Programme of Epidemiological Studies of Lixisenatide and other GLP-1 Receptor Agonists

Peter Boyle
Maria Bota
Philippe Autier
Mathieu Boniol
Chris Robertson

International Prevention Research Institute
95 cours Lafayette
69006 Lyon
France

(Revised) December 02, 2013

IPRI International Prevention Research Institute

Contents

I Background and Preamble

It is estimated that 347 million people worldwide have diabetes[1] and that diabetes deaths will increase by two thirds between 2008 and 2030 (WHO Diabetes, Factsheet No 312, September 2012 http://www.who.int/mediacentre/factsheets/fs312/en/index.html).

To maintain glycaemic control as diabetes progresses over time, patients with type 2 diabetes mellitus (T2DM) require systematic, individualized and gradually intensified interventions involving different levels of diet, exercise and oral or systemic therapies, alone or in combination. Medicinal treatment generally begins with an oral anti-diabetic agent and as the disease progresses over time, patients may require treatment with insulin.

Glucagon-like peptide 1 receptor agonists (GLP-1 RA) belong to a new class of anti-diabetic therapy that mimic the action of the GLP-1 hormone by stimulating the release of insulin by the pancreas thereby reducing blood glucose levels. They have several advantages as compared to earlier generation medications. In addition to having gluco-regulatory effects, they are not associated with oedema, they have a low incidence of hypoglycaemia and promote weight loss. At the present time, there are two GLP-1 RA approved and on the market: exenatide (in two formulations: Byetta and Bydurean, Amylin Pharmaceuticals, Inc., San Diego, CA, USA) and liraglutide (Victoza, Novo Nordisk, Inc., Copenhagen, Denmark). Even though the efficacy and safety of exenatide and liraglutide have been established through clinical trials, recent reports have raised concerns about the risk of developing acute pancreatitis, pancreatic cancer and thyroid cancer in patients who are take these drugs.

Two protocols for pharmaco-epidemiological studies that address the risk of acute pancreatitis, pancreatic cancer and thyroid cancer have been prepared to parallel the launch of a new diabetes treatment, Lixisenatide – a new GLP-1 receptor agonist recently approved to the European Medicines Agency.

The first study has a retrospective cohort design that aims to estimate incidence rates of these adverse events (acute pancreatitis, pancreatic cancer and thyroid cancer, in particular medullary thyroid cancer) in adult patients with T2DM who are either treated with currently approved GLP-1 receptor agonists (cohort 1) or other anti-diabetics (cohort 2). The study will be carried out in 3 countries: Denmark, Norway and Sweden. Given our knowledge of the biology of cancer in particular, the follow-up time is very short being a maximum of five years use of GLP-1 RAs in patients with diabetes. However, this study is being conducted in view of previous reports of potential excesses of cancer observed over a shorter period of potential exposure.

The second study aims to monitor occurrences of these events of interest among adult T2DM patients treated with Lixisenatide after EMA approval through patient registers in

[1] Definition of diabetes used for the estimates: fasting glucose >= 7.0 mmol/L or on medication.

Denmark, Norway and Sweden. This study will enable more relevant clinical parameters to be collected. This study is important given the previous experience of patients using GLP-1 receptor agonists with a short exposure time. It is essential to monitor any possible excess of the three conditions which have been associated with use of drugs in this class, i.e. pancreatic cancer, thyroid cancer, in particular medullary thyroid cancer and acute pancreatitis.

These studies will complement one another with the information found during the Database Study providing key information for inclusion in the design and interpretation of the Register Study.

Two outline protocols have been submitted to the European Medicines Agency (EMA) and have been commented upon by the Rapporteurs: the final versions are attached as Appendix I. The following protocols will continue to be developed taking into consideration these comments. For the purposes of this initial protocol, consideration will be restricted to developing the protocol for the three countries initially suggested: Denmark, Norway and Sweden. Similarly, only the GLP-1 RAs which are currently on the market are considered for the first part of the study, but the protocol can change and adapt if new GLP-1 products are introduced on the market during the study progress.

The protocols for the two studies have been developed according to the guidelines of the European Medicine Agency (*Guideline on good pharmacovigilance practices (GVP). Module VIII – Post-authorisation safety studies. 9 July 2012 (EMA/330405/2012)*). The background and rationale for the two studies share many common features and these have been mentioned once in detail in the protocol of the first study and the second time in summary form in the protocol of the second study. Of note, the first study will allow fine tuning some technical details for the second study, for instance sample size issues and profile of the population at risk and characteristics of diabetic patients prescribed GLP-1s.

When there is a reference to pancreatitis in the text, it can be assumed that it is meant as Acute Pancreatitis unless specifically reffered to as Chronic Pancreatitis.

II Database study of GLP-1 Receptor Agonists and Risk of Acute Pancreatitis, Pancreatic Cancer and Thyroid Cancer, in Particular Medullary Thyroid Cancer

Format and Content of Study Protocol

II.1 Title

Database Study of GLP-1 Receptor Agonists and Risk of Acute Pancreatitis, Pancreas Cancer and Thyroid Cancer, in Particular Medullary Thyroid Cancer. Version 02 of December, 2013

II.2 Marketing Authorisation Holder

The marketing authorization holder (MAH) is Sanofi.

II.3 Responsible Parties

Principal Investigator	*Peter Boyle PhD DSc FRSE FFPH FRCPSG FRCP FMedSci
Senior Investigator	*Philippe Autier MD PhD
Study Coordinator	*Maria Bota MSc/MEng
Study Statisticians	*Mathieu Boniol PhD
	*Chris Robertson PhD

Local Investigator, Denmark	Henrik Toft Sørenson MD
Local Investigator, Denmark	Timothy L Lash PhD
Local Investigator, Norway	Lars Vatten MD PhD
Local Investigator, Sweden	Rickard Ljung MD PhD

*A brief *Curriculum Vitae* is attached as Appendix IV.

II.4 Abstract

Title Database study of GLP-1 Receptor Agonists (RAs) and Risk of Acute Pancreatitis, Pancreatic Cancer and Thyroid Cancer, in Particular Medullary Thyroid Cancer [Version 02 of December, 2013]. Principal Investigator Professor Peter Boyle, International Prevention Research Institute, Lyon, France.

Rationale and Background. GLP-1 RA have been a focus of attention since the signalling of certain (rare but serious) adverse effects potentially associated with their use: acute pancreatitis, pancreatic cancer and thyroid cancer, in particular medullary thyroid cancer. With increasing follow-up time available, it is opportune to examine such associations in high-quality prescription databases.

Research Question and Objectives. This study is designed to focus on the risk associated with use of GLP-1 RA and will investigate the primary hypotheses that adult patients prescribed GLP-1 RA: (1) have an increased risk of acute pancreatitis when compared to patients prescribed other types of anti-diabetic drugs; (2) have an increased risk of pancreatic cancer when compared to patients prescribed other types of anti-diabetic drugs; and (3) have an increased risk of thyroid cancer, in particular medullary thyroid cancer when compared to patients prescribed other types of anti-diabetic drugs. Through this investigation, this study will establish the profile of users of GLP-1 RAs and of other anti-diabetic medications.

Study Design A series of retrospective cohort studies will be conducted based on prescription databases in Denmark, Norway, and Sweden, with a view to country-specific analysis and a planned meta-analysis of the three studies.

Population Everyone prescribed an anti-diabetic medication in Denmark, Norway and Sweden since the day on which the first GLP-1 agonist was approved for use.

Variables For each patient, information regarding all anti-diabetic medications prescribed in the study period will be recorded together with basic information such as age and gender. Patients who develop pancreatic and thyroid cancer, in particular medullary thyroid cancer will be identified as well anyone who is diagnosed with acute pancreatitis.

Data Sources Patients will be identified in the National Prescription Database and will be linked to the National Death Indices, National Cancer Registries and National Hospital Discharge schemes to identify cases of cancer, acute pancreatitis and anyone who has died.

Study Size Under conservative assumptions, approximately 37,000 GLP-1 RA treated patients will be eligible for this study by the end of 2011. Assuming an incidence rate of 65.6 per 100,000 p-y for acute pancreatitis, the study will be able to detect (at 5% significance level and 80% power) a minimum risk of 1.53. For an incidence rate of 29.19 per 100,000 p-y for pancreatic cancer and 6.13 for thyroid cancer, the study will

be able to detect a minimum risk of 1.96 for pancreatic cancer and 3.40 for thyroid cancer respectively.

Milestones Key milestones include that data collection will be concluded by mid-2014 and the report will be submitted to the CHMP in December 2014. After receiving the comments of the Rapporteurs, the Report will be finalized in the first quarter of 2015 and an article for a peer-reviewed submitted shortly thereafter.

II.5 Amendments and Updates

This is the initial protocol and any amendments will be placed here in a timely manner.

II.6 Milestones (events in months)

T0	Study preparation starts
T3	Protocol agreed and submitted to CHMP EMA
T6	Development of data collection module
T6	Final agreement on Protocol from CHMP
T8	Preliminary Pilot Testing of data collection and data transfer
T9	IRB/Ethics Approval as required at each site.
T10	Data collection begins in each country
T12	Interim report submitted to CHMP/EMA
T18	Data Collection complete
T21	Data Cleaning and Data Analysis.
T24	Submission of Report to CHMP/EMA
T26	Comments received from Rapporteurs
T27	Finalization of Report
T28	Submission of Article to peer-reviewed journal

II.7 Rationale and Background

Glucagon-like peptide 1 receptor agonist (GLP-1 RA) is a new class of blood glucose lowering drugs indicated in the treatment of type 2 diabetes mellitus (T2DM). It is an agonist molecule to the incretin (gastrointestinal hormone) GLP-1 which stimulates glucose-dependant secretion of insulin. GLP-1 is rapidly inactivated by the dipeptdyl peptidase-1 (DPP-4) (half-life of about 2 minutes), hence the need for a GLP analogue or agonist with greater resistance to DDP-4 degradation. GLP-1 regulates glucose levels by stimulating glucose-dependent insulin secretion and biosynthesis, and by suppressing glucagon secretion, delayed gastric emptying and promoting satiety.

There are currently 2 GLP-1 RA products on the market, one of which (exenatide) is available in two formulations (Byetta and Bydureon):

- Exenatide (also Exendin-4) marketed as Byetta by Amylin Pharmaceuticals, Inc., (San Diego, California, United States of America was launched in 2005 in the USA and approved in 2006 in the European Union and is administered subcutaneously twice daily; Exenatide marketed as Bydureon by Amylin Pharmaceuticals, Inc., (San Diego, California, United States of America) was approved on the market in 2012 and is administered subcutaneously once weekly.

- Liraglutide, marketed as Victoza by Novo Nordisk, Inc. (Copenhagen, Denmark). Liraglutide was approved by the European Medicines Agency (EMA) in July 2009 and by the United States Food and Drug Administration (FDA) in January 2010. Liraglutide, a once-daily glucagon-like peptide-1 receptor agonist, is approved for use as monotherapy in the USA and Japan (but not in Europe or Canada) and in combination with selected oral agents (all regions) for the treatment of patients with type 2 diabetes. Guidance from local advisory bodies is emerging on the most appropriate place for liraglutide in the treatment pathway. It is apparent from its phase 3 clinical trial programme that liraglutide provides superior glycaemic control compared with that achieved with other antidiabetic agents used early in the treatment pathway (e.g. glimepiride and sitagliptin). Key additional benefits include a low incidence of hypoglycaemia and clinically relevant weight loss, although these benefits may be attenuated by concomitant sulphonylurea treatment and, in the case of hypoglycaemia, reduction of the sulphonylurea dose may be necessary.

Safety concerns

GLP-1 receptor agonists have been demonstrated to have impact on glycaemic control, to be associated with weight loss and to carry a low risk of hypoglycaemia (Bergenstal et al, 2012; Scott et al, 2012; Nauck et al, 2012; Alves et al, 2012; Gough, 2012; Scott et al, 2012; Shyangdan et al, 2011). However, these drugs have been a focus of attention since they may be associated with the occurrence of certain rare but serious adverses events: acute pancreatitis, pancreatic cancer and thyroid cancer (especially medullary carcinoma of the thyroid).

Acute Pancreatitis

Spontaneous (post-marketing) reports of acute pancreatitis among type 2 diabetes patients on GLP-1 agonists were submitted to the FDA Adverse Event Reporting System [FDA alert: information for healthcare professionals: exenatide (marketed as Byetta). FDA: Postmarket Drug Safety Information for Patients and Providers, available at: http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm124713.htm]. Since the introduction on the market in 2005 until 8/18/2008, 36 cases of acute pancreatitis were reported in patients taking Byetta. As a result of these spontaneous results the FDA required the manufacturer to include a warning for the risk of pancreatitis on the prescribing information of exenatide.

Also, at the introduction on the market of the new molecule liraglutide (marketed as Victoza), patients were warned about the potential risks of pancreatitis, as there was a 4:1 imbalance http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm198543.htm) of the pancreatitis cases in patients using Victoza compared to patients using another diabetes medicine in five clinical trials.

However the preclinical and clinical evidence over the mechanism linking GLP-1 RA and acute pancreatitis is conflicting (Anderson et al, 2010; Elashoff et al, 2011; Drucker et al 2011). Preclinical studies showed equally a negative effect of incretin based drugs on the risk of developing pancreatitis (Matveyenko et al, 2009; Nachani et al, 2010) as well as a null effect or a positive effect (Engel et al, 2010; Tatarliewicz et al, 2010).

The clinical data are equally contradictory. A recent meta-analysis was carried out in order to assess the risk of acute pancreatitis and overall cancer with use of exenatide and liraglutide separately (Alves et al, 2012). The Summary Odds Ratio (SOR) based on 13 studies of exenatide that reported acute pancreatitis outcome was found to be 0.84 [95% CI, 0.58; 1.22]. The 13 studies included 3 cohort studies [Doré et al.2009; Doré et al.2011; Garg et al, 2010; Wenten et al, 2012) and 10 randomized controlled trials out of which 6 reported zero cases of pancreatitis, hence the odds ratio is zero. The overall Summary Odds Ratio based on 12 RCT of liraglutide that report acute pancreatitis outcome was found to be 0.97 [95% CI, 0.21; 4.39], out of which 8 studies reported zero cases of acute pancreatitis. There have been no post-market observational studies for liraglutide and acute pancreatitis so far. These results are weakened by limitations such as the fact that they are based on small studies, underpowered to detect rare adverse effects and of short duration.

A number of other studies have been reported:

- Romley et al (2012) conducted a study of exenatide therapy and the risk of pancreatitis and pancreatic cancer in a privately insured population. This is a retrospective cohort study on type 2 DM patients with employer provided health insurance from 2007 to 2009. Among the 268,561 patients included in the study, 2.6% used exenatide. The hospitalization rate for acute pancreatitis among patients who used at least one exenatide prescription was 1.96 per 1000 patients compared to 2.49 per 1000 patients who never used exenatide (p-value = 0.167).

- MacConell et al (2012) examined the safety and tolerability of exenatide twice daily in patients with type 2 diabetes with an integrated analysis of 5594 patients from 19 placebo-controlled and comparator-controlled clinical trials This is an integrated analysis of 19 RCT carried out by the manufacturer. The incidence rates for pancreatitis were not statistically different between groups.

- Elashoff et al (2011) reported on the disproportion of the FDA-AERS database of reported adverse events showed an increased risk of acute pancreatitis with exenatide: OR = 10.68 (p-value vs control drugs=2 x 10e-16). However, this must be interpreted bearing in mind the known limitations of this database (e.g. http://www.ncbi.nlm.nih.gov/pubmed/15317031).

The literature can be summarised by observing that the small number of reported events and other design limitations of the studies currently available does not allow for clear conclusions to be drawn, one way or another, at the present time.

Pancreatic Cancer

Besides observing a high number of pancreatitis cases, Elashoff et al (2011) also reported on pancreatic cancer in patients treated with exenatide [OR=2.95 (p value vs control drugs=9 x 10e-5)]. There are no further clinical studies that address this issue. Experimental data show that GLP-1 agonists increase beta-cell mass in rodents, But human trials do not support the rodent data (Brubaker et al, 2009).

Thyroid Cancer

The rodent calcitonin producing C-cell expresses GLP-1Rs, and sustained GLP-1R activation results in increased calcitonin secretion, C-cell hyperplasia and medullary thyroid cancer, predominantly in rats. In contrast, C cells within the monkey and human thyroid gland exhibit lower levels of GLP-1R expression, and prolonged administration of liraglutide at very high doses does not produce C-cell proliferation in monkeys (Drucker et al, 2011; Bjerre Knudsen et al, 2010).

A review on the association between glucagon-like peptide-1 receptor agonists and thyroid cancer (Chiu et al., 2012) concludes that GLP-1 agonists might increase the risk of thyroid C-cell pathology in rodents, but its risk in humans awaits investigation.

Therefore, the effects of GLP-1 on human cancer development, including pancreas and thyroid cancer, are overall unknown and difficult to be extrapolated from pre-clinical studies. In addition, the small number of cases and the lack of biological plausibility raise doubts between the use of GLP-1 agonists and the occurrence of cancer (pancreatic, thyroid or overall). Therefore longer-term, better designed epidemiological studies are required, in order to assess any risks of pancreas cancer and (medullary) carcinoma of the thyroid associated with GLP-1 RA use.

Design of Investigative Studies

Protocols for two studies have been prepared and are presented below. The rationale behind both studies revolves chiefly around the concept of performing the Registry study in the same populations where the incidence rates of acute pancreatitis, pancreatic cancer and (medullary) thyroid cancer in adult patients with type 2 diabetes treated with GLP-1 agonists (i.e., exenatide and liraglutide) and other anti-diabetics are established.

Very limited background information is available in the literature for the incidence rates of acute pancreatitis, pancreatic cancer and thyroid cancer, in particular medullary thyroid cancer in adult type 2 diabetes patients treated with GLP-1 agonists (i.e., exenatide and liraglutide) and other anti-diabetics. Therefore, the data from such a study will help contextualize these events expected to be observed in the patient registry of lixisenatide.

II.8. Research Question and Objectives

A series of cohort studies will be conducted based on prescription databases in Denmark, Norway, and Sweden, with a view to country-specific analysis and a planned meta-analysis of the three studies.

The primary objectives of this study are to estimate:

1. Incidence rates of acute pancreatitis (ICD10 K85) among adult type 2 diabetes patients treated with GLP-1 receptor agonists (i.e. exenatide and liraglutide), as well as patients treated with other anti-diabetic drugs and to examine the risk of acute pancreatitis in users of GLP-1 receptor agonists compared to users of other anti-diabetic medications;

2. Incidence rates of pancreatic cancer (ICD10 C25) among adult type 2 diabetes patients treated with GLP-1 receptor agonists (i.e. exenatide and liraglutide), as well as patients treated with other anti-diabetic drugs and to examine the risk of pancreatic cancer in users of GLP-1 receptor agonists compared to users of other anti-diabetic medications;

3. Incidence rates of thyroid cancer (ICD10 C73) (especially medullary thyroid cancer) among adult type 2 diabetes patients treated with GLP-1 receptor agonists (i.e. exenatide and liraglutide), as well as patients treated with other anti-diabetic drugs and to examine the odds ratio of medullary thyroid cancer in users of GLP-1 receptor agonists compared to users of other anti-diabetic medications.

Declaration of Study Hypotheses

This study is designed to focus on the risk associated with use of GLP-1 agonists and will investigate the following primary hypotheses:

1. That adult patients prescribed GLP-1 RAs have an increased risk of acute pancreatitis when compared to patients prescribed other types of anti-diabetic drugs;

2. That adult patients prescribed GLP-1 RAs have an increased risk of pancreatic cancer when compared to patients prescribed other types of anti-diabetic drugs;

3. That adult patients prescribed GLP-1 RAs have an increased risk of medullary thyroid cancer when compared to patients prescribed other types of anti-diabetic drugs.

II.9 Research Methods

II.9.1 Study Design

The study will have a retrospective observational (cohort) design using prescription databases as a source of patients prescribed anti-diabetic medications (cohort members) in three countries in northern Europe: Denmark, Norway and Sweden. Each has a database which has been used effectively in studies of this design and also has a National Cancer Registry, a National Death Registry and a Hospital Discharge Registry available for record linkage, as well as other sources of information on confounders which can be linked to the cohort.

In designing this series of studies, there were several key considerations that were identified as important to take into account. Recruitment of centers for the study was based on the availability of a population-based prescription register. This would allow the identification of a cohort of patients treated with anti-diabetic medications. "High-quality" mainly refers to the validity of demographic and clinical information on patients.

However, outcomes, mainly acute pancreatitis, can be subject to misclassification because of the difficulty to establish diagnosis. Furthermore, surveillance and information bias may influence the reliability of information reported in hospital discharges. Surveillance bias would occur as a consequence of doctors being aware that GLP-1 RAs intake may be linked to acute pancreatitis. Surveillance bias of GLP1 agonist users may end up in more abdominal diseases classified as pancreatitis simply because clinicians were more inclined to diagnose "pancreatitis" among patients taking GLP-1 agonist that consulted for abdominal symptoms and who were more likely to do so since abdominal pain has been reported more frequently among users of GL RAs.

The availability of reliable information on anti-diabetic treatments, not only on a cross-sectional basis but also during the whole course of diabetes, was another key requirement. It is expected that a sizable proportion of patients could change their treatment during the analysis period.

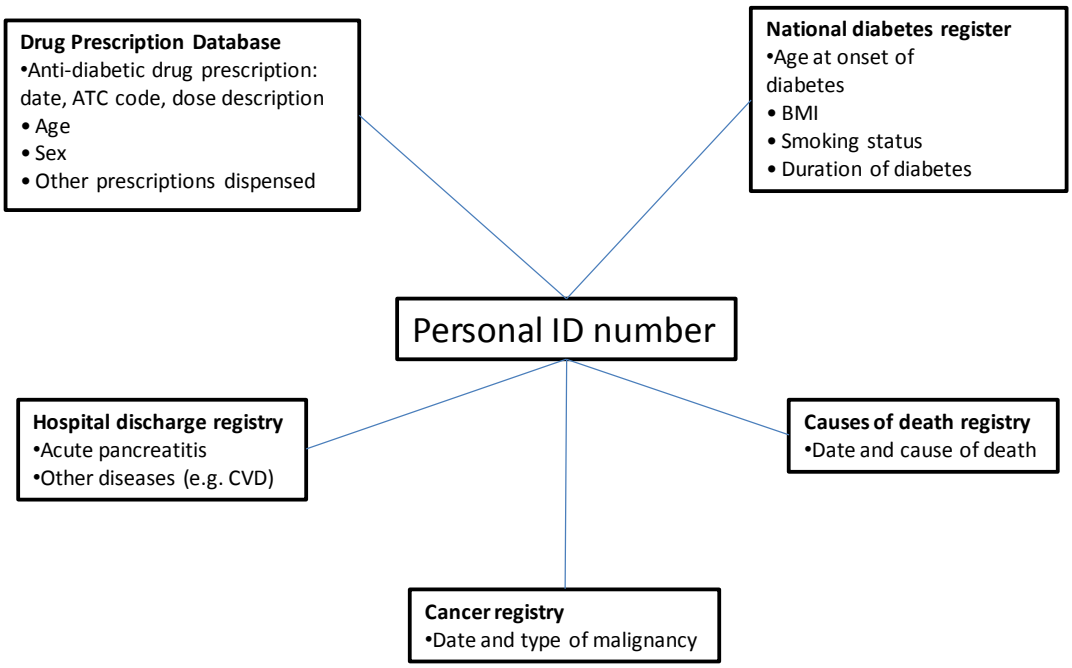
II.9.2 Setting

The study will include Denmark, Norway and Sweden. These countries were been chosen because each has:

(1) A high-quality prescription registry that is population-based.
(2) A high-quality cancer registry, which covers the entire population included in the prescription database.
(3) A national hospital discharge registry, which covers the entire population included in the prescription database
(4) A national death register, which can be used for record linkage to ascertain the date of death of any cohort member who died.
(5) A source of information on key confounders (notably BMI), either in the prescription database itself, in a diabetes registry or in other available databases or large prospective studies.

The study population will include adult T2DM patients in Denmark, Norway and Sweden treated with exenatide or liraglutide (cohort 1) and these groups will be compared with patients treated with other anti-diabetics (cohort 2). Patients with previous diagnosis of the outcomes of interest will be excluded.

A unique personal identity number will be used to link together the information from the several population based registries, as shown in Figure 1:



The source of the cohorts will be mainly represented by the drug prescription registries. Patients with diabetes will be identified as having been prescribed at least one prescription for an anti-diabetic drug, i.e. ATC code 'A10' and subcategories.

High completeness of follow-up is expected, as well as high accuracy of data, which will allow capture of the variables of most interest; this is supported by our previous study (glargine and risk of cancer).

A detailed table of characteristics of the cohort included in the analysis will be provided after consultation with the local investigators.

II.9.3 Variables

The study population will include adult T2DM patients in Denmark, Norway and Sweden treated with exenatide or liraglutide (cohort 1) and these groups will be compared with patients treated with other anti-diabetics (cohort 2).

Patients with the following conditions will be excluded from the study:

1) Individuals less than 18 years of age at the cohort entry;
2) Individuals with a diagnosis of thyroid cancer, pancreatic cancer, or any pancreatitis prior to cohort entry.

Dates

The start of the study, i.e. the date at which follow up begins, will vary over centres and will be the date that GLP-1 RAs (exenatide in both formulations and liraglutide) were first available in the country or the date that the prescription registry has valid data from (whichever came last). From past experience from working on these databases (Boyle et al, 2013) we learnt that all three prescription registries were set up before the EU approval dates for exenatide. Therefore, the study period is defined as starting on 28 November 2006 (the EU approval dates are 28 November 2006 for exenatide and 02 July 2009 for liraglutide).

The end of the study is the date at which the follow up ceases for subjects who are still under observation (i.e. have not died or have not had pancreatitis/pancreatic cancer/thyroid cancer or known to be lost to follow up, perhaps because they have emigrated). [Note that patients with either one of the indicated adverse events will continue to be followed-up to monitor the diagnosis of another adverse event]. This date will be the date to which the hospital discharge registry and the cancer registry data are validated, 31 December 2013 for acute pancreatitis (in the Hospital Discharge Register) and through 31 December 2012 for pancreatic and thyroid cancer (in the National Cancer Registries). These initial dates may be extended in an additional follow-up of the study cohorts at the end of the 5 years; this remains to be re-viewed by the end of the 4th year of study.

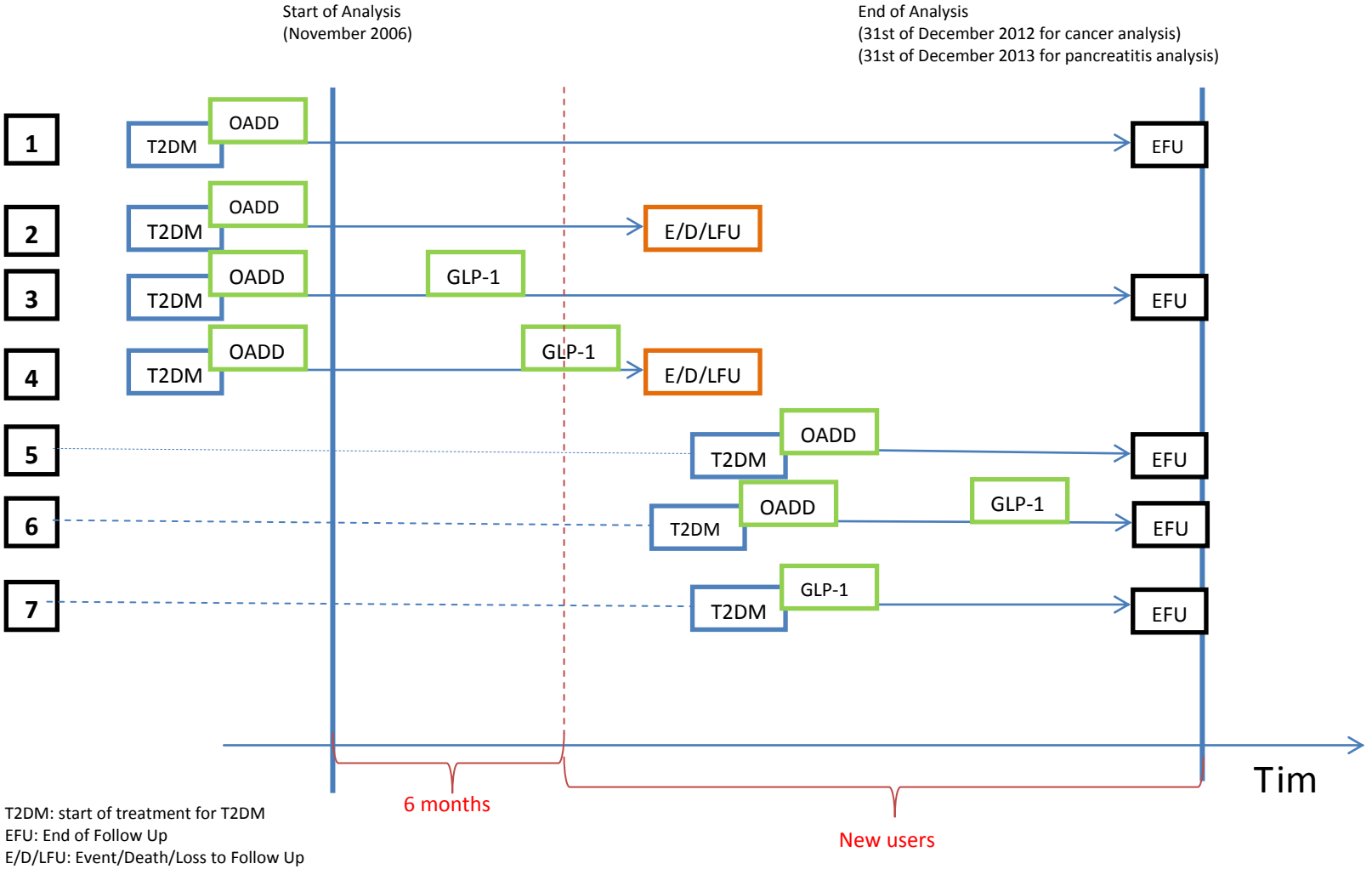
All patients who appear in the prescription registries of the countries with a record of prescription for anti-diabetes medication between the start date and end date for the centre are included in the analysis. Any patient without a record of prescription of any type of anti-diabetic medication will be excluded, as well as patients younger than 18 years at their start date. Patients with a cancer diagnosed prior to their start date (3 months after their date of first receiving anti-diabetic medication) will be excluded in the analysis as it is very unlikely that the cancer could be associated with the anti-diabetic treatment. We exclude the first 3 months from the beginning of anti-diabetes treatment because of the possibility that diabetes was caused by (or diagnosed following clinical workup for) cancer (reverse causality). As three months may be considered rather short and arbitrary length of the immortal time period to be excluded, a sensitivity analysis for exclusion of 6 months immortal time will be done. An eligible diabetes prescription is defined as only those occurring three months (or six months) or more before the censoring date (cancer, death and last date in registry). However, the three month (or six months) window will not apply for patients diagnosed with acute pancreatitis where, theoretically, this could be a rapid and acute response to an external stimulus such as therapy.

The starting date for an individual in the study is the date of first prescription of either exenatide or liraglutide for cohort 1 or the date of first prescription of other anti-diabetics (e.g., oral anti-diabetics, insulins) for cohort 2 during the study period.

A new user approach will be favoured in order to reduce prevalent user bias and confounding from covariates that could be associated with drug use (Ray, 2003). New users are defined as patients who initiated **either GLP-1 treatment or other anti-diabetic drugs** at least 6 months after the start date of the study (this will include patients who are treatment naive in regards to any anti-diabetic medication although this group will be very few in numbers). The 6 months 'criterion' was defined in previous work on these databases (Boyle et al, 2013). Figure II.9.3.1 shows possible patient trajectories; incident users (with no history of anti-diabetic treatment) are patients 5, 6 and 7 on this diagram. As all prescription databases were set up relatively recently (i.e. 2004-2005), and we will have many patients in the cohort that developed diabetes long before that, the new user approach will deal with patients for whom we have complete data on the history of anti-diabetic medication.

The period of follow-up begins at that time or three months later until a specified event takes place, either (1) date of cancer/or acute pancreatitis diagnosis; (2) date of death (right censoring, only if death occurred before the last date of available data in registry); and, (3) last date of available data in cancer registry.

Figure II.9.3.1: possible patient trajectories



T2DM: start of treatment for T2DM
EFU: End of Follow Up
E/D/LFU: Event/Death/Loss to Follow Up
OADD: Other Anti-Diabetic Drugs
GLP-1: Glucagon like peptide-1 receptor agonist

Outcome

Acute pancreatitis cases will be identified from the hospital discharge registers. The diagnosis of acute pancreatitis is a clinical diagnosis that hinges on the presence of abdominal pain and elevation of two biomarkers, themselves not diagnostic. One potential issue to be faced is that abdominal pain can be an unwanted side effect of the use of GLP-1 medication and this could lead to diagnostic bias.

Cases of all thyroid cancers (especially medullary thyroid cancer) and pancreatic cancer will be identified from the national cancer registers. However, data on the cancer cases for a given year are typically considered incomplete until approximately one year after the year ends. Therefore, it will be possible to use the national cancer registries in these three countries to identify incident cancers occurring until the end of 2012, if the analysis of thyroid cancer is planned to be performed in early 2014.

A potentially major issue surrounds the well-documented under-diagnosis of pancreatic cancer in some Cancer Registries. Kilander et al (2012) recently examined this situation in the Swedish Cancer Registry. From a total of 31,067 cases of pancreatic cancer, 44% were registered in the Hospital Patient Discharge Register but not in the Cancer Registry indicating an overwhelming under-reporting of pancreatic cancer in the Cancer Registry. Thus, diagnoses of pancreatic cancer will be sought in both the Cancer Registry and the Hospital Patient Discharge Registry in each of the countries.

Covariates

The key variables in the study will be obtained from the prescription databases (age, gender, insulin and other diabetes medications and other prescriptions); the hospital discharge registries (date of diagnosis, gallstones and obstruction of the pancreatic duct); the cancer registries (date of diagnosis, cancer site, histology and outcome of cancer); and the national death registers (date and cause of death).

All analyses will be stratified by age and gender and in addition by treatment history.

In order to improve the analysis all efforts will be made to collect additional information on several other potential confounding variables.

Potential confounders for pancreas cancer will include smoking history, alcohol intake, family history of pancreas cancer, a previous diagnosis of Multiple Endocrine Neoplasia (especially MEN1) and chronic pancreatitis.

Potential confounders for acute pancreatitis will include duration of diabetes, presence of gallstones, prior use of anti-diabetic medications, alcohol intake and obstruction of the pancreatic duct.

Potential confounders for thyroid cancer will include duration of diabetes, prior use of anti-diabetics, radiation treatment to the head and neck, iodine intake, hormonal and reproductive treatment, history of goiter or benign thyroid nodules, history of cancer, diagnosis of Multiple Endocrine Neoplasia type 2 (MEN2), and family history of medullary thyroid cancer at the baseline.

The availability of these additional data will differ between the individual countries. A dictionary of compatible covariate information will be compiled at the outset of the study to enable information common to more than one study to be collected and recorded in a manner that will enable the data to be used across studies.

Missing values for these variables will inevitably vary in proportion between variables and possibly between countries. The Biostatistical Advisory Group, a sub-committee of the Scientific Advisory Committee, will recommend a strategy for dealing with missing values taking into account the magnitude of the missing information for any one variable and any variation between countries (see below).

II.9.4 Data Sources

Denmark

The study will draw on health care databases covering the entire Danish population (approximately 5.3 million). The Danish National Health Service provides all inhabitants with free access to general practitioners and hospitals and refunds a variable proportion of prescription medication costs.

The Danish Civil Registration System keeps records on gender, date of birth, change of address, date of emigration and changes in vital status since 1968 (Frank, 2000). The records carry a 10-digit civil registration number (CRN), assigned to every Danish citizen and used in all Danish registers, enabling unambiguous record linkage between them. The CRN will enable the project to establish, for each individual under study, a complete hospital and prescription history since 1995.

The Register of Medicinal Products contains data from 1995 on almost all prescription drugs dispensed at all Danish pharmacies, including patients' CRN, the type of drug according to the anatomical therapeutic chemical classification system, and the date of dispensing the drug.

The Danish National Patient Registry (Andersen et al., 1999) collects data on all hospitalizations from Danish hospitals since 1977, including dates of admission and discharge, procedure(s) performed and up to 20 discharge diagnoses coded by physicians according to the International Classification of Diseases (8th revision [ICD-8] until the end of 1993 and 10th revision [ICD-10] thereafter). Inpatient admissions have always been collected; outpatient, day patient, and emergency room admissions have been collected since 1994.

Denmark has a high-quality National Cancer Registry which has existed since the early 1940s. Coverage and data quality have been shown to be complete from a variety of studies conducted using this resource and many influential epidemiological studies have been conducted and completed using it.

Data on covariates will be obtained from the patient registry and the Register of Medicinal Product Statistics, the Integrated Database for Labour Market Research at Statistics Denmark (Statistics Denmark, 1991) and, for a subset, data from the Laboratory Information System in Aarhus and North Jutland Counties. Additional covariate data will be collected in a subset by linkage with the diabetes national indicator project, the general practitioner's database, and annual cross-sectional studies of health behaviors in the Danish population.

Norway

Norway has a high quality National Population Registry with information on date of birth, gender, date of death, emigration/immigration history etc.

Since 2004, Norway has had a National Prescription Registry. Information is recorded from all prescribed drugs (excluding in-hospital medication), and includes data on the patient (gender, age, place of residence), the prescribing doctor (gender, age, place of residence) and time of prescription (calendar date).

In this study, individual data from the prescription registry will be linked to individual data at the Norwegian Cancer Registry.

In addition, Norway has a National Hospital Discharge scheme that records every period of hospitalization in the country together with diseases coded at discharge. Norway has also a high quality National Cancer Registry with demonstrated complete coverage and data quality.

However, the above mentioned data sources do not include information on other important covariates, therefore, we will supplement the main study with data from a large population based study (CONOR) in Norway that contains comprehensive information on the relevant covariates.

The CONOR Study is a collaboration of four separate cohorts from four regions of Norway, including the Tromsø Study (northern region), the HUNT Study (middle region), the HUSK Study (western region) and the HUBRO Study (Oslo region). Currently, the collaboration is based on core common information on 185,000 participants. Its data contains information on age, sex, height and weight (BMI), waist and hip circumference, smoking habits, prevalent diabetes, and physical activity, in addition to data on a number of laboratory parameters at baseline, including blood pressure and serum lipids (total cholesterol, HDL-cholesterol and triglycerides).

Sweden

The Swedish cohort will comprise patients included in the Prescribed Drug Register, who have been prescribed GLP-1 agonists or other anti-diabetic drugs. By linkage to the regional cancer registries in Sweden as well as hospital discharge registries, information on cancer incidence and pancreatitis will be obtained.

Sweden has a highly efficient National Population and Death Register where record linkage has been done effectively on such studies. This gives coverage of all deaths in Sweden and the ability for record linkage ensures that all members of the cohort who die can be identified. In addition, Sweden has a number of other national registers that may be used to add information on potentially confounding factors.

Overall

The personal identification number will be used to link unambigously the databases in each country. The ATC coding system (Anatomic Therapeutic Coding) will be used to identify exposure: all patients having been prescribed drugs for the treatment of diabetes (ATC code A10 and subcategories) will be retrieved and linked to the other databases: they will be followed via cancer and hospital discharge registries. The ICD10 codes will be used for outcome assessment: acute pancreatitis (K85), pancreatic cancer (C25) and thyroid cancer (C73), especially medullary thyroid cancer (Thyroid cancer is a distinct entity in the ICD10 and the tumour type can be determined by the ICD-O code).

II.9.5 Study size (Sample size and study power)

A key consideration in designing studies is the requirement for a large enough number of events (pancreatitis, pancreatic cancer and thyroid cancer) to provide adequate statistical power to detect an effect. A conservative approach to estimating statistical power has been adopted, since the cumulative rate of events will be greatly increased as longer follow-up time is available.

Assuming an average prevalence of T2DM of 5% (Carstensen et al, 2008) for a total adult population (20+ years) in the 3 countries (Denmark, Norway and Sweden) of 15,000,000, our study population will reach approximately 750,000 subjects.

In terms of exposure to GLP-1 RAs the literature search resulted into a very heterogeneous range of values. An estimation in the THIN database (based on records from a sample of UK GPs) up to the end of 2010 revealed that about 2% of type 2 diabetes patients were treated by GLP-1 agonists. This is likely to be underestimated, knowing that the UK system is usually slower in adopting new drugs. Several cohort studies in the US gave different estimations of exposure to GLP-1 RA: 17% (Garg et al, 2010) 11% (Doré et al, 2009), 2.6% (Romley et al, 2012), that may overestimate use in

Europe because adoption of new drugs is faster in the USA. Since liraglutide is manufactured and marketed by a Danish pharmaceutical company (Novo Nordisk), the proportion of type 2 diabetes patients treated with liraglutide in the Nordic countries is likely to be higher than that observed in the THIN database. We have therefore assumed that a proportion of 5 to 10% of the diabetic patients are exposed to GLP-1 RAs and the following sample size/power calculations are done for these 2 hypothetical values. Conservatively assuming an average follow up of one year for these patients and 5% of diabetics exposed to GLP-1, then 37,000 person-years (p-y) of total follow-up time will be eligible for this study by the end of 2011. Idem, if 10% of diabetics are exposed to GLP-1, then 74,000 person-years (p-y) of total follow-up time will be eligible for this study by the end of 2011.

The incidence rate of acute pancreatitis was estimated using age-specific data from Sandzen et al. (2009) for the period 1998-2003 among the Swedish population, weighted by the age distribution among the diabetic population (Diabetes in the UK April 2012 available at: http://www.diabetes.org.uk/Documents/Reports/Diabetes-in-the-UK-2012.pdf, Carstensen et al., 2008). Age specific incidence rate for pancreatic and thyroid cancer were derived from NORDCAN (www.dep.iarc.fr/nordcan.htm) and also weighted by the age distribution among the diabetic population. The estimated diabetes-age adjusted incidence rates are shown in Table **II.9.5.**1:

Table II.9.5.1: Projected age adjusted incidence rate

Outcome	Diabetes age adjusted incidence rate (per 100,000)
Pancreatitis	65.57
Pancreatic cancer	29.19
Thyroid cancer	6.13

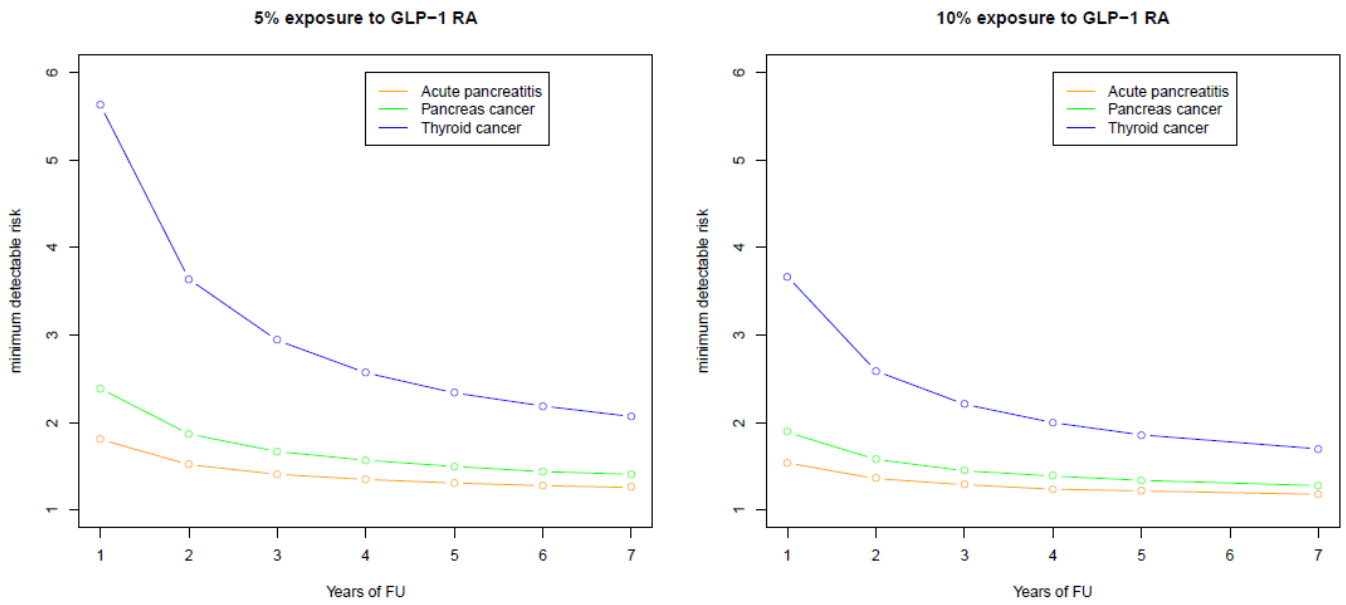
Under these assumptions, the minimal detectable risks (with 90% power and 95% confidence level, model: Poisson distribution) are shown in Table II.9.5.2 (sample size calculations using the methodology of Gu et al. 2008):

Table II.9.5. 2: Minimum detectable risk for one year of follow-up

Exposure to GLP-1 among diabetics	Acute Pancreatitis	Pancreatic cancer	Thyroid cancer
5%	1.80	2.40	5.63
10%	1.54	1.89	3.67

The database study will be completed in 2014. Figure II.9.5.2 shows the evolution of the minimum detectable risk with increasing years of follow-up, for 5% and 10% of exposure to GLP-1 among the diabetic population:

Figure II.9.5.2: Minimum detectable risk



The estimation of sample size and study power for the primary and secondary objectives will be further defined after consultation with local Principal Investigators and external experts.

II.9.6 Data Management

In each centre data will be linked between the different data sources (population registry, prescription registry, hospital discharge registry, cancer registry) through an anonymized unique identification number. Linking the population registry, the prescription registry and the cancer registry has already been tested and proved to be effective through our previous database study (Boyle et al, 2012). However, linking with the hospital discharge registry requires a procedure preventing introduction of information bias in the study.

All patients identified to have had an anti-diabetic treatment in the prescription database (regardless of the type of medication taken) will be linked to the Hospital Discharge Registry. All discharge information will be retrieved for all the diabetic patients (with an

anti-diabetic prescription) and searched for codes or keywords that indicate a pancreatic related disease focussing on acute pancreatitis and pancreatic cancer.

Each national centre will be responsible for the data storage and data management of the individual-level data, following all national and European directives regarding the well being and rights of each study subject. Each centre has an excellent track record of successfully undertaking similar research respecting all moral and legal requirements.

For data analysis, a two stage process will be adopted because it is not possible to share individual level data. In each country an individual level analysis will be carried out using a common statistical methodology. The anonymous results (statistical model coeffiecients) will be transferred to the coordinating center IPRI in a secured way (password protected). Pooling of the within study effects in a meta-analysis (Thompson et al, 2010), will then be carried out at I-PRI. This same procedure was used successfully in the earlier study. Notably, no identifiable data will be made available outside the country where the data are obtained.

II.9.7 Statistical Analysis

Full details of the statistical analysis will be determined prior to the end of the period of data collection and discussed and approved by the Biostatistics Advisory Committee. This is in a similar manner to the approach adopted in the *Northern European Database Study of Glargine and Cancer* (Boyle et al, 2013). The philosophical approach to the statistical analysis will be in the spirit of this previous study, whose statistical analysis plan is attached as Appendix III.

1. Incidence rates and 95% confidence intervals (CI) of pancreatitis, pancreatic cancer and thyroid cancer among the patients treated with GLP-1 RAs as well as those patients treated with other anti-diabetic medications will be derived. In addition, fitting a Poisson regression model may be considered.

2. Hazard ratios (95% CIs) of pancreatitis, pancreatic cancer and thyroid cancer associated with the treatment of GLP-1 RAs versus other anti-diabetics will be estimated using time-dependent Cox proportional hazards survival analysis. The potential confounding factors listed above will be adjusted for in the analyses (to be further discussed and refined by external experts).

The two types of analyses above (intent-to-treat analysis and an analysis by censoring the follow up time at the end of treatment of either GLP-1 RAs or other anti-diabetics) will be stratified by age, sex, previous anti-diabetic treatments (such as insulin, metformin etc) and other confounding factors in function of their availability.

3. Profile of GLP-1 users as compared to users of other anti-diabetics, for instance: age, sex, previous prescriptions, further covariates when available.

A major strength of the study will be that the Protocol will be followed to the largest extent possible and, notably, the statistical analyses will be restricted to the study hypotheses which have been declared.

II.9.8 Quality Control

The three countries involved in this study have databases which have all been demonstrated to be of the highest quality and completeness. The three countries chosen also have long-established and high-quality National Cancer Registries and Hospital Discharge Registers with diagnostic information. In addition, each of these countries has a National Mortality Database served by long-standing cause of death schemes. The three countries participated in the *Northern European Database Study of Glargine and Cancer* and have a substantial track-record of undertaking cutting-edge pharmaco-epidemiological studies.

With high-quality data available regarding exposure and the endpoints of interest, the study will be further strengthened by identical analyses being carried out in each centre using a common statistical methodology.

IPRI will ensure the coordination of the project through the **Coordination Office.** The Office will comprise the IPRI Principal Investigators and Senior Staff (Peter Boyle, Philippe Autier, Irene Leigh, Mathieu Boniol, Chris Robertson and Maria Bota): Maria Bota shall act as the Project Manager, will be available for daily contact with each of the national studies and responsible for developing the study database and preparing it for statistical analysis. In addition, Masters-level appointee(s) will work within the Office, coordinating study materials and correspondence, as needed.

The **Scientific Committee** for the study will comprise two representatives of IPRI (Peter Boyle, and Philippe Autier) and two representatives of each of the national studies: Henrik Toft Sørensen and Timothy Lash (in Denmark), Lars Vatten and Bjørn Olav Åsvold (in Norway), Rickard Ljung and Anders Ekbom (in Sweden). This group will be responsible for preparing the operational protocol for the study which shall then be passed to the Scientific Committee for approval. The Scientific Committee will ensure the conduct of the study according to the protocol in each of the participating countries, it will be responsible for the statistical analysis, the interpretation of the results and the preparation of the reports. The ultimate responsibility for the study lies with the Scientific Committee. It will meet regularly throughout the study period.

An independent, external **Scientific Steering Committee** will be appointed to oversee the study and advise on treatment, methodological and biostatistical issues. This group will meet regularly throughout the duration of the study and incorporate a **Biostatistical Advisory Group**, to advise on all aspects of the design and data analysis.

This Group will comprise Professor Geremia Bolli (University of Perugia, Italy), Professor Hertzel Gerstein (McMaster University, Hamilton, Canada), Professor Derek LeRoith (Mount Sinai, New York, United States of America), Professor Stuart J Pocock (University College London, UK); Professor Ian Ford (Robertson Centre for Biostatistics, University of Glasgow, UK) and Professor Theodore Holford (Department of Biostatistics, Yale University, USA).

II.9.9 Limitations of research methods

Administrative databases such as those employed in this study suffer from several key limitations including that the reason why a particular treatment was chosen is unknown and the reasons why therapy changed is also unknown. This contributes to the situation of confounding by indication, which can be a major source of concern in such studies leaving findings and conclusions open to a certain level of uncertainty. The Investigators are experienced epidemiologists who have worked extensively with such databases and can maximise the information which can be extracted from such material without over-interpreting what is possible.

Adjustment for confounding will not be available for the entire cohorts established but will only be available for a proportion of patients in the cohort.

II.10 Protection of Human Subjects

Each national centre will be responsible for following all national and European directives regarding the well-being and rights of each study subject. Each centre has an excellent track record of successfully undertaking similar research respecting all moral and legal requirements. At the central office (iPRI, Lyon) no identifiable data will be received from the individual centres.

All approvals necessary to undertake this study will be obtained in each country. In addition, the study protocol and the national approvals will be submitted to the IPRI Ethics Committee who will give tertiary ethical approval.

II.11 Management and Reporting of Adverse events/ reactions

Reporting of adverse events or adverse reactions on individual patients is not appropriate to this form of study where there is no contact between the investigators and the patients.

II.12 Plans for disseminating and communicating study results

At the end of the study, a full Report will be prepared and the MAH will submit this to the CHMP of the EMA. Once the comments of the Rapporteurs have been received, any modifications necessary will be made to the Report which will then be finalised. A manuscript presenting the results of the study will be prepared for publication in a peer-reviewed scientific journal and the findings presented at major scientific meetings of relevance to the subject matter e.g. at the Annual meeting of the European Association for the Study of Diabetes (EASD), at the Annual Meeting of the American Diabetes Association (ADA) and the Annual meeting of the American Society for Clinical Oncology (ASCO).

II.13 References cited in the text

Alves C, Batel-Marques F and Macedo AF. A meta-analysis of serious adverse events reported with exenatide and liraglutide: Acute pancreatitis and cancer. Diabetes Res Clin Pract. 2012 Sep 22. pii: S0168-8227(12)00312-9. doi: 10.1016/j.diabres.2012.09.008. [Epub ahead of print]

Andersen TF, Madsen M, Jørgensen J, Mellemkjoer L, Olsen JH. The Danish National Hospital Register. A valuable source of data for modern health sciences. Dan Med Bull 1999;46:263-8.

Anderson SL, Trujillo JM. Association of pancreatitis with glucagon-like peptide-1 agonist use. Ann Pharmacother. 2010 May;44(5):904-9. Epub 2010 Apr 6.

Bergenstal RM, Li Y, Booker Porter TK, Weaver C and Jenny Han M. Exenatide Once Weekly Improved Glycaemic Control, Cardiometabolic Risk Factors, and a Composite Index of an HbA1c<7%, without Weight Gain or Hypoglycaemia, Over 52 Weeks. Diabetes Obes Metab. 2012 Oct 18. doi: 10.1111/dom.12026.

Bjerre Knudsen L, Madsen LW, Andersen S, Almholt K, de Boer AS, Drucker DJ, Gotfredsen C, Egerod FL, Hegelund AC, Jacobsen H, Jacobsen SD, Moses AC, Mølck AM, Nielsen HS, Nowak J, Solberg H, Thi TD, Zdravkovic M 2010 Glucagon-like peptide-1 receptor agonists activate rodent thyroid C-cells causing calcitonin release and C-cell proliferation. Endocrinology 151:1473–1486

Boyle P, Bota M, Sorensen HT, Tuomilehto J, Ljung R, Colhoun H, Vatten L, Ulrichsen SP, Lash TL, Jacobsen JB, Sund R, Ekbom A, Kieler H, Livingstone S, Levin D, Osvold BO, Haglund B, Autier P, Pasterk M, Boniol M, Boffetta P and Robertson C. Northern European Database Study of Insulin and Cancer (manuscript submitted for publication)

Brubaker PL. Minireview: Update on Incretin Biology: Focus on Glucagon-Like Peptide-1. Endocrinology, May 2010, 151(5):1984–1989.

Carstensen B, Kristensen J K, Ottosen P, Borch-Johnsen K, The Danish National Diabetes Register: trends in incidence, prevalence and mortality. Diabetologia (2008) 51:2187–2196

Chiu WY, Shih SR and Tseng CH. A review on the association between glucagon-like peptide-1 receptor agonists and thyroid cancer. Exp Diabetes Res. 2012;2012:924168. doi: 10.1155/2012/924168. Epub 2012 May 28.

Dore DD, Seeger JD, Arnold Chan K Use of a claims-based active drug safety surveillance system to assess the risk of acute pancreatitis with exenatide or sitagliptin compared to metformin or glyburide. Curr Med Res Opin 2009; 25:1019–1027

Dore DD, Bloomgren GL, Wenten M, Hoffman C, Clifford CR, Quinn SG, Braun DK, Noel RA, Seeger JD. A cohort study of acute pancreatitis in relation to exenatide use. Diabetes Obes Metab 14 February 2011 doi: 10.1111/j.1463–1326.2011.01376.x

Drucker et al., Safety of incretin based therapies, J Clin Endocrinol Metab, Jul 2011, 96(7):2027-2031

Elashoff M, Matveyenko AV, Gier B, Elashoff R, Butler PC. Pancreatitis, pancreatic, and thyroid cancer with glucagon-like peptide-1-based therapies. Gastroenterology. 2011 Jul;141(1):150-6. Epub 2011 Feb 18.

Engel SS, Williams-Herman DE, Golm GT, Clay RJ, Machotka SV, Kaufman KD and Goldstein BJ 2010 Sitagliptin: review of preclinical and clinical data regarding incidence of pancreatitis. Int J Clin Pract 64:984–990

Frank L. Epidemiology. When an entire country is a cohort. Science 2000;287:2398-9.

Garg R, Chen W and Pendergrass W. Acute pancreatitis in type 2 diabetes treated with exenatide or sitagliptin: a retrospective observational pharmacy claims analysis. Diabetes Care 2010; 33:2349–2354

Gier B, Matveyenko AV, Kirakossian D, Dawson D, Dry SM, Butler PC. Chronic GLP-1 receptor activation by exendin-4 induces expansion of pancreatic duct glands in rats and accelerates formation of dysplastic lesions and chronic pancreatitis in the Kras(G12D) mouse model. Diabetes. 2012 May;61(5):1250-62. Epub 2012 Jan 20.

Gier B, Butler PC, Lai CK, Kirakossian D, DeNicola MM, Yeh MW. Glucagon like peptide-1 receptor expression in the human thyroid gland. J Clin Endocrinol Metab. 2012 Jan;97(1):121-31. Epub 2011 Oct 26.

Gough SC. Liraglutide: from clinical trials to clinical practice. Diabetes Obes Metab. 2012 Apr;14 Suppl 2:33-40. doi: 10.1111/j.1463-1326.2012.01576.x.

Gu K, Ng HK, Tang ML, Schucany WR. Testing the ratio of two Poisson rates. Biom J. 2008;50(2):283-98.

Kilander C, Mattsson F, Ljung R, Lagergren J and Sadr-Azodi O. Systematic under-reporting of the population-based incidence of pancreatic and biliary tract cancers,. (submitted for publication).

Knudsen LB, Kiel D, Teng M, Behrens C, Bhumralkar D, Kodra JT, Holst JJ, Jeppesen CB, Johnson MD, de Jong JC, Jorgensen AS, Kercher T, Kostrowicki J, Madsen P, Olesen PH, Petersen JS, Poulsen F, Sidelmann UG, Sturis J, Truesdale L, May J, Lau J. Small-molecule agonists for the glucagon-like peptide 1 receptor. Proc Natl Acad Sci U S A. 2007 Jan 16;104(3):937-42. Epub 2007 Jan 9.

McConell L, Brown C, Gurney K and Han J. Safety and tolerability of exenatide twice daily in patients with type 2 diabetes: integrated analysis of 5594 patients from 19 placebo-controlled and comparator-controlled clinical trials. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy 2012; 5: 29-41

Matveyenko AV, Dry S, Cox HI, Moshtaghian A, Gurlo T, GalassoR, Butler AE and Butler PC. Beneficial endocrine but adverse exocrine effects of sitagliptin in the human islet amyloid polypeptide transgenic rat model of type 2 diabetes: interactions with metformin. Diabetes 2009; 58:1604–1615

Nachnani JS, Bulchandani DG, Nookala A, Herndon B, Molteni A, Pandya P, Taylor R, Quinn T, Weide L and Alba LM. Biochemical and histological effects of exendin-4 (exenatide) on the rat pancreas. Diabetologia 2010; 53:153–159

Nauck M, Frid A, Hermansen K, Thomsen AB, During M, Shah N, Tankova T, Mitha I, Matthews DR. Long-term efficacy and safety comparison of liraglutide, glimepiride and placebo, all in combination with metformin in type 2 diabetes: 2-year results from the LEAD-2 study. Diabetes Obes Metab. 2012 Sep 17. doi: 10.1111/dom.12012. [Epub ahead of print]

Ray AW. Evaluating medication effects outside of clinical trials: new-user designs. Am J Epidemiol 2003;158:915-920.

Romley JA, Goldman DP, Solomon M, McFadden D and Peters AL. Exenatide therapy and risk of pancreatitis and pancreatic cancer in a privately insured population. Diabetes Technology and Therapeutics 2012; 14 (10): 1-10

Sandzen B, Rosenmuller M, Haapamaki MM, Nilsson E, Stenlund H, Oman M. First attack of acute pancreatitis in Sweden 1988-2003: incidence, aetiological classification, procedures and mortality – a register study. BMC Gastroenterology 2009, 9:18

Scott DA, Boye KS, Timlin L, Clark JF and Best JH. A network meta-analysis to compare glycaemic control in patients with type 2 diabetes treated with exenatide once weekly or

liraglutide once daily in comparison with insulin glargine, exenatide twice daily or placebo. Diabetes Obes Metab. 2012 Sep 7. doi: 10.1111/dom.12007. [Epub ahead of print]

Shyangdan DS, Royle P, Clar C, Sharma P, Waugh N and Snaith A. Glucagon-like peptide analogues for type 2 diabetes mellitus. Cochrane Database Syst Rev. 2011 Oct 5;(10):CD006423.

Tatarkiewicz K, Smith PA, Sablan EJ, Polizzi CJ, Aumann DE, Villescaz C, Hargrove DM, Gedulin BR, Lu MG, Adams L, Whisenant T, Roy D and Parkes DG. Exenatide does not evoke pancreatitis and attenuates chemically induced pancreatitis in normal and diabetic rodents. Am J Physiol Endocrinol Metab 2010; 299:E1076–E1086

Thompson S, Kaptoge S, White I, Wood A, Perry P, Danesh J; Emerging Risk Factors Collaboration. Statistical methods for the time-to-event analysis of individual participant data from multiple epidemiological studies. Int J Epidemiol. 2010 Oct;39(5):1345-59. Epub 2010 May 3.

Wenten M, Gaebler JA, Hussein M, Pelletier EM, Smith DB, Girase P, Noel RA, Braun DK and Bloomgren GL. Relative risk of acute pancreatitis in initiators of exenatide twice daily compared with other anti-diabetic medication: a follow-up study. Diabet Med. 2012 Nov;29(11):1412-8. doi: 10.1111/j.1464-5491.2012.03652.x.

III Patient Registry of Lixisenatide Use in Adult Type 2 Diabetes

Format and Content of Study Protocol

III.1 Title

Patient Registry of Lixisenatide Use in Adult Type 2 Diabetes

III.2 Marketing Authorization Holder

The marketing authorization holder (MAH) is Sanofi.

III.3 Responsible Parties

Principal Investigator	*Peter Boyle PhD DSc FRSE FFPH FRCPSG FRCP FMedSci
Senior Investigator	*Philippe Autier MD PhD
Study Coordinator	*Maria Bota MSc/MEng
Study Statisticians	*Mathieu Boniol PhD
	*Chris Robertson PhD

Local Investigator, Denmark	Henrik Toft Sørenson MD
Local Investigator, Denmark	Timothy L Lash PhD
Local Investigator, Norway	Lars Vatten MD PhD
Local Investigator, Sweden	Rickard Ljung MD PhD

*A brief *Curriculum Vitae* is attached as Appendix IV.

III.4 Abstract

Title Patient Registry of Lixisenatide Use in Adult Type 2 Diabetes

Rationale and Background. GLP-1 RAs have been a focus of attention since the signalling of certain (rare but serious) adverse effects reported with their use: pancreatitis, pancreatic cancer and thyroid cancer (especially medullary carcinoma). A new GLP-1 RA (i.e. lixisenatide) treatment for type 2 diabetes will soon be available on the market. An active surveillance approach is more useful for monitoring products after launch by providing a system for reporting these adverse effects and by collecting information on the exposed population.

Research Question and Objectives. In the context of pharmacovigilance activity of the EU RMP (European Union Risk Management Plan), it has been agreed with the European Medicines Agency (EMA) to develop a registry to monitor the occurrences of events of interest including acute pancreatitis, pancreatic cancer and thyroid cancer, especially medullary carcinoma of the thyroid, among adult type 2 diabetes patients treated with lixisenatide.

Study Design This will take the form of a Patient Registry involving patients with lixisenatide in Denmark, Norway and Sweden.

Population Diabetic patients prescribed with lixisenatide in Denmark, Norway and Sweden since the day on which lixisenatide was approved for use.

Variables For each patient, information regarding all anti-diabetic medications prescribed in the study period will be recorded together with basic information such as age and gender. Patients who develop cancer will be identified as will anyone who is diagnosed with pancreatitis, and their complete clinical information will be retrieved and collected from existing national registers and databases annually: smoking history, a previous diagnosis of Multiple Endocrine Neoplasia (especially MEN1), chronic pancreatitis, duration of diabetes, gallstones, prior use of other anti-diabetics, alcohol intake, obstruction of the pancreatic duct, radiation treatment to the head and neck, iodine intake, hormonal and reproductive treatment, diagnosis of Multiple Endocrine Neoplasia type 2 (MEN2), history of goitre or benign thyroid nodules, history of cancer, and family history of medullary thyroid cancer.

Data Sources Patients will be identified in the National Prescription Database. They will be linked to the National Death Indices, National Cancer Registries and National Hospital Discharge schemes to identify cases of cancer, pancreatitis and anyone who has died. Clinical data for all patients with the outcome of interest will also be retrieved from National Hospital Discharge schemes. Additional data will be collected from other (country specific) available data sources.

Study Size For a 1% exposure to lixisenatide among diabetic patients, thus 38 expected cases of pancreatitis, the power of the study in order to detect an observed vs

expected ratio of pancreatitis of 1.5 will be of 83% (significance level=0.05). Futhermore, the study will be able to detect an observed vs expected ratio of pancreatic cancer of 1.5 with 59% power (significance level=0.05), and an observed vs expected ratio of 2 with 92% power (significance level=0.05). However, for 1% exposure to lixisenatide, the study is underpowered to detect these same ratios of thyroid cancer, it will be able to detect with power of 92% an observed vs expected ratio of 2 (significance level=0.05) for 5% exposure to lixisenatide among the diabetic population.

Data analysis Descriptive analysis will be performed and total follow-up time for lixisenatide users will be calculated. For pancreatitis, pancreatic cancer and thyroid cancer, the expected number of cases will be estimated annually after launch using the background rates obtained from the retrospective databases study. If the observed number of cases for the events of interest, respectively, is significantly higher than the expected number of cases, further investigation may be warranted following discussion with the regulatory authorities.

Milestones The registry will be initiated after the launch of lixisenatide and preparations will begin with immediate effect to ensure that the systems are in place prior to launch. Status reports will be submitted to the Agency annually, together with the RMP update as planned. Final report will be submitted to the Agency at the end of the registry.

III.5 Amendments and Updates

This is the initial protocol and any amendments will be placed here in a timely manner.

III.6 Milestones (events in months)

The registry will be initiated after the launch of lixisenatide and preparations will begin with immediate effect to ensure that the systems are in place prior to launch. Status reports will be submitted to the Agency annually, together with the RMP update as planned. Final report will be submitted to the Agency at the end of the registry.

However, if a sufficient number of participants are captured for any outcome(s) of interest earlier before the end of registry, the final data analysis for the particular outcome(s) will be started immediately and the study report will be made available within 12 months.

Start of preparatory phase	T0	Development of draft Protocol
	T0+1	Meeting with Sanofi Global Pharmacovigilance and Epidemiology, Regulatory, and Medical Affairs
	T0+1	Establishment of Scientific and Steering Committee
	T0+2	Meeting of local Principal Investigators to refine protocol
	T0+3	Protocol agreed and submitted to CHMP EMA
	T0+6	Development of data collection module
	T0+7	Synthesis of background information on disease rates in populations
	T0+8	Preliminary Pilot Testing of data collection and data transfer
	T0+9	Final agreement on Protocol from CHMP
	T0+9	IRB/Ethics Approval
	T0+10	Registry ready to launch
Start of data collection	Date of market authorization for Lixisenatide – T	
End of data collection	2018	
Study progress reports	Yearly	
Interim reports	Yearly	
Final study report	2017 for Acute pancreatitis 2019 for pancreatic and thyroid cancer	

III.7 Rationale and Background

GLP-1 RAs have been a focus of attention since the signalling of certain (rare but serious) adverse effects reported with their use: pancreatitis, pancreatic cancer and thyroid cancer (especially medullary carcinoma, a rare tumour of the thyroid gland).

Glucagon-like peptide 1 receptor agonist (GLP-1 RA) is a new class of blood glucose lowering drugs indicated in the treatment of type 2 diabetes mellitus (T2DM). It is an agonist molecule to the incretin (gastrointestinal hormone) GLP-1 which stimulates glucose-dependant secretion of insulin. GLP-1 is rapidly inactivated by the dipeptdyl peptidase-1 (DPP-4) (half life of about 2 minutes), hence the need for a GLP analogue or agonist with greater resistance to DDP-4 degradation. GLP-1 regulates glucose levels by stimulating glucose-dependent insulin secretion and biosynthesis, and by suppressing glucagon secretion, delayed gastric emptying and promoting satiety.

There are currently 2 GLP-1 RA products on the market, one of which (exenatide) is available in two formulations (Byetta and Bydureon):

- Exenatide (also Exendin-4) marketed as Byetta by Amylin Pharmaceuticals, Inc., (San Diego, California, United States of America was launched in 2005 in the USA and approved in 2006 in the European Union and is administered subcutaneously twice daily; Exenatide marketed as Bydureon by Amylin Pharmaceuticals, Inc., (San Diego, California, United States of America) was approved on the market in 2012 and is administered subcutaneously once weekly.

- Liraglutide, marketed as Victoza by Novo Nordisk, Inc. (Copenhagen, Denmark). Liraglutide was approved by the European Medicines Agency (EMA) in July 2009 and by the United States Food and Drug Administration (FDA) in January 2010. Liraglutide, a once-daily glucagon-like peptide-1 receptor agonist, is approved for use as monotherapy in the USA and Japan (but not in Europe or Canada) and in combination with selected oral agents (all regions) for the treatment of patients with type 2 diabetes. Guidance from local advisory bodies is emerging on the most appropriate place for liraglutide in the treatment pathway. It is apparent from its phase 3 clinical trial programme that liraglutide provides superior glycaemic control compared with that achieved with other antidiabetic agents used early in the treatment pathway (e.g. glimepiride and sitagliptin). Key additional benefits include a low incidence of hypoglycaemia and clinically relevant weight loss, although these benefits may be ameliorated by concomitant sulphonylurea treatment and, in the case of hypoglycaemia, reduction of the sulphonylurea dose may be necessary.

Safety concerns

GLP-1 receptor agonists have been demonstrated to have impact on glycaemic control, to be associated with weight loss and to carry a low risk of hypoglycaemia (Bergenstal

et al, 2012; Scott et al, 2012; Nauck et al, 2012; Alves et al, 2012; Gough, 2012; Scott et al, 2012; Shyangdan et al, 2011). However, these drugs have been a focus of attention since they may be associated with the occurrence of certain (rare but serious) adverse: acute pancreatitis, pancreatic cancer and thyroid cancer (especially medullary carcinoma of the thyroid).

Acute Pancreatitis

Spontaneous (post-marketing) reports of acute pancreatitis among type 2 diabetes patients on GLP-1 agonists were submitted to the FDA Adverse Event Reporting System [FDA alert: information for healthcare professionals: exenatide (marketed as Byetta). FDA: Postmarket Drug Safety Information for Patients and Providers, available at: http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm124713.htm]. Since the introduction on the market in 2005 until 8/18/2008, 36 cases of acute pancreatitis were reported in patients taking Byetta. As a result of these spontaneous results the FDA required the manufacturer to include a warning for the risk of pancreatitis on the prescribing information of exenatide.

Also, at the introduction on the market of the new molecule liraglutide (marketed as Victoza), patients were warned about the potential risks of pancreatitis, as there was a 4:1 imbalance of the pancreatitis cases in patients using Victoza compared to patients using another diabetes medicine in 5 clinical trials [source: http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm198543.htm]

However the preclinical and clinical evidence over the mechanism linking GLP-1 RA and acute pancreatitis is conflicting (Anderson et al, 2010; Elashoff et al, 2011; Drucker et al 2011). Preclinical studies showed equally a negative effect of incretin based drugs on the risk of developing pancreatitis (Matveyenko et al, 2009; Nachani et al, 2010) as well as a null effect or a positive effect (Engel et al, 2010; Tatarliewicz et al, 2010).

The clinical data are equally contradictory. A recent meta-analysis was carried out in order to assess the risk of acute pancreatitis and overall cancer with use of exenatide and liraglutide separately (Alves et al, 2012). The Summary Odds Ratio (SOR) based on 13 studies of exenatide that reported acute pancreatitis outcome was found to be 0.84 [95% CI, 0.58; 1.22]. The 13 studies included 3 cohort studies [Doré et al.2009; Doré et al.2011; Garg et al, 2010; Wenten et al, 2012) and 10 randomized controlled trials out of which 6 reported zero cases of pancreatitis, hence the odds ratio was zero. The overall Summary Odds Ratio based on 12 RCT of liraglutide that report acute pancreatitis outcome was found to be 0.97 [95% CI, 0.21; 4.39], out of which 8 studies reported zero cases of acute pancreatitis. There have been no post-market observational studies for liraglutide and acute pancreatitis so far. These results are weakened by limitations such as the fact that they are based on small studies, underpowered to detect rare adverse effects and of short duration.

A number of other studies have been reported:

- Romley et al (2012) conducted a study of exenatide therapy and the risk of pancreatitis and pancreatic cancer in a privately insured population. This is a retrospective cohort study on type 2 DM patients with employer provided health insurance from 2007 to 2009. Among the 268,561 patients included in the study, only 2.6% used exenatide. The hospitalization rate for acute pancreatitis among patients who used at least one exenatide prescription was 1.96 per 1000 patients compared to 2.49 per 1000 patients who never used exenatide (p-value = 0.167).

- MacConell et al (2012) examined the safety and tolerability of exenatide twice daily in patients with type 2 diabetes with an integrated analysis of 5594 patients from 19 placebo-controlled and comparator-controlled clinical trials This is an integrated analysis of 19 RCT carried out by the manufacturer. The incidence rates for pancreatitis were not statistically different between groups.

- Elashoff et al (2011) reported on the disproportion of the FDA-AERS database of reported adverse events showed an increased risk of acute pancreatitis with exenatide: OR = 10.68 (p-value vs control drugs=2 x 10e-16). However, this must be interpreted bearing in mind the known limitations of this database (e.g. http://www.ncbi.nlm.nih.gov/pubmed/15317031).

  The literature can be summarised by observing that the small number of reported events and other design limitations of the studies currently available does not allow for clear conclusions to be drawn, one way or another, at the present time.

Pancreatic Cancer

Besides observing a high number of pancreatitis cases, Elashoff et al (2011) also reported on pancreatic cancer in patients treated with exenatide [OR=2.95 (p value vs control drugs=9 x 10e-5)]). There are no further clinical studies that address this issue. Experimental data show that GLP-1 agonists increase beta-cell mass in rodents, But human trials do not support the rodent data (Brubaker et al, 2009)..

Thyroid Cancer

The rodent calcitonin producing C-cell expresses GLP-1Rs, and sustained GLP-1R activation results in increased calcitonin secretion, C-cell hyperplasia and medullary thyroid cancer, predominantly in rats. In contrast, C cells within the monkey and human thyroid gland exhibit lower levels of GLP-1R expression, and prolonged administration of liraglutide at very high doses does not produce C-cell proliferation in monkeys (Drucker et al, 2011; Bjerre Knudsen et al, 2010).

A review on the association between glucagon-like peptide-1 receptor agonists and thyroid cancer (Chiu et al., 2012) concludes that GLP-1 agonists might increase the risk of thyroid C-cell pathology in rodents, but its risk in humans awaits confirmation.

Therefore, the effects of GLP-1 on human cancer development are overall unknown and difficult to be extrapolated from pre-clinical studies. In addition, the small number of cases and the lack of biological plausibility raise doubts between the use of GLP-1 agonists and the occurrence of cancer (pancreatic, thyroid or overall). Therefore longer-term, better designed epidemiological studies are required, in order to assess any risks associated with GLP-1 RA use.

Design of Investigative Study

Two studies have been prepared and the patient registry is presented below. The rationale behind both studies revolves chiefly around the concept of performing the Registry study in the same populations where the incidence rates of acute pancreatitis, pancreatic cancer and thyroid cancer, in particular medullary thyroid cancer in adult patients with type 2 diabetes treated with GLP-1 agonists (i.e., exenatide and liraglutide) and other anti-diabetics are established.

Very limited background information is available in the literature for the incidence rates of acute pancreatitis, pancreatic cancer and (medullary) thyroid cancer in adult type 2 diabetes patients treated with GLP-1 agonists (i.e., exenatide and liraglutide) and other anti-diabetics. Therefore, the data from such a study will help contextualize these events expected to be observed in the patient registry of lixisenatide.

"On 15 November 2012, the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion, recommending the granting of a marketing authorisation for the medicinal product Lyxumia. The active substance of Lyxumia is lixisenatide, a glucagon-like-peptide-1 (GLP-1) analogue medicinal product. Like native GLP-1, lixisenatide stimulates insulin release from the pancreatic islets, suppresses glucagon secretion, delays gastric emptying and reduces body weight. A pharmacovigilance plan for Lyxumia will be implemented as part of the marketing authorisation." (from EMA - Lyxumia).

The pharmacovigilance plan includes setting up a patient registry of type 2 diabetic patients taking lixisenatide. This would represent a proactive risk assessment in the post approval setting that allows for prospective follow-up and monitoring of occurrences of any of the outcomes of interest, i.e. pancreatitis, pancreatic cancer and thyroid cancer (especially medullary carcinoma of the thyroid).

The registry population will be representative of the population actually using the product since it should include all patients regardless of age, comorbidities or concurrent treatments. Follow up duration will be long enough to encompass delayed risks, consequences of long term use and effects of various combinations and alternations of treatments if any.

III.8 Research Question and Objectives

Study objectives

In the context of pharmacovigilance activity of the EU RMP (European Union Risk Management Plan), it has been agreed with the European Medicines Agency (EMA) to develop a Patient Registry of patients with diabetes exposed to lixisenatide.

The primary objectives of this study are to monitor the occurrences of:

1. acute pancreatitis,
2. pancreatic cancer
3. thyroid cancer, especially medullary carcinoma of the thyroid,

among adult type 2 diabetes patients treated with lixisenatide and to compare their risks with that of users of (1) other GLP-1 receptor agonists from the Database Study ; (2) other diabetic medications from the Database Study; and (3) the general population. The assembled cohort will be constantly monitored for these events to detect and emerging signal as quickly as possible.

Declaration of Study Hypotheses

This study is designed to focus on the risk associated with use of lixisenatide and will investigate the following primary hypotheses:

1. That adult patients prescribed lixisenatide have an increased risk of acute pancreatitis when compared to the expected risk calculated for the other GLP-1 RA users;

2. That adult patients prescribed lixisenatide have an increased risk of pancreatic cancer when compared to the expected risk calculated for the other GLP-1 RA users;

3. That adult patients prescribed lixisenatide have an increased risk of thyroid cancer (especially medullary carcinoma of the thyroid) when compared to the expected risk calculated for the other GLP-1 RA users;

Comparison of the incidence of these three conditions among users of lixisenatide and users of other GLP-1 receptor agonists will be available from the companion study among databases. This will provide an important background when interpreting any Odds Ratio found.

Secondary Hypotheses

4. That adult patients prescribed lixisenatide have an increased risk of pancreatitis when compared to the expected risk calculated for other diabetic medications (which will also be divided into groups of oral medications (an indicator of less severe diabetes) and insulin (an indicator of more severe diabetes);

5. That adult patients prescribed lixisenatide have an increased risk of pancreatic cancer when compared to the expected risk calculated for other diabetic medications (which will also be divided into groups of oral medications (an indicator of less severe diabetes) and insulin (an indicator of more severe diabetes);

6. That adult patients prescribed lixisenatide have an increased risk of thyroid cancer (especially medullary carcinoma of the thyroid) when compared to the expected risk calculated for other diabetic medications (which will also be divided into groups of oral medications (an indicator of less severe diabetes) and insulin (an indicator of more severe diabetes);

What is requested is to monitor the occurrence of pancreatitis, pancreas cancer and thyroid cancer in patients with diabetes receiving lixisenatide and to identify any potential signal indicating an increased level of pancreatitis, pancreas cancer and thyroid cancer as reliably and as quickly as possible. Comparisons need to be made with the background rate in patients with diabetes and also the general population before conclusions can be drawn. [Patients with diabetes have a background increased risk of both pancreatitis and pancreas cancer].

The comparison between risk of outcome events with different treatments will require to be handled very carefully. The only way to make such comparisons in an unbiased manner would be via a randomised clinical trial. In the observational studies proposed herein there are other factors, such as patient characteristics and physician choice, which may influence treatment choice. The products in question will not be distributed to patients in a randomised manner.

Importantly, comparison of risk of the endpoints (Pancreatitis, Pancreas Cancer, Thyroid cancer) in this setting is fraught with hazard particularly when comparing patients receiving lixisenatide with the use of all other anti-diabetic medications. This latter group will comprise a group of patients with a wide range of treatments associated with diabetes of different durations and different levels of severity, from less severe (e.g. patients prescribed metformin) to more severe (e.g. patients with basal and prandial insulins). Care will be taken to separate this group into patients with oral anti-diabetic medications and those requiring insulin: at least this will provide two comparison groups at different levels of diabetes severity.

A comparison of cases observed and the numbers observed given the rates in the general population will also be made although there are quite severe issues regarding comparability of the groups which make interpretation complicated. The observation periods are not contemporaneous which introduces a potential source of confounding and/or information bias arising from potential differential diagnostic accuracy in the two time periods. This will be addressed in the statistical analysis and interpretation.

III.9 Research Methods

III.9.1 Study design

This will take the form of a Patient Registry involving patients treated with lixisenatide in Denmark, Norway and Sweden. Additional sources of data will be sought among leading diabetes centres to identify more detailed clinical information. The study design will be the same in all 3 countries, but the data management procedure will differ between the centres, therefore some 'technical' details of the study implementations will be properly defined after consultation with each separate centre.

Prior to the full Registry study commencing, it will be essential to determine the most efficient manner in each country to develop the Register and to obtain the follow-up information. During this phase, it will be possible to refine the study design and, particularly, the methodology employed in each country.

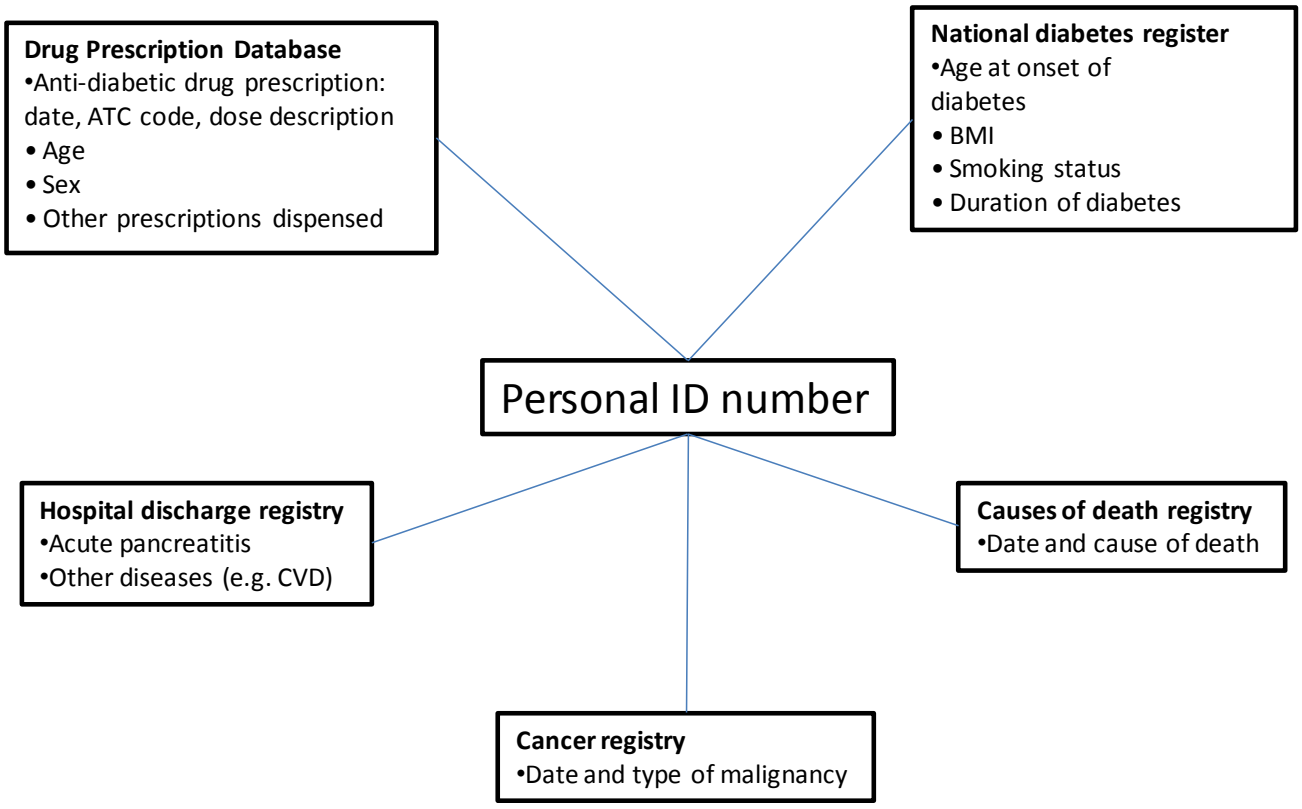
III.9.2 Setting

The study will be based in Denmark, Norway and Sweden. These countries have been chosen because each has:

1. A high-quality prescription registry that is population-based.
2. A high-quality cancer registry, which covers the entire population included in the prescription database.
3. A national hospital discharge registry, which covers the entire population included in the prescription database
4. A national death register, which can be used for record linkage to ascertain the date of death of any patient in the patient registry who died.
5. A source of information on key confounders (notably BMI), either in the prescription database itself, in a diabetes registry or in other available databases or large prospective studies.

A unique personal identity number will be used to link together the information from the several population based registries, as shown in the figure below:

Figure III.9.2



The source of the cohorts will be mainly represented by the drug prescription registries.

The study population will include patients with type 2 diabetes treated with lixisenatide after launch. The study period will start from the lixisenatide launch and last for 5 years.

The patients will be identified as having been prescribed at least one prescription for the GLP-1 RA lixisenatide.

High completeness of follow-up is expected, as well as high accuracy of data, which will allow capture of the variables of most interest.

The study entry date will be defined as the date of the first prescription of lixisenatide after launch. The follow-up will end at the earliest of the following: 1) death or 2) the end of the register.

Data from national registers and databases in Denmark, Norway and Sweden will be used as the primary data source to identify lixisenatide treated patients for this registry. In Denmark, Norway and Sweden, national prescription databases have been established and are linkable to other national registers and databases (e.g., National Cancer Registry, Cause of Death Registry, and Hospital Discharge Registry) via National Registration Identification number.

A detailed table of characteristics of the cohort included in the analysis will be provided after consultation with the local investigators.

III.9.3 Variables (Outcome, Exposure, Risk factors, Confounding variables)

For each patient, information regarding all anti-diabetic medications prescribed in the study period will be recorded together with basic information such as age and gender.

Patients who develop pancreatic cancer and thyroid cancer will be identified as well anyone who is diagnosed with pancreatitis, and their complete clinical information will be retrieved and collected from existing national registers and databases annually: smoking history, a previous diagnosis of Multiple Endocrine Neoplasia (especially MEN1), chronic pancreatitis, duration of diabetes, gallstones, prior use of other anti-diabetics, alcohol intake, obstruction of the pancreatic duct, radiation treatment to the head and neck, iodine intake, hormonal and reproductive treatment, diagnosis of Multiple Endocrine Neoplasia type 2 (MEN2), history of goitre or benign thyroid nodules, history of cancer, and family history of medullary thyroid cancer.

Outcomes of interest

Acute pancreatitis cases will be identified from the hospital discharge registers. Cases of thyroid cancer and pancreatic cancer will be identified from the national cancer registers. However, data on the cancer cases for a given year are typically considered incomplete until approximately one year after the year ends. For example, it will be possible to use the national cancer registries to identify incident cancers occurring until the end of 2013, if the analysis of thyroid cancer is planned to be performed in early 2015.

Exposure assessment and follow-up time

Patients with one or more prescriptions of lixisenatide will be identified from the national prescription registers and included in the register.

For acute pancreatitis, the exposure duration on lixisenatide will begin accumulating on the first day of lixisenatide prescription and continue with the subsequent continuous use of lixisenatide until:

1) the end of the lixisenatide treatment (in addition to a grace period of up to 30 days, to account for non-adherence),

2) the occurrence of acute pancreatitis, or;

3) the end of registry, whichever comes first.

For thyroid cancer and pancreatic cancer, the exposure duration will start from the first day of lixisenatide prescription and continue until either (1) the occurrence of thyroid cancer or pancreatic cancer, or (2) the end of registry, whichever comes first.

III.9.4 Data Sources

Patient registry data sources are the same as for the data base study (Section II.9.4)

Patients will be identified in the National Prescription Database. They will be linked to the National Death Indices, National Cancer Registries and National Hospital Discharge schemes to identify cases of cancer, pancreatitis and anyone who has died. Clinical data for all patients with the outcome of interest will also be retrieved from National Hospital Discharge schemes. Additional data will be collected from other (country specific) available data sources.

The personal identification number will be used to link unambigously the databases in each country. The ATC coding system (Anatomic Therapeutic Coding) will be used to identify exposure: all patients having been prescribed drugs for the treatment of diabetes (ATC code A10 and subcategories) will be retrieved and linked to the other databases: they will be followed via cancer and hospital discharge registries. The ICD10 codes will be used for outcome assessment: acute pancreatitis (K85), pancreatic cancer (C25) and thyroid cancer (C73), especially medullary thyroid cancer.

III.9.5 Study Size

All available data following the launch of lixisenatide will be analyzed for the final analyses. The data from the three participating countries will be combined together for the analysis. The estimation of sample size and study power for the objectives of this study will be further defined after consultation with local Principal Investigators and external experts.

According to estimates provided by the International Diabetes Federation for 2013, there were 1,049,810 prevalent cases of diabetes among adults aged 20-79 in the three countries combined (346,730 in Denmark; 209,870 in Norway; and 493,210 in Sweden). In addition, assuming a crude incidence rate of diabetes of 364 per 100,000 person-years (calculated using data for 1995-2006, from Carstensen et al, 2008), then for a total adult population of 15,000,000 persons, approximately 55,000 new cases of diabetes will be diagnosed every year in the three countries combined. This provides an estimate of the numbers of new cases of diabetes that are potentially eligible for the study. Not all of these patients will be candidates for treatment with lixisenatide for a variety of reasons. However, various scenarios about the prevalence of patients prescribed lixisenatide are made in order to estimate the statistical power of the Registry study. These estimates are presented in Table III.9.5.1 and Table III.9.5.2.

Using these hypothetical numbers, the number of patient-years accumulated over a period of 5 years of registry were calculated as follows:

1st year of registry:

no_records_yr1 = %lixi * prevalence_diabetes = %lixi * 1,049,810

2nd year of registry:

no_records_yr2 = no_records_yr1 + new_records_yr2
= no_records_yr1 + %lixi * new_cases_diabetes
= no_records_yr1 + %lixi * 55,000

3rd year of registry:

no_records_yr3 = no_records_yr2 + new_records_yr3
= no_records_yr1 + 2 * %lixi * new_cases_diabetes

etc…

Thus the number of person-years accumulated over 5 years is:

Person-years_over_5_years = no_records_yr1 + no_records_yr2+..+ no_records_yr5
=5*(%lixi*prevalence_diabetes)+10*(%lixi*new_cases_diabetes)

The number of expected cases of pancreatitis were calculated using the incidence rate shown above (65.57 per 100,000 person-years). The power of the study was then calculated for the expected number of cases as a mean of Poisson law (Breslow and Day, 1987) and a range of expected vs observed ratios. The results are shown in Table III.9.5.1.

Table III.9.5.1: Estimates of statistical power for Registry Study for pancreatitis under different scenarios for prevalence of prescription of lixisenatide.

Pancreatitis (incidence rate=65.57/100,000 pyrs)					
% exposure to lixisenatide	Pyrs accumulated over 5 years	No of expected cases	Power in order to detect obs/exp+=1.2	Power in order to detect obs/exp+=1.5	Power in order to detect obs/exp+=2
0.10%	5799.05	3.8	0.10*	0.17	0.39
0.20%	11598.1	7.6	0.13*	0.26	0.64
0.50%	28995.25	19.0	0.18	0.60	0.97
0.80%	46392.4	30.4	0.27	0.79	1.00
1.00%	57990.5	38.0	0.29	0.83	1.00
1.50%	86985.75	57.0	0.37	0.93	1.00
2%	115981	76.0	0.47	0.98	1.00
5%	289952.5	190.1	0.38*	1.00	1.00
10%	579905	380.2	0.60*	1.00	1.00
*Calculated using normal approximation					
+obs/exp stands for 'observed vs expected ratio'					

These numbers are certainly underestimated, as the incidence of diabetes has been steadily increasing worldwide. Even so, for a 1% exposure to lixisenatide among diabetic patients, thus 38 expected cases of pancreatitis, the power of the study in order to

detect an observed vs expected ratio of pancreatitis of 1.5 will be of 83% (significance level=0.05).

Table III.9.5.2 shows the power calculation for the Patient Registry Study and cancer (pancreatic cancer and thyroid cancer). For 1% of exposure to lixisenatide among the diabetic population the study will be able to detect an observed vs expected ratio of pancreatic cancer of 1.5 with 59% power (significance level=0.05), and an observed vs expected ratio of 2 with 92% power (significance level=0.05). For 1% exposure to lixisenatide, the study is underpowered to detect these same ratios of thyroid cancer, it will be able to detect with power of 92% an observed vs expected ratio of 2 (significance level=0.05) for 5% exposure to lixisenatide among the diabetic population.

Table III.9.5.2 : Estimates of statistical power for Registry Study for pancreas cancer and thyroid cancer under different scenarios for prevalence of prescription of lixisenatide.

Pancreatic cancer (incidence rate=29.19/100,000 pyrs)				
% exposure to lixisenatide	**Pyrs accumulated over 5 years**	**No of expected cases**	**Power in order to detect obs/exp+=1.5**	**Power in order to detect obs/exp+=2**
0.10%	5799.05	1.7	0.07	0.14
0.20%	11598.1	3.4	0.17	0.39
0.50%	28995.25	8.5	0.32	0.73
0.80%	46392.4	13.5	0.48	0.90
1.00%	57990.5	16.9	0.59	0.92
1.50%	86985.75	25.4	0.74	>0.98
2%	115981	33.9	0.79	1.00
5%	289952.5	84.6	0.99	1.00
10%	579905	169.3	1.00	1.00
Thyroid cancer (incidence rate=6.13/100,000 pyrs)				
% exposure to lixisenatide	**Pyrs accumulated over 5 years**	**No of expected cases**	**Power in order to detect obs/exp+=1.5**	**Power in order to detect obs/exp+=2**
0.10%	5799.05	0.4	<0.07	<0.14
0.20%	11598.1	0.7	<0.07	<0.14
0.50%	28995.25	1.8	0.07	0.14
0.80%	46392.4	2.8	0.08	0.21
1.00%	57990.5	3.6	0.17	0.39
1.50%	86985.75	5.3	0.22	0.54
2%	115981	7.1	0.26	0.64
5%	289952.5	17.8	0.59	0.92
10%	579905	35.5	0.83	1.00
+obs/exp stands for 'observed vs expected ratio'				

Thus, a prevalence of 0.08% of patients with diabetes prescribed lixisenatide would give the study an 80% power to detect a risk of 1.5. Similar calculations reveal that for pancreas cancer the corresponding prevalence of lixisenatide prescription to give 80% power would be 2% and for thyroid cancer 9%.

III.9.6 Data Management

Once the study population well defined via prescription registries, it will be essential to collect the follow-up data efficiently.

Adequate training of the staff will be essential in order to correctly recognize and report all events of interest. Systematic collection of follow-up data, routine follow-up of all registry patients for the key adverse effects previously identified, as well as all other information.

In each centre data will be linked between the different data sources (population registry, prescription registry, hospital discharge registry, cancer registry) through an anonymized unique identification number. Linking the population registry, the prescription registry and the cancer registry has already been tested and proved to be effective through our previous database study (Boyle et al, 2013). However, linking with the hospital discharge registry requires a procedure preventing introduction of information bias in the study.

All patients identified to have had an anti-diabetic treatment in the prescription database (regardless of the type of medication taken) will be linked to the Hospital Discharge Registry. All discharge information will be retrieved for all the diabetic patients (with an anti-diabetic prescription) and searched for codes or keywords that indicate a pancreas related disease. For the purpose of this task, in each country a Medical Adjudication Committee (MAC) will be assembled, composed of at least two internists, who will be blinded as to treatments taken by patients. The MAC will examine all charts of potential pancreatitis patients receiving lixisenatide and also patients receiving other GLP-1 receptor agonists. They will be responsible for:

- Establishing a disease definition for acute pancreatitis[2];
- Identify codes or keywords in hospital discharge records possibly associated with pancreatitis;
- Contact hospitals (through a standardized questionnaire) for getting full information on the data the diagnosis of pancreatitis was based on
- Review data for establishing whether pancreatitis was present.

After that the MAC assessment will be entered in the study database, the analyses in function of the treatment type (lixisenatide, other GLP-1 RAs or other anti-diabetic drugs) will be made following a review by the MAC of some patients not thought to have pancreatitis (to confirm the absence of the disease).

[2] An external blinded committee (Pancreatic Safety Assessment Committee or PSAC) has been appointed to review all pancreatic adverse events occurring in clinical trials of lixisenatide. The PSAC Charter has not been finalized, yet. However, the criteria for adjudication of acute pancreatitis will be adapted from those proposed by Banks, Freeman, and the Practice Parameters Committee of the American College of Gastroenterology (Am J. of Gastroenterology 2006;101:2379-2400) and Frossard et al. (Lancet 2008;371:143-52.).

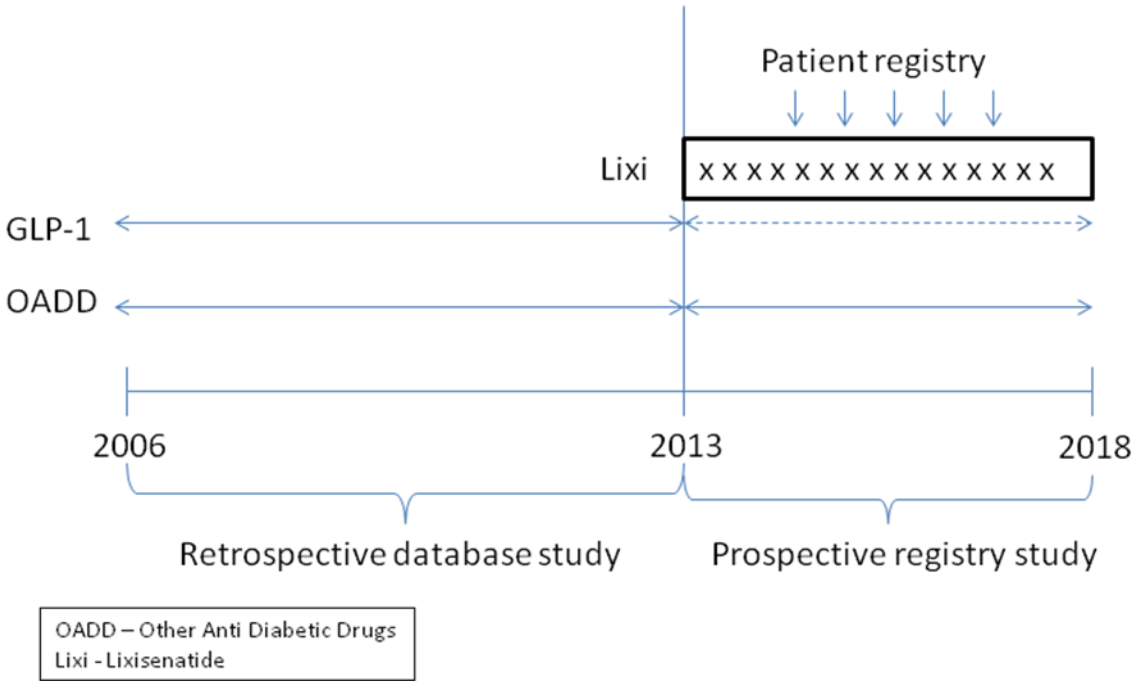
Similarly to the Database Study, each national centre will be responsible for the data storage and data management of the individual-level data, following all national and European directives regarding the well being and rights of each study subject. Each centre has an excellent track record of successfully undertaking similar research respecting all moral and legal requirements.

Only de-identified data will be stored at IPRI, and this will be done in a secure manner: data will password protected, and stored on local machines.

III.9.7 Data Analysis

Descriptive analysis will be performed and total follow-up time for lixisenatide users will be calculated.

Figure II.9.7.3: General study overview



For acute pancreatitis, pancreatic cancer and thyroid cancer, the expected number of cases will be estimated annually after launch using the background rates obtained from the retrospective databases study.

If the observed number of cases for the events of interest, respectively, is significantly higher than the expected number of cases, further investigation may be warranted following discussion with the regulatory authorities.

III.9.8 Quality Control

An independent **Scientific Steering Committee** will be appointed to oversee the study and advise on treatment, methodological and biostatistical issues. This group will meet regularly throughout the duration of the study and incorporate a **Biostatistical Advisory Group**, to advise on all aspects of the design and data analysis.

The **Scientific Steering Committee** will comprise:

Professor Geremia Bolli
University of Perugia
Perugia, Italy

Professor Stuart Pocock
University College London
London, United Kingdom

Professor Ian Ford
Robertson centre for Biostatistics
University of Glasgow,
Glasgow, United Kingdom

Professor Theodore Holford
Department of Biostatistics
Yale University School of Public Health
New Haven, United States of America

Professor Hertzel Gerstein
McMaster University,
Hamilton, Canada

Professor Derek LeRoith
Mount Sinai Hospital
New York, United States of America.

A Medical Adjudication Commitee (MAC), comprising of at least 2 medical internists in each country will be appointed. Their role will be to: 1) Establish the case definition for acute pancreatitis; 2) identify codes and keywords related to pancreatitis 3) Communicate with hospitals for data on diagnosis; 4) Verify the diagnosis on the basis of information transmitted by hospitals.

III.9.9 Limitations of Research methods

Several issues relating to confounding should be overcome by the prospective registry design. Although not a randomised study, this registry study will enable significant progress to be made over and above a classical database study. In particular, there will be the opportunity to have better information about the basis of the diagnoses of interest and also access to information about the patient's diabetic history and treatment, issues such as why a particular treatment choice was made and why any change was made to treatment will be accessible. The study will also allow methodological investigations of differences between the retrospective database studies being conducted in the same populations and the prospective Register study.

III.10 Protection of Human Subjects

Each national centre will be responsible for following all national and European directives regarding the well-being and rights of each study subject. Each centre has an excellent track record of successfully undertaking similar research respecting all moral and legal requirements. At the central office (iPRI, Lyon) no identifiable data will be received from the individual centres.

III.11 Management and Reporting of adverse events/reactions

All approvals necessary to undertake this study will be obtained in each country. In addition, the study protocol and the national approvals will be submitted to the IPRI Ethics Committee who will give tertiary ethical approval.

Reporting of adverse events or adverse reactions on individual patients is not appropriate to this form of study where there is no contact between the investigators and the patients.

III.12 Plans for disseminating and communicating study results

At the end of the study, a full Report will be prepared and the MAH will submit this to the CHMP of the EMA. Once the comments of the Rapporteurs have been received, any modifications necessary will be made to the Report which will then be finalised. A manuscript presenting the results of the study will be prepared for publication in a peer-reviewed scientific journal and the findings presented at major scientific meetings of relevance to the subject matter e.g. at the Annual meeting of the European Association for the Study of Diabetes (EASD), at the Annual Meeting of the American Diabetes Association (ADA) and the Annual meeting of the American Society for Clinical Oncology (ASCO).

III.13 References

Alves C, Batel-Marques F and Macedo AF. A meta-analysis of serious adverse events reported with exenatide and liraglutide: Acute pancreatitis and cancer. Diabetes Res Clin Pract. 2012 Sep 22. pii: S0168-8227(12)00312-9. doi: 10.1016/j.diabres.2012.09.008. [Epub ahead of print]

Andersen TF, Madsen M, Jørgensen J, Mellemkjoer L, Olsen JH. The Danish National Hospital Register. A valuable source of data for modern health sciences. Dan Med Bull 1999;46:263-8.

Anderson SL, Trujillo JM. Association of pancreatitis with glucagon-like peptide-1 agonist use. Ann Pharmacother. 2010 May;44(5):904-9. Epub 2010 Apr 6.

Bergenstal RM, Li Y, Booker Porter TK, Weaver C and Jenny Han M. Exenatide Once Weekly Improved Glycaemic Control, Cardiometabolic Risk Factors, and a Composite Index of an HbA1c<7%, without Weight Gain or Hypoglycaemia, Over 52 Weeks. Diabetes Obes Metab. 2012 Oct 18. doi: 10.1111/dom.12026.

Bjerre Knudsen L, Madsen LW, Andersen S, Almholt K, de Boer AS, Drucker DJ, Gotfredsen C, Egerod FL, Hegelund AC, Jacobsen H, Jacobsen SD, Moses AC, Mølck AM, Nielsen HS, Nowak J, Solberg H, Thi TD, Zdravkovic M 2010 Glucagon-like peptide-1 receptor agonists activate rodent thyroid C-cells causing calcitonin release and C-cell proliferation. Endocrinology 151:1473–1486

Boyle P, Bota M, Sorensen HT, Tuomilehto J, Ljung R, Colhoun H, Vatten L, Ulrichsen SP, Lash TL, Jacobsen JB, Sund R, Ekbom A, Kieler H, Livingstone S, Levin D, Osvold BO, Haglund B, Autier P, Pasterk M, Boniol M, Boffetta P and Robertson C. Northern European Database Study of Insulin and Cancer (manuscript submitted for publication)

Brubaker PL. Minireview: Update on Incretin Biology: Focus on Glucagon-Like Peptide-1. Endocrinology, May 2010, 151(5):1984–1989.

Carstensen B, Kristensen J K, Ottosen P, Borch-Johnsen K, The Danish National Diabetes Register: trends in incidence, prevalence and mortality. Diabetologia (2008) 51:2187–2196

Chiu WY, Shih SR and Tseng CH. A review on the association between glucagon-like peptide-1 receptor agonists and thyroid cancer. Exp Diabetes Res. 2012;2012:924168. doi: 10.1155/2012/924168. Epub 2012 May 28.

Dore DD, Seeger JD, Arnold Chan K Use of a claims-based active drug safety surveillance system to assess the risk of acute pancreatitis with exenatide or sitagliptin compared to metformin or glyburide. Curr Med Res Opin 2009; 25:1019–1027

Dore DD, Bloomgren GL, Wenten M, Hoffman C, Clifford CR, Quinn SG, Braun DK, Noel RA, Seeger JD. A cohort study of acute pancreatitis in relation to exenatide use. Diabetes Obes Metab 14 February 2011 doi: 10.1111/j.1463–1326.2011.01376.x

Drucker et al., Safety of incretin based therapies, J Clin Endocrinol Metab, Jul 2011, 96(7):2027-2031

Elashoff M, Matveyenko AV, Gier B, Elashoff R, Butler PC. Pancreatitis, pancreatic, and thyroid cancer with glucagon-like peptide-1-based therapies. Gastroenterology. 2011 Jul;141(1):150-6. Epub 2011 Feb 18.

Engel SS, Williams-Herman DE, Golm GT, Clay RJ, Machotka SV, Kaufman KD and Goldstein BJ 2010 Sitagliptin: review of preclinical and clinical data regarding incidence of pancreatitis. Int J Clin Pract 64:984–990

Frank L. Epidemiology. When an entire country is a cohort. Science 2000;287:2398-9.

Garg R, Chen W and Pendergrass W. Acute pancreatitis in type 2 diabetes treated with exenatide or sitagliptin: a retrospective observational pharmacy claims analysis. Diabetes Care 2010; 33:2349–2354

Gier B, Matveyenko AV, Kirakossian D, Dawson D, Dry SM, Butler PC. Chronic GLP-1 receptor activation by exendin-4 induces expansion of pancreatic duct glands in rats and accelerates formation of dysplastic lesions and chronic pancreatitis in the Kras(G12D) mouse model. Diabetes. 2012 May;61(5):1250-62. Epub 2012 Jan 20.

Gier B, Butler PC, Lai CK, Kirakossian D, DeNicola MM, Yeh MW. Glucagon like peptide-1 receptor expression in the human thyroid gland. J Clin Endocrinol Metab. 2012 Jan;97(1):121-31. Epub 2011 Oct 26.

Gough SC. Liraglutide: from clinical trials to clinical practice. Diabetes Obes Metab. 2012 Apr;14 Suppl 2:33-40. doi: 10.1111/j.1463-1326.2012.01576.x.

Gu K, Ng HK, Tang ML, Schucany WR. Testing the ratio of two Poisson rates. Biom J. 2008;50(2):283-98.

Kilander C, Mattsson F, Ljung R, Lagergren J and Sadr-Azodi O. Systematic under-reporting of the population-based incidence of pancreatic and biliary tract cancers,. (submitted for publication).

Knudsen LB, Kiel D, Teng M, Behrens C, Bhumralkar D, Kodra JT, Holst JJ, Jeppesen CB, Johnson MD, de Jong JC, Jorgensen AS, Kercher T, Kostrowicki J, Madsen P, Olesen PH, Petersen JS, Poulsen F, Sidelmann UG, Sturis J, Truesdale L, May J, Lau J. Small-molecule agonists for the glucagon-like peptide 1 receptor. Proc Natl Acad Sci U S A. 2007 Jan 16;104(3):937-42. Epub 2007 Jan 9.

McConell L, Brown C, Gurney K and Han J. Safety and tolerability of exenatide twice daily in patients with type 2 diabetes: integrated analysis of 5594 patients from 19 placebo-controlled and comparator-controlled clinical trials. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy 2012; 5: 29-41

Matveyenko AV, Dry S, Cox HI, Moshtaghian A, Gurlo T, GalassoR, Butler AE and Butler PC. Beneficial endocrine but adverse exocrine effects of sitagliptin in the human islet amyloid polypeptide transgenic rat model of type 2 diabetes: interactions with metformin. Diabetes 2009; 58:1604–1615

Nachnani JS, Bulchandani DG, Nookala A, Herndon B, Molteni A, Pandya P, Taylor R, Quinn T, Weide L and Alba LM. Biochemical and histological effects of exendin-4 (exenatide) on the rat pancreas. Diabetologia 2010; 53:153–159

Nauck M, Frid A, Hermansen K, Thomsen AB, During M, Shah N, Tankova T, Mitha I, Matthews DR. Long-term efficacy and safety comparison of liraglutide, glimepiride and placebo, all in combination with metformin in type 2 diabetes: 2-year results from the LEAD-2 study. Diabetes Obes Metab. 2012 Sep 17. doi: 10.1111/dom.12012. [Epub ahead of print]

Ray AW. Evaluating medication effects outside of clinical trials: new-user designs. Am J Epidemiol 2003;158:915-920.

Romley JA, Goldman DP, Solomon M, McFadden D and Peters AL. Exenatide therapy and risk of pancreatitis and pancreatic cancer in a privately insured population. Diabetes Technology and Therapeutics 2012; 14 (10): 1-10

Sandzen B, Rosenmuller M, Haapamaki MM, Nilsson E, Stenlund H, Oman M. First attack of acute pancreatitis in Sweden 1988-2003: incidence, aetiological classification, procedures and mortality – a register study. BMC Gastroenterology 2009, 9:18

Scott DA, Boye KS, Timlin L, Clark JF and Best JH. A network meta-analysis to compare glycaemic control in patients with type 2 diabetes treated with exenatide once weekly or liraglutide once daily in comparison with insulin glargine, exenatide twice daily or placebo. Diabetes Obes Metab. 2012 Sep 7. doi: 10.1111/dom.12007. [Epub ahead of print]

Shyangdan DS, Royle P, Clar C, Sharma P, Waugh N and Snaith A. Glucagon-like peptide analogues for type 2 diabetes mellitus. Cochrane Database Syst Rev. 2011 Oct 5;(10):CD006423.

Tatarkiewicz K, Smith PA, Sablan EJ, Polizzi CJ, Aumann DE, Villescaz C, Hargrove DM, Gedulin BR, Lu MG, Adams L, Whisenant T, Roy D and Parkes DG. Exenatide does not evoke pancreatitis and attenuates chemically induced pancreatitis in normal and diabetic rodents. Am J Physiol Endocrinol Metab 2010; 299:E1076–E1086

Thompson S, Kaptoge S, White I, Wood A, Perry P, Danesh J; Emerging Risk Factors Collaboration. Statistical methods for the time-to-event analysis of individual participant data from multiple epidemiological studies. Int J Epidemiol. 2010 Oct;39(5):1345-59. Epub 2010 May 3.

Wenten M, Gaebler JA, Hussein M, Pelletier EM, Smith DB, Girase P, Noel RA, Braun DK and Bloomgren GL. Relative risk of acute pancreatitis in initiators of exenatide twice daily compared with other anti-diabetic medication: a follow-up study. Diabet Med. 2012 Nov;29(11):1412-8. doi: 10.1111/j.1464-5491.2012.03652.x.

International Prevention Research Institute

Appendix I

Lixisenatide

Final Study Synopsis for the database post-approval in EU -10042011

International Prevention Research Institute

Study Synopsis for a Retrospective Database Study

Title:	Incidence Rates of Acute Pancreatitis, Pancreatic Cancer and Thyroid Cancer, Notably Medullary Carcinoma of the Thyroid, in Adult Patients with Type 2 Diabetes Mellitus Treated with GLP-1 Receptor Agonists and Other Anti-diabetics in Sweden, Denmark and Norway.
Background:	Limited background information is available in the literature for the incidence rates of acute pancreatitis, pancreatic cancer and thyroid cancer, in particular medullary thyroid carcinoma (MTC), in adult patients with type 2 diabetes mellitus (T2DM) treated with glucagon-like peptide-1 (GLP-1) receptor agonists (i.e., exenatide, liraglutide) and other anti-diabetics (e.g., oral anti-diabetics, insulins). Results from such a study will help contextualize the data potentially observed in the patient registry of Lixisenatide.
Objectives:	Primary objective: To estimate the incidence rates of acute pancreatitis, pancreatic cancer and thyroid cancer, in particular MTC, among adult T2DM patients treated with GLP-1 receptor agonists as well as the ones treated with other anti-diabetics. Secondary objective: To evaluate the potential association between acute pancreatitis, pancreatic cancer and thyroid cancer, in particular MTC, and the use of GLP-1 receptor agonists versus other anti-diabetics among adult T2DM patients.
Study design:	Retrospective cohort study using existing databases and registers in Sweden, Denmark and Norway.

Study population:	Study population will include adult T2DM patients treated with exenatide or liraglutide (cohort 1) versus the ones treated with other anti-diabetics (cohort 2). Patients with the following conditions will be excluded from the study: 1) individuals less than 18 years of age at the cohort entry; 2) individuals with a diagnosis of thyroid cancer, pancreatic cancer, or any pancreatitis prior to cohort entry. The study period is defined as 28 November 2006 through 31 December 2012 for acute pancreatitis and through 31 December 2012 for pancreatic and thyroid cancer (the EU approval dates are 28 November 2006 for exenatide and 02 July 2009 for liraglutide). Cohort entry date will be defined as the date of the first prescription of either exenatide or liraglutide for cohort 1 or the data of first prescription of other anti-diabetics (e.g., oral anti-diabetics, insulins) for cohort 2 during the study period. The follow-up will end at the earliest of the following: 1) diagnosis of acute pancreatitis, pancreatic cancer and thyroid cancer, respectively, for each event of interest, 2) death, or 3) the end of the study as mentioned above. Data from national registers and databases in Sweden, Denmark, and Norway will serve as the data source for this study. In three Nordic countries, national prescription databases have been established and are linkable to other national registers and databases (e.g., National Cancer Registry, Cause of Death Registry, and Hospital Discharge Registry) via National Registration Identification Numbers. Therefore, in this study, the patients treated with GLP-1 receptor agonists and other anti-diabetics will be identified in the prescription databases. The relevant data will be retrieved and linked with other databases and registries. All the relevant data from these three countries will be analyzed together in the final analysis.

Exposure measurement:	The exposure duration of GLP-1 receptor agonists will begin accumulating on the first day of GLP-1 receptor agonist prescription and continue with the subsequent continuous use of GLP-1 receptor agonists until: 1) the end of the GLP-1 receptor agonist treatment (in addition to a grace period of up to 30 days, to account for non-adherence), 2) the occurrence of the outcome, or 3) the end of study period, whichever comes first. The same will be applied to other anti-diabetics for the measurement of exposure duration. More details on exposure measurement will be defined based on the further discussion with external experts.
Outcomes of interest:	Acute pancreatitis cases will be identified from the hospital discharge registers. Cases of thyroid cancer and pancreatic cancer will be identified from the national cancer registers. However, data on the cancer cases for a given year are typically considered incomplete until approximately one year after the year ends. Therefore, if the analysis of pancreatic and thyroid cancer is planned to be performed in early 2014, the complete data for incident cancer cases occurred by the end of 2012 can be obtained from the national cancer registers in these four countries.
Covariates:	Potential confounders for acute pancreatitis will include age, gender, duration of T2DM, gallstones, prior use of anti-diabetics, alcohol intake, obstruction of the pancreatic duct, and post-endoscopic retrograde cholangiopancreatography (ERCP) status at the baseline. Potential confounders for thyroid cancer will include age, gender, duration of T2DM, prior use of anti-diabetics, radiation treatment to the head and neck, iodine intake, hormonal and reproductive treatment, history of goiter or benign thyroid nodules, and family history of thyroid cancer or multiple endocrine neoplasia at the baseline. Potential confounders for pancreatic cancer will include age, gender, race, duration of T2DM, prior use of anti-diabetics, alcohol intake, smoking, chronic pancreatitis, cholecystectomy, family history of pancreatic cancer, obesity, cirrhosis of the liver, and H. pylori infection at the baseline. In addition, as much data on confounders that can be identified will be abstracted and used in the final analysis.

Sample size and study power	A preliminary estimation in UK-The Health Improvement Network (THIN) database (up to the end of 2010) revealed that about 2% of T2DM patients were treated by GLP-1 receptor agonists (i.e., exenatide or liraglutide). It is likely that the proportion of T2DM patients treated by either exenatide or liraglutide in Nordic countries is similar to that observed in the THIN database. If assuming 2% of the T2DM patients will be treated with GLP-1 receptor agonists in Sweden, Denmark and Norway, approximately 15,000 GLP-1 receptor agonists treated patients will be eligible for this study by the end of 2012. Conservatively, assuming an average follow up of one year for these patients, 15,000 person-years (p-y) of total follow-up time will be eligible for this study by the end of 2012.
Sample size and study power	Assuming an incidence rate of 4.2 per 1,000 p-y for acute pancreatitis (1), a study with 15,000 p-y of follow-up time will provide a precision of ± 1.0/1,000 (3.2 - 5.2 per 1,000 p-y). Assuming an incidence rate of 1.1 per 10,000 p-y for thyroid cancer (http://seer.cancer.gov/), a study with 15,000 p-y of follow-up time will provide a precision of ± 2/10,000 (0.0 – 3.0 per 10,000 p-y). Assuming an incidence rate of 1.2 per 10,000 p-y for pancreatic cancer (http://seer.cancer.gov/), a study with 15,000 p-y of follow-up time will provide a precision of ± 2/10,000 (0.0 – 3.0 per 10,000 p-y). The estimation of sample size and study power for the secondary objective will be further defined after consultation with external experts and provided in the study protocol.

Statistical analyses:	1, Incidence rates and 95% confidence intervals (CI) of acute pancreatitis, pancreatic cancer and thyroid cancer among the patients treated with GLP-1 receptor agonists as well as those patients treated with other anti-diabetics will be derived. 2, Hazard ratios (95% CIs) of acute pancreatitis, pancreatic cancer and thyroid cancer associated with the treatment of GLP-1 receptor agonists versus other anti-diabetics will be estimated using time-dependent Cox proportional hazards survival analysis. The potential confounding factors listed above will be adjusted in the analyses (to be further discussed and refined by external experts). Two types of analyses are planned for this study, including an intent- to-treat like analysis and an analysis by censoring the follow up time at the end of treatment of either GLP-1 receptor agonists or other anti-diabetics. The database will be established in such a manner that it can be updated on a continual (annual) basis to provide increasingly precise estimates of the incidence rates and hazard ratios described above.
Timelines:	The analysis for acute pancreatitis will be performed after the launch of lixisenatide. In order to obtain the complete data for the cancer cases reported into the national cancer registries in 2012 (for the reason described in above Section "Outcomes of Interest"), the analysis for pancreatic and thyroid cancer, in particular MTC, will be performed in 2014. The detailed timelines will be defined in the study protocol.

References:

1. Noel RA, Braun DK, Patterson RE, Bloomgren GL. Increased risk of acute pancreatitis and biliary disease observed in patients with type 2 diabetes: a retrospective cohort study. Diabetes Care 2009;32:834-8

IPRI International Prevention Research Institute

Appendix II

Curriculum Vitae of Principal Investigators

Peter Boyle, Maria Bota, Mathieu Boniol, Philippe Autier, Chris Robertson

International Prevention Research Institute

CV Peter Boyle

IPRI International Prevention Research Institute

CURRICULUM VITAE

Peter Boyle

BSc PhD DSc (Med) DSc (*hc*)
FRSE FFPH FRCPS (Glas) FRCP (Edin) FMedSci

Knight's Cross of Order of Merit of Republic of Poland

Fellow, National Academy of Scotland
Fellow, Academy of Medical Science (United Kingdom)
Honorary Member, Hungarian Academy of Science

January, 2013

CURRICULUM VITAE

Name: Peter Boyle
Place of Birth: Glasgow
Nationality: British
Civil Status: Married with three grown-up children.
Languages English (native)
French (read, write and speak well)
Italian (read well, speak well and write minimally)

Education and Qualifications:

1974	B.Sc. Statistics, University of Glasgow
1985	Ph.D. Faculty of Medicine, University of Glasgow
2000	FRSE Fellow of Royal Society of Edinburgh
2003	FFPH Fellow, Faculty of Public Health Medicine (United Kingdom)
2003	FRCPS(Glas) Fellow, Royal College of Physicians and Surgeons of Glasgow
2006	FMedSci Fellow, Academy Medical Sciences
2006	DSc (Med) Faculty of Medicine, University of Glasgow
2006	DSc (*honoris causi*) Faculty of Science, University of Aberdeen.
2007	FRCP (Edin) Fellow, Royal College of Physicians of Edinburgh
2012	LlD (*honoris causi*), University of Dundee.

Academic Appointments:

1974-77	*Statistician*, University Department of Medicine, Glasgow. , UK
1977-80	*Statistician*, West of Scotland Cancer Surveillance Unit, Glasgow, UK
1980-84	*Senior Statistician*, West of Scotland Cancer Surveillance Unit, Glasgow, UK.
1984-1987	*Instructor and Assistant Professor*, Departments of Biostatistics and Epidemiology, Harvard School of Public Health, Boston, USA
1984-87	*Instructor and Assistant Professor*, Division of Biostatistics and Epidemiology, Dana-Farber Cancer Institute, Boston, USA
1986-89	*Senior Scientist*, SEARCH Programme, Unit of Analytical Epidemiology, International Agency for Research on Cancer, Lyon, France
1990-91	*Head*, SEARCH Programme, Unit of Analytical Epidemiology, International Agency for Research on Cancer, Lyon, France
1991-	Chairman, Department of Epidemiology and Biostatistics, and Director, Division of Cancer Control, European Institute of Oncology, Milan, Italy.
2004-2008	Director, International Agency for Research on Cancer, Lyon, France.
2009-	President, International Prevention Research Institute (Lyon, France)
1996 - 2005	*Professor of Cancer Epidemiology*, The University of Birmingham, UK

1998 -	Visiting Professor, University of Glasgow, United Kingdom
1996-2004	*Professor*, Postgraduate School of Pathology, University of Milan, Italy
2003-	Professor of Cancer Prevention and Control, University of Oxford, UK.
1996-2003	*Director*, World Health Organisation Collaborative Centre for Statistical Modelling in Epidemiology of Chronic Diseases.
2009-	Honorary Professor, University of Dundee, United Kingdom
2009-	Professor Adjunct, Yale University, New Haven, USA

Employment History

1974-1977. I was appointed Research Assistant (Statistician) in the Department of Medicine in the University of Glasgow in 1974. My work involved interaction with clinicians and other researchers on statistical aspects of their research work.

1977-1980. In 1977, I was appointed Statistician at the West of Scotland Cancer Surveillance Unit located at Ruchill Hospital in Glasgow. The work involved providing statistical support to the West of Scotland Cancer Registry, to the newly formed West of Scotland Oncological Association and to clinicians and other scientists engaged in cancer research and clinical trials.

1980-1984. I was promoted to Senior Statistician in the West of Scotland Cancer Surveillance Unit. The areas of responsibility remained the same but there was an additional level of responsibility. I supervised the work of the registry clerical and administrative staff (6 wte positions) and one junior statistician. During this period of employment, I had a sabbatical when I was awarded an IARC Research Training Fellowship to spend one year at the International Agency for Research on Cancer (Lyon, France) and four months at Harvard School of Public Health (Boston, Massachusetts).

1984-1987. I was appointed initially as Instructor and then as Assistant Professor in the Departments of Epidemiology and Biostatistics at Harvard School of Public Health (Boston, Massachusetts). I had a simultaneously appointment as Instructor and then Assistant Professor in the Department of Biostatistics and Epidemiology at the Dana-Farber Cancer Institute (Boston, Massachusetts). I provided epidemiological support at the Dana-Farber and was involved in research and teaching activities at the School of Public of Health. I supervised my first two doctoral students. I was given a initial leave of absence to take up a position at the International Agency for Research on Cancer (Lyon, France). I left to take up a higher position and to work in an international environment.

1986-1990. I was appointed as Senior Scientist to lead the SEARCH (Surveillance of Environmental Aspects Related to Cancer in Humans) programme of the International Agency for Research on Cancer (IARC). This is part of the World Health Organisation and based in Lyon, France. I had a staff of 6 scientists and an in-house

research budget of 350,000 dollars per annum. The programme attracted research funding for participating research teams in the participating countries.

1990-1991. I was promoted Head, SEARCH Programme at the IARC. The duties remained the same but the programme had expanded and there were more studies to supervise and coordinate. I left to take up a challenging job as the first employee of the newly created European Institute of Oncology.

1991-2003. I was appointed as the Director of the Division of Epidemiology and Biostatistics at the European Institute of Oncology. This was a newly created Institute which opened its hospital operation in 1994 (with 260 beds). I headed a Research Group which initially comprised three Senior Scientists, six technical assistants and two secretaries. The initial core funding for the research programme was approximately 1 million Euros. This built up to an international programme with five Senior Scientists, ten PhD/MSc assistants, five post-docs, 3-5 PhD students, an administrative assistant and two personal assistants. The final core budget was approximately 2 million Euros and we had over 2 million Euros in Research Grants when I left. I left on being elected Director of the IARC by the Member States.

2004-2008. I was elected Director of the International Agency for Research on Cancer (World Health Organisation) at the meeting of the Governing Council in May 2003 and took up post on 1st January 2004. This one of eight elected positions within the World Health Organisation and I was the first United Kingdom citizen to hold such a position within WHO. I was responsible for 350 personnel and the biennial budget was grown from 35.8 million dollars (for 2002-2003) to 44.7 million dollars (for 2008-2009). External research funding grew from an average of 10 million US dollars per annum before my arrival to an average of 23 million dollars per annum in the first four years (such funding was 34 million dollars in 2007). Five new participating States were introduced, enlarging the Agency from 16 to 21 members.

2009 to present. After completion of my mandate at IARC, I created the International Prevention Research Institute which is initially based in Lyon. This is a new concept in biomedical research combining a thorough, high-level, academic approach coupled with a practical focus on providing clear information about evidence-based clinical, epidemiological and prevention strategies. iPRI serves as an independent authoritative source of advice on critical risk issues and as a high-level training centre in all aspects of Prevention research. An academic partnership has been created with the University of Dundee and IPRI-Dundee has been formally established. IPRI comprises 8 partners initially and has a budget estimated to be 6-8 million Euros in 2010. With an outstanding faculty and international expertise, our mission is to bring the available excellence in scientific method to clarify critical issues in disease determination and prevention in order to contribute to the improvement in health of populations worldwide.

Major Research Contributions

I have had a productive research career in Epidemiology and I am a recognised leader in the global cancer control movement. In the latter role I have proved to be an efficient catalyst for important international collaborations particularly in low- and medium-income countries and, in particularly, providing a forum for collaboration among National Cancer Institutes. In my personal research, I have been active in several areas and we will highlight three below where hmy work has made a difference to disease prevention and clinical management.

In the area of **Tobacco Control,** I was a Member of the European Cancer Advisory Board. In this role I was able to develop the proposal for a European Union Tobacco Directive with its scientific justification. I worked closely as scientific advisor to the Commissioner, Mr David Byrne, and to the European Commission on the *European Tobacco Contents Directive* which was voted into law by the European Parliament in 2002. This European-wide law restricted the tar, nicotine and CO2 contents of cigarettes which could be sold in Europe, which banned the use of descriptors such a *Light* and *Low* and legislated for stronger health warnings and graphic pictures on packets of cigarettes sold throughout Europe. This was the first European law on Tobacco and paved the way for subsequent anti-tobacco legislation in the European Union and its Member States. Notably, I worked closely with several National Governments on the introduction of bans on smoking in bars, restaurants and public places.

I was the driving force behind the development of the four versions of the ***European Code Against Cancer***, in 1988, 1993, 2003 and 2009. This process involved a Europe wide consultation from experts from a wide variety of fields and developed a series of recommendations to the general public to reduce the incidence and mortality of cancer. The *European Code Against Cancer* (the first and second version) was the basis of the *Europe Against Cancer Programme* target to reduce the number of cancer deaths in the European Union between 1985 and 2000. Although mortality rates were rising when the plan was launched in 1985, a 9.5% reduction in the number of cancer deaths expected in 2000 was achieved, preventing 98,000 cancer deaths each year.

In my work in **Urological Disease,** I have applied an evidence-based approach to modifying the impact on treatment choices and outcome. My meta-analysis of the Phase III clinical trials of *finasteride* demonstrated that this drug was effective only in men with enlarged prostates. I was also able to demonstrate that finasteride reduced the risk of Acute Urinary Retention. I performed subsequent meta-analysis which demonstrated the effectiveness of *terasozin* and *permixon*, and the efficacy of Trans Urethral Needle Ablation (TUNA) in Benign Prostatic Hyperplasia. These findings have influenced clinical practice in benign prostatic hyperplasia in helping clarify what is the right treatment for a particular patient and this is reflected currently in international treatment guidelines. In addition, my work in Urology also included a pooled analysis of the world's three leading Dialysis Registries, involving over 900,000 patients, dialysed but not transplanted, followed up for cancer; the demonstration that testicular cancer mortality rates were reduced following the

implementation of effective therapy which, unfortunately, was not the case in countries of Central and Eastern Europe.

My research work has greatly influenced treatment outcomes and, together with my work in cancer control, has undoubtedly led to the prevention of many deaths.

External Appointments

1987-1996- Visiting Lecturer, Harvard School of Public Health, Boston.
1994- Honorary Lecturer, University Department of Surgery and Department of Epidemiology and Community Medicine, University College Dublin, Ireland.
1994- Honorary Senior Lecturer, Eastman Institute of Dental Health Science, London.
1996-2002 Adjunct Professor, Department of Epidemiology and Family Medicine, University of Pittsburgh, Pittsburgh, United States.
1999-2003 Honorary Professor, National School of Public Health Carlos III, Madrid, Spain
1999-2003 Scientific Advisor in Prevention and Control, ICRF, London
1999-2002 Chairman, Prevention and Control, ICRF, London.
1999-2002 Adjunct Member, Memorial Sloan Kettering Cancer Institute, New York.
2003- Director Emeritus, European Institute of Oncology (Milan, Italy)
2007 - Advisor, National Cancer Center of Korea
2009- Affiliate, R. Samuel McLaughlin Centre for Population Health Risk Assessment, University of Ottawa, Canada.
2009- External Member, University of Otaga, Dunedin, New Zealand.

Professional Qualifications

1974 *Fellow*, Royal Statistical Society
1979 *Fellow*, Institute of Statisticians
1993 *Chartered Statistician*, Royal Statistical Society

Honours, and Awards Won in Competition:

1981 *Travel Fellowship,* British Association for Research on Cancer
1981 *International Cancer Research Technology Transfer (ICRETT) Fellowship* (UICC)
1981 *Cancer Research Training Fellowship* , International Agency for Research on Cancer
1981 *Training Award* Greater Glasgow Health Board
1981 *Travel Fellowship,* Churchill Scholarship Trust for Scotland

1982 *Research Training Fellowship* International Agency for Research on Cancer (declined)
1994 *Premio La Madonnina* - City of Milan, Italy
1995 *Addlemen Visiting Professor*, University of Toronto, Canada.
1997 *Visiting Professor*, Institute of Urology, Moscow State University, Moscow, Russia
1998- Visiting Professor, Department of Urology, University of Innsbruck, Innsbruck, Austria.
1996 Honorary Member, Argentine Medical Association.
2000 *Knight's Cross of Order of Merit* of Republic of Poland
2000 *Fellow of Royal Society of Edinburgh*.
2002 Award from President of Israel for Lifetime Contribution to Cancer Research, on Occasion of 50th Anniversary of Israel Cancer Association, Jerusalem, 2002.
2003 Honorary Member, Hungarian Cancer Society.
2003 Honorary Member, European Society for Therapeutic Radiology and Oncology (ESTRO)
2006 Award of Honorary Doctor of Science by University of Aberdeen.
2006 Elected Fellow of Academy of Medical Science.
2006 Elected Fellow of Royal College of Physicians of Edinburgh.
2006 Elected Full member of ESMO (first non-Medical Oncologist elected to Full Membership).
2008 Gold Award of the Health Promotion Foundation of Poland.
2010 Elected Honorary Member of Hungarian Academy of Science.
2012 Award of Honorary Doctor of Laws by University of Dundee.

Invited Eponymous Lectures

Royal College of Physicians of Canada Lecturer, Canadian Urological Association, Canada (1998)
Europa Donna Lecture, Second European Breast Cancer Conference, Barcelona, Spain (2001)
Adelman Lecture, Princess Margaret Hospital, Toronto, Canada (2000)
Aneurin Bevin NHS Lecture, British Association of Cancer Research, Leeds (2002)
Kodak Lecture, British Association for Mammographic Screening, Edinburgh (2002)
Giullian Lecture, Italian Sociaty of Urology, Venice (2002)
Millins Symposium Lecture, Royal College of Surgeons of Ireland, Dublin, Ireland (2002)
BJU Int lecture, British Association of Urological Surgeons, Harrogate, UK (2003)
Davidson Lecture, Royal College of Physicians of Edinburgh (Aberdeen, 2008)
Annual Acta Oncologica Lecture 2008, Danish Oncological Society (Vejle, 2008)

Plenary Lectures at international meetings including the *American Society for Clinical Oncology*; the *American Association for Cancer Research*; the *European Association of Urology*, the *European Respiratory Society*, the *European Breast Cancer Meeting*, the *European Association for Cancer Research*, the *European Society for Mastology*,

the *European Cardiology Association*, the *European Society for Medical Oncology*, the *European Cancer and Clinical Oncology* meeting, the *European Society for Radiology and Therapeutics in Oncology*, *Canadian Urological Association*, *Asian Urological Association*, *Princess Takamatsu Symposium*, *Singapore Medical Association*, *Malayasian Urological Association*, *Australasian Urological Association*, *Yugoslavian Urological Association*, *Greek Urological Association*, *Danish Oncological Society*, *Polish Urological Society*, *Israel Cancer Society*, *Luxembourg Cancer Society, Hong Kong Medical Society*, *Chinese Association of Urology*, *Cancer Prevention Association of Thailand*, *Hungarian Oncological Society*, *Portugese Urological Association*, *Italian Association for Clinical Oncology*, *German Association for Medical Documentation*, *International Union Against Cancer*, *Finnish Cancer Society*, *Luxembourg Medical Society*, *South African Urological Association*, *Portuguese Oncological Society*, *British Association for Cancer Research*, *Hungarian Urological Association* and *Czechoslovakian Urological Association*.

Invited lectures at Scientific Meetings organised in Portugal, Spain, Italy, France, Germany, Austria, Belgium, Netherlands, United Kingdom, Ireland, Greece, Finland, Norway, Sweden, Denmark, Luxembourg, Slovenia, Slovakia, Czech Republic, Switzerland, Yugoslavia, Hungary, Poland, Lithuania, Russian Federation, United States, Cuba, Canada, Brazil, Argentine, Singapore, Malaya, Korea, China, Hong Kong, Japan, India, Sri Lanka, Thailand, Israel, Abu Dhabi, Australia, Jordan and New Zealand.

Major Committee Assignments

1986-92 Secretary, Epidemiology and Prevention Branch, EORTC, Brussels
1988-92 Scientific Advisory Committee (Breur Committee), EORTC, Brussels
1989-97 Chairman, Epidemiology and Prevention Branch, European Society of Mastology
1989-03 International Prostate Health Council
1990-91 Professorial Appointments Committee, Faculty of Medicine, University of Lausanne
1991-97 Treasurer and Member of Executive Board, European Society of Mastology
1992-97 Chairman, Epidemiology and Prevention Branch, EORTC.
1992-96 Secretary, Scientific Advisory Committee (Breur Committee), EORTC.
1992-99 Scientific Advisory Board, European School of Oncology, Milan
1993 Scientific Committee, ECCO8 Meeting (1996)
1994-95 Chairman, Committee to revise *European Code Against Cancer*.
1995-96 Chairman, Committee to prepare *EuropeanTobacco Control* recommendations.
1996- Member, Cancer Advisory Board of European Commission.
1997- Chairman, Scientific Committee, European Commisssion Tobacco Fund.
1998 Scientific Committee, Institut Gustav-Roussy (Villejuif, France)

1998-4	Chairman, European Commission Expert Committee Cancer Plan, 2000-
1998-2002	Scientific Advisory Committee, ICRF, London
1999-2002	Chairman, Scientific Evaluation Committee, European Tobacco Fund, EC.
2000-2003	Scientific Committee, Center for Cancer Detection and Prevention, St Gallen.
2001-2003	Italian Representative, European Commission Advisory Committee on Tobacco.
2000-01	Member, Italian National Oncological Commission, Ministry of Health, Italy.
2001-02	Member, Electromagnetic Fields Commission, Ministry of Health, Italy
2002	Chairman, Commission to Investigate Clustering of Leukaemia in Children, around *Radio Vaticana* Transmitter, Ministry of Health, Italy.
2002-	Member, CEO Advisory Committeee, American Cancer Society.
2003	Member, General Motors Prize (Mott) Committee
2003--	Member, International Affairs Committee, AACR
2006--	Member, Multidisciplinary Oncology Committee, ESMO.
2008-2010	Member, International Affairs Committee, ASCO.
2011-	Member, International Advisory Panel, Strathclyde University.
2012 -	Member, Steering Committee *Pink Ribbon Red Ribbon* Initiative
2012	Co-chair. Targets and Metrics Committee, PRRR.

Editorial Boards

Editorships:

Journal of Epidemiology and Biostatistics (with Carlo La Vecchia and Alec Walker)(1995-2003)
European Journal of Cancer (1990-1994).

Associate Editorships,
Oncology and Haematology Literature Service (1993-98),
Annals of Oncology (1999-)
British Journal of Urology International (2002-).
Onkologie (2010 -)

Editorial Board Member,
Cancer Causes and Control (1990-1994), Swiss Journal of Social and Preventive Medicine (1990-), British Journal of Cancer (1990-1997), Prospectives (1990-99), BPH Observer (1990-99), The Breast (1991-97), Oral Oncology (1991-), European R and D Database (1993-98), Lung Cancer (1995-), Journal of Radiation Therapy (1996-), European Cancer News (1996-98), Journal of Gynecologic Oncology (1996-), Annals of Oncology (1996-), URO (Portuguese Journal of Urology) (1996-), Breast Cancer Online (1999-),

Lancet (2003-), Nature Clinical Practice Urology (2004-), Molecular Oncology (2006-), Hematologia (2010-).

Selected Publications of Peter Boyle

1. Cairns, J. and **Boyle, P**. Cancer chemotherapy. Science, 1983, 220, 252-256.

2. Kerr, D.J., Burt, A.D., Brewin, T.B. and **Boyle, P**. Divergence between mortality and incidence rates of thyroid cancer in Scotland.. Lancet, 1985, ii (8447), 149.

3. Macfarlane, G.J., **Boyle, P**. and Scully, C. (letter) Rising mortality from cancer of the tongue in Young Scottish Males. Lancet 1987, ii:912.

4. Scully, C., **Boyle, P**. and Prime, S. Oral Cancer (Editorial). Lancet ii (8658), 1989: 311-312

5. **Boyle, P**., Maisonneuve, P., and Kaye, S.B. Testicular Cancer in Central Europe. Lancet 1990, 335:1033.

6. Lowenfels AB, Cavallini G, Ammann RW, Lankisch PG, Andersen JR, Dimagno EP, Andren-Sandberg A, Domellof L, Maisonneuve P, Di Francesco V, Lohr-Happe A, Krag E, Melton LJ, Pitchumoni CS, Wynn PS and **Boyle, P**. Pancreatitis and the risk of Pancreatic Cancer. New Eng.J.Med. 1993, 328 20:1433-1437

7. **Boyle P**. The Hazards of Passive and Active Smoking. New Engl.J.Med. 1993, 328:1708-1709

8. **Boyle P**, La Vecchia C, Negri E, Lucchini F and Levi F. Trends in diet-related cancers in Japan: a conundrum? (Letter). Lancet 1993, 342:752

9. **Boyle, P**, Macfarlane GJ and Scully C . Oral Cancer: necessity for Prevention Strategies (Editorial). Lancet 1993, 342:1129

10. **Boyle P**. The Hazards of Active and Passive Smoking. Letter to the Editor. N.Engl.J.Med. 1993, 329 (21): 1581

11. Zakelj M. and **Boyle P**. Breast Cancer Detection and Oral Contraceptive use in Slovenia (letter). Lancet, 1994, 343: 1166-1167

12. Neglia J, FitzSimmons S, Maisonneuve P, Schoni M, Schoni-Affolter F, Corey M, Lowenfels A, **Boyle P**, Dozor A, Durie P. The Risk of Cancer Among Patients with Cystic Fibrosis. N Engl J Med 1995, 332:494-499

13. Plesko I, Ondrus D, **Boyle P**. Testicular cancer incidence and mortality in Slovakia, 1968-1990. Lancet 1996, 347, 900-901

14. Buccianti G, Ravasi B, Cresseri D, Maisonneuve P, **Boyle P**, Locatelli F. Cancer in patients on renal replacement therapy in Lombardy, Italy. (Letter). Lancet, 1996; 347 (8993): 59-60.

15. *Collaborative Group on Hormonal Factors in Breast Cancer* (includes **P Boyle**). Breast cancer and hormonal contraceptives: collaborative reanalysis of individual data on 53.297 women with breast cancer and 100.239 women without breast cancer from 54 epidemiological studies. Lancet, 1996, 347: 1713-1727.

16. **Boyle P.** Global burden of cancer. Lancet (suppl), 1997, 349: 23-26.

17. Osborne M., **Boyle P**., Lipkin M. Cancer Prevention. Lancet, 1997, 349 (suppl): 27-30.

18. Becker N., **Boyle P**. Decline in mortality from testicular Cancer in West Germany after re-unification. Letter) Lancet, 350: 744.

19. Gray N., **Boyle P**. Attacks on tobacco Industry (Letter). Lancet, 350: 890, 1997.

20. *Collaborative Group on Hormonal Factors in Breast Cancer* (includes **P Boyle**), Breast Cancer and Hormone Replacement Therapy. Lancet, 1997, 350: 1047-1059.

21. Franklyn J.A., Maisonneuve P., Sheppard M.C., Betteridge J., **Boyle P**. Mortality after the Treatment of Hyperthyroidism with Radioactive Iodine. New Engl J Med, 338: 712-8, 1998.

22. **Boyle P**., Horton R., Radda G., Sharp D., Veronesi U., Walker A.M. Open debate on HRT. Lancet, 352: 836, 1998

23. Veronesi U., Maisonneuve P., Costa A., Sacchini V., Maltoni C., Robertson C., Rotmensz N., **Boyle P**. on behalf of the Italian Tamoxifen Study Group. Prevention of Breast cancer with Tamoxifen. The Italian Randomised Trial among Hysterectomised women. The Lancet, 352: 93-97, 1998.

24. Gray N., **Boyle P**., Zatonski W. Tar concentrations in cigarettes and carcinogen content. Lancet, 352:787-788, 1998.

25. Autier P., **Boyle P**., J.F.Dore'. Letter: Sorting the hype from the facts in melanoma. Lancet, 352: 738-739, 1998.

26. **Boyle P**. Expanding on epidemiology's first principles. Book review: Modern Epidemiology by K. Rothman et al. Lancet, 352:1635-1636, 1998

27. Veronesi U., Maisonneuve P., Costa A., Rotmensz N., **Boyle P**. Drop-outs in Tamoxifen Prevention Trials. Lancet, 353:244,1999

28. Franklyn J.A., Maisonneuve P., Sheppard M., Betteridge J., **Boyle P**. Cancer Incidence and mortality after radioiodine treatment for hyperthyroidism: a population-based cohort study. The Lancet, 353: 2111-2115, 1999

29. Maisonneuve P., Agodoa L., Gellert R., Stewart J.H., Buccianti G., Lowenfels A.B., Wolfe R.A., Jones E., Disney A., Briggs D., McCredie M., **Boyle P**. Cancer in end stage renal disease patients undergoing dialysis: results from an international collaborative study. Lancet, 1999; 354: 93-96.

30. Clinical Synthesis Panel on HRT. Clinical Synthesis Conference on Hormonal Replacement Therapy. Lancet 1999; 354: 152-156.

31. Gray N., Zatonski W., **Boyle P**. Regulation of carcinogens in cigarettes. The Lancet, 18 (354): 1036, 1999

32. **Boyle P**, Horton R, Walker AM, Sharp D and Delmas P. Clinical Synthesis Meeting on Osteoporosis. Lancet 1999; Nov 13;354(9191):1664.

33. Levi F, La Vecchia C, **Boyle P,** Lucchini F, Negri E. Western and eastern European trends in testicular cancer mortality. Lancet 2001 Jun 9;3 57 (9271):1853-4.

34. Parle JV, Maisonneuve P, Sheppard MC, **Boyle P**, Franklyn JA. Prediction of all-cause and cardiovascular mortality in elderly people from one low serum thyrotropin result: a 10-year cohort study. Lancet 2001 Sep 15;358(9285):861-5

35. *Collaborative Group on Hormonal Factors in Breast Cancer* (includes **P Boyle**). Familial breast cancer: collaborative reanalysis of individual data from 52 epidemiological studies including 58,209 women with breast cancer and 101,986 women without the disease. Lancet 2001 Oct 27;358(9291):1389-99

36. Veronesi U, Maisonneuve P., Sacchini V., Rotmensz N., **Boyle P** Tamoxifen for breast cancer among hysterectomised women. Lancet 2002; 359: 1122-4.

37. *Collaborative Group on Hormonal Factors in Breast Cancer* (includes **P Boyle**). Breast cancer and breast feeding: collaborative reanalysis of individual data from 47 epidemiological studies in 30 countries, including 50302 women with breast cancer and 96973 women without the disease. Lancet. 2002 Jul 20;360(9328):187-95.

38. Veronesi U, Maisonneuve P, Rotmensz N and **Boyle P**. Tamoxifen for breast cancer in hysterectomised women (Letter). Lancet 2002; 360 (9347): 1784-1785.

39. Cuzick J, Powles T, Veronesi U, Forbes J, Edwards R, Ashley S and **Boyle P**. Overview of main Outcomes in Breast Cancer Prevention Trials. Lancet 2003; 361: 296-300.

40. Pastorino U, Bellomi M, Landoni C, DE Fiori E, Arnaldi P, Picchio M, Pelosi G, **Boyle P** and Fazio F. Early lung-cancer detection with spiral CT and positron emission tomography: two years results. Lancet 2003; 362: 593-597.
41. Gray N and **Boyle P**. The Future of the Nicotine Addiction Market. (Commentary) Lancet 2003 Sep 13;362(9387):845-6.

42. Collaborative Group on Hormonal Factors in Breast Cancer (includes **P Boyle**). Breast cancer and abortion: collaborative reanalysis of data from 53 epidemiological studies, including 83 000 women with breast cancer from 16 countries. Lancet 2004; 363: 1007-16

43. Veronesi U, **Boyle P**, Goldhirsch A, Orrechia R and Viale G. Seminar on Breast Cancer. Lancet. 2005 May 365 (9472):1727-41.
44. **Boyle P**, Ariyaratne M, Bartelink H, Baselga J, Berns A, Brawley OW, Burns H, Davidov M, Dinshaw K, Dresler C, Eggermont AM, Gajurel D, Gordina G, Gray N, Kakizoe T, Karki BS, Kásler M, Kerr DJ, Khayat D, Kiselev A, Khuhaprema T, Klocker H, Levshin V, Martin-Moreno JM, McVie JG, Mendelsohn J, Napalkov NP, Ngoma TA, Park JG, Philip T, Pötschke-Langer M, Poudal HN, Rajan B, Ringborg U, Rodger A, Seffrin JR, Shanta V, Shrestha MM, Thomas R, Tursz T, de Valeriola D, Veronesi U, Wiestler OD, Zaridze D, Zatonski W and Zeng YX. Curbing tobacco's toll starts with the professionals: World No Tobacco Day. The Lancet (11th June) 2005; 365: 1990-1992

45. **Boyle P**, Ariyaratne MA, Barrington R, Bartelink H, Bartsch G, Berns A, de Valeriola D, Dinshaw KA, Eggermont AM, Gray N, Kakizoe T, Karki BS, Kaslar M, Kerr DJ, Khayat D, Khuhaprema T, Kim IH, Martin-Moreno J, McVie G, Park JG, Philip T, Ringborg U, Rodger A, Seffrin JR, Semiglazov V, Soo KC, Sun YT, Thomas R, Tursz T, Veronesi U, Wiestler O, Yoo KY, Zatonski W and Zhao P. Tobacco: deadly in any form or disguise. Lancet. 2006 May 27;367(9524):1710-2.

46. **Boyle P**. The Globalisation of Cancer. Lancet 2006; 368: 629-630

47. **Boyle P**. Book Review: Conspiracy theories of cancer, Lancet 2007; 370: 1751

48. Hainaut P and **Boyle P**. Curbing the Liver Cancer Epidemic in Africa. Lancet 2008; 371(9610): 367-368.

PUBLICATIONS 1 Books

Kemp, I.W., **Boyle, P.**, Smans, M. and Muir, C.S. "Cancer Incidence in Scotland: Atlas and Epidemiological Perspective". IARC Scientific Publication No. 72, IARC, Lyon (1985).

Boyle, P., Muir, C.S., Grundmann, E. (Eds.). "Cancer Mapping". Recent Results in Cancer Research, Vol. 114, Springer-Verlag, Heidelberg, 1989

Zatonski, W., **Boyle P**. and Tcyznski, J. (eds). "Cancer Epidemiology: Vital Statistics through Prevention". Interpresse, Warsaw, 1990.

Katsouyanni, K., Kogevinas, M., Dontas, N., Maisonneuve, P., **Boyle, P**. and Trichopoulos, D. Cancer Mortality in Greece, 1960-1985. Hellenic Cancer Society, Athens, Greece, 1990.

Veronesi, U., **Boyle, P.**, Ciatto, J., Goldhirsch, A., van der Schueren, E., Pastorino, U. Textbooks for General Practitioners, II. Breast Cancer. Springer-Verlag, Heidelberg, 1990.

Levi, F., La Vecchia, C., Negri, E., Randriamiharisoa, A. and **Boyle, P**. Le cancer en l'an 2000: Les modèles statistiques âge/période/cohorte pour la projection de la mortalité cancéreuse en Suisse. Ligue Suisse Contre le Cancer, Berne, 1991

Macfarlane GJ, Maisonneuve P and **Boyle P.** SEARCH: A computer Package to assist the statistical analysis of Case-Control Studies. IARC Technical Report, IARC, Lyon, 1991

Smans, M., **Boyle, P**. and Muir, C.S. (eds) "Cancer Mortality Atlas of EEC'. IARC Scientific Publication No 107, IARC, Lyon, 1993.

Black RJ, Macfarlane GJ, Maisonneuve P, and **Boyle P**. Cancer Incidence and Mortality in Scotland 1960-89. Information and Statistics Division National Health Service in Scotland / Cancer Research Campaign / The Government Statistical Service / European Institute of Oncology , 1995.

Zatonski W, Smans M, Tyczynski J, **Boyle P**. "Cancer Mortality Atlas in Central Europe". IARC Scientific Publications No. 134. IARC, Lyon , 1996.

Alexander, F.E. and **Boyle, P**. (Eds) "Statistical Methods in Cancer Research: IV Analysis of disease clustering". IARC, Lyon 1996.

Griffiths K, Aldercreutz H, **Boyle P**, Denis L, Morton M. "Nutrition and Cancer", ISIS Medical Communications. Oxford, 1996.

Kirby R, Roehrborn C, McConnell J, Fitzpatrick J and **Boyle P** (Eds)."Textbook of Benign Prostatic Hyperplasia", ISIS Medical Communications, Oxford, 1996.

Aapro M., Audisio R., **Boyle P.**, McCaffrey-Boyle D., Corner J., Monfardini S., Redmond K. (eds.) Cancer in the Elderly, a nursing and medical perspective. ESO Scientific Updates 2, Amsterdam: Elsevier, 1997.

Kirby R., McConnell J.D., Fitzpatrick J.M., Roehrborn C.G., **Boyle P**. Ipertrofia Prostatica Benigna Vol. I- II, Milano: UTET Periodici, 1997.

Boyle P., La Vecchia C., Walker AM. (eds). FIGO Annual Report on the Results of Treatment in Gynaecological Cancer, 24th Volume Statements of results obtained in patients treated in 1993-1995, Journal of Epidemiology and Biostatistics, Vol 6. Oxford: Isis Medical Communications, 2001.

McArdle CS, Kerr DJ and **Boyle P** (Eds). Monographs in Oncology. Volume I. Colorectal Cancer, ISIS Medical Publications, Oxford (2000).

Kirby RS, McConnell JD, Fitzpatrick J, Roehrborn CG, Wyllie M and Boyle P (Eds). Therapeutic Treatment for Benign Prostatic Hyperplasia. Informa Healthcare, London (2005)

Boyle P, Gray N, Zatonski W, Henningfield J and Seffrin J. Tobacco: Public Health Disaster of the Twentieth Century. Oxford University Press, Oxford (2004)

Boyle P and Smans M. Cancer Mortality Atlas of European Union, 1993-1997. IARC Press, IARC (Lyon) (2008)

Curado MP, Edwards BK, Shin HR, Storm HH, Heanue M, Ferlay J and **Boyle P**. eds. Cancer incidence in five continents. Vol. IX (9). Lyon, France: IARC Press, 2007. (IARC Scientific publications no. 160.)

Boyle P and Levin B (Eds). World Cancer Report 2008. IARC, Lyon (2008)

Boyle P and Levin (Eds). Dünya Kanser Raporu 2008. IARC, Lyon (2008)

Boyle P, Gray N, Zatonski W, Henningfield J and Seffrin J. Tobacco: Science, Policy and Public Health. 2nd Edition. Oxford University Press, Oxford (2010)

Zheng T, Boffetta P and **Boyle P**. Epidemiology and Biostatistics. iPRI Scientific Publication No 1, iPRI, Lyon, France

Boyle P, Boffetta P, Zatonski W, Rehm J, Burns HJG and Lowenfels A. Alcohol: Science, Policy and Public Health. Oxford University Press, Oxford (in preparation).

Boyle P, Brawley O, Burns HJG, Adebawomo C, Sullivan R and Milburn A. Deprivation: Science, Policy and Public Health. Oxford University Press, Oxford (in preparation).

Publications 2 Scientific Articles *(excluding published abstracts)*

1. Boyle P., Parbrook G.D. The inter-relation of personality and post-operative factors. Brit. J. Anaesth., 49: 259-264, 1977.

2. Ramsay L.E., Boyle P., Ramsay, M.H. Factors influencing serum potassium in treated hypertension. Quarterly J. Med., 46, 401-409,1977.

3. Parbrook E.O., Parbrook G.D. Boyle P. Comparison of synchronised and manual use of audio tape slide programmes. Anaesthesia., 32: 614-619, 1977.

4. Nichols G., Ramsay L.E., Boyle P. The Elag-Koln automatic blood pressure recorder - a clinical appraisal. Brit. Heart J., 29: 795-801, 1977.

5. Winchester J.F., Kellett R.J., Boddy P., Boyle P., Dargie H.J., Mahaffey H.J., Mahaffey K.E., Ward D.M., Kennedy A.C. Metolazone and bendroflumethazide in hypertension: physiologic and metabolic observations. Clin. Pharmacol. Ther., 28: 611-618, 1980.

6. Stephen K.W., Kirkwood M., Boyle P., Young K.C., Gillespie F.C., Campbell D. Fissure sealing with nuva-seal and alpha-seal: two year data. J. Dentistry, 9: 53-57, 1981.

7. Stephen K.W., Boyle I.T., Campbell D., MacNee S., Fyffe J.A., Jenkins A.S., Boyle P. A four-year double-blind fluoridated school milk study in a vitamin-D deficient area. Brit. Dent. J., 151: 287-292, 1981.

8. Scully C., Eckersall P.D., Emond R.T.D., Boyle P., Beeley J. Serum alpha-amylase isozymes in mumps: estimation of salivary and pancreatic isozymes by isoelectric focusing. Clinica. Chimica. Acta., 113: 281-291, 1981.

9. McInnes G.T., Quigley E.M.M., Boyle P. Alcohol withdrawal and blood pressure. Scot. Med. J., 26: 176-177, 1981.

10. Ferguson M.M., Carter J.C., Boyle P., McKay-Hart D., Lindsay R. Oral symptoms related to the female climacteric. J. Roy. Soc. Med., 74: 492-498, 1981.

11. Scully C, Boyle P.Nucleic acid-metabolising enzymes as markers in oral squamous carcinoma. IRCS Med. Sc., 9: 542-543, 1981.

12. Scully C., Spandidos D., Ward-Booth P., Boyle P., MacGregor I. Serum alkaline deoxyribonuclease in oral cancer and premalignant lesions. Biomedicine, 35: 179-180, 1981.

13. Mills P.R., Spooner R.J., Russell R.I., Boyle P., MacSween R.N.M. Serum glutamate dehydrogenase as a marker of hepatocyte necrosis in alcoholic liver disease. Brit. Med. J., 283: 754-755, 1981.

14. Boyle P., Scully C. Changing morbidity and mortality from oral cancer in Scotland. IRCS Med. Sci., 9: 883, 1981.

15. Scully C., Barkus T., Boyle P., MacGregor I., Ward-Booth P. Immune complexes in oral cancer. IRCS Med. Sci., 9: 872, 1981.

16. Robertson A.G., Boyle P., Yosef H.M., Gillis C.R., Flatman G.E. Cancer of the larynx in West of Scotland. A review of the results and a consideration of new therapeutic approaches. Am. J. Clin. Oncol. (CTT), 5: 527-533, 1982.

17. Mills P.R., Boyle P., Quigley E.M.M., MacSween R.N.M., Watkinson G. Primary biliary cirrhosis. An increase in the incidence of associated extrahepatic malignant neoplasm? J. Clin. Path., 35: 541-543, 1982.

18. Boyle P., Robertson A.G., Gillis C.R., Flatman G.E., Scully, C. Epidemiology of laryngeal cancer in Scotland. IRCS Med. Sci., 10: 61-62, 1982.

19. Scully C., Boyle P. Beta-2 micro-globulin in Lichen Planus. J. Dent. Res., 61, 758-760, 1982.

20. Boyle P., Scully C. Epidemiological aspects of oral cancer. Acta Stomatologica Internationalia, 3: 193-200, 1982.

21. Ridley W.J., Jackson P., Stewart J.H., Boyle P. Role of the ante-natal radiography in the management of breech deliveries. Brit. J. Obs. Gynecol., 89: 342-347, 1982.

22. Scully C., Barkus T., Boyle P., McGregor I., Ward-Booth P. Circulating immune complexes detected by binding of radio labelled protein A in patients with oral cancer and oral premalignant lesions. J. Clin. Lab. Immunol., 8, 113-115, 1982.

23. Scully C., Boyle P., Yap P.L. Immunoglobulins G, M, A, D and E in Behcet's syndrome. Clinica Chimica Acta., 120: 237-242, 1982.

24. Scully C., Eglin R.P., Ward-Booth P., McGregor I.A., Boyle P. Human oral squamous cell carcinoma: evidence for RNA complementary to herpes simplex virus DNA. IRCS Med. Sci., 10: 531-532 1982.

25. Mackay A., Boyle P., Brown J.J., Forrest H., Graham A.G., Lever A.F., Robertson J.I.S., Semple P.F. The decision on surgery in renal artery stenosis. Quarterly J. Med., 52: 363-381, 1983.

26. Scully C., Yap P.L., Boyle P. IgD and IgE concentrations in patients with recurrent apthous stomatitis. Arch. Dermatol., 119, 31-34, 1983.

27. Scully C., Boyle P. Oral cancer: new immunological observations. Acta. Stomatologica Internationalia., 4: 17-19, 1983.

28. Scully C., Boyle P. Screening for medical problems in dentistry: 1. Reliability of a self-administered questionnaire. Comm. Dent. Oral Epidemiol., 11:105-108, 1983.

29. Boyle P., Day N.E., Magnus K. Mathematical modelling of malignant melanoma trends in Norway, 1953-1978, Am. J. Epidemiol., 118:887-896, 1983.

30. Boyle P., Scully C., Smans M., Robertson A.G. Lip cancer mortality in Great Britain. IRCS Med. Sci., 11:178-179, 1983.

31. Cairns J., Boyle P. Cancer chemotherapy. Science, 220:252-256, 1983.

32. Boyle P., Soukop M., Scully C., Robertson A.G., Burns H.J.G., Gillis C.R. Improving prognosis of Hodgkin's disease in Scotland. IRCS Med. Sci., 11,:754-755, 1983.

33. Boyle P., Zaridze D.G. Colorectal cancer as a disease of the environment. Ecol. Dis., 2:241-248, 1983.

34. Stephen K.W., Boyle I.T., Campbell D., McNee S., Boyle P. A five-year double-blind fluoridated milk study in Scottish school children. Comm. Dent. Oral Epidemiol., 223-229, 1984.

35. Zaridze D.G., Boyle P., Smans M. International trends in prostatic cancer. Int. J. Cancer, 33:223-230, 1984.

36. Cowans B., Burns H.J.G., Boyle P. Ledingham I.M. The relative prognostic value of lactate and haemodynamic measurements in early shock. Anaesthesia, 39:750-755, 1984.

37. Cunningham D., Soukop M., McArdle C., Carter D.C., Smyth J., Allen S.G., Kaye, S.B., Sangster, G., Calman, K.C., Hutcheon, A. Boyle, P. Advanced gastric cancer: experience in Scotland using 5-fluoruracil, adriamycin and mytomycin-C. Brit. J. Surg., 71:673-676, 1984.

38. Galloway D.J., Boyle P., Davidson P.M., George W.D. Electro-analgesia following abdominal surgery: a clinical assessment. Surgery, Gynaecology and Obstetrics, 159:453-456, 1984.

39. Gillis C.R., Hole D.J., Hawthorne V., Boyle P. The effect of environmental tobacco smoking in two urban communities in western Scotland. Eur. J. Res. Dis. (supp), 65:121-126, 1984.

40. Galloway D.J., Burns H.J.G., Bear H., Boyle P., Jarrett F., George W.D. Colorectal cancer in young adults. Clin. Oncol., 10:205-211, 1984.

41. Ferguson M.M., Carter J., Boyle P. An epidemiological study of factors associated with recurrent aphthae in women. J. Oral Med., 39:212-217, 1984.

42. Robertson A.G., McGregor I.A., Flatman G.E., Soutar D.S., Boyle P. The role of radical surgery and post-operative radiotherapy in the management of intra-oral carcinoma. Brit. J. Plastic Surg., 29:314-320, 1985.

43. Zaridze D.G., Kuvshinov J.P., Matiakin E., Polakov B.I., Boyle P., Blettner M. Chemoprevention of oral and esophageal cancer in Uzbekistan, USSR. NCI Monograph, Fourth Pacific Basin Symposium on Epidemiology, Bethesda, NCI, 259-262, 1985.

44. Boyle P., Zaridze D.G., Smans M. Descriptive epidemiology of colorectal cancer. Int. J. Cancer., 36:9-18, 1985.

45. Burt A.D., Kerr D.J., Brown I.L., Boyle P. Lymphoid and epitelial markers in small cell anaplastic thyroid tumours. J. Clin. Path., 38:893-896, 1985.

46. McCall D.R., Watkins T.R., Stephen K.W., MacFarlane G.J., Boyle P. APF gel application: further intra-oral loss and distribution studies. Brit. Dent. J., 159: 82-84, 1985.

47. Goudie B.M., Burt A.D., Boyle P., MacFarlane G.J., Birnie G.G., Mills P.R., Gillis C.R., Watkinson G., MacSween R.N.M. Breast cancer in women with primary biliary cirrhosis. Brit. Med. J., 291(6509), 1597-1598, 1985.

48. Kerr D.J., Burt A.D., Brewin T.B., Boyle P. Divergence between mortality and incidence rates of thyroid cancer in Scotland. Lancet, ii (8447):149, 1985.

49. Nichols R.J., Galloway D.J., Mason A.Y., Boyle P. Clinical local staging of rectal cancer. Brit. J. Surg., 72:51-52, 1985.

50. Yeung Laiwah A.C., MacPhee G.J.A., Boyle P., Moore M., Goldberg A. Autonomic neuropathy in acute intermittent porphyria. Neurosurg. Psychiatry, 48 (10):1025-1030, 1985.

51. Goudie B.M., Burt A.D., Boyle P., MacFarlane G.J., Birnie G.G., Gillis C.R., MacSween R.N.M., Watkinson G. Breast cancer in women with primary biliary cirrhosis. Br. Med. J., 292(6516): 340-341 1986.

52. Robertson A.G., MacGregor I.A., Soutar D.S., Ferguson M.M., Flatman G.E., Boyle, P. Post-operative radiotherapy in the management of advanced intra-oral cancers. Clin. Radiol., 37: 173-178 1986.

53. Robertson C., Boyle P. Age, period and cohort models: the use of individual records. Statistics in Medicine, 5: 527-538, 1986.

54. Kerr D.J., Burt A.D., Boyle P., Macfarlane G.J., Storer A.M., Brewin T.B. Prognostic Factors in Thyroid Tumours. Brit. J. Cancer, 54: 475-482, 1986.

55. Galloway D.J., Owen, R.W., Jarrett F., Boyle P., Hill M.J., George, W.D. Experimental colorectal cancer: the relationship of diet and faecal bile acid concentration to tumour induction. Brit. J. Surgery, 73: 233-237, 1986.

56. Katsouyani K., Trichopoulos D., Boyle P., Xirouchaki E., Trichopoulou A., Lisseos B., Vasilaros S. MacMahon B.Diet and Breast Cancer: A case-control study in Greece. Int. J. Cancer 38:815-820, 1986.

57. Boyle P., Kaye S.B., Robertson A.G. Improving prognosis of testicular cancer in Scotland. ICRS Med. Sci., 14: 976-977, 1986.

58. Freer C.B., Boyle P., Ryan M. A study of attendance patterns in general practice over three years. Health Bull., 44: 78-80, 1986.

59. Boyle P., Robertson C. Statistical modelling of lung cancer and laryngeal cancer incidence data in Scotland, 1960-1979. Amer. J. Epidem., 125: 731-744, 1987.

60. Boyle P., Robertson C. Breast Cancer and Colon Cancer Incidence in Females in Scotland, 1960-84. J. Natl. Cancer Inst., 79:1175-1179, 1987.

61. Galloway D.J., Jarrett F., Boyle P., Carr C., Indran M., Owen R.W., George W.D. Morphological and cell kinetic effects of dietary manipulation during colorectal carcinogenesis. GUT, 28: 754-763, 1987.

62. Macfarlane G.J., Boyle P., Scully C. Rising mortality from cancer of the tongue in Young Scottish Males. (letter), Lancet ii: 912, 1987.

63. Robertson A.G., Boyle P., Deuchars F., Robertson C. Carcinoma of the Larynx. J. Surg. Oncol., 35: 217-222, 1987.

64. Zaridze D.G., Boyle P. Cancer of the prostate: epidemiology and aetiology. Brit. J. Urology, 59: 493-503, 1987.

65. Boyle P., Kaye S.B., Robertson A.G. Changes in Testicular Cancer in Scotland. Eur. J. Clin. Oncol., 23(6): 827-830, 1987.

66. Boyle P., Robertson C. Age-period-cohort modelling of malignant melanoma incidence in Scotland, 1960-1984. Amer. J. Epidem. 126: 766, 1987.

67. Goddard M.J., Krewski D., Boyle P. SEARCH - A Programme of IARC. Chronic Disease in Canada 9(2): 31-34, 1987.

68. Katsouyani K., Willett W., Trichopoulos D., Boyle P., Trichopoulou A., Vasilaros S., Papadiamantis J., MacMahon B. Risk of breast cancer among Greek women in relation to nutrient intake. Cancer 61: 181-185, 1988.

69. Robertson J., Boyle P., Imrie C.W. Patients with ampullary carcinoma are prone to other malignant tumours. Brit. J. Cancer 58: 216-28, 1988.

70. Boyle P., Soukop M., Scully C., Robertson A.G., Burns H.J.G, Gillis C.R. Improving prognosis of Hodgkin's Disease in Scotland. Eur. J. Cancer. Clin. Oncol. 24: 229-234, 1988.

71. Gillis C.R., Hole D.J., Boyle P. Cigarette smoking and male lung cancer in an area of very high incidence: report of a case-control study in the West of Scotland. J. Epid. Comm. Health. 42(1): 38-43, 1988.

72. Boyle P., Leake R.E. Progress in Understanding Breast Cancer: Epidemiologic and Biologic Interactions. Breast Cancer Res. Treat. 11: 91-112, 1988.

73. Boyle P., Robertson C. Re: Statistical Modelling of Cancer Data. Am J. Epid. 129: 225-226, 1988.

74. Cuzick J., Boyle, P. Trends in Cervix Cancer Mortality. Cancer Surveys 7(3): 417-439, 1988.

75. Goudie B.M., Burt A.D., Macfarlane G.J., Boyle P., Gillis C.R., Watkinson G. Risk factors and Prognosis in Primary Biliary Cirrhosis. Amer. J. Gastroenterology 84: 713-720, 1989.

76. La Vecchia C., Boyle P., Cislaghi C., Decarli A., Negri, E. Descriptive Epidemiology of Hodgkin's Disease in Italy. Tumori, 75:401-405, 1989.

77. Boyle P. Breast Cancer - Do Dietary Factors Matter? Update 38 (7): 725-726,810, 1989.

78. Boyle P., Hsieh C.C., Maisonneuve P., La Vecchia C., Macfarlane G.J., Trichopoulos D., Walker A.M. Epidemiology of Pancreas Cancer. Int. J. Pancreatology, 5 (4):327-346, 1989.

79. Mack T., Boyle, P., Pour P. Pancreas Cancer: Integration of Epidemiology and Laboratory. Int. J. Pancreatology 5(4): 4-9, 1989.

80. Scully C., Boyle P., Prime S. Oral Cancer (Editorial). Lancet ii (8658): 311-312, 1989.

81. Mack T., Boyle P., Pour P. M. Summary of the Second Meeting of the International Pancreatic Cancer Study Group (IPCSG) Int. Journ of Pancreatology, 5:387-389, 1989.

82. La Vecchia C., Negri E., Boyle P. Reproductive Factors and Breast Cancer: An Overview. Soz. Praeventivmed 34: 101-107, 1989.

83. La Vecchia C., Negri E., Boyle P. Alcohol and Breast Cancer: Update from an Italian case-control study. Eur. J. Cancer and Clin. Oncol., 25:1711-1717, 1989

84. Levi F., Maisonneuve P., Filiberti R, La Vecchia C., Boyle P. Patterns of Cancer Incidence and Mortality in Europe. Swiss J. Preventive and Social Medicine Supp. 2: 1-84, 1989.

85. Boyle P., Macfarlane G.J., Maisonneuve P., Zheng T., Scully C., Tedesco B. Epidemiology of Mouth Cancer in 1989: a review. J. Roy. Soc. Med. 83: 724-730, 1990.

86. La Vecchia C., Boyle P., Cislaghi C., Decarli A., Negri E. Descriptive Epidemiology of Cancers of the Upper Digestive and Respiratory Tract in Italy. Rev. Epi. Sante Publ., 38:271-273, 1990.

87. La Vecchia C., Bruzzi P., Boyle P. Some further consideration on the role of oral contraceptives in breast carcinogenesis. Tumori, 76:220-224, 1990.

88. La Vecchia C., Negri E., d'Avanzo B., Ferraroni M., Gramenzi A., Savoldelli R., Boyle P., Franceschi S. Medical history, diet and pancreatic cancer. Oncology, 47:463-466, 1990.

89. Kaye S.B., Boyle P. The Impact of Chemotherapy in Germ-cell Tumours. Cancer Surveys 8: 631-646, 1990.

90. Negri E., La Vecchia C., Levi F., Decarli A., Boyle P. The Application of Age-Period and Cohort Models to predict Swiss Cancer Mortality. J. Cancer Res. Clin. Oncol., 116:207-214, 1990.

91. Parazzini F., La Vecchia C., Negri E., Bruzzi P., Palli D., Boyle P. Anthropometric Variables and Risk of Breast Cancer. Int. J. Cancer, 45:397-402, 1990.

92. Levi F., Maisonneuve P., Boyle P., Filiberti R., La Vecchia C. Incidence and Mortality of Tumours in Europe. Epidemiol.Prev., 12:56-62, 1990

93. Negri E., La Vecchia C., Decarli A., Boyle P. Projections of Mortality from Major Cancer Sites in Italy. Tumori, 76:420-428, 1990.

94. La Vecchia C., Negri E., Parazzini F., Boyle P., D'Avanzo B., Levi F., Gentile A., Franceschi S. Height and cancer risk in a network of case-control studies from Northern Italy. Int. J. Cancer, 45, 275-279, 1990.

95. La Vecchia C., Negri E., D'Avanzo B., Boyle P. Reported Alcohol Intake and Symptomatic Gallstones (letter to Editor). New Engl. J. Med., 322, 473 , 1990.

96. Boyle P., Tomatis L. Cancer Mortality in Italy. Tumori, 76:85-86, 1990.

97. Moller H., Boyle P., Maisonneuve P., La Vecchia C., Jensen O.M. Changing mortality of male oesophageal cancer in Denmark and other European countries in relation to increasing levels of alcohol consumption. Cancer Caus. Control, 1: 173-181, 1990.

98. La Vecchia C., Negri E., D'Avanzo B., Franceschi S., Decarli A., Boyle, P. Dietary Indicators of Laryngeal Cancer Risk. Cancer Research, 50: 4497-4500, 1990.

99. Boyle P. Breast Cancer and Dietary Factors (Editorial). Hospital Update, 16:11-15, 1990.

100. Boyle P., Maisonneuve P., Kaye S.B. Testicular Cancer in Central Europe. Lancet, 335:1033, 1990.

101. D'Avanzo B., Negri E., La Vecchia C., Gramenzi A., Bianchi C., Franceschi S., Boyle, P. Cigarette Smoking and Bladder Cancer. Eur. J. Cancer, 26 (6):714-718, 1990.

102. Bouchardy C., Clavel F., La Vecchia C., Raymond L., Boyle P. Alcohol, Beer and Cancer of the Pancreas. Int. J. Cancer, 45: 842-846, 1990.

103. La Vecchia C., Franceschi S., Bruzzi P., Parazzini F., Boyle, P. The relationship between oral contraceptive use, cancer and vascular disease. Drug Safety 5 (6): 436-446, 1990.

104. Boyle P., Zheng T., Macfarlane G.J., McGinn R., Maisonneuve P., La Vecchia C., Scully C. Recent advances in the etiology and epidemiology of Head and Neck Cancer. Current Opinion in Oncology, 2: 539-545, 1990.

105. Levi F., Ollyo J.B., La Vecchia C., Boyle P., Monnier P., Savary M. The Consumption of Tobacco, Alcohol and the Risk of Adenocarcinoma in Barrett's Oesophagus, Int. J. Cancer, 45: 852-854, 1990.

106.La Vecchia C., Negri E., D'Avanzo B., Boyle P., Franceschi S. Medical History and Primary Liver Cancer. Cancer Res. 50: 6274-6277, 1990.

107.Negri, E., La Vecchia C., D'Avanzo B., Gentile A., Boyle P., Franceschi S. Salt Preference and Risk of Gastrointestinal Cancers. Nutr. Cancer, 14: 227-232, 1990.

108.Franceschi S., La Vecchia C., Negri E., Parazzini F., Boyle P. Breast cancer risk and history of selected medical conditions linked with female hormones. Eur. J. Cancer 26: 781-786, 1990.

109.Oishi K., Okada K., Yoshida O., Yamabe H., Ohno Y., Hayes R.B., Schroeder F.H., Boyle P. A case-control study of prostatic cancer in Kyoto, Japan: sexual risk factors. The Prostate, 17: 269-279, 1990.

110.Boyle P. SEARCH Programme of the IARC (Editorial). Eur. J. Cancer 26 (5): 547-549, 1990.

111.Ad Hoc Working Group (Boyle P., Cardis E., Coleman M.P., Saracci R., Ahlbom A., Feychting M. and 18 others). Extremely low-frequency electric and magnetic fields and risk of human cancer. Bioelectromagnetics, 11: 91-99, 1990.

112.Zheng T., Boyle P., Hu H.F., Duan J., Ma L., Shiu L., Niu S., MacMahon B. Tobacco smoking, alcohol consumption and risk of oral cancer: a case-control study in Beijing, People's Republic of China. Cancer Causes and Control, 1: 173-180, 1990.

113.Zheng T., Boyle P., Hu J., Duan P., Jiang D., Ma L., Shui L., Niu S., Scully C., MacMahon B. Dentition, oral hygiene and risk of oral cancer: a case-control study in Beijing, People's Republic of China. Cancer Causes and Control, 1: 235-242, 1990.

114.Adami H.-O., Adams G.E.D., Boyle P., Ewertz M., Lee N.C., Lund E., Miller A.B., Olsson H., Steel M., Tricholoulos D., Tulinius H. Breast Cancer Etiology. Int. J. Cancer suppl., 5: 22-39, 1990.

115.Boyle P. Cigarette Smoking and Pancreas Cancer. Tobacco Alert (October), 2: 8-12, 1990.

116.Boyle P., Maisonneuve P., Saracci R., Muir C.S. Is the Increased Incidence of Primary Malignant Brain Tumours in the Elderly Real? (Editorial). J. Natl. Cancer Inst., 82: 1594-1597, 1990.

117.Katsouyanni K., Kogevinas M., Dontas N., Maisonneuve P., Boyle P., Trichopoulos D. Cancer Mortality in Greece, 1960-1985. Hellenic Cancer Society, Athens, Greece, 1990.

118.Boyle P. Epidemiology of Benign Prostatic Hyperplasia. Prospectives, 1(3): 1-4, 1990.

119.Muir C.S., Boyle P. The Burden of Cancer in Europe. Eur. J. Cancer, 26: 1111-1113, 1990.

120.Hsieh C.C., Maisonneuve P., Boyle P., Macfarlane G.J., Robertson C. Analysis of quantitative data by quantiles in epidemiologic studies: classification according to cases, noncases or all subjects. Epidemiology, 2: 137-140, 1991.

121.Baghurst P.A., McMichael A.J., Slavotnik A.H., Baghurst K.I., Walker A.M., Boyle P.A case-control study of diet and cancer of the pancreas. Amer. J. Epidem., 134: 167-179, 1991.

122.Levi F., La Vecchia C., Randriamiharisoa A., Boyle P. Cancer mortality in young adults in Switzerland, 1951-1989. J.Cancer Res.Clin.Oncol., 117:497-501, 1991.

123.La Vecchia C., Levi F., Franceschi S., Boyle P. Assessment of screening for cancer. Journal of Technicology Assessment in Health Care, 7 (3):275-285, 1991.

124.La Vecchia C., Negri E., D'Avanzo B., Boyle P. Risk factors for gallstone disease requiring surgery. Int. J. Epidemiol., 20: 209-215, 1991.

125.Boyle P., McGinn R., Maisonneuve P., La Vecchia C. Epidemiology of Benign Prostatic Hyperplasia: Present Knowledge and Studies Needed. Eur.Urology, 20(suppl 2): 3-10, 1991.La Vecchia C., Negri E., D'Avanzo B., Franceschi S., Boyle P. Dairy products and the risk of prostatic cancer. Oncology 48: 406-410, 1991.

126.Zatonski W., Przwoniak K., Howe G.R., Maisonneuve P., Walker A.M., Boyle P. Nutritional Factors and Pancreatic Cancer: A Case-control study from South-West Poland. Int. J. Cancer, 48: 390-394, 1991.

127.La Vecchia C., Negri E., D'Avanzo B., Boyle P., Franceschi S.Dietary indicators of oral and pharyngeal cancer. Int. J. Epidemiol., 20: 39-44, 1991.

128.D'Avanzo B., Negri E., Gramenzi A., Franceschi S., Parazzini F., Boyle P., La Vecchia C. Fats in seasoning and breast cancer risk: an Italian case-control study. Eur. J. Cancer, 27: 420-423, 1991.

129.Ghadirian P., Simard A., Baillargeon J., Maisonneuve P., Boyle P. Nutritional Factors and Pancreatic Cancer in the Francophone Community in Montreal, Canada. Int. J. Cancer, 47: 1-6, 1991.

130.La Vecchia C., Boyle P., Franceschi S., Levi F., Maisonneuve P., Negri E., Lucchini F., Smans M. Smoking and Cancer with Emphasis on Europe, Eur. J. Cancer, 27: 94-104, 1991.

131.Zheng T., Boyle P. A case-control study of oral cancer in Beijing. Tobacco Alert, (July ,126), 1991.

132.Boyle P. Cancer Incidence Registration. Eur. J. Cancer, 27: 112-113, 1991.

133.Cockett AT, Aso Y., Denis L., Khoury S., Barry MJ., Boyle P., (and 17 others). Recommendations du Comite' de Consensus de l'OMS concernant l'evaluation diagnostique de l'HPB. Progress en Urologie 1:957-972, 1991.

134.Gray J.M.B., Beard K., Lawson DH., Kemp I., Trotter P., Boyle P. Long-term Phenothiazine use and Breast and Pancreatic Cancer in Scottish In-patients. Pharmaceut.Med., 5:107-112, 1991.

135.Bueno de Mesquita B., Maisonneuve P., Moerman C.J., Runia S., Boyle P. Life-time history of smoking and exocrine carcinoma of the pancreas. A population-based case-control study in the Netherlands. Int.J.Cancer, 49:816-822, 1991.

136.Katsouyanni K., Boyle P., Trichopoulos D. Diet and urine estrogens among postmenopausal women. Oncology, 48:490-494, 1991.

137.De Vries N., Boyle P. Alcohol verhoogt risico voor Kanker van de Bovenste Voedsel- en lucht wegen. Kanker (the Netherlands), 15:240-241, 1991.

138.La Vecchia C., Levi F., Lucchini F., Kaye S.B., Boyle P. Hodgkin's Disease Mortality in Europe. Brit. J. Cancer, 64: 723-734, 1991.

139.Negri E., Franceschi S., Tzonou A., Booth M., La Vecchia C., Parazzini F., Beral V., Boyle P., Trichopoulos D. Pooled analysis of three European case-control studies: I. Reproductive factors and risk of epithelial ovarian cancer. Int. J. Cancer, 49:50-56, 1991.

140.Ghadirian P., Boyle P., Simard A., Baillargeon J., Maisonneuve P., Perret C. Reported Family Aggregation of Pancreatic Cancer within a population based case-control study in the Francophone Community in Montreal, Canada. Int. J.Pancreatol., 10:183-196, 1991.

141.La Vecchia C., Levi F., Lucchini F., Evstifeeva T., Boyle P. Cancer Mortality in the Union of Soviet Socialist Republics (USSR), 1986-88. Int. J. Cancer, 49:678-683, 1991.

142.La Vecchia C., Negri E., Franceschi S., D'Avanzo B., Boyle P. Tea consumption and cancer risk. Nutrition and Cancer, 17:27-32, 1992.

143.Howe G.R., Ghadirian P., Bueno de Mesquita H.B., Zatonski W., Baghurst P.A., Miller A.B., Simard A., Baillargeon J., de Waard F., Przewozniak K., McMichael A.J., Hsieh C.C., Maisonneuve P., Boyle P., Walker A.M. A collaborative case-control study of nutrient intake and pancreatic cancer within the SEARCH Programme. Int.J.Cancer, 51 : 365-372, 1992.

144.Zheng T., Mayne S.T., Boyle P., Holford T.R., Flannery J.T. Epidemiology of Non-Hodgkin's Lymphoma in Connecticut, 1935-1988. Cancer, 70:840-849, 1992.

145.La Vecchia C., Lucchini F., Negri E., Boyle P., Maisonneuve P., Levi F. Trends of Cancer Mortality in Europe, 1955-89. I. Digestive Sites. Eur. J. Cancer, 28:132-235, 1992.

146.La Vecchia C., Lucchini F., Negri E., Boyle P., Maisonneuve P., Levi F. Trends of Cancer Mortality in Europe, 1955-89. II Respiratory tract, bone, connective and soft tissue sarcomas, and skin. Eur. J. Cancer, 28:514-599, 1992.

147.La Vecchia C., Lucchini F., Negri E., Boyle P., Maisonneuve P., Levi F. Trends of Cancer Mortality in Europe, 1955-89. III Breast and Genital Sites. Eur. J. Cancer, 28:927-998, 1992.

148.La Vecchia C., Lucchini F., Negri E. Boyle P., Maisonneuve P., Levi F. Trends in Cancer Mortality in Europe, 1955-89. IV, Urinary tract, eye, brain and nerves, and thyroid. Eur.J.Cancer, 28:1210-1281, 1992.

149.La Vecchia C., Lucchini F., Negri E., Boyle P., Maisonneuve P., Levi F. Trends in Cancer Mortality in Europe, 1955-89 V Lymphohaemopoietic and all cancers. Eur.J.Cancer, 28:1509-1581, 1992.

150.Boyle P. Trends in Cancer Mortality in Europe (editorial). Eur.J.Cancer, 28:7-8, 1992.

151.Boyle P. In-My-View: Population Studies in Benign Prostatic Hyperplasia. Prospectives 2:5-6, 1992.

152.Boyle P., Macfarlane G.J., Zheng T., Maisonneuve P., Evstifeeva T., Scully C. Recent Advances in Epidemiology of Head and Neck Cancer. Current Opinion in Oncology, 4:471-477, 1992.

153.Zatonski W., La Vecchia C., Przewozniak K., Maisonneuve P., Lowenfels A.B., Boyle P. Risk factors for Gallbladder Cancer. A Polish case-control study. International Journal of Cancer, 51:707-711, 1992.

154.Boyle P. Book Review: Nutrients and Cancer Prevention, Eur.J.Cancer, 28: 236 - 237, 1992.

155.Scully C., Boyle P., Tedesco B. The recognition and diagnosis of cancer arising in the mouth. Postgraduate Doctor, 15:134-141, 1992.

156.Boyle P. Cancer: An Increasing Research Priority. Medicographia, 14:3-9, 1992.

157.Boyle P. Some remarks on the Epidemiology of Benign Prostatic Hyperplasia. European Urology Today, 2:10-11, 1992.

158.Boyle P. Book Review: "Human Carcinogen Exposure: Biomonitoring and Risk Assessment". Eur. J.Cancer, 28A:1929, 1992.

159.Boyle P. Editorial: Epidemiology in Central and Eastern Europe. Epidemiology, 3:391-394, 1992.

160.Boyle P. Screening for Prostatic Diseases. Prospectives, 3:1-5, 1992.

161.Boyle P. Book Review: Observation and Inference: An Introduction to the Methods of Epidemiology. Cancer Causes Control, 3:183, 1992.

162.Bueno de Mesquita H.B., Maisonneuve P., Moerman C.J., Runia S., Boyle P. Lifetime consumption of alcoholic beverages, tea and coffee and exocrine carcinoma of the pancreas: A population-based case- control study in the Netherlands. Int.J.Cancer, 50:514-522, 1992.

163.Levi F., La Vecchia C., Lucchini F., Negri E., Boyle P. Patterns of Childhood Cancer. Incidence and Mortality in Europe. Eur. J. Cancer, 28A:2028-2049, 1992.

164.Macfarlane G.J., Boyle P., Scully C. Oral Cancer in Scotland: Changing Incidence and Mortality. Brit.Med.J. 305:1121-1123, 1992.

165.Scully C., Boyle P.Vitamin A related compounds in the chemoprevention of potentially malignant oral lesions and carcinoma. Eur.J.Cancer. B: Oral Oncology 2:87-89, 1992.

166.Zheng T., Mayne St., Holford T.R., Boyle P., Flannery J. Time Trend and Age-Period-Cohort Effects on Incidence of Esophageal Cancer in Connecticut, 1935-89. Cancer Causes Control 3:481-492, 1992.

167.Zatonski W.A., Boyle P., Przwoniak K., Maisonneuve P., Drosik W., Walker A.M. Cigarette smoking, alcohol, tea and coffee consumption and pancreas cancer risk: a case-control study from Opole, Poland. Int. J. Cancer, 53:601-607, 1993.

168.Zheng T., Boyle P., Willett W.C., Hu H.F., Duan J., Evstifeeva T., Niu S., MacMahon B. A Case-Control Study of Oral Cancer in Beijing, People's Republic of China. Associations with Nutrient Intakes, Foods and Food Groups. Oral Oncology, 29B, 1:45-55, 1993.

169.La Vecchia C., Negri E., Franceschi S., D'Avanzo B., Boyle P. Marital Status, indicators of sexual activity and prostatic cancer. J.Epidemiol.Comm.Health, 47:450-453, 1993.

170.Zaridze D.G., Evstifeeva T., Babaeva M., Boyle, P. Fats used in seasoning and breast cancer risk: a case-control study in Moscow, Russia. Annals Oncology, 4:495-498, 1993.

171.Boyle P. The Hazards of Active and Passive Smoking. Letter to the Editor. N.Engl.J.Med., 329 (21): 1581, 1993.

172.Boyle P., La Vecchia C., Negri E., Lucchini F., Levi F. Trends in diet-related cancers in Japan: a conundrum? (Letter) Lancet, 342: 752, 1993.

173.Boyle P., Macfarlane G.J., Scully C. Oral Cancer: necessity for Prevention Strategies (Editorial). Lancet, 342:1129, 1993.

174.Boyle P., Zaridze D.G. Risk factors for prostate and testicular cancer. Eur.J.Cancer, 7: 1048-1055, 1993.

175.Boyle P. The Hazards of Passive and Active Smoking. New Engl.J.Med., 328:1708-1709, 1993.

176.Boyle B., Chilvers C., Ferraz E., Hulka B., King R., La Vecchia C., Petitti D., Lumbiganon P., Skegg D., Thomas D., Viegas O., Jordan A., Forthney J., Peterson H., Ramachandran P., Spirtas R.Depot-medroxyprogesterone acetate (DMPA) and cancer: Memorandum from a WHO meeting Bulletin World Health Organization, 71(6):669-676, 1993.

177.Franceschi S., Boyle P., Maisonneuve P., La Vecchia C., Burt A.D., Kerr D.J., Macfarlane G.J., Alexander W.D.The Epidemiology of Thyroid Carcinoma. Critical Reviews in Oncogenesis, 4:25-52, 1993.

178.La Vecchia C., Boyle P. Trends in the tobacco-related cancer epidemic in Europe. Cancer Detection and Prevention, 17(4/5):495-506, 1993.

179.La Vecchia C., Franceschi S., Talamini R., Negri E., Boyle P., D'Avanzo B. Marital Status, Indicators of sexual activity and prostate cancer. J.Epid.Comm.Health, 47:450-453, 1993.

180.La Vecchia C., Levi F., Lucchini F., Negri E., Boyle P. Trends in Cancer Mortality in the USSR, 1965-90. Int.J.Cancer, 56:31-39, 1993.

181.La Vecchia C., Lucchini F., Negri E., Boyle P., Levi F. Trends in Cancer Mortality, 1955-89: Asia, Africa and Oceania. Eur.J.Cancer, 29A-15:2168-2211, 1993.

182.La Vecchia C., Lucchini F., Negri E., Boyle P., Levi F. Trends in cancer mortality in the Americas, 1955-1989. Eur.J.Cancer, 29A:431-470, 1993.

183.Levi F., La Vecchia C., Lucchini F., Boyle P. Cancer Incidence and mortality in Europe, 1983-87.Soz Praventivmed 1993, Suppl. 3, 38: S155-S229, 1993.

184.Lowenfels A.B., Cavallini G., Ammann R.W., Lankisch P.G., Andersen J.R, Dimagno E.P., Andren-Sandberg A., Domellof L.., Maisonneuve P., Di Francesco V., Lohr-Happe A., Krag E., Melton L.J., Pitchumoni C.S., Wynn P.S., Boyle P. Pancreatitis and the risk of Pancreatic Cancer. New Eng.J.Med., 328, 20:1433-1437, 1993.

185.Macfarlane G.J., Boyle P., Evstifeeva T., Scully C. Epidemiological Aspects of Lip cancer in Scotland. J.Oral Epi. Comm.Dent., 21:279-82, 1993.

186.Macfarlane G.J., Evstifeeva T., Scully C., Boyle P.The Descriptive Epidemiology of Pharyngeal Cancer in Scotland. European Journal of Epidemiology, 9 (6): 587-590, 1993.

187.Martin-Moreno J.M., Boyle P., Gorgojo L., Maisonneuve P., Fernandez-Rodriguez J.C., Willett W.C., Salvini S. Development and validation of a food frequency questionnaire in Spain. Int.J.Epidemiol., 22, 3:512-519, 1993.

188.Martin-Moreno J.M., Willett W.C., Gorgojo L., Boyle P., Gonzales J., Villar F., Maisonneuve P. Alcoholic beverage consumption and risk of breast cancer in Spain. Cancer Causes and Control, 4:345-353, 1993.

189.Robertson A.G., Robertson C., Boyle P., Symonds R.P., Wheldon T.E. The Effect of Differing Radiotherapeutic Schedules on the Response of Glottic Carcinoma of the Larynx. Eur. J. Cancer, 4 (29A): 501-510, 1993.

190.Schroeder F., Boyle P. Screening for Prostate Cancer: Necessity or Nonsense? Eur. J. Cancer, 5 (29A): 656-661, 1993.

191.Wald N.J., Chamberlain J., Hackshaw A., Anderson T., Boyle P., Forrest P., Frischbier H.J., Hakama M., Rutqvist L.E., Schaffer P., Seradour B., Tabar L., Rosselli Del Turco M., E. Von der Schueren. Report of the European Society of Mastology (EUSOMA). Breast Cancer Screening Evaluation Committee. The Breast, 2:209-216, 1993

192.Zaridze D.G., Evstifeeva T., Boyle P. Chemoprevention of oral Leukoplakia and chronic esophagitis in an area of high incidence of oral and esophageal cancer. Annals Epidemiol., 3:225-234, 1993.

193.Zheng T., Mayne S.T., Holford T.R., Boyle P., Wenliang L., Chen Y., Mador M., Flannery J. The time trend and age-period-cohort effects on incidence of Adenocarcinoma of the stomach in Connecticut, from 1955-1989. Cancer 72, 2:330-340, 1993.

194.Boyle P. Diet in the Aetiology of Cancer (Editorial). Eur.J.Cancer, 30A, No.2, p. 133, 1994.

195.Boyle P. New Insights into the Epidemiology and Natural History of Benign Prostatic Hyperplasia. Prog.Clin.Biol.Res., 386:3-18, 1994.

196.Boyle P. Dietary factors in the Aetiology of Cancer (Editorial). Oncology and Haematology Literature Service, 1 (2):7-8, 1994.

197.Boyle P. Epidemiology of Benign Prostatic Hyperplasia: risk factors and concomitance with Hypertension.Brit.J.Clin.Practice, 74:18-22, 1994.

198.Boyle P., Maisonneuve P., Rotmensz N., Sacchini V., Costa A. Prevention of breast cancer with Tamoxifen Oncology in Practice, 3/94: 9-11, 1994.

199.La Vecchia C., D'Avanzo B., Negri E., Franceschi S., Boyle P. Gastrectomy and subsequent risk of oesophageal cancer in Milan. Journal of Epidemiology and Community Health, 48:310-312, 1994.

200.La Vecchia C., Negri E., Franceschi S., D'Avanzo B., Boyle P. A case-control study of diabetes mellitus and cancer risk. Br.J.Cancer., 70:950-953, 1994.

201.Macfarlane G.J., Plesko I., Kramarova E., Obsitnikova A., Boyle P. Epidemiological features of gastric and oesophageal cancers in Slovakia. British Journal of Cancer, 70:177-179, 1994.

202.Macfarlane G.J., Evstifeeva T.V., Robertson C., Boyle P., Scully C. Trends of oral cancer mortality among females worldwide. Cancer Causes and Control, 5: 255-258, 1994.

203.Franceschi S., Levi F., Lucchini F., Negri E., Boyle P., La Vecchia C. Trends in Cancer Mortality in Young Adults in Europe, 1955-1989. Eur.J.Cancer, 30A:2096-2118, 1994.

204.Katsouyanni K., Trichopoulou A., Stuver S., Garas Y., Kritselis A., Kyriakou G., Stoïkidou M., Boyle P., Trichopoulos D. The association of fat and other

macronutrients with breast cancer: a case-control study from Greece. Brit.J.Cancer, 70: 537-541, 1994.

205.Macfarlane G.J., Boyle P., Evstifeeva T.V., Robertson C., Scully C. Rising Trends of Oral Cancer Mortality World-wide, The return of an old Public Health Problem. Cancer Causes and Control, 5: 259-265, 1994.

206.Hopper J.L., Giles G.G., McCredie M.R.E., Boyle P. Background, Rationale and Protocol for a Case-Control-Family study of breast cancer. The Breast, 3:79-86, 1994.

207.Macfarlane G.J., Boyle P. The Epidemiology of Oesophageal Cancer in the United Kingdom and other European Countries. J.Roy.Soc.Med., 87:334-337, 1994.

208.Filippini G., Farinotti M., Lovicu G., Maisonneuve P., Boyle P. Mothers' active and passive smoking during pregnancy and risk of brain tumour in children. Int.J.Cancer, 57: 769-774, 1994.

209.Hietanen E., Bartsch H., Bereziat J.C., Camus A.M., McClinton S., Eremin O., Davidson L., Boyle P. Diet and Oxidative Stress in Breast, Colon and Prostate cancer patients: a case-control study. European Journal of Clinical Nutrition, 48: 575-586, 1994.

210.Lowenfels A.B., Maisonneuve P., Cavallini G., Amann R.V., Lankisch P.G., Andersen J.R., Dimagno E.P., Andren-Sandberg A., Domellof L., and the International Pancreatitis Study Group: Listed Authors plus Vincenzo Di Francesco, Paolo Pederzoli, Annette Lohr-Happe, Einar Krag, Peter Boyle, C.S. Pitchumoni, Pe Shein Wynn, and Joseph Melton. Prognosis of Chronic Pancreatitis: an International Multicenter Study Amer.J.Gastroenterology, 9:1467-1471, 1994.

211.Martin-Moreno J.M., Boyle P., Gorgojo L., Maisonneuve P., Fernandez-Rodriguez J.C., Willett W.C., Banegas J.R, Artalejo F.R. Dietary fat, olive oil intake and breast cancer risk. Int. J. Cancer, 58:774-780, 1994.

212.McCredie M., Maisonneuve P., Boyle P. Antenatal Risk Factors for Malignant Brain Tumours in New South Wales Children. Int.J.Cancer, 56: 6-10, 1994.

213.McCredie M., Maisonneuve P., Boyle P. Perinatal and early postnatal risks for malignant brain tumours in New South Wales Children. Int. J. Cancer, 56:11-15, 1994.

214.Sagnier P.P., Macfarlane G.J., Richard F., Botto H., Teillac P., Boyle P. Results of an Epidemiological Survey Employing a Modified American Urological Association Symptom Index for Benign Prostatic Hyperplasia in France. J. Urology, 151:1266-1270, 1994.

215.Sagnier P.P., Richard F., Botto H., Teillac P., Dreyfus J.P., Boyle P. Adaptation et validation en langue française du score international des symptomes de l'hypertrophie benigne de la prostate. Prog.Urol., 4: 532-540, 1994.

216.Vela Navarrete R., Martin-Moreno J.M., Calahorra F.J., Damian Moreno J., Herandez Coronado A., Boyle P. Validacion cultural y linguistica, en castellano del baremo internacional de sintomas prostaticos (I-PSS). Actas Urologicas Espanolas, 18: 841-847, 1994.

217.Zheng T., Holford T.R., Boyle P., Chen Y., Ward B.A., Flannery J., Mayne S.T. Time Trend and Age-Period-Cohort Effect of Histologic types of Lung Cancer in Connecticut, 1960-89. Cancer 74, 5:1556-1567, 1994.

218.Zakelj M., Boyle P. Breast Cancer Detection and Oral Contraceptive use in Slovenia (letter). Lancet, 343:1166-1167, 1994.

219.Robertson C., Boyle P., Hsieh C.C., Macfarlane G.J., Maisonneuve P. Some statistical considerations in the analysis of case-control studies when the exposure variables are continuous measurements. Epidemiology, 5(2):164-170, 1994.

220.Macfarlane G.J., Boyle P., Evstifeeva T.V., Robertson C., Scully C. Rising Trends of Oral Cancer Mortality World-wide among women. Cancer Causes and Control, 5:255-258, 1994.

221.Axon A., Boyle P., Riddel R.H., Grandjouan S., Hardcastle J., Yoshida S. Summary of a Working Party on the Surveillance of Premalignant Lesions. Am.J. Gastroenterol., 89:160-168, 1994.

222.Boyle P., Maisonneuve P. Lung Cancer and Tobacco Smoking. Lung Cancer, 12:167-181, 1995.

223.Levi F., La Vecchia C., Lucchini F., Boyle P., Negri E. Patterns of childhood cancer mortality: America, Asia and Oceania. Eur.J.Cancer, 31A: 771-782, 1995.

224.Macfarlane G.J., Zheng T., Marshall J.R., Boffetta P., Niu S., Brasure J., Merletti F., Boyle P. Alcohol, Tobacco, Diet and the risk of oral cancer: A pooled analysis of three case-control studies. European Journal of Cancer part B - Oral Oncology, 31B: 181-187, 1995.

225.Macfarlane G.J, Evstifeeva T.V, Boyle P., Grufferman S. International patterns of occurrence of Hodgkin's Disease in children and young adult males. Int. J. Cancer, 61:165-169, 1995.

226.Napalkov P., Maisonneuve P., Boyle P. Worldwide patterns of prevalence and mortality from Benign Prostatic Hyperplasia. Urology, 46 (Supplement 3A): 41-46, 1995.

227.Boyle P., Maisonneuve P., Dore' J.F. Epidemiology of Malignant Melanoma. Brit.Med.Bull., 3:523-547, 1995.

228.Boyle P., Napalkov P. The Epidemiology of Benign Prostatic Hyperplasia and observations on concomitant hypertension. Scand. J.Urol. Nephrol., 29:7-12, 1995.

229.Neglia J., FitzSimmons S., Maisonneuve P., Schoni M., Schoni-Affolter F., Corey M., Lowenfels A., Boyle P., Dozor A., Durie P. The Risk of Cancer Among Patients with Cystic Fibrosis. New Engl. J. Med., 332:494-499, 1995.

230.Boyle P., Chiesa F., Scully C. Chemoprevention and Oral Cancer - (More) trials and (more) tribulations. European Journal of Cancer B. Oral Oncology, 1 (1): 2, 1995.

231.Boyle P. Book Review: R. Doll, J.F. Fraumeni Jr., Muir C.S., Trends in Cancer Incidence and Mortality, Cancer Surveys, Vol. 19/20. Statistics in Medicine, 14: 2507-2508, 1995 (IF 1.085).

232.Boyle P. Progress in Preventing Death from Colorectal Cancer.Editorial. Brit. J.Cancer., 72: 528-530, 1995.

233.Macfarlane G.J., Sagnier P.P., Richard F., Teillac P., Botto H., Boyle P. Determinants of treatment-seeking behaviour for urinary symptoms in older men. Br. J. Urol., 76 (6): 714-718, 1995.

234.Macfarlane G., Evstifeeva T., Boyle P., Grufferman S. International patterns in the occurence of Hodkgin's disease in children and young adult males. Int. J. Cancer, 6: 165-169, 1995.

235.Boyle P., Macfarlane G.J., Blot W.J., Chiesa F., Lefebvre J.L., Mano Azul A., de Vries N., Scully C. European School of Oncology Advisory Report to the European Commission for the Europe Against Cancer Programme: Oral Carcinogenesis in Europe. Oral Oncology, 31B:75-85,1995.

236.Sagnier P.P., Macfarlane G.J., Teillac P., Botto H., Richard F., Boyle P. Impact of Symptoms of Prostatism on level of Bother and Quality of Life of men in the French Community. J Urology, 153: 669-673, 1995.

237.Boyle P. Tobacco Smoking: The Worsening of the Epidemic. Editorial for: Literature Reviews. Oncology and Haematology, 3:4-6, 1995.

238.Boyle P. Tobacco and Cancer, the European Perspective. Annals of Oncology, 6: 435-439, 1995.

239.Fernandez E., La Vecchia C., Porta M., Negri E., D'Avanzo B., Boyle P. Pancreatitis and the risk of pancreatic cancer. Pancreas, 2 (11):185-189, 1995.

240.Veronesi U., Costa A., Sacchini V., Luini A., Bonanni B., Veronesi P., Rotmensz N., Boyle P. Etude italienne de chimioprevention du cancer du sein avec le tamoxifene. Contracept. Fertil. Sex., 23: 258-260 1995.

241.Boyle P., Maisonneuve P., Napalkov P. Geographical and temporal patterns of incidence and mortality from prostate cancer. Urology 46 (Suppl 3A): 47-55, 1995.

242.Primic Zakelj M., Evstifeeva T., Ravnihar B., Boyle P. Breast cancer risk and oral contraceptive use in Slovenian women aged 25-54. Int J Cancer, 62: 414-420, 1995.

243.Zheng T., Holford T.R., Ward B.A., McKay J., Flannery J., Boyle P. Time Trend in Pancreatic Cancer Incidence in Connecticut, 1935-1990. Int. J. Cancer, 61: 622-627, 1995.

244.Veronesi U., Costa A., Boyle P., Maisonneuve P., Rotmensz N., Zecchini A.M., Barberini M., Bestetti F., Bettega D., Bocciolone L., Bonanni B., Bruno S., Canigiula L., Cassano E., Farante G., Lampreda C., Mascotti G., Ponzone V., Sacchini V., Salvioni A., Travaglini R., Veronesi P., Zocca A., D'Aiuto G., Oliviero P., Rotunno L., Sottana F., Gucciardo G., Marini P., Muraca M.G., Scillone L., Veronesi A., Pizzichetta M., Conforti S., Palazzo S., Audisio R.A., Ravaioli R., Rulli A., Pluchinotta A., Modena S., Molino A.M., Zannoni E., Valentini M., Depalma P., Baratelli G., Barros A., Bernardo G., Bocchiotti G., Bonsignori M., Bottinelli G., Carnaghi P., Colombo P., Cresta C., D'Amore L., Della Torre L., Donadello N., Dossena G., Ferrari A., Frasson A., Guidetti R., Leonardi F., Luerti M., Magro A.G., Pagni P., Raia F., Rocci R., Schittuli F., Tommasini A., Zanella B., Albisetti W., Coopmans De Yoldi G., Decensi A., Di Maggio C., Guazzi M., Luini A., Maltoni C., Mannucci P.M., Pardi G., Podda M., Ravasi G., Scaltrini G., Turbati M. Prevention of breast cancer with Tamoxifen: The Italian study in Hysterectomized women. The Breast, 4: 267-272, 1995.

245.Robertson C., Boyle P., Hsieh C.C., Macfarlane G., Maisonneuve P. Interpretation and Analyses of differential exposure variability and zero-exposure categories for continuous exposures. Epidemiology 6(3):335, 1995.

246.Boyle P., Primic-Zakelj M. Review article. European Code Against Cancer. Journal of Slovene Medical Society, 64:447-452, 1995.

247.Boyle P., Veronesi U., Tubiana M., Alexander F.E., Calais da Silva F., Denis L.J., Freire J.M., Hakama M., Hirsch A., Kroes R., La Vecchia C., Maisonneuve P., Martin-Moreno J.M., Newton-Bishop J., Pinborg J.J., Saracci R., Scully C., Standaert B., Storm H., Blanco S., Malbois R., Bleehen N., Dicato M., Plesnicar S. Special Paper. European School of Oncology Advisory Report to the European Commission for the "Europe Against Cancer Programme"European Code Against Cancer. Eur. J. Cancer, 9: 1395-1405, 1995.

248.Boyle P. The Revised European Code Against Cancer. Oncology in Practice, 3: 4-8, 1995.

249.Boyle P., Primic Zakelj M. Eropski Kodeds Proti Raku. Zdravstveno Varstvo, 34: 411-2, 1995.

250.Boyle P., Primic Zakelj M. European Code against Cancer. Radiol. Oncol., 29: 248-9, 1995.

251.Boyle P., Maisonneuve P and Steg A. Decrease in mortality from benign prostatic hyperplasia: a major unheralded health triumph. Journal Urology, 155:176-180, 1996.

252.Zheng T., Holford T.R., Chen Y., Ma J.Z., Flannery J., Liu W., Russi M., Boyle P. The Time Trend and Age-period Cohort Effect on Incidence of Thyroid Cancer in Connecticut, 1935-1992. Int. J. Cancer, 67: 504-509, 1996.

253.Boyle P., Maisonneuve P., Napalkov P. The incidence of Prostate Cancer will double by the Year 2030: The Argument For. Eur. Urol., 29:3-9, 1996.

254.*Collaborative Group on Hormonal Factors in Breast Cancer* Breast cancer and hormonal contraceptives: Further Results. Contraception, 54 (Suppl. 3):1S-106S, 1996.

255.Marshall J., Boyle P. Nutrition and Oral Cancer. Cancer Cause Control , 7 (1): 101-111, 1996.

256.Plesko I., Ondrus D., Boyle P. Testicular cancer incidence and mortality in Slovakia, 1968-1990. Lancet, 347: 900-901, 1996.

257.Macfarlane G.J., Botto H. Sagnier P.P., Teillac P., Richard F., Boyle P. The relationship between sexual life and urinary condition in the French community. J. Clin. Epidemiol., 49(10): 1171-1176, 1996.

258.Salvini S., Gnagnarella P., Parpinel M.T., Boyle P., Decarli A., Ferraroni M., Giacosa A., La Vecchia C., Negri E., Franceschi S. The Food Composition

Database for an Italian Food Frequency Questionnaire. Journal of Food Composition and Analysis, 9:57-71, 1996.

259.Buccianti G., Maisonneuve P., Ravasi B., Cresseri D., Locatelli F., Boyle P. Cancer among patients on renal replacement therapy. A population-based survey in Lombardia, Italy. Int. J. Cancer, 66:591-593, 1996.

260.Sagnier P., Girman C., Garraway M., Jumamoto T., Lieber M., Richard F., Macfarlane G., Guess H., Jacobsen S., Tsukamoto T., Boyle P. International Comparison of the Community Prevalence of Symptoms of Prostatism in Four Countries. Eur. Urol., 29: 15-20, 1996.

261.Boyle P., Napalkov P. Epidemiology of Benign Prostatic Hyperplasia: Current Perspectives. European Urology 29 (1): 7-11, 1996.

262.Cattaruzza M.S., Maisonneuve P., Boyle P. Occasional Review: Epidemiology of Laryngeal Cancer. Oral Oncol., Eur.J.Cancer, 32B:293-305, 1996.

263.Boyle P., Gould L., Roehrborn C. Prostate Volume Predicts Outcome of Treatment of Benign Prostatic Hyperplasia with Finasteride. Meta-Analysis of Randomized Clinical Trials.Urology, 48(3): 398-405, 1996.

264.Negri E., La Vecchia C., Levi F., Franceschi S., Serra-Majem L., Boyle P. Comparative Descriptive Epidemiology of Oral and Esophageal Cancers in Europe. Eur. J. Cancer Prev., 5: 267-280, 1996.

265.Zheng T., Holford T.R., Zheng M.A., Ward B., Falnnery J., Boyle P. Continuing increase in incidence of germ-cell testis cancer in young adults: experience from Connecticut, USA, 1935-1992. Int. J.Cancer 65, 723-729, 1996.

266.Schöni H.M., Maisonneuve P., Schöni-Affolter F., Lowenfels A.B., Boyle P., Members of the CF/CSG Group.Cancer risk in patients with cystic fibrosis: the European data. J. Roy. Soc. Med., 89 (27): 38-43 1996.

267.Zheng T., Holford T.R., Ma Z., Chen Y., Liu W., Ward B.A., Boyle P. The Continuing Increase in Adenocarcinoma of the Uterine Cervix: A Birth Cohort Phenomenon. Int. J. Epi., 25 (2): 252-258, 1996.

268.Boyle, P. Continual importance of descriptive epidemiology in cancer research (Editorial). Ann. Oncol., 7: 439-440, 1996.

269.Boyle P. Prostate Cancer: Creation and Control of an Epidemic. J. Epi. Bio., (1) 2: 65-67, 1996.

270.Boyle P., Kornacker M., Diehl V. Europäischer Kodex gegen den Krebs. Empfehlungen Medizinische Klinik, 91: 262-267, 1996.

271.Boyle P., Kubik A. Revidované Zneni Europského Kodexu Proti Zhoubným Nàdorum. Cas. Lek. ces., 22: 711-715, 1996.

272.Zheng T., Holford R., Chen Y., Ma J.Z., Mayne S.T., Boyle P., Flannery J. Time Trend and Age-Period Cohort Effect on Incidence of Bladder Cancer in Connecticut,1935-1992. Int. J. Cancer, 68: 172-176, 1996.

273.Buccianti G., Ravasi B., Cresseri D., Maisonneuve P., Boyle P., Locatelli F. Cancer in patients on renal replacement therapy in Lombardy, Italy. (Letter). The Lancet, 347 (8993): 59-60, 1996.

274.Boyle P., La Vecchia C. Introducing the Journal of Epidemiology and Biostatistics.Editorial. J. Epi. Bio., 1: 1-2, 1996.

275.Boyle P. The Epidemiology of Malignant Melanoma Rev. Argent. Canc. XXIV (1): 26-32, 1996.

276.Boyle P., Plesko I. Európsky kódex proti rakovine. Slovensky Lekár, 4: 30-35, 1996.

277.Boyle P. Exogenous Hormones and Cancer Risk in Women. What should women be advised to do? Eur. Cancer News, 8:4-7, 1996.

278.Boyle P., Eckhardt S. Európai Rákellenes Kódex. Magyar Onkológia, 2:68-75, 1996.

279.Alexander F.E., Wray N., Boyle P., Bring J., Coebergh J.W., Draper G., Levi F., McKinney P.A., Michaelis J., Peris-Bonet R., Petridou E., Pukkala E. Storm H., Terracini B., Vatten L. Review: Clustering of childhood leukemia leukaemia: a European study in progress. J.Epi.Bio., 1: 13-22, 1996.

280.Boyle P. L'epidemiologia del cancro in Europa. Le Scienze, 339:88-89, 1996.

281.Boyle P. European Cancer Experts Recommendations for Tobacco Control. Eur.Canc.News., 9(9) 8-11, 1996.

282.Rocco F., De Cobelli O., Maffezzini M., Franchini V., Scardino E., Carmignani L., Andres M., Frea B., Crispino S., Tancini G., Paolorossi F., Boyle P., Maisonneuve P. Neoadjuvant chemotherapy and conservative surgery for locally advanced transitional cell bladder cancer. J. Chemotherapy, 8 (4): 326-327, 1996.

283.*Collaborative Group on Hormonal Factors in Breast Cancer*. Breast cancer and hormonal contraceptives: collaborative reanalysis of individual data on 53.297 women with breast cancer and 100.239 women without breast cancer from 54 epidemioological studies. Lancet, 347: 1713-1727, 1996.

284.Boyle P. European cancer experts' recommendations for tobacco control. J. Epi. Bio., 1(3):121-123, 1996.

285.Zatonski W.A., Boyle P. Health transformations in Poland after 1988. J. Epi. Bio., 1(4): 183-197, 1996.

286.Andreoni B., Crosta C., Biffi R., Marzona L., Pozzi S., Lotti M. e C.T.S.U.O. Regione Lombardia. Attivazione nella Regione Lombardia del Trial multicentrico "Once only sigmoidoscopy"per lo screening del carcinoma colorettale. Minerva Chir.(Suppl. 1 al N.6), 51: 43-50, 1996.

287.Boyle P., Primic Zakelj M. Eropski Kodeds Proti Raku. European Code Against Cancer. Obzornik Zdravstvene nege, 30: 3-5, 1996.

288.Boyle P, Maisonneuve P, Bueno de Mesquita B, Ghadirian P, Howe GR, Zatonski W, Baghurst P, Moerman CJ, Simard A, Miller AB, Przewoniak K, McMichael AJ, Hsieh CC, Walker AM. Cigarette smoking and pancreas cancer: a case control study of the search programme of the IARC. *Int J Cancer* 1996 Jul 3;67(1):63-71

289.Zatonski W., Lowenfels A.B., Boyle P., Maisonneuve P., Bueno de Mesquita B., Ghadirian P., Jain M., Preznowiak K., Baghurst P., Moerman C.D., Simard A., Howe G.R., McMichael A.J., Hsieh C.C., Walker A.M. Epidemiological aspects of gallbladder cancer: a case-control study of the SEARCH Programme of the IARC. J.N.C.I., 89 (15): 1132-1138, 1997.

290.Boyle P., Krewski D., Ashmore J.P., Cardis E., Zielinski J.M. Radiation Epidemiology and National Dose Registers. Proceedings of the Workshop held at University of Toronto, 13-14 July 1992. Eur. J.Cancer, 33: (Suppl. 3):S1-S2, 1997.

291.Ghadirian P., Lacroix A., Maisonneuve P., Perret C., Potvin C., Gravel D., Bernard D., Boyle P. Nutritional Factors and Colon Carcinoma. A case-control study involving French Canadians in Montreal, Quebec, Canada. Cancer, 80:858-864, 1997.

292.Fernandez E., La Vecchia C., Porta M., Negri E., D'Avanzo B., Boyle P. Pancreatitis and the risk of Pancreatic Cancer: In Response to Gullo & Pezzilli. Pancreas, 14:106-107, 1997.

293.Lowenfels A.B., Maisonneuve P., DiMagno E., Elitsur Y., Gates L.K., Perrault J., Whitcomb D.C. and the International Hereditary Pancreatitis Study Group. Hereditary Pancreatitis and the Risk of Pancreatic Cancer. J. Natl. Cancer I., 89 (6): 442-446, 1997.

294.Zheng T., Holford T.R., Chen Y., Ward B., Liu W., Flannery J., Boyle P. Are Cancers of the Salivary Gland Increasing? Experience from Connecticut, USA. Int. J. Epidemiol., 26: 264-271, 1997.

295.Zheng T., Holford T.R., Chen Y., Ward B., Liu W., Flannery J., Boyle P. Are Cancers of the Salivary Gland Increasing? Experience from Connecticut, USA. Int. J. Epidemiol., 26: 264-271, 1997.

296.Zheng T., Holford T.R., Chen Y., Ma Z., Liu W.L., Flannery J., Boyle P. Lymphocytic Leukemias in Connecticut, USA: Time Trends and Racial Differences, 1935-1992. J. Epi. Bio., 1(4): 219-225, 1997.

297.Chen Y., Zheng T., Chou M., Boyle P., Holford T.R. The increase of Hodgkin's disease incidence among young adults: experience in Connecticut 1935-1992. Cancer, 79 (11): 2209-2218, 1997.

298.Zheng T., Holford T., Chen Y., Jiang P., Zhang B., Boyle P. Risk of Tongue Cancer Associated with Tobacco Smoking and Alcohol Consumption: A Case-Control Study. Oral Oncol., 33 (2): 82-85, 1997.

299.Boyle P. European Cancer Experts Recommendations for Tobacco Control. Annal. Oncol., 8:9-13, 1997.

300.Boyle P. Cancer, Cigarette smoking and premature death in Europe. A review including the Recommendations of European Cancer Experts Consensus Meeting, Helsinki, October 1996. Lung Cancer, 17: 1-60, 1997.

301.Boyle P., Krewski D., Ashmore J.P., Cardis E., Zielinski J.M. Radiation Epidemiology and National Dose Registers. Eur. J.Cancer, 33: Suppl. 3,S1-S2, 1997.

302.Andersen J.T., Nickel J.C., Marshall V.R., Schulman C.C. and Boyle P. Finasteride significantly reduces acute urinary retention and the need of surgery in patients with symptomatic Benign Prostatic Hyperplasia. Urology, 49:839-845, 1997.

303.Boyle P. Global burden of cancer. Lancet, 349 (Oncology Supplement II): 23-26, 1997.

304.Autier P., Dore' J.F., Cesarini J.P., Boyle P. and the epidemiology & Prevention subgroup, the EORTC Melanoma Cooperative Group and the EORTC Prevention Research Division. Should subjects who used psoralen suntan activators be screened for Melanoma? Ann. Oncol., 8(5):435-437, 1997.

305.Osborne M., Boyle P., Lipkin M. Cancer Prevention. Lancet, 349 (Oncology supplement II): 27-30, 1997.

306.Boyle P. Cultural and linguistic validation of questionnaires for use in international studies: the nine-item BPH-specific quality of life scale. Eur. Urol., 32 (suppl 2): 50-52, 1997.

307.Becker N., Boyle P. Decline in mortality from testicular Cancer in West Germany after re-unification. (Research Letter) Lancet, 350: 744, 1997.

308.Boyle P., La Vecchia C. Journal of Epidemiology and Biostatistics: the first year. J. Epi. Bio., 2 (1): 7, 1997.

309.Boyle P. Editorial: Some current issues in population screening for cancer. J. Epi. Bio., 2 (1): 1-4, 1997.

310.Gray N., Boyle P. Attacks on tobacco Industry (The US Settlement) (Letter). The Lancet, 350: 890, 1997.

311.Tradati N., Grigolato R., Calabrese L., Costa L., Giugliano G., Morelli F., Scully C., Boyle P., Chiesa F. Oral Leukoplakias: to treat or not to treat? Oral Oncology, 33 (5): 317-321, 1997.

312.Collaborative group on hormonal factors in breast cancer. Breast Cancer and Hormone Replacement Therapy. Lancet, 350: 1047-1059, 1997

313.Zakelj M., Robertson C., Boyle P., Hsieh C., Effect of Parity and age at delivery on breast cancer risk in slovenian Women aged 25-54, , Int. J Cancer, 73:1-9, 1997 (3.403)

314.Boyle P. Editorial: Epidemiology of scientific misconduct. J. Epi. Bio., 2(2): 61-63, 1997.

315.Boyle P., Maisonneuve P., Napalkov P. Commentary: Urological cancers: epidemiological overview of a neglected problem. J. Epi. Bio., 2 (3):125-145, 1997.

316.Boyle P. Editorial. Gynaecological cancer survival: monitoring international and temporal variation. J Epi Bio, 2 (4): 185-186, 1997.

317.Boyle P. Cancer, Cigarette Smoking and premature death in Europe. In: European Strategy to promote Health and non-smoking. Europe Against Cancer. High level Cancer Experts Committee. Consensus Conference on Tobacco, Helsinki, October 2nd, 1996. Oy Edita AB, Helsinki 1997.

318.Robertson C. and Boyle P. Statistical Modelling of Breast Cancer Incidence and Mortality Rates in Scotland. Brit J Cancer, 76 (9): 1248-1252, 1997

319.Franklyn J.A., Maisonneuve P., Sheppard M.C., Betteridge J., Boyle P. Mortality after the Treatment of Hyperthyroidism with Radioactive Iodine. New Engl J Med, 338: 712-8, 1998.

320.LaVecchia C, Negri E, Levi F, Lucchini, Boyle P.Cancer Mortality in Europe: Effects of age, Cohort of Birth and Period of Death. Eur J Cancer, 34 (1): 118-141, 1998.

321.Alexander F., Boyle P., Carli P.M., Coebergh J.W., Draper G., Ekbom A., Levi F., McKinney P.A., McWhirter W., Magnani C., Michaelis J., Olsen J.H., Peris-Bonet R., Petridou E., Pukkala E., Terracini B., Vatten L. on behalf of the EUROCLUS project. Spatial Temporal Patterns in Childhood Leukaemia: further evidence for an infectious origin. Brit J Cancer, 77:812-817, 1998 (IF 3.666)

322.Decensi A., Bonanni B., Guerrieri-Gonzaga A., Gandini S., Robertson C., Johansson H., Travaglini R., Sandri M.T., Tessadrelli A., Farante G., Salinaro F., Bettega D., Barreca A., Boyle P., Costa A., Veronesi U. Biologic activity of Tamoxifen at low doses in healthy women. JNCI, 90 (19): 1461-1468, 1998

323.Alexander F., Boyle P., Carli P.M., Coebergh J.W., Draper G., Ekbom A., Levi F., McKinney P.A., McWhirter W., Michaelis J., Peris-Bonet R., Petridou E., Pompe-Kirn V., Plesko I., Pukkala E., Rahu M., Storm H., Terracini B., Vatten L., Wray N. on behalf pf the EUROCLUS project. Spatial Clustering of Childhood Leukaemia: Summary Results from the EUROCLUS project. Brit J Cancer , 77:818-824, 1998 (IF 3.666)

324.Robertson C. and Boyle P. Statistical Modelling of Breast Cancer Incidence and Mortality Rates in Scotland. Brit J Cancer, 76 (9): 1248-1252, 1997

325.LaVecchia C, Negri E, Levi F, Lucchini, Boyle P. Cancer Mortality in Europe: Effects of age, Cohort of Birth and Period of Death., Eur J Cancer, 34 (1); 118-141, 1998.

326.Mezzetti M., La Vecchia C., Decarli A., Boyle P., Talamini R., Franceschi S. Population Attributable risk for breast cancer : diet, nutrition and physical exercise. J Natl Cancer Inst, 90: 389-94, 1998.

327.Calabrese L., Tradati N., Nickolas T.L., Giugliano G., Zurrida S., Scully C., Boyle P., Chiesa F. Review. Cancer screening in otorhinolaryngology. European J Cancer, 34: 1-4, 1998

328.Robertson C., Boyle P. Modeling Temporal Aspects of an Exposure *(Letter).* Epidemiology, 9 (3): 361-362, 1998.

329.Dore J-F., Maisonneuve P., Cattaruzza M.S., Autier P., Cochran A.J., Boyle P. A molecular epidemiological approach to the study of expression of a metastasis marker in primary melanomas and its correlation with individual patients's risk of recurrence or metastasis. Melanoma Research, Suppl. 7(2): 121-125, 1997.

330.Ghadirian P, Lacroix A, Perret C, Robidoux A, Falardeau M, Maisonneuve P, Boyle P. Breast Cancer Risk and Nutrient Intake Among French Canadians in Montreal: a Case Control Study.The Breast, 7: 108-113, 1998

331.Boyle P. Osservazioni relative all'epidemiologia della ritenzione urinaria acuta. (Some Remarks on the Epidemiology of Acute Urinary Retention). Archivio Italiano Urologia Andrologia, spec.-suppl al n. 2, 1998.

332.Robertson C., Boyle P. Age-Period-Cohort of Chronic Disease Rates - I Modelling Approach. Statist. Med., 17: 1305-1323, 1998.

333.Bartsch H, Malaveille C., Lowenfels A.B., Maisonneuve P., Hautefeuille A., Boyle P. and the International Pancreatic Disease Study Group. Genetic polymorphism of N-acetyltransferases, glutathione S-transferase M1 and NAD(P)H: quinone oxidoreductase in relation to malignant and benign pancreatic disease risk. Eur J of Cancer Prevention, 7: 215-223, 1998.

334.Veronesi U., Maisonneuve P., Costa A., Sacchini V., Maltoni C., Robertson C., Rotmensz N., Boyle P. on behalf of the Italian Tamoxifen Study Group. Prevention of Breast cancer with Tamoxifen. The Italian Randomised Trial among Hysterectomised women. The Lancet, 352: 93-97, 1998.

335.Boyle P., Autier P. Editorial: Colorectal Cancer Screening. Health policy or a continuing Research Issue? Annals of Oncology, 9:581-584, 1998.

336.Robertson C. and Boyle P. Age-Period-Cohort of Chronic Disease Rates - II Graphical Approaches. Statist. Med., 17:1325-1340, 1998.

337.Robertson C., Boyle P. Age at any birth and Breast Cancer Risk. Stat.Med., 17: 431-445, 1998. (IF 1.250)

338.Decensi A., Robertson C., Rotmensz N., Severi G., Maisonneuve P., Sacchini V., Boyle P., Costa A., Veronesi U. on behalf of the Italian Chemoprevention Group. Effect of Tamoxifen and Transdermal hormone replacemente therapy on cardiovascular risk factors in a prevention trial. Brit. J. Cancer, 78(50): 572-578, 1998.

339.Gray N., Boyle P., Zatonski W. Tar concentrations in cigarettes and carcinogen content. Lancet, 352:787-788, 1998.

340.Levi F., Lucchini F., Boyle P., Negri E., La Vecchia C. Cancer Incidence and mortality in Europe, 1988-92. J. Epi. Bio, 3(3), Suppl, 1998.

341.Autier P., Boyle P., J.F.Dore'. Letter: Sorting the hype from the facts in melanoma. Lancet, 352: 738-739, 1998.

342.Boyle P., Horton R., Radda G., Sharp D., Veronesi U., Walker A.M. Open debate on HRT. Lancet, 352:836, 1998.

343.Ghadirian P., Maisonneuve P., Perret C., Lacroix A., Boyle P. Epidemiology of sociodemographic characteristics, lifestyle, medical history and colon cancer: A case-control study among French Canadians in Montreal. Cancer Detect. Prev. 22 (5): 396-404, 1998

344.Boyle P., Keech M., Nonis A., Fourcade R., Hobbs R., Kiemeney L.A.M., Lee Chungwook., Maier W., Watson M., Robertson C. The UrEpik Study: A cross-sectional survey of benign prostatic hyperplasia, urinary incontinence and male erectile dysfunction, prostatitis and interstitial cystitis in the United Kingdom, France, the Netherlands and Korea. J Epi Bio, 3 (2):179-187, 1998.

345.Ghadirian P., Lacroix A., Perret C., Maisonneuve P., Boyle P. Sociodemographic characteristics, smoking, medical and family history and breast cancer. Cancer Detection and Prevention, 22 (6): 485-494, 1998

346.Boyle P. Prostate Specific Antigen (PSA) testing as screening for prostate cancer. The Current Controversy. Ann. Oncol., 9:1263-1264, 1998. (IF 2,736)

347.Boyle P. Expanding on epidemiology's first principles. Book review: Modern Epidemiology by K. Rothman et al. Lancet, 352:1635-1636, 1998

348.Langman MJS, Boyle P. Chemoprevention of Colorectal Cancer. Gut, 43(4): 578-585, 1998

349.Girman C.J., Jacobsen S.J., Tsukamoto T., Richard F.,Garraway M., Sagnier P.P, Guess H.A., Rhodes T., Boyle P., Lieber M.M. Health-Related quality of life associated with lower urinary tract symptoms in four countries. Urology, 51:428-436, 1998

350.Denis L., Pagano F., Nonis A., Robertson C., Romano P., Boyle P. A double-blind placebo-controlled trial to assess the efficacy and tolerability of Mepartricin in the treatment of BPH. Prostate, 37:246-252, 1998 IF 2.552

351.Veronesi U., Maisonneuve P., Costa A., Rotmensz N., Boyle P. Drop-outs in Tamoxifen Prevention Trials. Lancet, 353:244,1999

352.Boyle P, Maisonneuve P, Autier P. Towards cancer control in women. J Epi Bio, 3(1):137-168, 1998

353.Boyle P. Epidemiology of Lung Cancer: a century of great success and ignominious failure. Respiratory Care Matters, 3 (4): 8-9, 1999.

354.Roehrborn C.G., Boyle P., Gould L., Waldstreicher J. Serum prostate-specific antigen as a predictor of prostate volume in men with BPH. Urology, 53(3)581-589, 1999.

355.Boyle P., La Vecchia C. Editorial: Preparing for the Millennium. J Epi Bio, 4 (1): 1-2, 1999.

356.Boyle P, Severi G. Epidemiology of Prostate Cancer Chemoprevention. Eur Urol, 35: 370-376, 1999.

357.Kirby R., Robertson C., Griffiths K., Denis L.J., Boyle P. Finasteride in association with either Flutamide or Goserelin as Combination Hormonal Therapy in Patients with stage M1 Carcinoma of the prostate. Prostate 1999; 40: 105-114

358.Alexander F.E., Boyle P., Carli M., Coebergh J.W., Ekbom A., Levi F., McKinney P.A., McWhirter W., Michaelis J., Peris-Bonet R., Petridou E., Pompe-Kirn V., Plesko I., Pukkala E., Rahu M., Stiller C.A., Storm H., Terracini B., Vatten L., Wray N., on behalf of the EUROCLUS project. Population density and childhood leukaemia: results of the EUROCLUS study. Eur J Cancer, 1999; 35 (3): 439-444.

359.Zheng T., Holford T.R., Mayne S.T., Owens P.H., Ward B., Carter D., Dubrow R., Zahm S.H., Tessari J D.and Boyle P. Environmental exposure to hexachlorobenzene (HCB) and risk of female breast cancer in Connecticut, USA. Cancer Epidemiology and Biomarkers 1999; 8: 407-411

360.Franklyn J.A., Maisonneuve P., Sheppard M., Betteridge J., Boyle P. Cancer Incidence and mortality after radioiodine treatment for hyperthyroidism: a population-based cohort study. The Lancet, 353: 2111-2115, 1999

361.Maisonneuve P., Agodoa L., Gellert R., Stewart J.H., Buccianti G., Lowenfels A.B., Wolfe R.A., Jones E., Disney A., Briggs D., McCredie M., Boyle P. Cancer in end stage renal disease patients undergoing dialysis: results from an international collaborative study. Lancet, 1999; 354: 93-96.

362.Clinical Synthesis Panel on HRT. Clinical Synthesis Conference on Hormonal; Replacement Therapy. Lancet 1999; 354: 152-156

363.Maisonneuve P., Agodoa L., Gellert R., Stewart J.H., Buccianti G., Lowenfels A.B., Wolfe R.A., Jones E., Disney A.P., Briggs D., McCredie M., Boyle P. Cancer in patients on dialysis for end-stage renal disease: an international collaborative study. Lancet, 354: 93-99, 1999

364.Zheng T., Holford T.R., Mayne S.T., Owens P.H., Ward B., Carter D., Dubrow R., Zahm S.H., Boyle P Tessari J.,. B-Benzene Hexachloride in Breast cancer adipose tissue and risk of breast carcinoma. Cancer Cancer, 85(10): 2212-2216, 1999.

365.Lowenfels A.B., Maisonneuve P., Boyle P., Zatonski W.A. Epidemiology of gallbladder cancer. Hepato-gastroenterology, 46:1529-1532, 1999

366.Clinical Synthesis Panel on HRT. Clinical Synthesis Conference: Hormone replacement therapy. Lancet, 354: 152-155, 1999

367.Robertson C., Gandini S.and Boyle P. Age-Period-Cohort Models: A Comparative Study of Available Methodologies. Journal of Clinical Epidemiology, 52 (6): 569-583, 1999

368.Levi F., Lucchini F., Negri E., Boyle P. and La Vecchia C. Cancer Mortality in Europe, 1990-1994, and an Overview of Trends from 1955 to 1994. The European Journal of Cancer, 35 (10) 1477-1516, 1999.

369.Gray N., Zatonski W., Boyle P. Regulation of carcinogens in cigarettes. The Lancet, 18 (354): 1036, 1999

370.Roehrborn C.G., Boyle P., Bergner D., Gray T., Gittelman M., Shown T., Melman A., Bracken RB., de Vere White R., Wang D., Waldstreicher J. Serum prostate-specific antigen and prostate volume predict long-term changes in symptoms and flow rate: results of a four-year, randomised trial comparing Finasteride versus placebo (PLESS Study Group). Urology 54: 662-669, 1999.

371.Zheng T., Holford TR., Mayne ST., Ward B., Carter D., Owens PH., Dubrow R., Zahn SH., Boyle P., Archibeque S., Tessari J. DDE and DDT in breast adipose tissue and risk of female breast cancer. Am J Epidemiol, 150(5): 453-8, 1999

372.Levi F., Lucchini F., Negri E., Boyle P. and La Vecchia C. Cancer Mortality in Europe, 1990-1994, and an Overview of Trends from 1955 to 1994. The European Journal of Cancer, 35: (10) 1477-1516, 1999.

373.Franceschi S., Levi F., Conti E., Talamini R., Negri E., Dal Maso L., Boyle P., Decarli A., La Vecchia C. Energy Intake and Dietary Pattern in Cancer of the Oral Cavity and Pharynx. Cancer Causes and Control, 10: 439-444, 1999.

374.Boyle P, Horton R, Walker AM, Sharp D and Delmas P. Clinical Synthesis Meeting on Osteoporosis. Lancet 1999; Nov 13;354(9191):1664.

375.Severi G, Plesko I, Robertson C, Obsitnikova A and Boyle P. Larynx cancer in Slovakia and the role of anatomical sites. Oral Oncology 1999; 35: 564-570

376.Clinical Synthesis Panel on HRT. Editorial: Hormone Replacement Therapy. Journal of Epidemiology and Biostatistics, 4 (3): 123-128, 1999.

377.Maisonneuve P., Agodoa L., Gellert R., Stewart J.H., Buccianti G., Lowenfels A.B., Wolfe R.A., Jones E., Disney A.P., Briggs D., McCredie M., Boyle P.

Distribution of primary renal diseases leading to end stage renal failure in the United States, Europe, and Australia and New Zealand: results from an International comparative study. Am. J. of Kidney Diseases, 2000: 35(1): 157-165.

378.Gandini S., Merzenich H., Robertson C., Boyle P. Review on diet and breast cancer risk: the role of vegetables and fruits consumption and related vitamins. European Journal of Cancer 2000; 36(5): 636-646.

379.Boyle P., Robertson C., Lowe F., Roehrborn C. Meta-analysis of clinical trials of Permixon in the treatement of BPH. Urology, 2000; 55(4): 533-539.

380.Zheng T, Holford TR, Mayne ST, Tessari J, Ward B, Carter D, Owens PH, Boyle P, Dubrow R, Archibeque-Engle S, Dawood O, Zahm SH. Risk of female breast cancer associated with serum polychlorinated biphenyls and 1,1-dichloro-2,2'-bis(p-chlorophenyl)ethylene. Cancer Epidemiol Biomarkers Prev. 2000 Feb;9(2):167-74.

381.Zheng T, Holford TR, Mayne ST, Owens PH, Zhang B, Boyle P, Carter D, Ward, B, Zhang Y, Zahm SH. Exposure to electromagnetic fields from use of electric blankets and other in-home electrical appliances and breast cancer risk. Amer J Epidemiol 2000 Jun 1;151(11):1103-11.

382.Severi G, Giles GG, Robertson C, Boyle P, Autier P. Mortality from cutaneous melanoma: evidence for contrasting trends. Br J Cancer 2000 Jun;82(11):1887-91

383.Boyle P, Langman JS. Epidemiology. BMJ. 2000 Sep 30;3 21(7264):805-808.

384.Autier P, Severi G, Boyle P, Dore JF. More About: Sunscreen Use and Duration of Sun Exposure: a Double-Blind, Randomized Trial. J Natl Cancer Inst. 2000 Sep 20;92(18):1532-1533.

385.Boyle P, Maisonneuve P, Autier P. Update on cancer control in women. Int J Gynaecol Obstet. 2000 Aug;70(2):263-303.

386.Zheng T, Holford TR, Tessari J, Mayne ST, Owens PH, Ward B, Carter D, Boyle P, Dubrow R, Archibeque-Engle S, Zahm SH. Breast cancer risk associated with congeners of polychlorinated biphenyls. Am J Epidemiol. 2000 Jul 1;152(1):50-8.

387.Gray NJ, Zaridze DG, Robertson C, Krivosheeva L, Sigacheva N, Boyle P, and the International Cigarette Variation Group. Variation within global cigarette brands in tar, nicotine, and certain nitrosamines: analytic study. Tobacco Control 2000; 9: 351-352

388.Boyle P., Gandini S., Robertson C., Zatonski W., Fagerstrom K., Slama K., Kunze M. Gray N. and the International Smokers Survey Group. Characteristics of Smokers'Attitudes Towards Stopping: Survey of 10,295 Smokers in Representative Samples from 17 European Countries. Eur J Publ Health 10: 5-14, 2000

389.Plesko I., Severi G., Obsitnikova A., Boyle P. Trends in the incidence of non-melanoma skin cancer in Slovakia, 1978-1995. Neoplasma, 47:132-147, 2000

390.Sonke G.S., Kolman D., de la Rosette J.J., Donkers L., Boyle P., Kiemeney L.A.L.M. Prevalentie van lagere urinewegsymptomen bij mannen en de invloed op hun kwaliteit van leven: de Boxmeer studie" (Prevalence of LUTS among men and influence on their QoL: the Boxmeer study. The Netherlands Tijdschrift voor Geneesunke. *Ned Tijdschr Geneeskd* 2000 Dec 30;144(53):2558-63

391.Ghadirian P., Maisonneuve P., Perret C., Kennedy G., Boyle P., Krewski D., Lacroix A. A case-control study of toenail selenium and cancer of the breast, colon and prostate. Cancer Detection and Prevention 24:305-313, 2000.

392.Zheng T, Holford, Tr Tessari, J. Mayne St., Zahm Sh., Owens Ph., Zhang B., Ward B., Carter D., Zhang Y., Zhang W., Dubrow R. Boyle P. Oxychlordane and trans-nonachlor in breast adipose tissue and risk of female breast cancer. J. Epi. Bio, 5: 153-160, 2000.

393.Gray N., Boyle P. The Regulation of Tobacco and Tobacco Smoke. Ann. Oncol., 11:909-914, 2000.

394.Boyle P, Bellanti JA and Robertson C. Meta-analysis of published clinical trials of Ribosomal vaccine (Ribomunyl) in prevention of respiratory infections. BioDrugs 2000; 145 (6): 389-408.

395.Holford TR, Zheng T, Mayne ST, Zahm SH, Tessari JD, Boyle P. Joint effects of nine polychlorinated biphenyl (PCB) congeners on breast cancer risk. *Int J Epidemiol* 2000 Dec;29(6):975-82

396.Robertson C, Perone C, Primic-Zakelj M, Kirn VP, Boyle P. Breast cancer incidence rates in Slovenia 1971-1993. *Int J Epidemiol* 2000 Dec;29(6):969-74

397.Levi F, La Vecchia C, Boyle P. The rise and fall of prostate cancer. *Eur J Cancer Prev* 2000 Dec;9(6):381-5

398.Gray N., Boyle P. Tobacco Industry must not dump its high nitrosamine tobacco on poor countries. BMJ, 2001; 322:557.

399.Kubik A, Zatloukal P, Boyle P, Robertson C, Gandini S, Tomasek L, Gray N, Havel L. A case-control study of lung cancer among Czech women. *Lung Cancer* 2001 Mar;31(2-3):111-118

400.Fagerstrom K, Boyle P, Kunze M and Zatonski W. The anti-smoking climate in EU countries and Poland. Lung Cancer. 2001 Apr;32(1):1-5.

401.Franceschi S, Dal Maso L, Augustin L, Negri E, Parpinel M, Boyle P, Jenkins DJ, La Vecchia C. Dietary glycemic load and colorectal cancer risk. Ann Oncol. 2001 Feb;12(2):173-8.

402.Meuleman EJ, Donkers LH, Robertson C, Keech M, Boyle P, Kiemeney LA. Ned Tijdschr Geneeskd. 2001 Mar 24;145(12):576-81. Dutch.

403.Boyle P, Gandini S, Baglietto S, Severi G and Robertson C. Epidemiology of Prostate Cancer. European Urology 2001: 39: 2-3.

404.Sasieni P, Cuzick J, Boyle P, Hince T, Kitchener H, Lilleyman J, McEwen J, Miles R, Roche M, Slevin MM, Vessey M, Wald N, Wilkins N and Young N. Routine audit is an ethical requirement of screening . Brit Med J 2001; 322:1179.

405.Zheng T, Holford TR, Mayne ST, Owens PH, Zhang Y, Zhang B, Boyle P, Zahm SH. Lactation and breast cancer risk: a case-control study in Connecticut. Br J Cancer 2001 Jun;84(11):1472-6.

406.Boyle P, Leon M, Autier P. Epidemiology of Osteoporosis. J Epidemiol Biostat 2001;6(2):185-92.

407.Levi F, La Vecchia C, Boyle P, Lucchini F, Negri E. Western and eastern European trends in testicular cancer mortality. Lancet 2001 Jun 9;3 57 (9271):1853-4.

408.Parle JV, Maisonneuve P, Sheppard MC, Boyle P, Franklyn JA. Prediction of all-cause and cardiovascular mortality in elderly people from one low serum thyrotropin result: a 10-year cohort study. Lancet 2001 Sep 15;358(9285):861-5

409.Giles GG, Severi G, McCredie MR, English DR, Johnson W, Hopper JL, Boyle P. Smoking and prostate cancer: findings from an Australian case-control study. Ann Oncol 2001 Jun;12(6):761-5

410.Robertson C, Van Den Donk M, Primic-Zakelj M, MacFarlane T and BoyleP. The association between induced and spontaneous abortion and risk of breast cancer in Slovenian women aged 25-54. The Breast 2001; 10: 291-198.

411.Bartsch G, Horninger W, Klocker H, Reissigl A, Oberaigner W, Schonitzer D, Severi G, Robertson C, Boyle P. Prostate cancer mortality after introduction of prostate-specific antigen mass screening in the Federal State of Tyrol, Austria. Urology 2001 Sep;58(3):417-24

412.Boyle P, Robertson C, Manski R, Padley RJ, Roehrborn CG. Meta-analysis of randomized trials of terazosin in the treatment of benign prostatic hyperplasia. Urology 2001 Nov; 58 (5):717-722.

413.Roehrborn CG, Bartsch G, Kirby R, Andriole G, Boyle P, de la Rosette J, Perrin P, Ramsey E, Nordling J, De Campos Freire G, Arap S. Guidelines for the diagnosis and treatment of benign prostatic hyperplasia: a comparative, international overview. Urology 2001 Nov;58 (5):642-50

414.Levi F, Lucchini F, Negri E, Boyle P and La Vecchia C. Changed trends of cancer mortality in the elderly. Annals Oncology 2001; 12: 1467-1477.

415.Boyle P and Zheng T. Environmental factors influencing the epidemiology of breast cancer. The Breast 2001; 10 (supp 3): 1-8.

416.Plesko I, Severi G, Obsitnikova A, Boyle P and Kubik A. Lung cancer incidence rates by histologic type: an example of trends in Eastern Europe--Slovakia 1978-95. Neoplasma. 2001;48(4):247-53.

417.Collaborative Group on Hormonal Factors in Breast Cancer (includes P Boyle). Familial breast cancer: collaborative reanalysis of individual data from 52 epidemiological studies including 58,209 women with breast cancer and 101,986 women without the disease. Lancet 2001 Oct 27;358(9291):1389-99

418.Fourcade RO, Chauvin I, Gaudin AF, Mazzetta C, Boyle P. [Frequency of Nocturia in Auxerre, France: the UrEpiK study]. Prog Urol 2001;11(6):1251-8.

419.Fourcade RO, Gaudin AF, Mazzetta C, Robertson C, Boyle P. [Prevalence of LUTS and Incontinence in the Auxerre, France: the UrEpiK study]. Presse Med 2002;31(5):202-10

420.Gray N and Boyle P. Regulation of cigarette emissions. Ann Oncol 2002 Jan;13(1):19-21

421.Boyle P. Faecal occult blood testing (FOBT) as screening for colorectal cancer: the current controversy. Ann Oncol 2002 Jan;13(1):6-8

422.Parle JV, Maisonneuve P, Sheppard MC, Boyle P and Franklyn JA. Mortality in elderly patients with subclinical hypertension. Lancet 2002 Mar 2;359(9308):799

423.Veronesi U, Maisonneuve P., Sacchini V., Rotmensz N., Boyle P Tamoxifen for breast cancer among hysterectomised women. Lancet 2002; 359: 1122-4.

424.Filippini G, Maisonneuve P, McCredie M, Peris-Bonet R, Modan B, Preston-Martin S, Mueller BA, Holly EA, Cordier S, Choi NW, Little J, Arslan A, Boyle P. Relation of childhood brain tumors to exposure of parents and children to tobacco smoke:

The Search international case-control study. Int J Cancer. 2002 Jul 10;100(2):206-13.

425.Debruyne F, Koch G, Boyle P, Da Silva FC, Gillenwater JG, Hamdy FC, Perrin P, Teillac P, Vela-Navarrete R, Raynaud JP. Comparison of a Phytotherapeutic Agent (Permixon) with an alpha-Blocker (Tamsulosin) in the Treatment of Benign Prostatic Hyperplasia: A 1-Year Randomized International Study. Eur Urol. 2002 May;41(5):497-507.

426.Giles GG, Severi G, Sinclair R, English DR, McCredie MR, Johnson W, Boyle P, Hopper JL. Related Articles Androgenetic alopecia and prostate cancer: findings from an Australian case-control study. Cancer Epidemiol Biomarkers Prev. 2002 Jun;11(6):549-53.

427.Collaborative Group on Hormonal Factors in Breast Cancer (includes P Boyle). Breast cancer and breastfeeding: collaborative reanalysis of individual data from 47 epidemiological studies in 30 countries, including 50302 women with breast cancer and 96973 women without the disease. Lancet. 2002 Jul 20;360(9328):187-95.

428.Zheng T, Holford TR, Mayne ST, Owens PH, Boyle P, Zhang B, Zhang YW, Zahm SH. Use of hair colouring products and breast cancer risk. a case-control study in Connecticut. Eur J Cancer 2002 Aug;38(12):1647-52

429.Levi F, Lucchini F, Negri E, Boyle P, Vecchia CL. Trends in mortality from Hodgkin's disease in western and eastern Europe. Br J Cancer 2002 Jul 29;87(3):291-3

430.Debruyne F, Koch G, Boyle P, Da Silva FC, Gillenwater JG, Hamdy FC, Perrin P, Teillac P, Vela-Navarrete R, Raynaud JP; groupe d'etude PERMAL. [Comparison of a Phytotherapeutic Agent (Permixon) with an alpha-Blocker (Tamsulosin) in the Treatment of Benign Prostatic Hyperplasia: A 1-Year Randomized International Study][In French] : Prog Urol 2002 Jun;12(3):384-92

431.Zheng T, Holford TR, Taylor Mayne S, Luo J, Hansen Owens P, Hoar Zahm S, Zhang B, Zhang Y, Zhang W, Jiang Y and Boyle P. A case-control study of occupation and breast-cancer risk in Connecticut. J Cancer Epidemiol Prev. 2002;7(1):3-11.

432.Roehrborn C, Boyle P, Nickel J, Hoefner K and Andriole G. Efficacy and safety of a dual inhibitor of 5-alpha-reductase types 1 and 2 (dutasteride) in men with benign prostatic hyperplasia. Urology. 2002 Sep;60(3):434.

433.Zheng T, Holford TR, Zahm SH, Owens PH, Boyle P, Zhang Y, Wise JP Sr, Stephenson LP and Ali-Osman F. Cigarette smoking, glutathione-s-transferase M1

and t1 genetic polymorphisms, and breast cancer risk (United States). Cancer Causes Control. 2002 Sep;13(7):637-45.

434.Rotmensz N, Decensi A, Maisonneuve P, Costa A, Sacchini V, Travaglini R, D'Aiuto G, Lovison F, Gucciardo G, Muraca MG, Pizzichetta MA, Conforti S, Robertson C, Boyle P, Veronesi U.Rationale for a study adding tamoxifen to HRT. Eur J Cancer. 2002 Sep;38(S6):22-23

435.Boyle P. Current Situation of Screening for Cancer. Ann Oncol. 2002;13 Suppl 4:189-98.

436.Collaborative Group on Hormonal Factors in Breast Cancer (includes P Boyle). Alcohol, tobacco and breast cancer - collaborative reanalysis of individual data from 53 epidemiological studies, including 58 515 women with breast cancer and 95 067 women without the disease. Brit J Cancer 2002; 87: 1234-1246.

437.La Vecchia C, Bruzzi P, Decarli A, Gaboardi F, Boyle P. An estimate of prostate cancer prevalence in Italy. Tumori 2002 Sep-Oct;88(5):367-9.

438.Veronesi U, Maisonneuve P, Rotmensz N, Boyle P Tamoxifen for breast cancer in hysterectomised women. : Lancet 2002;360(9347):1785

439.Boyle P, Leon ME. Epidemiology of colorectal cancer. Br Med Bull 2002;64:1-25

440.Trabattoni D, Bartorelli AL, Montorsi P, Fabbiocchi F, Loaldi A, Galli S, Ravagnani P, Cozzi S, Grancini L, Liverani A, Leon ME, Robertson C, Boyle P. Comparison of outcomes in women and men treated with coronary stent implantation. Catheter Cardiovasc Interv 2003 Jan;58(1):20-8

441.Stewart JH, Buccianti G, Agodoa L, Gellert R, McCredie MR, Lowenfels AB, Disney AP, Wolfe RA, Boyle P, Maisonneuve. Cancers of the kidney and urinary tract in patients on dialysis for end-stage renal disease: analysis of data from the United States, Europe, and Australia and New Zealand. J Am Soc Nephrol 2003 Jan;14(1):197-207

442.Giles GG, Severi G, English DR, McCredie MR, MacInnis R, Boyle P, Hopper JL. Early growth, adult body size and prostate cancer risk. : Int J Cancer 2003 Jan 10;103(2):241-5

443.Veronesi U, P Maisonneuve, N Rotmensz, A Costa, V Sacchini, R Travaglini, G D'Aiuto, F Lovison, G Gucciardo, MG Muraca, MA Pizzichetta, S Conforti, A Decensi, C Robertson and P Boyle on behalf of the Italian Tamoxifen Study group. Tamoxifen and the prevention of hormonally dependent breast cancer in higher risk women : The Italian Randomized Trial Among Hysterectomized Women. J Natl Cancer Inst 2003; 95: 160-165.

444.Cuzick J, Powles T, Veronesi U, Forbes J, Edwards R, Ashley S and Boyle P. Overview of main Outcomes in Breast Cancer Prevention Trials. Lancet 2003; 361: 296-300.

445.Boyle P. Screening. Eur J Respirator Disease 2003 ; 21: 3s-16s

446.Zheng T, Holford TR, Zahm SH, Owens PH, Boyle P, Zhang Y, Zhang B, Wise JP, Stephenson LR and Ali-Osman F. Glutathione S-transferase M1 and T1 genetic polymorphisms, alcohol consumption and breast cancer risk. Brit J Cancer 2003; 88: 58-62.

447.Kirby R.S., Altwein J.E., Bartsch G., Boyle P., Jardin A., Roehrborn C., Cary M.M., Sweeney M., Grossman E.B. The Efficacy and Tolerability of Doxazosin and Finasteride, Alone or in combination, in the Treatment of Symptomatic Benign Prostatic Hyperplasia: Results of the Prospective European Doxazosin and Comination Therapy (PREDICT) Trial. Urology 2003 Jan;61(1):119-26.

448.Boyle P, Golia S, Daly P, Johnston P and Robertson C. Cancer Mortality in Ireland. Ann Oncol 2003;14:323-32.

449.Levi F, Lucchini F, Negri E, Boyle P and La Vecchia C. Mortality from major cancer sites in the European Union, 1955-1998. Ann Oncol 2003 Mar;14(3):490-5

450.Levi F, Lucchini F, Boyle P, Negri E and La Vecchia C. Testicular Cancer Mortality in Eastern Europe. Int J Cancer 2003 (Jul 1);105(4):574

451.Levi F, Lucchini F, Negri E, Boyle P and La Vecchia C. Recent trends in mortality from benign prostatic hyperplasia. The Prostate 2003 Aug 1;56(3):207-11.

452.Boyle P, Severi G and Giles GG. Epidemiology of Prostate Cancer. Urol. Clinics North America 2003 May;30(2):209-17.

453.Boyle P. Global Summit on Mammographic Screening. (Editorial) Annals Oncology 2003 Aug;14(8):1159-60.

454.Giles GG, Severi G, English DR, McCredie MRE, Borland R, Boyle P and Hopper JL. Sexual factors and prostate cancer. BJU Int 2003; 92: 211-216.

455.Severi G, Giles GG, Southey MC, Tesoriero A, Tilley W, Nufing, Morris H, English DR, McCredie MRE, Boyle P and Hopper JL. No association between *ELAC2/HPC2* polymorphisms and serum prostate-specific antigen level or prostate cancer. J Natl Cancer Inst 2003 Jun 4;95(11):818-24

456.Boyle P Screening for Prostate Cancer - Have you had your cholesterol measured? BJU Int 2003; 92: 191-200.

457.Boyle P, d'Onofrio A, Maisonneuve P, Severi G, Robertson C, Tubiana M and Veronesi U. Measuring Progress Against Cancer In Europe: Has the 15% Decline targeted for 2000 come about? Annals Oncology 2003; 14: 1312-1325.

458.Boyle P, Autier P, Bartelink H, Baselga J, Boffetta P, Burn J, Burns HJG, Christensen L, Denis L, Dicato M, Diehl V, Doll R, Franceschi S, Gillis CR, Gray N, Gricuite L, Hackshaw A, Kasler M, Kogevinas M, Kvinnsland S, La Vecchia C, Levi F, McVie JG, Maisonneuve P, Martin-Moreno JM, Newton Bishop J, Oleari F, Perrin P, Richards M, Ringborg U, Siracka E, Quinn M, Storm H, Tubiana M, Tursz T, Veronesi U, Wald N, Weber W, Zaridze DG, Zatonski W and zur Hausen H. European Code Against Cancer and Scientific Justification: Third Version (2003). Annals Oncol 2003; 14: 973-1005.

459.Quinn MJ, d'Onofrio A, Møller B, Black R, Martinez-Garcia C, Møller H, Rahu M, Robertson C, Schouten L, La Vecchia C and Boyle P. Cancer Mortality Trends in the EU and Acceeding States up to 2015. Annals Oncol 2003; 14: 1148-1152.

460.O'Leary MP, Roehrborn C, Andriole G, Nickel C, Boyle P and Hofner K. Improvements in benign prostatic hyperplasia-specific quality of life with dutasteride, the novel dual 5alpha-reductase inhibitor. BJU Int. 2003 Aug;92(3):262-266

461.Autier P, Boyle P, Buyse M, Bleiberg H. Is FOB screening really the answer for lowering mortality in colorectal cancer? Recent Results Cancer Res. 2003;163:254-63

462.Veronesi U, Maisonneuve P, Rotmensz N, Decensi A, Viale G and Boyle P. Re: Italian Randomized Trial Among Women with Hysterectomy: Tamoxifen and Hormone-Dependent Breast Cancer in High-Risk Women. The Authors Response. J Natl Cancer Inst 2003; 95: 918-919

463.Pastorino U, Bellomi M, Landoni C, DE Fiori E, Arnaldi P, Picchio M, Pelosi G, Boyle P and Fazio F. Early lung-cancer detection with spiral CT and positron emission tomography: two years results. Lancet 2003; 362: 593-597.

464.Boyle P and Fitzpatrick JM. Prevalence of Benign Urological Disease in Communities. BJU Int. 2003 Sep;92(4):342-3

465.Boyle P, Robertson C, Mazzetta C, Keech M, Hobbs R, Fourcade R, Kiemeney L, Lee C and the UrEpiK Study Group. The prevalence of lower urinary tract symptoms in men and women in four centres. The UREPIK study. BJU Int. 2003 Sep;92(4):409-414

466.Boyle P, Robertson C, Mazzetta C, Keech M, Hobbs R, Fourcade R, Kiemeney L, Lee C and the UrEpiK Study Group.. The relationship between lower urinary tract

symptoms and health status The UREPIK study. BJU Int. 2003 Oct;92(6):575-580.

467.Boyle P, Robertson C, Mazzetta C, Keech M, Hobbs R, Fourcade R, Kiemeney L, Lee C and the UrEpiK Study Group. The association between Lower Urinary Tract Symptoms and Erectile Dysfunction across four centers. The UREPIK study. BJU Int. 2003 Nov;92(7):719-725.

468.Boyle P, Robertson C, Mazzetta C, Keech M, Hobbs R, Fourcade R, Kiemeney L, Lee C and the UrEpiK Study Group.. The prevalence of male urinary incontinence across four centres The UREPIK study. BJU Int. 2003 Dec;92(9):943-947

469.Boyle P, Diehm C and Robertson C. Meta-analysis of Clinical Trials of Cyclo 3 Fort in the Treatment of Chronic Venous Insufficiency. Int Angiol. 2003 Sep;22(3):250-62

470.Gray N and Boyle P. The Future of the Nicotine Addiction Market. (Commentary) Lancet 2003 Sep 13;362(9387):845-6.

471.Boyle P. Tobacco control, screening, and collaboration are priorities for IARC, incoming director says. Interview with Peter Boyle. J Natl Cancer Inst. 2003 Nov 19;95(22):1653-5

472.Rosen R, Altwein J, Boyle P, Kirby RS, Lukacs B, Meuleman E, O'Leary MJ, Puppo P, Robertson C and Giuliano F. Lower Urinary Tract Symptoms and Male Sexual Dysfunction: The Multinational Survey of the Ageing Male (MSAM-7). Eur Urol 2003; 44(6): 637-649.

473.Boyle P. Mammographic Screening: after the dust has settled. Breast. 2003 Dec;12(6):351-6

474.Boyle P. Recommendation for mammographic screening after the dust settles. Breast. 2003 Mar;12 Suppl 1:S3.

475.Boyle P, Leon ME, Maisonneuve P and Autier P. Cancer Control In Women: Update 2003. Int J Gynaecol Obstet 2003 Oct;83 Suppl 1:179-202.

476.Morton LM, Holford TR, Leaderer B, Boyle P, Zham SH, Zhang Y, FlynnS, Tallini G, Zhang B, Owens P and Zheng T. Cigarette smoking and risk of non-Hodgkin Lymphoma subtypes among women. Brit J Cancer 2003; 89: 2087-2092.

477.Morton LM, Holford T, Leaderer B, Boyle P, Zahm SH, Zhang Y, Flynn F, Tallini G, Owens PH, Zhang B, Zheng T. Alcohol Use and risk of non-Hodgkin Lymphoma among Connecticut women. Cancer Causes Control 2003 Sep;14(7):687-94.

478.Boyle P. Testicular Cancer: The Challenge for Cancer Control. Lancet Oncology 2004; 5: 56-61.

479.Boyle P, Dore JF, Autier P and Ringborg U. Cancer of the Skin: A Forgotten Problem in Europe. Annals Oncology 2004; 15(1): 5-6.

480.Hodge A, English D, McCredie M, Severi G, Boyle P, Hopper JL and Giles GG. Foods, nutrients and prostate cancer. Cancer Causes Control. 2004 Feb;15(1):11-20.

481.Gray NE and Boyle P. The Case of the Disappearing Nitrosamines. A Potentially Global Phenomenon. Tobacco Control. 2004 Mar;13(1):13-6.

482.Zheng T, Holford T, Leaderer B, Zhang Y, Boyle P, Zahm SH, Flynn S, Tallini G, Zhang B, Zhou K, Owens PH, Rothman R, Lan Q and Boyle, P. Diet and nutrient intakes and risk of non-Hodgkin Lymphoma in Connecticut women. Am J Epidemiol. 2004 Mar 1;159(5):454-66.

483.Zhang Y, Holford TR, Leaderer B, Boyle P, Zahm SH, Flynn S, Tallini G, Owens PH and Zheng T. Hair Coloring Product Use And Risk of Non-Hodgkin's Lymphoma: A Population-based Case-Control Study In Connecticut. Amer J Epid 2004; 159: 148-154.

484.Morton LM, Engels EA, Holford TR, Leaderer B, Zhang Y, Zahm SH, Boyle P, Zhang B, Flynn S, Tallini G, Owens PH, Zheng T. Hepatitis C virus and risk of non-Hodgkin lymphoma: a population-based case-control study among Connecticut women. Cancer Epidemiol Biomarkers Prev. 2004 Mar;13(3):425-30.

485.Zhang Y, Holford TR, Leaderer B, Zahm SH, Boyle P, Morton LM, Zhang B, Zou K, Flynn S, Tallini G, Owens PH and Zheng T. Prior Medical Conditions and Medication Use and Risk of Non-Hodgkin Lymphoma in Connecticut United States Women. Cancer Causes Control 2004; 15(4): 419-428.

486.Zhang Y, Holford TR, Leaderer B, Boyle P, Zahm SH, Owens PH, Morton M, Zhang B, Zou K, Flynn S, Tallini G, and Zheng T. Blood Transfusion and Risk of Non-Hodgkin's Lymphoma in Connecticut Women. Am J Epidemiol 2004 Aug; 160(4): 325-30.

487.Zhang Y, Holford TR, Leaderer B, Boyle P, Zahm SH, Zhang B, Zou K, Morton LM, Owens PH, Flynn S, Tallini G and Zheng T. Menstrual and reproductive factors and risk of non-Hodgkin's lymphoma among Connecticut women. Am J Epidemiol. 2004 Oct 15;160(8):766-73.

488.Collaborative Group on Hormonal Factors in Breast Cancer (includes P Boyle). Breast cancer and abortion: collaborative reanalysis of data from 53 epidemiological studies, including 83 000 women with breast cancer from 16 countries. Lancet 2004; 363: 1007-16

489.Boyle P, Robertson C, Lowe F and Roehrborn C. Updated Meta analysis of Clinical trials of Permixon® in the treatment of Symptomatic Benign Prostatic Hyperplasia. BJUInt. 2004 Apr;93(6):751-6.

490.Morton LM, Holford T, Leaderer B, Boyle P, Zahm SH, Zhang Y, Flynn F, Tallini G, Owens PH and Zheng T. Hepatitis B virus and risk of non-Hodgkin's lymphoma: a population-based case-control study in Connecticut women. Int J cancer (in press).

491.Boyle P, Roehrborn C, Harkaway R, Logie J, de la Rosette J and Emberton M. 5-alpha reductase inhibition provides superior benefits to alpha blockade by preventing AUR and BPH-related surgery. Eur Urology 2004; 45(5): 626-627.

492.Levi F, Lucchini F, Negri E, Boyle P and La Vecchia C. Cancer Mortality in Europe, 1995-1999, and an overview of trends since 1960. Int J Cancer 2004 Jun 10;110(2):155-69.

493.Levi F, Lucchini F, Negri E, Boyle P and La Vecchia C. The leveling of Prostate Cancer Mortality in Western Europe. The Prostate 2004; 60(1): 46-52.

494.Debruyne F, Boyle P, Calais Da Silva F, Gillenwater JG, Hamdy FC, Perrin P, Teillac P, Vela-Navarrete R, Raynaud JP, Schulman CC. Evaluation of the Clinical Benefit of Permixon and Tamsulosin in Severe BPH Patients-PERMAL Study Subset Analysis. Eur Urol. 2004 Jun;45(6):773-80.

495.Horninger W, Berger A, Pelzer A, Klocker H, Oberaigner W, Schonitzer D, Severi G, Robertson C, Boyle P, Bartsch G. Screening for prostate cancer: updated experience from the tyrol study. Curr Urol Rep. 2004 Jun;5(3):220-5.

496.Boyle P, Mezzetti M, Vecchia CL, Franceschi S, Decarli A, Robertson C. Contribution of three components to individual cancer risk predicting breast cancer risk in Italy. Eur J Cancer Prev. 2004 Jun;13(3):183-191.

497.Gnagnarella P, Parpinel M, Salvini S, Franceschi S, Palli D and Boyle P. The update of the Italian Food Composition Database. J Food Comp Analysis 2004, 17: 509-522.

498.Boyle P, Robertson C, Vaughan D and Fitzpatrick JM. Meta-analysis of Transurethral Needle Ablation (TUNA) for the treatment of symptomatic benign prostatic hyperplasia. BJUInt 2004 Jul;94(1):83-8.

499.Gray N and Boyle P. Publishing tobacco tar measurements on packets. BMJ 2004 Oct 9; 329 (7470): 813-4.

500.Rosen R, Altwein J, Boyle P, Kirby RS, Lukacs B, Meuleman E, O'Leary MP, Puppo P, Robertson C and Giuliano F. [Lower urinary tract symptoms and male sexual

dysfunction: the multinational survey of the aging.male (MSAM-7)] Prog Urol. 2004 Jun;14(3):332-44. French.

501.Debruyne F, Boyle P, Calais da Silva F, Gillenwater JG, Hamdy FC, Perrin P, Teillac P, Vela-Navarrete R, Raynaud JP, Schulman C. [Evaluation of the clinical benefit of Permixon and tamsulosin in severe BPH patients--PERMAL study subset analysis] Prog Urol. 2004 Jun;14(3):326-31. French.

502.Levi F, Lucchini F, Negri E, Zatonski W, Boyle P and La Vecchia C. Trends in cancer mortality in the European Union and accession countries, 1980-2000. Ann Oncol. 2004 Sep;15(9):1425-31.

503.Robertson C. Runzi N, Idris N and Boyle P. Beyond Classical Meta Analysis: Can inadequately reported studies be included? Drug Discovery Today 2004; 9 (21): 924-931.

504.Creasman WT, Kohler MF, Odicino F, Maisonneuve P and Boyle P. Prognosis of papillary serous, clear cell, and grade 3 stage I carcinoma of the endometrium. Gynecol Oncol. 2004 Dec;95(3):593-6.

505.Zhang Y, Wise JP, Holford TR, Xie H, Boyle P, Zahm SH, Rusiecki J, Zou K, Zhang B, Zhu Y, Owens PH and Zheng T. Serum Polychlorinated Biphenyls, Cytochrome P-450 1A1 Polymorphisms, and Risk of Breast Cancer in Connecticut Women. Am J Epidemiol. 2004 Dec 15;160(12):1177-83.

506.Vandoninck V, Bemelmans BL, Mazzetta C, Robertson C, Keech M, Boyle P and Kiemeney LA. The prevalence of urinary incontinence in community-dwelling married women: a matter of definition. BJU Int. 2004 Dec;94(9):1291-5

507.Boyle P, Vainio H, Smith R, Benamouzig R, Lee WC, Segnan N, Takima K and Tsubono Y..Workgroup I: criteria for screening. UICC International Workshop on Facilitating Screening for Colorectal Cancer, Oslo, Norway (29 and 30 June 2002). Ann Oncol. 2005 Jan;16(1):25-30.

508.Gandini S, Sera F, Cattaruzza MS, Picconi O, Boyle P and Melchi CF. Meta-analysis of risk factors for cutaneous melanoma: I. Common and atypical naevi. Eur J Cancer 2005 Jan;41(1):28-44.

509.Gandini S, Sera F, Cattaruzza MS, Pasquini P, Picconi O, Boyle P and Melchi CF. Meta-analysis of risk factors for cutaneous melanoma: II Sun exposure. Eur J Cancer. 2005 Jan;41(1):45-60.

510.Gandini S, Sera F, Cattaruzza MS, Pasquini P, Zanetti R, Masini C, Boyle P and Melchi CF. Meta-analysis of risk factors for cutaneous melanoma: III. Family history, actinic damage and phenotypic factors. Eur J Cancer. 2005 Aug 24

511.Decensi A, Maisonneuve P, Rotmensz N, Bettega D, Costa A, Sacchini V, Salvioni A, Travaglini R, Oliviero P, D'Aiuto G, Gulisano M, Gucciardo G, Del Turco MR, Pizzichetta MA, Conforti S, Bonanni B, Boyle P and Veronesi U. Effect of tamoxifen on venous thromboembolic events in a breast cancer prevention trial Circulation. 2005 Feb 8;111(5):650-6.

512.Veronesi U, Boyle P, Goldhirsch A, Orrechia R and Viale G. Seminar on Breast Cancer. Lancet. 2005 May 365 (9472):1727-41.

513.Boyle P and Ferlay J. Cancer incidence and mortality in Europe, 2004. Annals Oncol 2005; 16: 481-488.

514.Boyle P. Tobacco Smoking and British Doctors' Cohort (Editorial). Brit J Cancer 2005; 92: 419-420.

515.Kreimer AR, Clifford GM, Boyle P and Franceschi S. Human papillomavirus types in head and neck squamous cell carcinomas worldwide: a systematic review. Cancer Epidemiol. Biomarkers Prev. 2005; 14(2): 467-75.

516.Horninger W, Berger A, Pelzer A, Klocker H, Oberaigner W, Schonitzer D, Severi G, Robertson C, Boyle P and Bartsch G. Screening for prostate cancer: updated experience from the Tyrol study. Can J Urol. 2005 Feb;12 (1 Supp1):7-13.

517.Bruno S, Maisonneuve P, Castellana P, Rotmensz N, Rossi S, Maggioni M, Persico M, Colombo A, Monasterolo F, Casadei-Giunchi D, Desiderio F, Stroffolini T, Decensi A, Veronesi U and the Italian Tamoxifen Study Group (includes Boyle P). Incidence and Risk Factors for non-alcoholic steatohepatitis in the Italian Tamoxifen Chemoprevention Trial BMJ 2005; 21st March 2005.

518.Gray N, Henningfield JE, Benowitz NL, Connolly GN, Dresler C, Fagerstrom K, Jarvis MJ and Boyle P. Toward a comprehensive long term nicotine policy. Tob Control. 2005 Jun;14(3):161-5.

519.Boyle P, Ariyaratne M, Bartelink H, Baselga J, Berns A, Brawley OW, Burns H, Davidov M, Dinshaw K, Dresler C, Eggermont AM, Gajurel D, Gordina G, Gray N, Kakizoe T, Karki BS, Kásler M, Kerr DJ, Khayat D, Kiselev A, Khuhaprema T, Klocker H, Levshin V, Martin-Moreno JM, McVie JG, Mendelsohn J, Napalkov NP, Ngoma TA, Park JG, Philip T, Pötschke-Langer M, Poudal HN, Rajan B, Ringborg U, Rodger A, Seffrin JR, Shanta V, Shrestha MM, Thomas R, Tursz T, de Valeriola D, Veronesi U, Wiestler OD, Zaridze D, Zatonski W and Zeng YX. Curbing

tobacco's toll starts with the professionals: World No Tobacco Day. The Lancet (11th June) 2005; 365: 1990-1992

520.Scully C and Boyle P. The role of the dental team in preventing and diagnosing cancer; 1. Cancer in general. Dent Update. 2005 May;32(4):204-6, 208-10, 212.

521.Boyle P and Ferlay J. Mortality and survival in breast and colorectal cancer. Nature Clinical Practice Oncology (2005) 2, 424-425

522.Cogliano VJ, Baan R, Straif K, Grosse Y, Secretan B, El Ghissassi and Boyle P. Transparency in the IARC Monographs. Lancet Oncology 2005; 6: 747.

523.Boyle P and Dresler C. Preventing the lung cancer epidemic. Annals Oncology 2005; 16: 1565-6.

524.Zhang Y, Lan Q, Rothman N, Zhu Y, Zahm SH, Wang SS, Holford TR, Leaderer B, Boyle P, Zhang B, Zou K, Chanock S and Zheng T. A putative exonic splicing polymorphism in the BCL6 gene and the risk of non-Hodgkin lymphoma. J Natl Cancer Inst. 2005 Nov 2;97(21):1616-8.

525.Veronesi U and Boyle P. Breast cancer – Authors' reply. The Lancet 366 (9497): 1606.

526.Boyle P. Breast cancer control: Signs of progress, but more work required. Breast 2005 Dec;14(6):429-38.

527.Baglietto L, Jenkins MA, Severi G, Giles GG, Bishop DT, Boyle P and Hopper JL. Measures of familial aggregation depend on definition of family history: meta-analysis for colorectal cancer. J Clin Epidemiol 2006 Feb;59(2):114-124.

528.Severi G, Morris HA, Macinnis RJ, English DR, Tilley W, Hopper JL, Boyle P and Giles GG. Circulating steroid hormones and the risk of prostate cancer. Cancer Epidemiol Biomarkers Prev. 2006 Jan;15(1):86-91

529.Zhu Y, Zheng T, Stevens RG, Zhang Y and Boyle P. Does "clock" matter in prostate cancer? Cancer Epidemiol Biomarkers Prev. 2006 Jan;15(1):3-5.

530.Lan Q, Zheng T, Rothman N, Zhang Y, Wang SS, Shen M, Berndt SI, Zahm SH, Holford TR, Leaderer B, Yeager M, Welch R, Boyle P, Zhang B, Zou K, Zhu Y and Chanock S. Cytokine polymorphisms in the Th1/Th2 pathway and susceptibility to non-Hodgkin lymphoma. Blood. 2006 Jan 31; [Epub ahead of print] PMID 16639601

531.Zatonski W, Mikucka M, La Vecchia C and Boyle P. Infant mortality in Central Europe: effects of transition. Gac Sanit. 2006 Jan-Feb;20(1):63-6.

532.Cardis E, Krewski D, Boniol M, Drozdovitch V, Darby SC, Gilbert ES, Akiba S, Benichou J, Ferlay J, Gandini S, Hill C, Howe G, Kesminiene A, Moser M, Sanchez M, Storm H, Voisin L and Boyle P. Estimates of the cancer burden in Europe from radioactive fallout from the Chernobyl accident. Int J Cancer. 2006 Apr 20; [Epub ahead of print]

533.Shen M, Zheng T, Lan Q, Zhang Y, Zahm SH, Wang SS, Holford TR, Leaderer B, Yeager M, Welch R, Kang D, Boyle P, Zhang B, Zou K, Zhu Y, Chanock S, Rothman N. Polymorphisms in DNA repair genes and risk of non-Hodgkin lymphoma among women in Connecticut. Hum Genet. 2006 Jul;119(6):659-68.

534.Boyle P, Ariyaratne MA, Barrington R, Bartelink H, Bartsch G, Berns A, de Valeriola D, Dinshaw KA, Eggermont AM, Gray N, Kakizoe T, Karki BS, Kaslar M, Kerr DJ, Khayat D, Khuhaprema T, Kim IH, Martin-Moreno J, McVie G, Park JG, Philip T, Ringborg U, Rodger A, Seffrin JR, Semiglazov V, Soo KC, Sun YT, Thomas R, Tursz T, Veronesi U, Wiestler O, Yoo KY, Zatonski W and Zhao P. Tobacco: deadly in any form or disguise. Lancet. 2006 May 27;367(9524):1710-2.

535.Severi G, Hayes VM, Neufing P, Padilla EJ, Tilley WD, Eggleton SA, Morris HA, English DR, Southey MC, Hopper JL, Sutherland RL, Boyle P and Giles GG. Variants in the prostate-specific antigen (PSA) gene and prostate cancer risk, survival, and circulating PSA. Cancer Epidemiol Biomarkers Prev. 2006 Jun;15(6):1142-7.

536.Severi G, Morris HA, MacInnis RJ, English DR, Tilley WD, Hopper JL, Boyle P and Giles GG. Circulating insulin-like growth factor-I and binding protein-3 and risk of prostate cancer. Cancer Epidemiol Biomarkers Prev. 2006 Jun;15(6):1137-41.

537.Boyle P. The Globalisation of Cancer. Lancet 2006; 368: 629-630

538.Lan Q, Zheng T, Chanock S, Zhang Y, Shen M, Wang SS, Berndt SI, Zahm SH, Holford TR, Leaderer B, Yeager M, Welch R, Hosgood D, Boyle P and Rothman N. Genetic variants in caspase genes and susceptibility to non-Hodgkin lymphoma. Carcinogenesis. 2007; 28(4): 823-827.

539.Zhu Y, Leaderer D, Guss C, Brown HN, Zhang Y, Boyle P, Stevens RG, Hoffman A, Qin Q, Han X and Zheng T. Ala394Thr polymorphism in the clock gene NPAS2: A circadian modifier for the risk of non-Hodgkin's lymphoma. Int J Cancer. 2007 (Jan 15); 120(2) :432-5.

540.Hayes VM, Severi G, Padilla EJ, Morris HA, Tilley WD, Southey MC, English DR, Sutherland RL, Hopper JL, Boyle P and Giles GG. 5-alpha-reductase type 2 gene variant associations with prostate cancer risk, circulating hormone levels and androgenetic alopecia. Int J Cancer 2007; 120(4): 776-780.

541.Lan Q, Zheng T, Shen M, Zhang Y, Wang SS, Zahm SH, Holford TR, Leaderer B, Boyle P and Chanock S. Genetic polymorphisms in the oxidative stress pathway and susceptibility to non-Hodgkin lymphoma. Hum Genet. 2007; 28(4): 823-7.

542.Zhang Y, Wang R, Holford TR, Leaderer B, Zahm SH, Boyle P, Zhu Y, Qin Q and Zheng T. Family history of hematopoietic and non-hematopoietic malignancies and risk of non-Hodgkin lymphoma. Cancer Causes Control. 2007; 18(4): 351-359.

543.Ferlay J, Autier P, Boniol M, Heanue M, Colombet M and Boyle P. Estimates of cancer incidence and mortality in Europe in 2006. Annals Oncology 2007; 18(3): 581-592.

544.Zhang Y, Holford TR, Leaderer B, Boyle P, Zhu Y, Wang R, Zou K, Zhang B, Wise JP Sr, Qin Q, Kilfoy B, Han J and Zheng T. Ultraviolet Radiation Exposure and Risk of Non-Hodgkin's Lymphoma. Am J Epidemiol. 2007; 165(11): 1255-1264.

545.Robertson C, Link CL, Onel E, Mazzetta C, Keech M, Hobbs R, Fourcade R, Kiemeney L, Lee C, Boyle P and McKinlay JB. The impact of lower urinary tract symptoms and comorbidities on quality of life: the BACH and UREPIK studies. BJU Int. 2007 Feb;99(2):347-54.

546.Boffetta P, McLaughlin JK, La Vecchia C, Autier P and Boyle P. "Environment" in cancer causation and aetiological fraction: Limitations and ambiguities. Carcinogenesis 2007; 28(5): 913-915.

547.Veronesi U, Maisonneuve P, Rotmensz N, Bonanni B, Boyle P, Viale G, Costa A, Sacchini V, Travaglini R, D'Aiuto G, Oliviero P, Lovison F, Gucciardo G, del Turco MR, Muraca MG, Pizzichetta MA, Conforti S, Decensi A; Italian Tamoxifen Study Group. Tamoxifen for the prevention of breast cancer: late results of the Italian Randomized Tamoxifen Prevention Trial among women with hysterectomy. J Natl Cancer Inst. 2007 May 2;99(9):727-37.

548. Scully C, Boyle P, Day T, Hill B, Joshi V, Leupold NE, Shah JP and Lefebvre JL. International Consortium on Head and Neck Cancer Awareness (ICOHANCA). Oral Oncol 2007: Oct;43(9):841-842.

549.Boyle P. Book Review: Conspiracy theories of cancer, Lancet 2007; 370: 1751

550.Ferlay J, Randi G, Bosetti C, Levi F, Negri E, Boyle P, La Vecchia C. Declining mortality from bladder cancer in Europe. BJU Int. 2008; 101(1): 11-19.

551.Severi G, Hayes VM, Tesoriero AA, Southey MC, Hoang HN, Padilla EJ, Morris HA, English DR, Sutherland RL, Boyle P, Hopper JL, Giles GG. The rs743572 common variant in the promoter of CYP17A1 is not associated with prostate cancer risk or circulating hormonal levels. BJU Int. 2008; 101(4): 492-6.

552.Koutros S, Zhang Y, Zhu Y, Mayne ST, Zahm SH, Holford TR, Leaderer BP, Boyle P, Zheng T. Nutrients Contributing to One-Carbon Metabolism and Risk of Non-Hodgkin Lymphoma Subtypes. Am J Epidemiol. 2008 Feb 1; 167(3): 287-94

553.Hainaut P and Boyle P. Curbing the Liver Cancer Epidemic in Africa. Lancet 2008; 371(9610): 367-368.

554.Gandini S, Botteri E, Iodice S, Boniol M, Lowenfels AB, Maisonneuve P and Boyle P. Tobacco smoking and cancer: A meta-analysis. Int J Cancer. 2008 Jan 1;122(1):155-64.

555.Levi F, Ferlay J, Galeone C, Lucchini F, Negri E, Boyle P and La Vecchia C. The changing pattern of Kidney Cancer incidence and mortality in Europe. BJU Int. 2008 Apr;101(8):949-58.

556.Autier P and Boyle P. Artificial ultraviolet sources and skin cancers: rationale for restricting access to sunbed use before 18 years of age. Nat Clin Pract Oncol 2008; 5(4): 178-9.

557.Bartsch G, Horninger W, Klocker H, Pelzer A, Bektic J, Oberaigner W, Schennach H, Schafer G, Frauscher F, Boniol M, Severi G, Robertson C and Boyle P on behalf of the Tyrol Prostate Cancer Screening Group. Tyrol Prostate Cancer Demonstration Project: Early Detection, Treatment, Outcome, Incidence and Mortality.BJU Int. 2008 Apr;101(7):809-16.

558.Boyle P. Favourable trends in cancer mortality in the European Union but no room for complacency. Annals Oncol 2008; 19: 605-606

559.Lingwood R, Boyle P, Milburn A, Arbuthnott J, McCaffrey R, Kerr SH and Kerr DJ. The Challenge of Cancer Control in Africa. Nature Rev Cancer 2008; 8(5): 398-403.

560.Park JG, Park JW, Kim DW, Seo HG, Nam BH, Lee JS, Choi JC, Kim IS and Boyle P. Factors influencing attitudes to legislation banning the manufacture and sale of tobacco products. Tob Control. 2008 Apr;17(2):142-3

561.Boyle P, Anderson B, Andersson LC, Ariyatne Y, Auleley G-R, Barbacid M, Bartelink H, Baselga J, Behbehani K,, Belardelli F, Berns A, Bishop J, Brawley O, Burns HJG, Clanton M, Cox B, Currow D, Dangou J-M, de Valeriola D, Dinshaw K, Eggermont A, Fitzpatrick JM, Forstmane M, Garaci E, Gavin AT, Kakizoe T, Kasler M, Keita N, Kerr DJ, Khayat D, Khleif S, Khuhaprema T, Knezevic T, Kubinova R, Mallath M, Martin-Moreno JM, McCance D, McVie JG, Merriman A, Ngoma T, Nowacki M, Orgelbrand J, Park J-G, Pierotti M, Pinillos Ashton L, Puska P, Escobar CVR, Rajan B, Rajkumar T, Ringborg U, Robetson C, Rodger A, Roovali L, Santini LA, Sarhan M, Seffrin J, Semiglazov V, Shrestra BM, Soo KC, Stamenic V, Tamblyn

C, Thomas R, Tuncer AM, Tursz T, Vaitkiene R, Vallejos C, Veronesi U, Wojtyla A, Yach D, Yoo K-Y, Zatonski W, Zaridze DG, Zeng Y-X, Zhao P and Zheng T. Need for Global Action for Cancer Control. Annals Oncology 2008; 19: 1519-1521.

562.Boffetta P, Tubiana M, Hill C, Boniol M, Aurengo A, Masse R, Valleron A-J, Monier R, de The G, Boyle P and Autier P. The Causes of Cancer in France. Annals Oncology 2008; (epub ahead of print) PMID 18765462

563.Boyle P, Boffetta P and Autier P. Diet, Nutrition and Cancer: Public, Media and Scientific Confusion. Annals Oncolgy 2008 Oct;19(10):1665-7.

564.Zhang Y, Guo GL, Han X, Zhu C, Kilfoy BA, Zhu Y, Boyle P and Zheng T. Do Polybrominated Diphenyl Ethers (PBDEs) Increase the Risk of Thyroid Cancer? Biosci Hypotheses. 2008;1(4):195-199

565.Wang R, Zhang Y, Lan Q, Holford TR, Leaderer B, Hoar Zahm S, Boyle P, Dosemeci M, Rothman N, Zhu Y, Qin Q and Zheng T. Occupational Exposure to Solvents and Risk of Non-Hodgkin Lymphoma in Connecticut Women. Am J Epidemiol. 2008 Dec 4. [Epub ahead of print]

566.Zaridze D, Maximovitch D, Lazarev A, Igitov V, Boroda A, Boreham J, Boyle P, Peto R and Boffetta P. Alcohol poisoning is a main determinant of recent mortality trends in Russia: evidence from a detailed analysis of mortality statistics and autopsies. Int J Epidemiol. 2009; 38(1):143-53.

567.Sun X, Huang J, Homma T, Kita D, Klocker H, Schafer G, Boyle P and Ohgaki H. Genetic Alterations in the PI3K Pathway in Prostate Cancer. Anticancer Res. 2009 May;29(5):1739-43

568.Boyle P, Heanue M, Robertson C, Ferlay J, Gavin A, Fitzpatrick J and Johnson PG. Cancer in Ireland, 1926-2005. Annals Oncology (in press).

569.Boyle P and Brawley OW. Prostate Screening: Evidence Weighs Against Population Screening.CA Cancer J Clin 2009 [doi: 10.3322/caac.20025]epub ahead of print.

570.Duell EJ, Maisonneuve P, Baghurst PA, Bueno-de-Mesquita HB, Ghadirian P, Miller AB, Zatonski W, Vrieling A, Boffetta P and Boyle P. Menstrual and reproductive factors and pancreatic cancer in the SEARCH program of the IARC. Cancer Causes Control. 2009 Aug 4. [Epub ahead of print]

571.Kilfoy BA, Zheng T, Lan Q, Han X, Holford T, Hein DW, Qin Q, Leaderer B, Morton LM, Yeager M, Boyle P, Zhao P, Chanock S, Rothman N and Zhang Y. Genetic variation in N-acetyltransferases 1 and 2, cigarette smoking, and risk of non-Hodgkin lymphoma. Cancer Causes Control. 2009 Oct 7. [Epub ahead of print]

572.Ma S, Zhang Y, Huang J, Han X, Holford T, Lan Q, Rothman N, Boyle P and Zheng T. Identification of Non-Hodgkin's Lymphoma Prognosis Signatures Using the CTGDR Method.. Bioinformatics. 2009 Oct 22. [Epub ahead of print].

573.La Vecchia C, Bosetti C, Lucchini F, Bertuccio P, Negri E, Boyle P and Levi F. Cancer mortality in Europe, 2000–2004, and an overview of trends since 1975. Annals Oncology [published online November 30, 2009 doi:10.1093/annonc/mdp530]

574.Boyle P and Boffetta P. Alcohol consumption and breast cancer risk. Breast Cancer Research 2009;11 Suppl 3:S3. Epub 2009 Dec 18.[PMID: 20030878]

575.Han X, Zheng T, Foss FM, Ma S, Holford T, Boyle P, Leaderer B, Zhao P, Dai M and Zhang Y. Alcohol consumption and non-Hodgkin lymphoma survival. J Ca Survivorship 2009 Dec 29. [Epub ahead of print]

576.Boyle P, Ford I, Robertson J, La Vecchia C, Boffetta P and Autier P. Essential considerations in the investigation of associations between insulin and cancer risk using prescription databases. Ecancermedicalscience. 2009;3:174. Epub 2009 Dec 11. [PMID: 22276024]

577.Maisonneuve P, Lowenfels AB, Bueno-de-Mesquita HB, Ghadirian P, Baghurst PA, Zatonski WA, Miller AB, Duell EJ, Boffetta P and Boyle P. Past Medical History and Pancreatic Cancer Risk: Results From a Multicenter Case-Control Study. Ann Epidemiol. 2010 Feb;20(2):92-98.

578.Kilfoy BA, Ward MH, Zheng T, Holford TR, Boyle P, Zhao P, Dai M, Leaderer B and Zhang Y. Risk of non-Hodgkin lymphoma and nitrate and nitrite from the diet in Connecticut women. Cancer Causes Control. 2010 Mar 5. [Epub ahead of print]

579.Boffetta P, Autier P, Boniol M, Boyle P, Hill C, Aurengo A, Masse R, de Thé G, Valleron AJ, Monier R and Tubiana M. An Estimate of Cancers Attributable to Occupational Exposures in France. J Occup Environ Med. 2010 Mar 30. [Epub ahead of print]

580.Conde L, Halperin E, Akers NK, Brown KM, Smedby KE, Rothman N, Nieters A, Slager SL, Brooks-Wilson A, Agana L, Riby J, Liu J, Adami HO, Darabi H, Hjalgrim H, Low HQ, Humphreys K, Melbye M, Chang ET, Glimelius B, Cozen W, Davis S, Hartge P, Morton LM, Schenk M, Wang SS, Armstrong B, Kricker A, Milliken S, Purdue MP, Vajdic CM, Boyle P, Lan Q, Zahm SH, Zhang Y, Zheng T, Becker N, Benavente Y, Boffetta P, Brennan P, Butterbach K, Cocco P, Foretova L, Maynadié M, de Sanjosé, S, Staines A, Spinelli JJ, Achenbach SJ, Call TG, Camp NJ, Glenn M, Caporaso NE, Cerhan JR, Cunningham JM, Goldin LR, Hanson CA, Kay NE, Lanasa MC, Leis JF, Marti GE, Rabe KG, Rassenti LZ, Spector LG, Strom SS, Vachon CM, Weinberg JB, Holly EA, Chanock S, Smith MT, Bracci PM and Skibola

CF. Genome-wide association study of follicular lymphoma identifies a risk locus at 6p21.32. Nat Genet. 2010 Jul 18. [Epub ahead of print].

581.Boyle P, Chapman CJ, Holdenrieder S, Murray A, Robertson C, Wood WC, Maddison P, Healey G, Fairley GH, Barnes AC and Robertson JF. Clinical validation of an autoantibody test for lung cancer. Ann Oncol. 2010 Jul 30. [Epub ahead of print]

582.Li Q, Zheng T, Holford TR, Boyle P, Zhang Y and Dai M. Light at night and breast cancer risk: results from a population-based case-control study in Connecticut, USA. Cancer Causes Control. 2010 Oct 7. [Epub ahead of print]

583.Chen Y, Zheng T, Lan Q, Foss F, Kim C, Chen X, Dai M, Li Y, Holford T, Leaderer B, Boyle P, Chanock SJ, Rothman N and Zhang Y. Cytokine polymorphisms in Th1/Th2 pathway, body mass index, and risk of non-Hodgkin lymphoma. Blood. 2010 Oct 15. [Epub ahead of print]

584.Boyle P and Howell A: The globalisation of breast cancer. *Breast Cancer Research* 2010, 12(Suppl 4):S7.

585.Barry KH, Zhang Y, Lan Q, Zahm SH, Holford TR, Leaderer B, Boyle P, Hosgood HD 3rd, Chanock S, Yeager M, Rothman N and Zheng T.. Genetic Variation in Metabolic Genes, Occupational Solvent Exposure, and Risk of Non-Hodgkin Lymphoma. Am J Epidemiol. 2011 Jan 12. [Epub ahead of print] PMID: 21228414

586.Pelucchi C, La Vecchia C, Bosetti C, Boyle P and Boffetta P. Exposure to acrylamide and human cancer--a review and meta-analysis of epidemiologic studies. Ann Oncol. 2011 Jan 13. [Epub ahead of print] PMID: 21239401

587.Boniol M, Doré JF and Boyle P. Re. Lehrer S, Green S, Stock RG (2011) Association between number of cell phone contracts and brain tumor incidence in nineteen U.S. States. J Neurooncol 101:505-507.

588.Smedby KE, Foo JN, Skibola CF, Darabi H, Conde L, Hjalgrim H, Kumar V, Chang ET, Rothman N, Cerhan JR, Brooks-Wilson AR, Rehnberg E, Irwan ID, Ryder LP, Brown PN, Bracci PM, Agana L, Riby J, Cozen W, Davis S, Hartge P, Morton LM, Severson RK, Wang SS, Slager SL, Fredericksen ZS, Novak AJ, Kay NE, Habermann TM, Armstrong B, Kricker A, Milliken S, Purdue MP, Vajdic CM, Boyle P, Lan Q, Zahm SH, Zhang Y, Zheng T, Leach S, Spinelli JJ, Smith MT, Chanock SJ, Padyukov L, Alfredsson L, Klareskog L, Glimelius B, Melbye M, Liu ET, Adami HO, Humphreys K, Liu J. GWAS of Follicular Lymphoma Reveals Allelic Heterogeneity at 6p21.32 and Suggests Shared Genetic Susceptibility with Diffuse Large B-cell Lymphoma. PLoS Genet 7(4): e1001378. doi:10.1371/journal.pgen.1001378

589.Lam S, Boyle P, Healey GF, Maddison P, Peek L, Murray A, Chapmand CJ, Allen J, Wood WC, Sewell HF and Robertson JF. EarlyCDT-Lung: An Immunobiomarker Test as an Aid to Early Detection of Lung Cancer. Cancer Prev Res 2011; 4(7): 1126-34

590.Bojar I, Bilinski P, Boyle P, Zatonski W, Marcinkowski J and Wojtyla A. Prevention of female reproductive system cancer among rural and urban Polish pregnant women.. Ann Agric Environ Med. 2011 Jun;18(1):183-8. [PMID: 21736284]

591.Wojtyla A, Bojar I, Boyle P, Zatonski W, Marcinkowski J and Bilinski P. Nutritional behaviours among pregnant women from rural and urban environments in Poland. Ann Agric Environ Med. 2011 Jun;18(1):169-74. [PMID:21736282]

592.Sullivan R, Peppercorn J, Sikora K, Zalcberg J, Meropol NJ, Amir E, Khayat D, Boyle P, Autier P, Tannock IF, Fojo T, Siderov J, Williamson S, Camporesi S, McVie JG, Purushotham AD, Naredi P, Eggermont A, Brennan MF, Steinberg ML, De Ridder M, McCloskey SA, Verellen D, Roberts T, Storme G, Hicks RJ, Ell PJ, Hirsch BR, Carbone DP, Schulman KA, Catchpole P, Taylor D, Geissler J, Brinker NG, Meltzer D, Kerr D, Aapro M. Delivering affordable cancer care in high-income countries. Lancet Oncol. 2011 Sep;12(10):933-80.

593.Bassig BA, Zheng T, Zhang Y, Berndt SI, Holford TR, Hosgood HD 3rd, Hu W, Leaderer B, Yeager M, Menashe I, Boyle P, Xu J, Zou K, Zhu Y, Chanock S, Rothman N and Lan Q. Polymorphisms in complement system genes and risk of non-Hodgkin lymphoma. Environ Mol Mutagen. 2011 Dec 15. doi: 10.1002/em.21675. [Epub ahead of print]

594.Zhu G, Pan D, Zheng T, Lan Q, Chen X, Chen Y, Kim C, Bi X, Holford T, Boyle P, Leaderer B, Chanock SJ, Rothman N, Zhang Y. Polymorphisms in Th1/Th2 cytokine genes, hormone replacement therapy, and risk of non-Hodgkin lymphoma. Front Oncol. 2011 Jul 28;1(21). pii: 00021.

595.Boyle P. Improving health in central and eastern europe. Ann Agric Environ Med. 2011 Dec 22;18(2):281-2.

596.Zatoński WA; Manczuk M, Sulkowska U, Didkowska J, Wojciechowska U, Tarkowski W, Przewozniak K, Gumkowski J, Janik-Koncewicz K, Boffetta P, Campos H, LaVecchia C, Powles J, Rehm J, Willet W, Negri E, Aaro L, Boyle P, Gilmore A, Jougla E, Moreno JM, Lowenfels A, Paccaud F, Peto R, Petric VK, Puska P, Klumbiene J, Pudule I, Kiivet R, Aaviksoo A, Albreht T, Kaposvari C, Dimitrov P, Holcatova I, Pilipcinova A, Poledne R, Marcinkova D, Furtunescu F,

Bagnardi V, Baliunas D, Brozova J, Vrbanova H, Bene M, West R, Jarvis M, Bohm G, Kunze M, Gisle L, Joossens L, Storm H, Laatikainen T, Wilquin JJ, Ratte S, Thyrian R, Gallus S, Zeegers T, Prins T, Munoz EF, Karlsson AS, Halicka E, Lund J, Moskalewicz J, Patra J, Pavillon G, Popova S, Scotti L and Taylor B. Epidemiological analysis of health situation development in Europe and its causes until 1990. Ann Agric Environ Med. 2011 Dec;18(2):194-202.

597. Li Q, Holford TR, Zhang Y, Boyle P, Mayne ST, Dai M and Zheng T. Dietary fiber intake and risk of breast cancer by menopausal and estrogen receptor status. Eur J Nutr. 2012 Feb 16. [Epub ahead of print]

598.Zhang Y, Zhu C, Curado MP, Zheng T and Boyle P. Changing patterns of bladder cancer in the USA: evidence of heterogeneous disease. BJU Int. 2012 Jan;109(1):52-6. doi: 10.1111/j.1464-410X.2011.10283.x. Epub 2011, May 18

599.Kim C, Zheng TZ, Lan Q, Chen Y, Foss FM, Chen X, Holford TR, Leaderer B, Boyle P, Chanock SJ, Rothman N and Zhang Y. Genetic polymorphisms in oxidative stress pathway genes and modification of BMI and risk of non-Hodgkin lymphoma. Cancer Epidemiol Biomarkers Prev. 2012 Feb 28. [Epub ahead of print]

600.Aschebrook-Kilfoy B, Ward MH, Zheng T, Holford TR, Boyle P, Leaderer B and Zhang Y. Dietary Nitrate and Nitrite Intake and Non-Hodgkin Lymphoma Survival. Nutr Cancer. 2012 Mar 16. [Epub ahead of print]

601.Jiao J, Zheng T, Lan Q, Chen Y, Deng Q, Bi X, Kim C, Holford T, Leaderer B, Boyle P, Ba Y, Xia Z, Chanock SJ, Rothman N and Zhang Y. Occupational solvent exposure, genetic variation of DNA repair genes, and therisk of non-Hodgkin's lymphoma. Eur J Cancer Prev. 2012 Mar 17. [Epub ahead of print]

602.Largent J, Oefelein M, Kaplan HM, Okerson T and Boyle P. Risk of lymphoma in women with breast implants: analysis of clinical studies. Eur J Cancer Prev. 2012 May;21(3):274-80.

603.Chapman CJ, Healey GF, Murray A, Boyle P, Robertson C, Peek LJ, Allen J, Thorpe AJ, Hamilton-Fairley G, Parsy-Kowalska CB, Macdonald IK, Jewell W, Maddison P and Robertson JF. EarlyCDT®-Lung test: improved clinical utility through additional autoantibody assays. Tumour Biol. 2012 Apr 11. [Epub ahead of print]

604.Deng Q, Zheng T, Lan Q, Lan Y, Holford T, Chen Y, Dai M, Leaderer B, Boyle P, Chanock SJ, Rothman N and Zhang Y. Occupational solvent exposure, genetic variation in immune genes, and the risk for non-Hodgkin lymphoma. Eur J Cancer Prev. 2012 May 18. [Epub ahead of print]

605.Bi X, Zheng T, Lan Q, Xu Z, Chen Y, Zhu G, Foss F, Kim C, Dai M, Zhao P, Holford T, Leaderer B, Boyle P, Deng Q, Chanock SJ, Rothman N and Zhang Y. Genetic polymorphisms in IL10RA and TNF modify the association between blood transfusion and risk of non-Hodgkin lymphoma. Am J Hematol. 2012 Apr 26. doi: 10.1002/ajh.23244. [Epub ahead of print]

606. Gandini S, Negri E, Boffetta P, La Vecchia C and Boyle P. Mouthwash and Oral Cancer Risk Quantitative Meta-analysis of Epidemiologic Studies. Ann Agric Environ Med. 2012 Jun 27;19(2):173-80.

607.Boniol M, Autier P, Boyle P and Gandini S. Cutaneous melanoma attributable to sunbed use: systematic review and meta-analysis. BMJ2012;345 doi: 10.1136/bmj.e4757(Published 24 July 2012)

608.Boyle, P, Boniol M, Koechlin A, Robertson C, Valentini F, Coppens K, Fairley L, Boniol-Rech M, Zheng T, Zhang Y, Pasterk M, Smans M, Curado MP, Mullie P, Gandini S, Bota M, Bolli G, Rosenstock J and Autier P. Diabetes and breast cancer risk: a meta-analysis. *British Journal of Cancer.* DOI: 10.1038/bjc.2012.414

609.Boniol M, Boyle P, Autier P, Ruffion A and Perrin P. Critical role of prostate biopsy mortality in the number of years of life gained and lost within a prostate cancer screening programme. BJU Int. 2012 Sep 18. doi: 10.1111/j.1464-410X.2012.11513.x. [Epub ahead of print]

610.Boyle P. Trople-negative Breast Cancer: epidemiological considerations and recommendations. Annals Oncol 2012; 23 (suppl 6):vi7=vi12

611.Hu W, Bassig BA, Xu J, Zheng T, Zhang Y, Berndt SI, Holford TR, Hosgood HD 3rd, Leaderer B, Yeager M, Menashe I, Boyle P, Zou K, Zhu Y, Chanock S, Lan Q and Rothman N. Polymorphisms in pattern-recognition genes in the innate immunity system and risk of non-Hodgkin lymphoma. Environ Mol Mutagen. 2012 Oct 11. doi: 10.1002/em.21739. [Epub ahead of print]

612.Boyle P, Koechlin A, Pizot C, Boniol M, Robertson C, Mullie P, Bolli G, Rosenstock J and Autier P. Blood glucose concentrations and breast cancer risk in women without diabetes: a meta-analysis. Eur J Nutr DOI 10.1007/s00394-012-0460-z

613.Lech-Maranda E, Bienvenu J, Broussais-Guillaumot F, Michallet AS, Warzocha K, Biliński P, Boyle P, Coiffier B and Salles G. Pretreatment Levels of Vascular Endothelial Growth Factor in Plasma Predict a Complete Remission Rate and Time to Relapse or Progression in Patients with Diffuse Large B-Cell Lymphoma. Arch Immunol Ther Exp (Warsz). 2013 Jan 3. [Epub ahead of print]

614.Autier P, Koechlin A, Boniol M, Mullie P, Bolli G, Rosenstock J and Boyle P. Serum insulin and C-peptide concentration and breast cancer: a meta-analysis. Cancer Causes Control. 2013 Feb 14. [Epub ahead of print]

615.Boniol M, Boyle P, Autier P, Ruffion A and Perrin P. Reply.: Critical role of prostate biopsy mortality in the number of years of life gained and lost within a prostate cancer screening programme. BJU Int. 2013 Mar;111(3):E17-8. doi: 10.1111/bju.12020_10.

International Prevention Research Institute

CV Maria Bota

Maria Bota
Vibert,
(27 years old, Romanian)

Address: 9 Rue Laurent
69006, Lyon, France
Tel. office : +33 (0)4 72 17 11 99
Tel. mobile : +33 (0)6 31 19 03 85
E-mail: maria.bota@i-pri.org

Research Officer Specialised in Biostatistics, Bioinformatics and Modeling

Professional and research experience

Since 2010 **International Prevention Research Institute (IPRI), Lyon, France**

Research officer: Participation in the coordination of international epidemiologic research projects, statistical analysis applied to public health, scientific document writing, and student supervision.

2009-2010 **Department of ecology and evolution, University of Lausanne, Switzerland**

(Dec 2009-Mar 2010) Software developer and analyst (Fixed-term contract): R-based development of gene set analysis tools for ant microarrays.

2009 **Sanofi Pasteur, Marcy L'Etoile, France**

(Feb-Aug) Internship: Modeling of vaccine degradation data in the context of stability studies.

2008-2009 **Institute of Molecular and Cellular Biology, University of Leeds, UK**

(Sep 2008-Jan 2009) Internship: Microarray data analysis. 'An expanded set of direct BLIMP-1 target genes' project.

2008 **IARC (International Agency for Research on cancer), Lyon, France**

(Jul-Aug) Internship: Data entry & data analysis: 'Long time trends of cancer, by country' project.

Education

2006-2009 **Master's Degree – Diplôme d'Ingénieur – specialised in Bioinformatics and modelling**
Institution: National Institute of Applied Sciences (INSA), Lyon, France
Principal subjects: biostatistics, bioinformatics, modeling of complex biological systems, computer sciences, applied maths.

2004-2006 **Bachelors' Degree - General Engineering Studies, European Section (EURINSA)**
Institution: National Institute of Applied Sciences (INSA), Lyon, France

2004 Baccalaureat sciences (Maths, Computer Sciences; English section) - 9.18/10
Institution: National College 'Fratii Buzesti', Romania

Skills and competences

Statistical packages R, Stata, Epi Info
Programming C/ C++, Python, Perl, MySQL
Languages/Other Latex, HTML
Software Microsoft Office Suite, UNIX (notions)

Languages

- Romanian (mother tongue)
- English (fluent)
- French (fluent)
- Spanish (basic level), German (beginner)

Honorary appointments

2012-2015 Honorary Lecturer, School of Nursing and Midwifery, University of Dundee, Scotland.

Teaching experience

May-July 2012 Co-Supervision (with Autier P.) of Master's student – Nada Assi (4 BIM, INSA de Lyon).
June-July 2012 Lecturer for the IPRI – Dundee epidemiology and global health summer school 2012.
http://www.dundee.ac.uk/cmdn/summer/

International Prevention Research Institute

June-July 2011 Teaching assistant for the IPRI – Dundee epidemiology and global health summer school 2011.

June-July 2010 Teaching assistant for the IPRI – Dundee epidemiology and global health summer school 2010.

Publications

2012 Boyle P, Boniol M, Koechlin A, Robertson C, Valentini F, Coppens K, Fairley LL, Boniol-Rech M, Zheng T, Zhang Y, Pasterk M, Smans M, Curado MP, Mullie P, Gandini S, Bota M, Bolli G, Rosenstock J and Autier P. **Diabetes and Breast cancer: a meta-analysis. Br J Cancer 2012; 107: 1608-17.**

2012 Murtagh MJ, Demir I, Jenkings KN, Wallace S, Murtagh B, Boniol M, Bota M, LaFlamme P, Boffetta P, Ferretti V, Burton PR. **Securing the Data Economy: Translating Privacy and Enacting Security in the Development of DataSHIELD. Public Health Genomics, 15, pp. 243-253.**

2010 Doody GM, Care MA, Burgoyne NJ, Bradford JR, Bota M, Bonifer C, Westhead DR, Tooze RM. **An extended set of PRDM1/BLIMP1 target genes links binding motif type to dynamic repression**. **Nucleic Acids Res. 2010 Sep;38(16):5336-50.**

Conference presentations

Maria Bota, Peter Boyle, Mathieu Boniol, Chris Robertson, **100 Years of cancer mortality in Scotland:**
2012 National Cancer Institute Directors Meeting, Lyon, France (oral presentation)

Philippe Autier, Mathieu Boniol, Alice Koechlin, Maria Bota, Chris Robertson, Julio Rosenstock, Geremia Bolli and Peter Boyle **Diabetes, related factors and breast cancer risk:**
2012 American Diabetes Association, Philadelphia, USA (poster)

Peter Boyle, Alice Koechlin, Mathieu Boniol, Chris Robertson, Maria Bota, Geremia B. Bolli and Julio Rosenstock, **Updated meta-analysis of cancer risk among users of insulin glargine:**
2012 American Diabetes Association, Philadelphia, USA (poster)

IPRI International Prevention Research Institute

CV Mathieu Boniol

Dr. Mathieu BONIOL
Born 09-08-1977, Married, 2 children

Work:
International Prevention Research Institute
95 cours Lafayette
69006 Lyon
France
Tel. 04 72 17 11 85
Mobile : 06 48 34 45 08
e-mail : mathieu.boniol@i-pri.org
Home:
280 Chemin des Fontanettes
38121 Chonas L'Amballan
France
Tel. 04 74 56 29 07
e-mail: mailingmat@yahoo.fr

OCCUPATION AND TRAINING

January 2010 – Present (Lyon) **International Prevention Research Institute**
Research Director

October 2006-December 2009 (Lyon) **International Agency for Research on Cancer**
Statistician **(**Fixed-term contract**)**

October 2004-September 2006 (Lyon) **International Agency for Research on Cancer**
Post-Doc (Special Training Award)

September 2001-September 2004 **INSERM Unit 590 (Centre Léon-Bérard, Lyon)**
PhD **-** Thesis Director : Jean-François Doré
« Role of host factors and solar exposure in the risk of cutaneous melanoma»

February 2002-September 2004 (Lyon) **International Agency for Research on Cancer**
Visiting Scientist
Atlas of cancer mortality in Europe. Supervisor: Michel Smans

June 2001 (2 weeks) **EORTC data center (Bruxelles, Belgium)**
ICRETT grant from UICC
Study of the period of diagnosis as prognostic factor for cutaneous melanoma in two randomized controlled trial of the EORTC Melanoma group

March 1999 - September 2001 **INSERM Unit 453 (Centre Léon-Bérard, Lyon)**
Training in epidemiology

August 1998 **PASTEUR MERIEUX S.V. (Marcy L'Etoile, France)**
Laboratory technician, Thymoglobuline department : production and treatment of thymocytes

EDUCATION

2001-2004 **PhD. Epidemiology** 'Doctorat d'épidémiologie'.
Université de Bourgogne (Dijon)
Mention très honorable avec les félicitations du jury

1999-2001 **Master in clinical epidemiology- option biostatistics**
* DEA Epidémiologie clinique et évaluation des actions de santé

Université de Bourgogne (Dijon). Mention bien (4ème/22)
* Maîtrise des sciences sanitaires et sociales (option Recherche Clinique)
Université Claude Bernard Lyon 1. Mention bien

1996-1999 **Bachelor in biostatistics.**
Université Claude Bernard Lyon 1.

PROFESSIONAL MEMBERSHIPS

Honorary lecturer, University of Dundee, United Kingdom.
President of the European Society of skin cancer prevention – EUROSKIN www.euroskin.eu
Member of "Physical agent" committee of the French cohort ELFE (INED, France)
Member of the EORTC Melanoma group
Member of the International Task Force on Skin Cancer Screening and Prevention (Hamburg, Germany)

REVIEWER AND EXPERTISE ACTIVITIES

Reviewer for: Acta Dermato-Venereologica, Annals of Oncology, Archives of Dermatology, Archives of Internal Medicine, Biomed Central Cancer, European Journal of Cancer, International Journal of Environmental Research and Public Health, JEADV, Lung Cancer, Melanoma Research, Surgical Oncology, The Breast, Travel Medicine and Infectious Disease. Grant applications reviewer for Cancer Research UK , INCa (Institut National du Cancer).
Expert for: WHO expert in the French AFSSET (Agence française de sécurité sanitaire de l'environnement et du travail) working group on radiofrequencies 2009, INVS (institut de veille sanitaire) working group on sunbeds. CNAM (Caisse d'assurance maladie) working group on prostate cancer screening

LANGUAGE

French
English (UN proficiency language certified)

INFORMATIC SKILLS

SAS, SPSS, Stata, Epi-info, R(notions), TreeAge, ArcGis, MapScan,
Basic, Turbo Pascal, Fortran, Java

HOBBIES AND PERSONNAL INTEREST

Music, cinema, swimming, role playing games, parlour games
Musician: Drums, Electric Guitar; style: rock, heavy metal

Mathieu BONIOL –Scientific publications

- Original peer reviewed articles

2013

Autier P, Boniol M. RE: Relationship between sunbed use and melanoma risk in a large case-control study in the United Kingdom. Int J Cancer. **2013**;132(8):1959.

Autier P, Koechlin A, Boniol M, Mullie P, Bolli G, Rosenstock J, Boyle P. Serum insulin and C-peptide concentration and breast cancer: a meta-analysis. Cancer Causes Control. **2013** Feb 14. [Epub ahead of print]

Autier P, Boniol M. Effect of screening mammography on breast cancer incidence. N Engl J Med. **2013**;368(7):677.

Rosenblatt E, Izewska J, Anacak Y, Pynda Y, Scalliet P, Boniol M, Autier P. Radiotherapy capacity in European countries: an analysis of the Directory of Radiotherapy Centres (DIRAC) database. Lancet Oncol. **2013**;14(2):e79-86.

2012

Autier P, Boniol M. Pitfalls in using case-control studies for the evaluation of the effectiveness of breast screening programmes. Eur J Cancer Prev. **2012** Dec 20. [Epub ahead of print]

Autier P, Boniol M. Breast cancer screening: evidence of benefit depends on the method used. BMC Med. **2012**;10:163.

Boniol M, Boyle P, Autier P, Ruffion A, Perrin P. Critical role of prostate biopsy mortality in the number of years of life gained and lost within a prostate cancer screening programme. BJU Int. **2012**;110(11):1648-52.

Boyle P, Koechlin A, Pizot C, Boniol M, Robertson C, Mullie P, Bolli G, Rosenstock J, Autier P. Blood glucose concentrations and breast cancer risk in women without diabetes: a meta-analysis. Eur J Nutr. **2012** Nov 3. [Epub ahead of print]

Boyle P, Boniol M, Koechlin A, Robertson C, Valentini F, Coppens K, Fairley LL, Boniol M, Zheng T, Zhang Y, Pasterk M, Smans M, Curado MP, Mullie P, Gandini S, Bota M, Bolli GB, Rosenstock J, Autier P. Diabetes and breast cancer risk: a meta-analysis. Br J Cancer. **2012**;107(9):1608-17.

Boniol M, Autier P, Boyle P, Gandini S. Cutaneous melanoma attributable to sunbed use: systematic review and meta-analysis. BMJ. **2012**;345:e4757.

Autier P, Koechlin A, Smans M, Vatten L, Boniol M. Mammography screening and breast cancer mortality in Sweden. J Natl Cancer Inst. **2012**;104(14):1080-93.

Autier P, Boniol M, Perrin P. Prostate-cancer mortality after PSA screening. N Engl J Med. **2012**;366(23):2230

Autier P, Boniol M. The incidence of advanced breast cancer in the West Midlands, United Kingdom. Eur J Cancer Prev. **2012**;21(3):217-21.

Murtagh MJ, Demir I, Jenkings KN, Wallace SE, Murtagh B, Boniol M, Bota M, Laflamme P, Boffetta P, Ferretti V, Burton PR. Securing the Data Economy: Translating Privacy and Enacting Security in the Development of DataSHIELD. Public Health Genomics. **2012**;15(5):243-53.

Autier P, Boniol M. Mammography screening and breast cancer mortality--letter. Cancer Epidemiol Biomarkers Prev. **2012**;21(5):869

Chaabna K, Boniol M, de Vuyst H, Vanhems P, Antônio de Ávila Vitoria M, Curado MP. Geographical patterns of Kaposi's sarcoma, nonHodgkin lymphomas, and cervical cancer associated with HIV infection in five African populations. Eur J Cancer Prev. **2012** ;21(1):1-9.

2011

Haukka J, Byrnes G, Boniol M, Autier P. Trends in breast cancer mortality in Sweden before and after implementation of mammography screening. PLoS One. **2011**;6(9):e22422.

Boniol M. Rapporteur's report on Session 2: Epidemiological findings. Prog Biophys Mol Biol. **2011** ;107(3):367-8
Gandini S, Autier P, Boniol M. Reviews on sun exposure and artificial light and melanoma. Prog Biophys Mol Biol. **2011** ; 107(3):362-6

Greinert R, Boniol M. Skin cancer - Primary and secondary prevention (information campaigns and screening) - With a focus on children & sunbeds. Prog Biophys Mol Biol. **2011** Sep 3. [Epub ahead of print]

Autier P, Boniol M, Gavin A, Vatten LJ. Breast cancer mortality in neighbouring European countries with different levels of screening but similar access to treatment: trend analysis of WHO mortality database. BMJ. **2011** Jul 28;343:d4411. doi: 10.1136/bmj.d4411.

Villar S, Le Roux-Goglin E, Gouas DA, Plymoth A, Ferro G, Boniol M, Lereau M, Bah E, Hall AJ, Wild CP, Mendy M, Norder H, van der Sande M, Whittle H, Friesen MD, Groopman JD, Hainaut P. Seasonal Variation in TP53 R249S-mutated Serum DNA With Aflatoxin Exposure And Hepatitis B Virus Infection. Environ Health Perspect. **2011** Jul 18. [Epub ahead of print]

Boniol M, Doré JF, Boyle P. Re. Lehrer S, Green S, Stock RG (2011) Association between number of cell phone contracts and brain tumor incidence in nineteen U.S. States. J Neurooncol 101:505-507. J Neurooncol. **2011** Apr 16. [Epub ahead of print]

Autier P, Boniol M, Doré JF. Is Sunscreen Use for Melanoma Prevention Valid for All Sun Exposure Circumstances? J Clin Oncol. **2011** Apr 4. [Epub ahead of print]

Autier P, Doré JF, Breitbart E, Greinert R, Pasterk M, Boniol M. The indoor tanning industry's double game. Lancet. **2011** Apr 16;377(9774):1299-301.

Chaillol I, Boniol M, Middleton R, Doré JF, Autier P, Gavin A. Seasonality of cutaneous melanoma diagnosis in Northern Ireland with a review. Melanoma Res. **2011** Apr;21(2):144-51.

Autier P, Boniol M, Middleton R, Doré JF, Héry C, Zheng T, Gavin A. Advanced breast cancer incidence following population-based mammographic screening. Ann Oncol. **2011** Jan 20. [Epub ahead of print]

Autier P, Boniol M. Caution needed for country-specific cancer survival. Lancet. **2011** Jan 8;377(9760):99-101.

Shin A, Park S, Shin HR, Park EH, Park SK, Oh JK, Lim MK, Choi BY, Boniol M, Boffetta P. Population attributable fraction of infection-related cancers in Korea. Ann Oncol. **2011** Mar 8. [Epub ahead of print]

Gandini S, Boniol M, Haukka J, Byrnes G, Cox B, Sneyd MJ, Mullie P, Autier P. Meta-analysis of observational studies of serum 25-hydroxyvitamin D levels and colorectal, breast and prostate cancer and colorectal adenoma. Int J Cancer. **2011** Mar 15;128(6):1414-24.

2010

Boniol M, Césarini P, Chignol MC, Césarini JP, Doré JF. [Why indoor tanning must be taxed? A proposal from La Sécurité Solaire, WHO collaborating centre]. Presse Med. **2010** Dec;39(12):1236-7.

Boniol M, Autier P. Prevalence of main cancer lifestyle risk factors in Europe in 2000. Eur J Cancer. **2010**;46(14):2534-44.

Autier P, Tryggvadóttir L, Sigurdsson T, Olafsdóttir E, Sigurgeirsson B, Jonasson JG, Olafsson JH, Byrnes GB, Héry C, Doré JF, Boniol M. Autier et al. Respond to "A Sunbed Epidemic?" Am J Epidemiol. **2010** Sep 2. [Epub ahead of print]

Héry C, Tryggvadóttir L, Sigurdsson T, Olafsdóttir E, Sigurgeirsson B, Jonasson JG, Olafsson JH, Boniol M, Byrnes GB, Doré JF, Autier P. A melanoma epidemic in Iceland: possible influence of sunbed use. Am J Epidemiol. **2010**;172(7):762-7.

Autier P, Boniol M, Lavecchia C, Vatten L, Gavin A, Héry C, Heanue M. Disparities in breast cancer mortality trends between 30 European countries: retrospective trend analysis of WHO mortality database. BMJ. **2010** Aug 11;341:c3620. doi: 10.1136/bmj.c3620.

Carvalho LV, Pereira EM, Frappart L, Boniol M, Bernardo WM, Tarricone V, Tavtigian S, Southey MC. Molecular characterization of breast cancer in young Brazilian women. Rev Assoc Med Bras. **2010**;56(3):278-87.

Shin HR, Joubert C, Boniol M, Hery C, Ahn SH, Won YJ, Nishino Y, Sobue T, Chen CJ, You SL, Mirasol-Lumague MR, Law SC, Mang O, Xiang YB, Chia KS, Rattanamongkolgul S, Chen JG, Curado MP, Autier P. Recent trends and patterns in breast cancer incidence among Eastern and Southeastern Asian women. Cancer Causes Control. **2010** Nov;21(11):1777-85.

Carsin AE, Drummond FJ, Black A, van Leeuwen PJ, Sharp L, Murray LJ, Connolly D, Egevad L, Boniol M, Autier P, Comber H, Gavin A. Impact of PSA testing and prostatic biopsy on cancer incidence and mortality: comparative study between the Republic of Ireland and Northern Ireland. Cancer Causes Control. **2010**;21(9):1523-31.

Renard F, Vankrunkelsven P, Van Eycken L, Henau K, Boniol M, Autier P. Decline in breast cancer incidence in the Flemish region of Belgium after a decline in hormonal replacement therapy. Ann Oncol. **2010** Dec;21(12):2356-60.

Doré JF, Boniol M, Telle-Lamberton M; Afsset Working Group on Radiofrequencies. Re: Time trends in brain tumor incidence rates in Denmark, Finland, Norway, and Sweden, 1974-2003. J Natl Cancer Inst. **2010** ;102(10):741-2

Geller AC, Greinert R, Sinclair C, Weinstock MA, Aitken J, Boniol M, Capellaro M, Doré JF, Elwood M, Fletcher SW, Gallagher R, Gandini S, Halpern AC, Katalinic A, Lucas R, Marghoob AA, Nolte S, Schüz J, Tucker MA, Volkmer B, Breitbart E. A nationwide population-based skin cancer screening in Germany: proceedings of the first meeting of the International Task Force on Skin Cancer Screening and Prevention (September 24 and 25, 2009). Cancer Epidemiol. **2010**;34(3):355-8.

Boffetta P, Autier P, Boniol M, Boyle P, Hill C, Aurengo A, Masse R, Thé G, Valleron AJ, Monier R, Tubiana M. An estimate of cancers attributable to occupational exposures in france. J Occup Environ Med. **2010** ;52(4):399-406.

Rey G, Boniol M, Jougla E. Estimating the number of alcohol-attributable deaths: methodological issues and illustration with French data for 2006. Addiction. **2010**;105(6):1018-29.

Shin HR, Boniol M, Joubert C, Hery C, Haukka J, Autier P, Nishino Y, Sobue T, Chen CJ, You SL, Ahn SH, Jung KW, Law SC, Mang O, Chia KS. Secular trends in breast cancer mortality in five East Asian populations: Hong Kong, Japan, Korea, Singapore and Taiwan.
Cancer Sci. **2010**; 101(5):1241-6.

2009

Autier P, Héry C, Haukka J, Boniol M, Byrnes G. Advanced breast cancer and breast cancer mortality in randomized controlled trials on mammography screening. J Clin Oncol. **2009** ;27(35):5919-23.

Caini S, Gandini S, Sera F, Raimondi S, Fargnoli MC, Boniol M, Armstrong BK. Meta-analysis of risk factors for cutaneous melanoma according to anatomical site and clinico-pathological variant Eur J Cancer. **2009**;45(17):3054-63.

Montella A, Gavin A, Middleton R, Autier P, Boniol M. Cutaneous melanoma mortality starting to change: A study of trends in Northern Ireland. Eur J Cancer. **2009**;45(13):2360-6.

Cantwell MM, Murray LJ, Catney D, Donnelly D, Autier P, Boniol M, Fox C, Middleton RJ, Dolan OM, Gavin AT. Second primary cancers in patients with skin cancer: a population-based study in Northern Ireland. Br J Cancer. **2009**;100(1):174-7.

Degrave E, Meeusen B, Grivegnée AR, Boniol M, Autier P. Causes of death among Belgian professional military radar operators: a 37-year retrospective cohort study. Int J Cancer. **2009**;124(4):945-51.

Boffetta P, Tubiana M, Hill C, Boniol M, Aurengo A, Masse R, Valleron AJ, Monier R, de Thé G, Boyle P, Autier P. The causes of cancer in France. Ann Oncol. **2009**;20(3):550-5.

2008

Berthiller J, Straif K, Boniol M, Voirin N, Benhaïm-Luzon V, Ayoub WB, Dari I, Laouamri S, Hamdi-Cherif M, Bartal M, Ayed FB, Sasco AJ. Cannabis smoking and risk of lung cancer in men: a pooled analysis of three studies in Maghreb. J Thorac Oncol. **2008**;3(12):1398-403.

Boniol M, Chignol MC, Dore JF. Sun protection among skin cancer-treated patients. J Eur Acad Dermatol Venereol. **2008** ;22(5):646-7

Héry C, Ferlay J, Boniol M, Autier P. Quantification of changes in breast cancer incidence and mortality since 1990 in 35 countries with Caucasian-majority populations. Ann Oncol. **2008**;19(6):1187-94

Bartsch G, Horninger W, Klocker H, Pelzer A, Bektic J, Oberaigner W, Schennach H, Schäfer G, Frauscher F, Boniol M, Severi G, Robertson C, Boyle P; Tyrol Prostate Cancer Screening Group. Tyrol Prostate Cancer Demonstration Project: early detection, treatment, outcome, incidence and mortality. BJU Int. **2008**;101(7):809-16.

Héry C, Ferlay J, Boniol M, Autier P. Changes in breast cancer incidence and mortality in middle-aged and elderly women in 28 countries with Caucasian majority populations. Ann Oncol. **2008**;19(5):1009-18

Gandini S, Botteri E, Iodice S, Boniol M, Lowenfels AB, Maisonneuve P, Boyle P. Tobacco smoking and cancer: a meta-analysis. Int J Cancer. **2008** 1;122(1):155-64.

Boniol M, Verriest JP, Pedeux R, Doré JF. Proportion of skin surface area of children and young adults from 2 to 18 years old. J Invest Dermatol. **2008**;128(2):461-4.

Boniol M, Dore JF, Autier P. Changing the labeling of sunscreen, will we transform sun avoiders into sunscreen users? J Invest Dermatol. **2008**;128(2):481

2007

Autier P, Boniol M, Héry C, Masuyer E, Ferlay J. Cancer survival statistics should be viewed with caution. Lancet Oncol. **2007**;8(12):1050-2

Boniol M, Autier P, Doré JF. Photoprotection. Lancet. **2007**;370(9597):1481-2

Autier P, Boniol M, Dore JF. Sunscreen use and increased duration of intentional sun exposure: Still a burning issue. Int J Cancer. **2007**;121(1):1-5

Ferlay J, Autier P, Boniol M, Heanue M, Colombet M, Boyle P. Estimates of the cancer incidence and mortality in Europe in 2006. Ann Oncol. **2007**;18(3):581-92.

2006

The International Agency for Research on Cancer Working Group on artificial ultraviolet (UV) light and skin cancer, Autier P, Boniol M, Boyle P, Daniel J, Dore JF, Gandini S, Green A, Newton-Bishop J, Weinstock MA, Westerdahl J, Secretan B, Walter SD. The association of use of sunbeds with cutaneous malignant melanoma and other skin cancers: A systematic review. Int J Cancer. **2006**;120:1116–22.

Voirin N, Berthillet J, Benhaim-Luzon V, Boniol M, Straif K, Ben Ayoud W, Ben Ayed F, Sasco A. Risk for lung cancer and past use of cannabis in Tunisia. J Thorac Oncol. **2006**;1:577–9.

Cardis E, Krewski D, Boniol M, Drozdovitch V, Darby SC, Gilbert ES, Akiba S, Benichou J, Ferlay J, Gandini S, Hill C, Howe G, Kesminiene A, Moser M, Sanchez M, Storm H, Voisin L, Boyle P. Estimates of the cancer burden in Europe from radioactive fallout from the Chernobyl accident. Int J Cancer. **2006** ;119(6):1224-35

Boniol M, Armstrong BK, Dore JF. Variation in incidence and fatality of melanoma by season of diagnosis in new South Wales, Australia. Cancer Epidemiol Biomarkers Prev. **2006**;15(3):524-6.

Pedeux R, Sales F, Pourchet J, Kallassy M, Fayolle C, Boniol M, Severi G, Ghanem G, Nakazawa HN, Autier P, Dore JF. Ultraviolet B sensitivity of peripheral lymphocytes as an independent risk factor for cutaneous melanoma. Eur J Cancer. **2006**;42(2):212-5.

2005

de Vries E, Boniol M, Severi G, Eggermont AM, Autier P, Bataille V, Dore JF, Coebergh JW. Public awareness about risk factors could pose problems for case-control studies: the example of sunbed use and cutaneous melanoma. Eur J Cancer. **2005**;41(14):2150-4.

Bataille V, Boniol M, De Vries E, Severi G, Brandberg Y, Sasieni P, Cuzick J, Eggermont A, Ringborg U, Grivegnee AR, Coebergh JW, Chignol MC, Dore JF, Autier P. A multicentre epidemiological study on sunbed use and cutaneous melanoma in Europe. Eur J Cancer. **2005**;41(14):2141-9.

Autier P, Severi G, Boniol M, de Vries E, Coebergh JW, Dore JF. Re: Sun exposure and mortality from melanoma. J Natl Cancer Inst. **2005**;97(15):1159.

Boniol M, De Vries E, Coebergh JW, Dore JF; EUROCARE Working Group. Seasonal variation in the occurrence of cutaneous melanoma in Europe: influence of latitude. An analysis using the EUROCARE group of registries. Eur J Cancer. **2005**;41(1):126-32.

2004

Autier P, Boniol M, Severi G, Pedeux R, Grivegnee AR, Dore JF. Sex differences in numbers of nevi on body sites of young European children: implications for the etiology of cutaneous melanoma. Cancer Epidemiol Biomarkers Prev. **2004**;13(12):2003-5.

de Vries E, Boniol M, Dore JF, Coebergh JW; EUROCARE working group. Lower incidence rates but thicker melanomas in Eastern Europe before 1992: a comparison with Western Europe. Eur J Cancer. **2004**;40(7):1045-52.

Beauchesne P, Pedeux R, Boniol M, Soler C. 99mTc-sestamibi brain SPECT after chemoradiotherapy is prognostic of survival in patients with high-grade glioma. J Nucl Med. **2004**;45(3):409-13.

Boniol M, Autier P, Dore JF. Re: A prospective study of pigmentation, sun exposure, and risk of cutaneous malignant melanoma in women. J Natl Cancer Inst. **2004**;96(4):335-6; author reply 336-8.

2003

Autier P, Coebergh JW, Boniol M, Dore JF, de Vries E, Eggermont AM. Management of melanoma patients: benefit of intense follow-up schedule is not demonstrated. J Clin Oncol. **2003**;21(19):3707.

Autier P, Severi G, Pedeux R, Cattaruzza MS, Boniol M, Grivegnee A, Dore JF; European Organisation for Research and Treatment of Cancer Melanoma Group. Number and size of nevi are influenced by different sun exposure components: implications for the etiology of cutaneous melanoma (Belgium, Germany, France, Italy). Cancer Causes Control. **2003**;14(5):453-9.

Beauchesne P, Soler C, Boniol M, Schmitt T. Response to a phase II study of concomitant-to-sequential use of etoposide and radiation therapy in newly diagnosed malignant gliomas. Am J Clin Oncol. **2003**;26(3):e22-7.

Pedeux R, Boniol M, Dore JF, Beauchesne P. Ultrafractionation radiation therapy of human gliomas: A preclinical model. Int J Cancer. **2003**;107(2):334.

2002

Pedeux R, Boniol M, Autier P, Doré JF. Re: DNA repair, dysplastic nevi, and sunlight sensitivity in the development of cutaneous malignant melanoma. J Natl Cancer Inst. **2002**;94(10):772-3

Severi G, Cattaruzza MS, Baglietto L, Boniol M, Dore JF, Grivegnee AR, Luther H, Autier P; European Organization for Research Treatment of Cancer (EORTC) Melanoma Cooperative Group. Sun exposure and sun protection in young European children: an EORTC multicentric study. Eur J Cancer. **2002**;38(6):820-6.

Boniol M, Sallin J, Dore JF. Time trends of cutaneous melanoma in Queensland, Australia and Central Europe. Cancer. **2002**;94(6):1902-3.

2001

Autier P, Boniol M, Severi G, Giles G, Cattaruzza MS, Luther H, Renard F, Grivegnee AR, Pedeux R, Dore JF; EPIMEL. The body site distribution of melanocytic naevi in 6-7 year old European children. Melanoma Res. **2001**;11(2):123-31.

Autier P, Boniol M, Severi G, Dore JF; European Organizatin for Research and Treatment of Cancer Melanoma Co-operative Group. Quantity of sunscreen used by European students. Br J Dermatol. **2001**;144(2):288-91.

2000

Autier P, Severi G, Dore JF, Boniol M. Has the sun protection factor had its day? Information on sunscreens should warn against excessive sun exposure. BMJ. **2000**;320(7244):1274-5.

- Other scientific activities (expert group, working group) and other publications (book and congress abstracts)

Boniol M, Coignard F, Vacquier B, Benmarhnia T, Gaillot de Saintignon J, Le Tertre A, Dore JF, Empereur-Bissonnet P. Evaluation de l'impact sanitaire de l'exposition aux ultraviolets délivrés par les appareils de bronzage artificiel sur le mélanome cutané en France. Bulletin d'Epidémiologie Hebdomadaire **2012**; 18-19, 210-213.

Gaillot de Saintignon J, Boniol M, Dore JF, Cesarini JP, Bessette D, Tordjman I.Retour sur les idées reçues qui motivent le recours au bronzage en cabine UV. Bulletin d'Epidémiologie Hebdomadaire **2012**; 18-19, 215-216.

Caisse Nationale d'Assurance Maladie (CNAM) working group on the evaluation of prostate cancer screening, Paris, 2012, CNAM.

InVS working group on the evaluation of the health impact of sunbed, Paris, **2011,** InVS.

INCA working group on 'Notes de synthèse sur l'effet potentiellement protecteur du rayonnement ultraviolet sur certains cancers internes (notamment colon et sein)', Paris, **2011**, INCa

INCa working group on 'Installations de bronzage UV : état des lieux des connaissances sur les risques de cancer et recommandations', Paris, **2010**, INCa

Afsset working group on 'Radiofrequences', Paris, **2009**, Afsset

Boniol M, Heanue M. Age-standardisation and denominators. In "Cancer Incidence in Five Continents Volume IX", Lyon, **2009**, IARC

IARC Working group on Vitamin D and cancer. IARC Working Group Reports Volume 5, Lyon, **2008,** IARC**.**

IARC Working group on Attributable Causes of Cancer in France in the year 2000. IARC Working Group Reports Volume 3, Lyon, **2007,** IARC**.**

Boniol M, Doré JF, Autier P, Smans M, Boyle P. Descriptive epidemiology of skin cancer incidence and mortality. pp. 203-223 In "*Skin Cancer Prevention*" Ringborg U, Brandberg Y, Breitbart EW, Greinert R, eds., Informa healthcare **2007**.

IARC Working group on risk of skin cancer and exposure to artificial light. IARC Working Group Reports Volume 1, Lyon, **2006,** IARC**.**

Doré JF, Boniol M. Environmental influences on cutaneous melanoma. In "*Textbook of Melanoma"* Thompson JF, Morton DL, Kroon BBR, eds., Martin Dunitz **2003**.

Doré JF, Pedeux R, Boniol M, Chignol MC, Autier P.(2001) Intermediate-effect biomarkers in prevention of skin cancer. pp.81-91 In "*Biomarkers in Cancer Chemoprevention*" Miller AB, Bartsch H, Bofetta P, Dragsted L, Vainio H, eds. IARC Scientific Publication N° 154. 1 Vol, Lyon, **2001**, IARC.

Doré JF, Boniol M. Faut-il conseiller l'usage des crèmes solaires chez l'enfant ? Les Nouvelles Dermatologiques **2001;**30:306-10.

Coebergh J, de Vries E, Soerjomataram I, Barendregt J, Oenema A, Lemmens VE, Kunst A, Boniol M, Autier PH, Klepp KI. Scenarios for Cancer prevention in Europe: the Eurocadet project. EJC Supp. **2009**;7(2):64-65.

Rey G, Boniol M, Jougla E. Estimating the number of alcohol-attributable deaths: methodological issues and illustration with French 2006 data. Alcoholism-Clinical and Experimental Research. **2010**;34(8):S108A.

Rosenblatt E, Izewska J, Anacak Y, Pynda Y, Boniol M, Autier R. Radiotherapy capacity in Europe 2009: results of the EUNICE project. EJC Suppl **2009**;7(2):158.

De Carvalho L, Tarricone V, Pereira E, Frappart L, Boniol M, Tavtigian SV, Southey MC. Molecular characterization of breast cancer in young Brazilian women. Histopathology. **2008**;53:33.

Boniol M, Cattaruzza MS, Wald L, Chignol MC, Richard MA, Leccia MT, Truchetet F, Renoirte C, Vereecken P, Autier P, Dore JF. Individual sun exposure can be assessed using meteorologic satellite measurements. Epidemiol. **2006**;17(6):S245-S245.

Boyle P, Boniol M, Dore JF, Chignol MC, Wald L. UV-FRANCE. Measurement of individual and population exposure to ultraviolet radiation based on data from meteorological satellites. Epidemiol. **2006**;17(6):S306-S306.

Bartsch G, Horninger W, Oberaigner W, Schonitzer D, Klocker H, Robertson C, Seven G, Boniol M, Boyle P. Tyrolean screening study: Update 2005 - Stage migration and decrease of mortality. J Urol. **2006**;175(4):S153-S154.

Bataille V, Boniol M, De Vries E, Severi G, Brandberg Y, Sasieni P, Cuzick J, Eggermont A, Ringborg U, Grivegnee AR, Coebergh JW, Dore JF, Autier P. Sunbed use and melanoma: a multi-centre case-control study of melanoma in Europe. Br J Dermatol. **2005**;153(S1):2.

Bartsch GC, Horninger W, Oberaigner W, Schonitzer D, Klocker H, Berger AP, Pelzer A, Bektic J, Robertson C, Severi G, Boniol M, Boyle P. Prostate cancer mortality following introduction of prostate specific antigen (PSA) mass screening in the Federal State of Tyrol, Austria: Follow-up until 2003. J Urol. **2005**;173(4):S146.

Bartsch G, Horninger W, Oberaigner W, Schonitzer D, Klocker H, Berger A, Pelzer A, Bektic J, Robertson C, Severi G, Boniol M, Boyle P. Prostate cancer mortality following introduction of prostate specific antigen (PSA) mass screening in the federal state of Tyrol, Austria: Follow-up until 2003. Eur Urol Suppl. **2005**;4(3):152.

De Vries E, Boniol M, Severi G, Brandberg Y, Eggermont A, Ringborg U, Grivegnee A, Coebergh JW, Dore JF, Autier P, Cuzick J, Batailler B. Sunbed use in melanoma cases and controls in Europe: a European Union multicentre case-control study. Br J Dermatol. **2003**;149(S64):87-88.

Pedeux R, Sales F, Pourchet J, Kallassy M, Boniol M, Severi G, Ghanem G, Nakazawa H, Autier P, Dore JF. Individual sensitivity to ultraviolet light: A new independent risk factor for cutaneous melanoma. Pigment Cell Research **2002**;15(S9):23.

Autier PH, Dore JF, Severi G, Pedeux R, Boniol M. Number and size of naevi are influenced by different sun exposure components: Implications for the aetiology of cutaneous melanoma. Pigment Cell Research. **2002**;15(S9):24.

- Selected invited oral presentations

- 7th International Conference on the science of exposure assessment (X2012), Edinburgh, United Kingdom, 2-5/07/2012 - "How to reduce the burden of skin cancer? Protective clothing, sunscreens, shading, avoiding sunbed use."
- Conference on "Ozone depletion, UV exposure and skin cancer" Copenhaguen, Denmark, 25/04/2012 - "Quantification of sun exposure in Europe and its effects on the development of skin cancer"
- Workshop on "health risks of sunbed use – needs, regulations and perspectives" at the Federal ministry of environment, Berlin, Germany, 23/04/2012 - "Sunbeds in Europe – the "double game" of the sunbed industry"
- Conference on "the epidemiology of cutaneous melanoma: from its prevention to its cure", Istituto Dermopatico dell'Immacolata (IDI), Roma, Italy, 01/12/2011 - "Eurosun project: strategies for decreasing skin cancer"

- International WHO-ICNIRP joint workshop on "Non-ionizing radiation & Children's health", Ljubljana, Slovenia, 18-20/05/2011- "Skin Cancer – primary and secondary prevention" and Epidemiology session's rapporteur
- INCa, Paris 06/05/2010 Meeting "*Developper la recherche translationnelle et Clinique Française dans le melanome*" - "Epidemiology of melanoma"
- World Melanoma congress 12-16/05/2009 Vienna, Austria – "Cutaneous melanoma mortality starting to change: a study of trends in Northern Ireland.".
- XXXème Cours de Dermatologie Pédiatrique, 14/04/2009 Arcachon, France : "Evolution de la surface cutanée chez l'enfant.".
- Societe francaise de dermatologie, Paris, France. 13/03/2008: " Récentes tendances d'incidence et de mortalité du mélanome cutané: impact de l'exposition solaire, de l'utilisation de solarium et du dépistage "
- RECIF, Lyon, France 27/03/2008: "Prostate Cancer.".
- Iarc 26-29/06/2007 Lyon, France (seminar, presentation to the director of DG Sanco at Iarc): "Estimating proportions of cancers attributable to lifestyle and environment in Europe: opportunities and methodological issues"
- Iarc seminar 28/11/2006 Lyon, France: "Exposure to sunbed and risk of cutaneous melanoma: a meta-analysis"
- Iarc Day 17/05/2006 Lyon, France: "Torture your data to find out about errors"
- Working group on avoidable causes of cancer 21-23/03/2005 Lyon, France: "Methodological issues on the calculation of attributable fraction"
- Several lecture on « Solar radiation and skin cancer » at Ecole pratique des hautes etudes, Lyon, France 2003-2009.
- World Melanoma congress 06/09/2005 Vancouver, Canada: Nodular melanoma incidence. Seasonal variation of melanoma incidence in NSW
- World Melanoma congress 2001 – Venice, Italy: Seasonal variation in melanoma incidence.

CV Philippe Autier

CURRICULUM VITAE

(September 2012)

Philippe AUTIER, M.D., M.P.H., Ph.D.
(Physician-Epidemiologist)

Citizenship: Belgian
Date of birth: December 29, 1956
Married, name of spouse: Anne Brédart, psychologist working at the Curie Cancer Institute in Paris

Children: Anton (21 years old) and Gilles (16 years old).

Place of residence:

33 rue Vaubecour
69002 Lyon
France

Professional address:

International Prevention Research Institute (iPRI)
www.i-pri.org

Legal address: 95 Cours Lafayette, 69006 Lyon, France

Office : Espace Européen, Bâtiment G
Chemin du Saquin
69130 Ecully (Lyon), France
Tel : +33 472 17 11 83 (direct)
+33 472 17 11 99 (reception)
E-mail : philippe.autier@i-pri.org

EDUCATION

DOCTOR IN MEDICINE 1975-82
Université Libre de Bruxelles (Bruxelles).

DIPLOMA OF DOCTOR IN TROPICAL MEDICINE TROPICALE 1982-83
Institut de Médecine Tropicale (Antwerpen)

EPIDEMIOLOGIC INTELLIGENCE SERVICE COURSE (September and October 1986) "Centers for Disease Control" (Atlanta, U.S.A) and the "Institut pour le Dévelopement de la Biostatistique et de l'Epidémiologie" (Paris, France).

MASTER IN PUBLIC HEALTH 1988-89
Harvard School of Public Health (Cambridge, Massachusetts, U.S.A). Studies done under the "Fullbright" status with a grant from the "Frank Boas Foundation";
Areas of concentration: Biostatistics, Epidemiology and Health Economics

WORLD HEALTH ORGANISATION SEMINAR FOR THE TRAINING OF CONSULTANTS FOR THE GLOBAL PROGRAM ON AIDS. September 1987, Genève (Switzerland).

COURSE OF MOLECULAR BIOLOGY FOR THE EPIDEMIOLOGIST.
International Agency for Research on Cancer, September 1990, Lyon (France).

COURSE OF BIOSTATISTICS APPLIED TO THE GENETIC ASPECTS OF CANCER. International Agency for Research on Cancer, August 1991, Lyon (France).

PhD DEGREE OBTAINED AT ERASMUS UNIVERSITY ROTTERDAM (THE NETHERLANDS)
Thesis entitled "Sunbed use, sunscreen use, childhood sun exposure and cutaneous melanoma", defended on 1éth of October 2012.

ACADEMIC POSITION

HONORARY PROFESSOR of EPIDEMIOLOGY at the University of Dundee, Scotland, UK.

International Prevention Research Institute

CURRENT POSITION

From December 2009 onwards

Vice-President Population Studies at the International Prevention Research Institute (iPRI). This position entails supervision of scientific works done by a team of biostatisticians (4), computer specialists (2), and assistants (3), as well as PhD students and students doing internship in biostatistics and epidemiology.

Ph Autier scientific activities mainly deal with etiologic researches based on epidemiological methods and meta-analytic methods, as well as clinical epidemiology. Main research areas are related to complex issues that need problem-solving approaches and connecting data from various sources.

Ph Autier supervised works done by a team of epidemiologists, statisticians, computer specialists, data managers and other functions. Ph Autier was responsible of result reporting, report writing and presentation of conclusions of projects to official bodies and companies.

Main working topics and research areas are:

1/ Performing research activities part of iPRI contractual agreements. On-going activities in 2012 are:

- Cancer risk associated with insulin and non-insulin treatments of diabetes mellitus, using data from European cohorts (mainly prescription databases), and systematic review and meta-analysis of published literature (Studies commissioned by the European Medicine Agency [EMEA, London]);
- Pharmacovigilance plans for new diabetes treatment, cancer and other adverse events in prescription databases and in cohorts (Studies commissioned by the European Medicine Agency [EMEA, London]).
- Meta-analyses of diabetes and metabolic conditions and cancer risk;
- Risk of oral cancer associated with mouthrinse preparations;
- Use of mouth rinse preparations and prevention of periodontal infections (plaque, gingivitis);
- Risk of cancer associated with carbonated beverages.

Results of all these activities are or will be published in peer-reviewed journals and/or submitted as official reports to regulatory bodies and/or public health institutions.

2/ Services and researches in **health technology assessment** (HTA) and **comparative (relative) effectiveness** research, with a focus on clinical and epidemiological designs and data gathering for documenting effectiveness and perform health economics evaluations. PA is doing health outcome research on clinical and public health indicators of efficacy and effectiveness (eg, survival, mortality, premature mortality, incidence, case-fatality, QALY and related indicators), especially on their strength and weaknesses. The emphasis is put on best use of already available data, published or non published, as well as already existing but unexploited databases and on-going epidemiological studies.

3/ Development of clinical, epidemiological projects for **testing new screening, new diagnosis tools or new biomarkers in cancer detection and screening**.

> From 2003 until 2011, the main topic of activity was a new ultrasound-based technologies (**HistoScanning,** www.histoscanning.com) enabling distinction between cancer and non cancerous tissues in solid organs. HistoScanning has been developed for the (early) detection of breast, prostate, thyroid and ovarian cancers. The main task of PA is to supervise clinical studies, provide statistical help to investigators, to analyse data and prepare publications.
>
> Current research support is provided to imaging modalities for prostate and breast cancer (e.g., real time elastography).

4/ Research on melanoma epidemiology and photoprotection. Extensive collaborations have been built with cancer registries in Northern Ireland, Scotland and the Netherlands.

5/ Epidemiological researches on the **human effects of vitamins** and related compounds. Current main topic of work is the **vitamin D**;

6/ Research on evaluation of screening activities in general populations through analysis of cancer registry data on trends in incidence of advanced cancer, and on cancer-specific mortality.

7/ PA is regularly solicited by biomedical companies as well as by public services (e.g., HTA agencies) to provide expertise in domains like clinical epidemiology, skin carcinogenesis, breast cancer, vitamin and hormone-related issues.

PREVIOUS POSITIONS

September 2005-November 2009

From September 1, 2005, Dr Ph Autier had a fixed-term position at the International Agency for Research on Cancer (IARC), at P5 level. He decided to leave the IARC for joining the **International Prevention Research Institute (iPRI)**

Official position of Ph Autier within the IARC is **Group Head (level P5)**, of Prevention Evaluation Group (five scientists, one secretary, PhD and post-doc students).

The overall duties of Ph Autier were to manage human resources, to set agendas and priorities, and to supervise scientific activities of the group.

Main projects headed by Ph Autier in February 2009 are:

1/ Coordination of studies on evaluation of **impact of cancer screening on cancer incidence and mortality.**

2/ Coordination of scientific activities on causes and prevention of skin cancers, mainly the cutaneous melanoma. Coordination of the **EUROSUN project**, funded by the Directorate General on Health and Consumers of the European Commission that has the goal to evaluation exposure to solar ultraviolet radiation of Europeans using measurements provided by meteorological satellites.

3/ Coordination of development of new biostatistical methods for **mathematical description of cancer development**, with a particular focus on finding statistical characteristics best suited for describing biological behaviours of aggressive and indolent cancers.

4/ Development of a new area in descriptive epidemiology, called "**descriptive oncology**" that has the purpose to collect, organize and analyze and display data on cancer incidence, mortality, risk factors, screening activities, therapeutic activities and infrastructures. These activities are to be considered as a further expansion of IARC activities centred on Cancer in Five Continents and Globocan.

5/ Coordination of a IARC Working Group on **vitamin D and cancer** (first report issued in September 2008).

Main activities at IARC from 2005 until end of 2008 were:

1/ **Cluster coordinator**, with duty of management five different groups (60 persons): (i) Descriptive Epidemiology group, in charge of production of Cancer in Five Continents (CI-V); (ii) Data Analysis and Interpretation Group, in charge of epidemiological analysis of descriptive epidemiology data; (iii) Biostatistics and Methodology Support Group, in charge of biostatistics analysis as a common resource for the IARC; (iv) Information Technology Services, in charge of computer and networking technical aspects for the IARC, and (v), the Radiation Group, in charge of studies on ionizing and non-ionizing radiation and cancer. In 2009, these coordination activities stopped with the withdrawal of "clusters" from the IARC scientific structure.

2/ Leader of the coordination team and responsible for the day-to-day management of the project "Feasibility Study for Coordination of National Cancer Activities (EUROCAN)" contracted with the European Union (DG RESEARCH). The goal of this project is to identify barriers hindering high level, efficient cancer research in the European Union, and to propose ways for improving coordination of cancer research (details on www.eurocanplus.eu). Final report of the Eurocan+Plus Project is released on 10 April 2004, and is freely available on www.eurocanplus.eu or at www.iarc.fr.

November 2003 to August 2005

Head of the Unit of Epidemiology and Prevention of the Jules Bordet Institute (Brussels).

The main occupation of Ph Autier was to act as medical director of Advanced Medical Diagnosis, a Belgian start-up company that created and patented a new mathematical method for cancer screening, called **HistoScanning** (www.histoscanning.com). Ph Autier was responsible for the development and coordination of clinical studies aiming at testing the medical value of that new technique for the early detection of ovarian, prostate and breast cancers. Studies unfold in renowned medical institutions : Karolinska Institutet (Stockholm, Sweden), University of Tübingen (Germany), Erasmus Hospital (Rotterdam, The Netherlands), Oncologische Centrum of Antwerp (Prof L Denis, Belgium), Jules Bordet Institute (Brussels, Belgium), Hopital La Pitié Salpétrière (Paris, France), European Institute of Oncology (Milano, Italy), Sint Georges Hospital (London, UK).

Ph. Autier also supervised studies done by a team of 6 persons in the field of :
(1) Cancer screening.
(2) Epidemiology of cutaneous melanoma.
(3) Disease control in villages affected by the presence of industrial waste disposals (projects done for the Belgian Government).

That position encompassed regular contacts with public health authorities of Belgium and France, with the European level (e.g., with DG SANCO and DG Research of the European Commission), and also with multilateral health agencies (e.g., WHO). These contacts were related to (1) the administration of research projects, (2) to the co-ordination of collaborative works, and (3) to the provision of expert advice (consulting).

July 2000 to October 2003

Head of the Centre of Epidemiology and Statistics of the Luxembourg Institute for Health, located at the "Centre de Recherche Publique Santé" (CRP-Santé) in Luxemburg. The CRP-Santé is an independent public institution, funded by the Ministry of Health and to the Ministry of Research and Education of the Grand Duchy of Luxemburg. The principal tasks consisted in:

- developing prospective epidemiological studies using the numerous health-related databases existing in Luxemburg, and to develop original designs in etiologic research and genetic epidemiology of cancers, cardiovascular diseases and metabolic diseases such as osteoporosis.
- Devising, conducting and coordinating epidemiological studies at European levels.

In 2000 and 2001, Philippe Autier was expert to the programme "Health and Pollution" of the European Commission, Directorate-General Health & Consumer Protection (DG SANCO), for Health and Environment programmes, and pollution related diseases.

1996-2000:

Deputy Director at the European Institute of Oncology, Milan (Italy): Ph Autier coordinated programmes in etiologic epidemiology programmes and in epidemiological researches on melanoma. Research projects co-ordinated by Ph. Autier were financed by the European Commission (50%), private companies (30%), and governments (20%). Among other projects, Ph Autier received grants from the Programme Europe Against Cancer of the European Commission for studies on sunscreen for skin cancer prevention. He also received a grant from the 3rd Framework Programme (BIOMED) of the European Commission for conducting a European multicentric study of sunbed use and cutaneous melanoma.

1994-1996:

Health Outcome Manager at Merck Sharp and Dohme (MSD), SA/NV, Belgium. Main task was to develop and conduct studies on health economic and evidence based medicine. Reporting was done to the Managing Director. Studies were usually developed with Belgian opinion leaders and with Merck headquarters in the USA.

Several publications were done from studies initiated by Ph Autier, on use of statins in Belgium and on economic aspects of fractures and of osteoporosis (see publication list).

1989-1993:

(a) **Head of the Epidemiology and Prevention Unit of the Jules Bordet Institute** (Oncology centre in Brussels), and of the Oeuvre Belge du Cancer (Agency active in cancer prevention and in the funding of researches). In 1991-93, teacher of clinical research methods at the PHARMED COURSE organised by the Free University of Brussels, intended for the training in the development of new drugs or of new medical technologies.

(b) Co-ordinator of the Brussels Breast Cancer Screening Programme implemented by the three universities operating in the Brussels area (funded by the European Commission and Belgian Governmental agencies).

1988-89: Studies in Boston, USA.

1985-1988:

Founder and epidemiologist at the European Association for Health and Development (AEDES, Brussels-Paris-Barcelona; www.aedes.be). AEDES is specialized in the management of pharmaceuticals and health services at country level and in the handling of epidemics or large scale nutritional problems. Most funds of AEDES come from the European Commission, the World Bank and private institutions.

Ph Autier launched and coordinated the first Early Warning Systems for famine prevention in Mali and Chad, projects funded by the European Commission. Ph Autier conducted also various missions of expertise in epidemiologist in Angola, Mozambique, Hong-Kong, Zaïre, and Sudan.

1982-1985:

Serviced as volunteer in the humanitarian non-governmental organization Médecins Sans Frontière in Honduras (in 1985 and 1986), and in Chad (1987-88). In Chad, Ph Autier was the "medical coordinator" of projects conducted by team of about 50 expatriates and 200 Chadian health workers.

LANGUAGES

French: Mother tongue
English: High fluency in speaking and writing
Dutch: Good knowledge
Spanish: Some knowledge
Italian: Some knowledge

MEMBERSHIPS

CORE GROUP MEMBER OF THE WHO WORKING GROUP ON INDOOR UV TANNING (Geneva)

MEMBER of the EDITORIAL BOARD (epidemiology and prevention) of the journal **MELANOMA RESEARCH** (from February 2009)

MEMBER of the EDITORIAL BOARD (epidemiology and prevention) of the **EUROPEAN JOURNAL OF CANCER**

MEMBER and Co-CHAIRMAN of ***EPIMEL***, the Epidemiology and Prevention section of the **EORTC Melanoma Co-operative Group** (EORTC is the European Organisation for Research and Treatment of Cancer).

MEMBER OF BOARD OF THE **EUROPEAN MELANOMA GROUP** (Scientific non-profit organisation)

PRESIDENT OF THE BOARD OF DIRECTOR OF THE **ASSOCIATION EUROPEENNE POUR LE DEVELOPMENT ET LA SANTÉ (AEDES)**, asbl, vzw (Brussels, Paris) (non profit private organisation under Belgian law)

FORMER PRESIDENT AND MEMBER OF BOARD OF THE **AEDES FOUNDATION** (Brussels, Public Foundation under Belgian law)

MEMBER OF THE BOARD OF THE **ASSOCIATION EUROPEENNE POUR LE DEVELOPMENT ET LA SANTÉ (AEDES)**, scrl, Brussels and Paris (www.aedes.be).

PAST PRESIDENT AND MEMBER OF THE BOARD OF ***EPISEARCH***, a non-profit organization under the Belgian law dedicated to the promotion of emerging innovative methods (in economics, biostatistics and data handling) for clinical and population studies.

IPRI International Prevention Research Institute

PUBLICATION LIST

(peer reviewed, no abstract)

1. Autier P, Boniol M, Boyle P. Re: The report of the Independent UK Panel on Breast Cancer Screening. Lancet 2013 (in press).

2. Autier P, Koechlin A, Boniol M, et al. Serum insulin and C-peptide concentration and breast cancer: A meta-analysis. *Cancer Causes Control* 2013 (Epub ahead of print).

3. Autier P, Boniol M. Effect of screening mammography on breast cancer incidence.N Engl J Med. 2013;368(7):677. doi: 10.1056/NEJMc1215494#SA1.

4. Rosenblatt E, Izewska J, Anacak Y, Pynda Y, Scalliet P, Boniol M, Autier P. Radiotherapy capacity in European countries: an analysis of the Directory of Radiotherapy Centres (DIRAC) database. *Lancet Oncol*. 2013 Feb;14(2):e79-86.

5. Autier P, Boniol M. Pitfalls in using case-control studies for the evaluation of the effectiveness of breast screening programmes. *Eur J Cancer Prev*. 2012 Dec 20. [Epub ahead of print]

6. Autier P, Boniol M. Breast cancer screening: evidence of benefit depends on the method used. *BMC Medicine* 2012 Dec 12; 10: 163.

7. Boyle P, Koechlin A, Pizot C, Boniol M, Robertson C, Mullie P, Bolli G, Rosenstock J, Autier P. Blood glucose concentrations and breast cancer risk in women without diabetes: a meta-analysis. *Eur J Nutr*. 2012 Nov 3. [Epub ahead of print]

8. Autier P. Risk factors for breast cancer for women aged 40 to 49 years. *Ann Intern Med*. 2012 Oct 2;157(7):529.

9. Boyle P, Boniol M, Koechlin A, Robertson C, Valentini F, Coppens K, Fairley LL, Boniol M, Zheng T, Zhang Y, Pasterk M, Smans M, Curado MP, Mullie P, Gandini S, Bota M, Bolli GB, Rosenstock J, Autier P. Diabetes and breast cancer risk: a meta-analysis. *Br J Cancer*. 2012; doi: 10.1038/bjc.2012.414.

10. Autier P, Boniol M. RE: Relationship between sunbed use and melanoma risk in a large case-control study in the United Kingdom, by F. Elliot and Colleagues, published in the International Journal of Cancer on June 15, 2012. *Int J Cancer*. 2012; doi: 10.1002/ijc.27848.

11. Boniol M, Boyle P, Autier P, Ruffion A, Perrin P. Critical role of prostate biopsy mortality in the number of years of life gained and lost within a prostate cancer screening programme. *BJU Int*. 2012 Sep 18. doi: 10.1111/j.1464-410X.2012.11513.x.

12. Autier P. Mammography screening before introduction of the national breast screening programme in Norway. *Int J Cancer*. 2012 Aug 30. doi: 10.1002/ijc.27806.

13. Autier P, Esserman LJ, Flowers CI, Houssami N. Breast cancer screening: the questions answered. *Nat Rev Clin Oncol*. 2012;9:599-605. doi: 10.1038/nrclinonc.2012.126.

14. Salomon G, Spethmann J, Beckmann A, Autier P, Moore C, Durner L, Sandmann M, Haese A, Schlomm T, Michl U, Heinzer H, Graefen M, Steuber T. Accuracy of HistoScanning™ for the prediction of a negative surgical margin in patients undergoing radical prostatectomy. *BJU Int*. 2012 Aug 9. doi: 10.1111/j.1464-410X.2012.11396.x.

15. Raimondi S, Gandini S, Fargnoli MC, Bagnardi V, Maisonneuve P, Specchia C, Kumar R, Nagore E, Han J, Hansson J, Kanetsky PA, Ghiorzo P, Gruis NA, Dwyer T, Blizzard L, Fernandez-de-Misa R, Branicki W, Debniak T, Morling N, Landi MT, Palmieri G, Ribas G, Stratigos A, Cornelius L, Motokawa T, Anno S, Helsing P, Wong TH, Autier P, García-Borrón JC, Little J, Newton-Bishop J, Sera F, Liu F, Kayser M, Nijsten T, Study Group G. Melanocortin-1 receptor, skin cancer and phenotypic characteristics (M-SKIP) project: study design and methods for pooling results of genetic epidemiological studies. *BMC Med Res Methodol*. 2012;12:116.

16. Boniol M, Autier P, Boyle P, Gandini S. Cutaneous melanoma attributable to sunbed use: systematic review and meta-analysis. *BMJ*. 2012 Jul 24;345:e4757. doi: 10.1136/bmj.e4757. Review.

17. Autier P, Koechlin A, Smans M, Vatten L, Boniol M. Mammography screening and breast cancer mortality in Sweden. *J Natl Cancer Inst* 2012; 104: 1080-93.

18. Autier P, Gandini S, Mullie P. A Systematic review: Influence of vitamin D Supplementation on serum 25-hydroxyvitamin D concentration. *J Clin Endocrinol Metab* 2012; 97(8):2606-13.

19. Coste J, Carel JC, Autier P. [The grey realities of population screening]. Rev Epidemiol Sante Publique. 2012 Jun;60(3):163-5. French. No abstract available.

20. Autier P, Boniol M, Perrin P. Prostate-cancer mortality after PSA screening. N Engl J Med. 2012 Jun 7;366(23):2230; author reply 2230-1. No abstract available.

21. Autier P, Boniol M. Mammography screening and breast cancer mortality--letter. Cancer Epidemiol Biomarkers Prev. 2012 May;21(5):869.

22. Autier P, Boniol M. The incidence of advanced breast cancer in the West Midlands, United Kingdom. *Eur J Cancer Prev*. 2012; 21: 217-21.

23. Vaes E, Manchanda R, Autier P, Nir R, Nir D, Bleiberg H, Robert A, Menon U. Differential diagnosis of adnexal masses: sequential use of the risk of malignancy index and HistoScanning, a novel computer-aided diagnostic tool. *Ultrasound Obstet Gynecol*. 2012; 39:91-8.

24. Gandini S, Autier P, Boniol M. Reviews on sun exposure and artificial light and melanoma. *Prog Biophys Mol Biol*. 2011 Dec;107(3):362-6.

25. Simmons LA, Autier P, Zát'ura F, Braeckman J, Peltier A, Romic I, Stenzl A, Treurnicht K, Walker T, Nir D, Moore CM, Emberton M. Detection, localisation and characterisation of prostate cancer by Prostate HistoScanning(™). *BJU Int* 2011; 110:28-35.

26. Selby P, Autier P. The impact of the process of clinical research on health service outcomes. *Ann Oncol*. 2011 Nov;22 Suppl 7:vii5-vii9.

27. Speeckaert R, Vermaelen K, van Geel N, Autier P, Lambert J, Haspeslagh M, van Gele M, Thielemans K, Neyns B, Roche N, Verbeke N, Deron P, Speeckaert M, Brochez L. Indoleamine 2,3-dioxygenase, a new prognostic marker in sentinel lymph nodes of melanoma patients. *Eur J Cancer*. 2012; 48(13):2004-11.

28. Autier P. Frequency, digital technology, and the efficiency of screening mammography. *Ann Intern Med.* 2011; 155:554-5.

29. Autier P. Breast cancer screening. *Eur J Cancer*.2011; 47S3:S133-S146.
30. Autier P. Glossary of essential terms used in cancer screening. *Eur J Cancer.* 2011; 47S3:S171-S175.

31. Bonneux LG, Autier P. [Population-based breast cancer screening is not worthwhile. Screening has little effect on mortality]. [Article in Dutch]. *Ned Tijdschr Geneeskd.* 2011;155(35):A3774.

32. Sullivan R, Peppercorn J, Sikora K, Zalcberg J, Meropol NJ, Amir E, Khayat D, Boyle P, Autier P, Tannock IF, Fojo T, Siderov J, Williamson S, Camporesi S, McVie JG, Purushotham AD, Naredi P, Eggermont A, Brennan MF, Steinberg ML, De Ridder M, McCloskey SA,Verellen D, Roberts T, Storme G, Hicks RJ, Ell PJ, Hirsch BR, Carbone DP, Schulman KA, Catchpole P, Taylor D, Geissler J, Brinker NG, Meltzer D, Kerr D, Aapro M. Delivering affordable cancer care in high-income countries. *Lancet Oncol*. 2011 Sep;12(10):933-80.

33. Haukka J, Byrnes G, Boniol M, Autier P. Trends in breast cancer mortality in Sweden before and after implementation of screening. *PLoS One* 2011 (in press).

34. Autier P, Boniol M, Gavin A, Vatten L. Breast cancer mortality in neighbouring European countries with different levels of screening but similar access to treatment: trend analysis of WHO mortality database. *BMJ* 2011; 343: d4411.

35. Autier P, Boniol M, Doré JF. Is sunscreen use for melanoma prevention valid for all sun exposure circumstances? *J Clin Oncol* 2011 29(14): e425-6.

36. Mullie P, Autier P. Relation of vitamin d deficiency to cardiovascular disease. *Am J Cardiol* 2011;107:956.

37. Mullie P, Autier P. Fatty fish and the relation between 25(OH) vitamin D and triacylglycerol. *Eur J Clin Nutr* 2011 Jan 19. [Epub ahead of print]

38. Gandini S, Boniol M, Haukka J, Byrnes G, Cox B, Sneyd MJ, Mullie P, Autier P. Meta-analysis of observational studies of serum 25-hydroxyvitamin D levels and colorectal, breast and prostate cancer and colorectal adenoma. *Int J Cancer* 2011;128:1414-24.

39. Boffetta P, Autier P. Is breast cancer associated with tobacco smoking? *BMJ* 2011; 342: d1093.

40. Autier P, Doré JF, Eggermont AM, Coebergh JW. Epidemiological evidence that UVA radiation is involved in the genesis of cutaneous melanoma. *Curr Opin Oncol* 2011;23:189-96.

41. Vaes E, Manchanda R, Nir R, Nir D, Bleiberg H, Autier P, Menon U, Robert A. Mathematical models to discriminate between benign and malignant adnexal masses: potential diagnostic improvement using ovarian HistoScanning. *Int J Gynecol Cancer* 2011 Jan;21(1):35-43.

42. Autier P, Doré JF, Breitbart E, Greinert R, Pasterk M, Boniol M. The indoor tanning industry's double game. *Lancet* 2011;16: 377(9774): 1299-301.

43. Chaillol I, Boniol M, Middleton R, Doré JF, Autier P, Gavin A. Seasonality of cutaneous melanoma diagnosis in Northern Ireland with a review. *Melanoma Res* 2011 Apr;21(2):144-51.

44. Autier P, Boniol M, Middleton R, Doré JF, Héry C, Zheng T, Gavin A. Advanced breast cancer incidence following population-based mammographic screening. *Ann Oncol* 2011; 22(8):1726-35.

45. Autier P, Boniol M. Caution needed for country-specific cancer survival. *Lancet* 2011 Jan 8;377(9760):99-101.

46. International Agency for Research on Cancer. A review of human carcinogens Monograph No 100 - Part D: radiation. *IARC Monographs*, Lyon, 2012.

47. Autier P, Tryggvadóttir L, Sigurdsson T, Olafsdóttir E, Sigurgeirsson B, Jonasson JG, Olafsson JH, Byrnes GB, Héry C, Doré JF, Boniol M. Autier et al. Respond to "A Sunbed Epidemic?" *Am J Epidemiol* 2010 Sep 2. [Epub ahead of print].

48. Héry C, Tryggvadóttir L, Sigurdsson T, Sigurdsson T, Ólafsdóttir E, Sigurgeirsson B, Jonasson JG, Olafsson JH, Boniol M, Byrnes GB, Jean-François Doré JF, Autier P. A melanoma epidemic in Iceland: Possible influence of sunbed use. *Am J Epidemiol* 2010 Oct 1;172(7):762-7. Epub 2010 Sep 2.

49. Boniol M, Autier P. Prevalence of main cancer lifestyle risk factors in Europe in 2000. *Eur J Cancer* 2010 Sep;46(14):2534-44.

50. Shin HR, Joubert C, Boniol M, Hery C, Ahn SH, Won YJ, Nishino Y, Sobue T, Chen CJ, You SL, Mirasol-Lumague MR, Law SC, Mang O, Xiang YB, Chia KS, Rattanamongkolgul S, Chen JG, Curado MP, Autier P. Recent trends and patterns in breast cancer incidence among Eastern and Southeastern Asian women. *Cancer Causes Control* 2010 Nov;21(11):1777-85. Epub 2010 Jun 18.

51. Carsin AE, Drummond FJ, Black A, van Leeuwen PJ, Sharp L, Murray LJ, Connolly D, Egevad L, Boniol M, Autier P, Comber H, Gavin A. Impact of PSA testing and prostatic biopsy on cancer incidence and mortality: comparative study between the Republic of Ireland and Northern Ireland. *Cancer Causes Control* 2010 Sep;21(9):1523-31. Epub 2010 Jun 1.

52. Autier P, Boniol M, La Vecchia C, Vatten L, Gavin A, Héry C, Heanue M. Disparities in breast cancer mortality trends between 30 European countries: retrospective trend analysis of WHO mortality database. *BMJ*. 2010 Aug 11;341:c3620. Erratum in: *BMJ*. 2010;341:c4480. LaVecchia, Carlo [corrected to La Vecchia, Carlo].

53. Renard F, Vankrunkelsven P, Van Eycken L, Henau K, Boniol M, Autier P. Decline in breast cancer incidence in the Flemish region of Belgium after a decline in hormonal replacement therapy. *Ann Oncol* 2010 Dec;21(12):2356-60. Epub May 3.

54. Boffetta P, Autier P, Boniol M, Boyle P, Hill C, Aurengo A, Masse R, Thé G, Valleron AJ, Monier R, Tubiana M. An estimate of cancers attributable to occupational exposures in France. *J Occup Environ Med* 2010 Apr;52(4):399-406.

55. Lucidarme O, Akakpo JP, Granberg S, Sideri M, Levavi H, Schneider A, Autier P, Nir D, Bleiberg H; Ovarian HistoScanning Clinical Study Group. A new computer-aided diagnostic tool for non-invasive characterisation of malignant ovarian masses: results of a multicentre validation study. *Eur Radiol* 2010 Aug;20(8):1822-30. Epub 2010 Mar 20.

56. Shin HR, Boniol M, Joubert C, Hery C, Haukka J, Autier P, Nishino Y, Sobue T, Chen CJ, You SL, Ahn SH, Jung KW, Law SC, Mang O, Chia KS. Secular trends in breast cancer mortality in five East Asian populations: Hong Kong, Japan, Korea, Singapore and Taiwan. *Cancer Sci*. 2010 May;101(5):1241-6. Epub 2010 Jan 31.

57. Sighoko D, Bah E, Haukka J, McCormack VA, Aka EP, Bourgeois D, Autier P, Byrnes G, Curado MP, Hainaut P. Population-based breast (female) and cervix cancer rates in The Gambia: evidence of ethnicity-related variations. *Int J Cancer* 2010 Feb 16. [Epub ahead of print]

58. Boyle P, Ford I, Robertson J, La Vecchia C, Boffetta P and Autier P. Essential considerations in the investigation of associations between insulin and cancer risk using prescription databases. Ecancermedicalscience. 2009;3:174. Epub 2009 Dec 11.

59. Autier P. Sunscreen abuse for intentional sun exposure. *Br J Dermatol* 2009; 161 Suppl 3: 40-5.

60. Autier P, Héry C, Haukka J, Boniol M, Byrnes G. Advanced breast cancer and breast cancer mortality in randomized controlled trials on mammography screening. *J Clin Oncology* 2009;27(35):5919-23.

61. Jenab M, McKay J, Bueno-de-Mesquita HB, van Duijnhoven FJ, Ferrari P, Slimani N, Jansen EH, Pischon T, Rinaldi S, Tjønneland A, Olsen A, Overvad K, Boutron-Ruault MC, Clavel-Chapelon F, Engel P, Kaaks R, Linseisen J, Boeing H, Fisher E, Trichopoulou A, Dilis V, Oustoglou E, Berrino F, Vineis P, Mattiello A, Masala G, Tumino R, Vrieling A, van Gils CH, Peeters PH, Brustad M, Lund E, Chirlaque MD, Barricarte A, Suárez LR, Molina E, Dorronsoro M, Sala N, Hallmans G, Palmqvist R, Roddam A, Key TJ, Khaw KT, Bingham S, Boffetta P, Autier P, Byrnes G, Norat T, Riboli E. : Vitamin D receptor and calcium sensing receptor polymorphisms and the risk of colorectal cancer in European population. *Cancer Epidemiol Biomarkers Prev*. 2009 Sep;18(9):2485-91.

62. Saadatian-Elahi M, Slimani N, Chajès V, Jenab M, Goudable J, Biessy C, Ferrari P, Byrnes G, Autier P, Peeters PH, Ocké M, Bueno de Mesquita B, Johansson I, Hallmans G, Manjer J, Wirfält E, González CA, Navarro C, Martinez C, Amiano P, Suárez LR, Ardanaz E, Tjønneland A, Halkjaer J, Overvad K, Jakobsen MU, Berrino F, Pala V, Palli D, Tumino R, Vineis P, Santucci de Magistris M, Spencer EA, Crowe FL, Bingham S, Khaw KT, Linseisen J, Rohrmann S, Boeing H, Noethlings U, Olsen KS, Skeie G, Lund E, Trichopoulou A, Oustoglou E, Clavel-Chapelon F, Riboli E.Plasma phospholipid fatty acid profiles and their association with food intakes: results from a cross-sectional study within the European Prospective Investigation into Cancer and Nutrition. *Am J Clin Nutr*. 2009 Jan;89(1):331-46.

63. Montella A, Gavin A, Middleton R, Autier P, Boniol M. Cutaneous melanoma mortality starting to change: A study of trends in Northern Ireland. *Eur J Cancer* 2009;45(13):2360-6.

64. Cantwell MC, Murray LJ, Catney D, Donnelly D, Autier P, et al. Second primary cancers in patients with skin cancer: A population-based study in Northern Ireland. *Br J Cancer* 2008.

65. Coordination and report writing of the report on Vitamin D and Cancer, IARC Working Group Report No. 5, International Agency for Research on Cancer, Lyon, 2008 (available at www.iarc.fr, search for "vitamin D").

66. Boffetta P, Tubiana M, Hill C, Boniol M, Aurengo A, Masse R, Valleron AJ, Monier R, de Thé G, Boyle P, Autier P. The causes of cancer in France. Ann Oncol. 2009; 20: 550-5.

67. Autier P, Ait Ouakrim D. Numbers of mammography equipments in thirty countries where significant mammography screening exists. *Br J Cancer*, 2008; 99: 1185-90.

68. Autier P. Two views of science and the real world. RE: Observational Research, Randomised Trials, and Two Views of Medical Science by Vandenbroucke JP *PLoS Medicine* Vol. 5, No. 3, e67 doi:10.1371/journal.pmed.0050067.

69. Braeckman J, Autier P, Soviany C, Nir R, Nir D, Michielsen D, Treurnicht K, Jarmulowicz M, Bleiberg H, Govindaraju S, Emberton M. The accuracy of transrectal ultrasonography supplemented with computer-aided ultrasonography for detecting small prostate cancers. *Br J Urology Int*, 2008; 102:1560-5.

70. Hery C, Ferlay J, Boniol M, Autier P. Changes in breast cancer incidence and mortality in middle-aged and elderly women in 28 countries with Caucasian majority populations. *Annals of Oncology*. doi:10.1093/annonc/mdm593.

71. Hery C, Ferlay J, Boniol M, Autier P. Quantification of changes in breast cancer incidence and mortality since 1990 in 35 countries with Caucasian-majority populations. *Annals of Oncology*. doi:10.1093/annonc/mdn025.

72. Autier P. Boyle P. Artificial ultraviolet sources and skin cancers : rationale for restricting access to sunbed use before 18 years of age. *Nat Clin Pract Oncol* 2008;5(4):178-179.

73. Boniol M, Dore JF, Autier P. Changing the labelling of Sunscreen, Will We Transform Sun Avoiders into Sunscreen Users? *J Invest Dermatol*. 2008; 128(2):481-482.

74. Autier P, Boniol M, Héry C, Masuyer E, Ferlay J. Cancer survival statistics should be viewed with caution. *Lancet Oncol*. 2007 Dec;8:1050-2.

75. Boniol M, Dore JF., Autier P. Photoprotection, *Lancet.* 2007;370:1481-2.

76. Braeckman J, Autier P, Garbar C, Marichal MP, Soviany C, Nir R, Nir D, Michielsen D, Bleiberg H, Egevad L, Emberton M. Computer-aided ultrasonography (HistoScanning): a novel technology for locating and characterizing prostate cancer. *BJU Int*. 2007:101:293-8.

77. Haentjens P, Autier P, Barette M, Venken K, Vandershcueren D, Boonen S, on behalf of the Hip Fracture Study Group. Survival and functional outcome according to hip fracture type: A one-year prospective cohort study in elderly women with an intertrochanteric or femoral neck fracture. *Bone*. 2007; 41:958-64.

78. IARC Working Group. Attributable Causes of Cancer in France in Year 2000. IARC Working Group Reports, vol. 3, International Agency for research on Cancer, Lyon, 2007 (freely available at www.iarc.fr).

79. Arbyn M, Autier P, Ferlay J. Burden of cervical cancer in the 27 member states of the European Union: estimates for 2004. *Ann Oncol*. 2007;18: 1423-1425.

80. Autier P, Gandini S. Vitamin D supplements and all-cause mortality: a meta-analysis of randomized control trials. *Arch Int Med* 2007;167: 1730-1737.

81. Linseisen J, Rohrmann S, Miller AB, Bueno-de-Mesquita HB, Büchner FL, Vineis P, Agudo A, Gram IT, Janson L, Krogh V, Overvad K, Rasmuson T, Schulz M, Pischon T, Kaaks R, Nieters A, Allen NE, Key TJ, Bingham S, Khaw KT, Amiano P, Barricarte A, Martinez C, Navarro C, Quirós R, Clavel-Chapelon F, Boutron-Ruault MC, Touvier M, Peeters PH, Berglund G, Hallmans G, Lund E, Palli D, Panico S, Tumino R, Tjønneland A, Olsen A, Trichopoulou A, Trichopoulos D, Autier P, Boffetta P, Slimani N, Riboli E. Fruit and vegetable consumption and lung cancer risk: updated information from the European Prospective Investigation into Cancer and Nutrition (EPIC). *Int J Cancer*. 2007;121(5):1103-14.

82. Autier P, Boniol M, Doré JF. Sunscreen use and increased duration of intentional sun exposure: Still a burning issue. *Int J Cancer* 2007;121(1):1-5.

83. Arbyn M, Raifu A, Autier P, Ferlay J. Burden of cervical cancer in Europe: estimates for 2004. *Ann Oncol* 2007;18(10):1708-15.

84. Boffetta P, McLaughlin JK, la Vecchia C, Autier P, Boyle P. "Environment" in cancer causation and aetiological fraction: Limitations and ambiguities. *Carcinogenesis* 2007;28(5):913-5.

85. Ferlay J, Autier P, Boniol M, Heanue M, Colombet M, Boyle P. Estimates of the cancer incidence and mortality in Europe in 2006. *Ann Oncol* 2007;18:581-92.

86. International Agency for Research on Cancer Working Group on artificial ultraviolet (UV) light and skin cancer. The association of use of sunbeds with cutaneous malignant melanoma and other skin cancers: A systematic review. *Int J Cancer* 2007; 120:1116-22. Review. Erratum in: *Int J Cancer* 2007;120:2526.

87. International Agency for Research on Cancer Working Group on artificial ultraviolet (UV) light and skin cancer. The association of use of sunbeds with cutaneous malignant melanoma and other skin cancers: A systematic review. *IARC Report*, Lyon, 2006 (freely available at www.iarc.fr).

88. Expert participant to IARC Monograph on Hormone Therapy and Oral Contraceptives, 2005. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Volume 91, Oestrogen-progestogen replacement therapy and combined oral contraceptives, International Agency for Research on Cancer. Lyon, 2007.

89. Bleiberg H, Grivegnee A, Hendlisz A, Autier P. Screening for colorectal cancer: the selection of patients at risk. *Rev Med Brux* 2006; 27: S221-3. (in French).

90. Scelo G, Boffetta P, Autier P, Hemminki K, Pukkala E, Olsen JH, Weiderpass E, Tracey E, Brewster DH, McBride ML, Kliewer EV, Tonita JM, Pompe-Kirn V, Chia KS, Jonasson JG, Martos C, Giblin M, Brennan P. Associations between ocular melanoma and other primary cancers: an international population-based study. *Int J Cancer* 2007;120:152-9.

91. Bleiberg H, Autier P, Huet F, Schrauwen AM, Staquet E, Delaunoit T, Hendlisz A, Wyns C, Panzer JM, Caucheteur B, Eisendrath P, Grivegnee A. Colorectal cancer (CRC) screening using sigmoidoscopy followed by colonoscopy: a feasibility and efficacy study on a cancer institute based population. *Ann Oncol* 2006;17:1328-32.

92. Pedeux R, Sales F, Pourchet J, Kallassy M, Fayolle C, Boniol M, Severi G, Ghanem G, Nakazawa HN, Autier P, Dore JF. Ultraviolet B sensitivity of peripheral lymphocytes as an independent risk factor for cutaneous melanoma. *Eur J Cancer* 2006; 42:212-5.

93. Autier P. Cutaneous malignant melanoma: The facts about sunscreens and sunbeds. *Anticancer Therapy Expert Rev Anticancer Ther* 2005;5:821-33.

94. de Vries E, Boniol M, Severi G, Eggermont AM, Autier P, Bataille V, Dore JF, Coebergh JW. Public awareness about risk factors could pose problems for case-control studies: The example of sunbed use and cutaneous melanoma. *Eur J Cancer* 2005; 41:2150-4.

95. Bataille V, Boniol M, De Vries E, Severi G, Brandberg Y, Sasieni P, Cuzick J, Eggermont A, Ringborg U, Grivegnee AR, Coebergh JW, Chignol MC, Dore JF, Autier P. A multicentre epidemiological study on sunbed use and cutaneous melanoma in Europe. *Eur J Cancer* 2005;41:2141-9.

96. Autier P, Severi G, Boniol M, de Vries E, Coebergh JW, Dore JF. Re: Sun exposure and mortality from melanoma. *J Natl Cancer Inst* 2005;97:1159.

97. Degrave E, Autier P, Grivegnée AR, Zizi M. Mortality among Belgian militaries and exposure to radars. *Eur J Epidemiol* 2005; 20: 677-681.

98. Haentjens P, Autier P, Barette M, Boonen S; Belgian Hip Fracture Study GroupPredictors of functional outcome following intracapsular hip fracture in elderly women. A one-year prospective cohort study. *Injury* 2005; 36:842-50.

99. Autier P, Boniol M, Severi G, Pedeux R, Grivegnée AR, Doré JF. Sex and body-distribution of nevi in European children: implications for the aetiology of cutaneous Melanoma. *Cancer Epidemiol Biomarkers Prev* 2004; 13: 2003-5.

100. Autier P. Perspectives in melanoma prevention: the case of sunbeds. *Eur J Cancer* 2004; 40: 2367-76.

101. Mullie P, Vansant G, Grivegnée AR, Autier P. Ontbijtfrequentie van Belgische mannelijke and vrouwelijke adolescenten tussen 12 and 15 jaar (IN DUTCH). *Tijdschrift voor Geneeskunde* 2004; 60:474-480.

102. Boniol M, Autier P, Doré JF. Re: A prospective study of pigmentation, sun exposure , and risk of cutaneous melanoma in women. *J Natl Cancer Inst* 2004; 96: 335-6.

103. Boyle P, Doré JF, Autier P, RingborgU. Cancer of the skin: a forgotten problem in Europe. *Ann Oncol* 2004; 15: 5-6.

104. Boyle P, Leon ME, Maisonneuve P, Autier P. Cancer control in women. Update 2003. *Int J Gynaecol Obstet* 2003; 83 Suppl. 1: 179-202.

105. Autier P, Creplet J, Vansant G, Brohet C, Paquot N, Muls E, Mullie P, Grivegnee AR. The impact of reimbursement criteria on the appropriateness of 'statin' prescribing. *J Cardiovasc Risk* 2003;10:456-62.

106. Boonen S, Autier P, Barette M, Vanderschueren D, Lips P, Haentjens P. Functional outcome and quality of life following hip fracture in elderly women: a prospective controlled study. *Osteoporos Int* 2003; 15: 87-94.

107. Haentjens P, Autier P, Collins J, Velkeniers B, Vanderschueren D, Boonen S. Colles fracture, spine fracture, and subsequent risk of hip fracture in men and women. A meta-analysis. *J Bone Joint Surg Am* 2003;85-A(10):1936-43.

108. Autier P, Coebergh JW, Boniol M, Dore JF, de Vries E, Eggermont AM. Management of melanoma patients: benefit of intense follow-up schedule is not demonstrated. *J Clin Oncol*. 2003;21:3707.

109. Haentjens P, Autier P, Barette M, Boonen S; Belgian Hip Fracture Study Group. Costs of care after hospital discharge among women with a femoral neck fracture*. Clin Orthop*. 2003; 414:250-8.

110. Autier P, Severi G, Pedeux R, Cattaruzza MS, Boniol M, Grivegnee A, Dore JF; European Organisation for Research and Treatment of Cancer Melanoma Group. Number and size of nevi are influenced by different sun exposure components: implications for the etiology of cutaneous melanoma (Belgium, Germany, France, Italy). *Cancer Causes Control.* 2003;14:453-9.

111. Autier P, Boyle P, Buyse M, Bleiberg H. Is FOB screening really the answer for lowering mortality in colorectal cancer? *Recent Results in Cancer Research* 2003;163:254-63.

112. Boyle P, Autier P, Bartelink H, Baselga J, Boffetta P, Burn J, Burns HJ, Christensen L, Denis L, Dicato M, Diehl V, Doll R, Franceschi S, Gillis CR, Gray N, Griciute L, Hackshaw A, Kasler M, Kogevinas M, Kvinnsland S, La Vecchia C, Levi F, McVie JG, Maisonneuve P, Martin-Moreno JM, Bishop JN, Oleari F, Perrin P, Quinn M, Richards M, Ringborg U, Scully C, Siracka E, Storm H, Tubiana M, Tursz T, Veronesi U, Wald N, Weber W, Zaridze DG, Zatonski W, zur Hausen H. European Code Against Cancer and scientific justification: third version (2003). *Ann Oncol.* 2003 Jul;14(7):973-1005.

113. Mullie P, Muls E, Vansant G, Grivegnée AR, Autier P. Over het gebruik van boter als smeervet bij cardiovasculaire risicofactoren en in functie van dieetinterventies / Ingediend (IN DUTCH) *Tijdschrift voor Geneeskunde* 2003;59:395-401.

114. Mullie P, Muls E, Vansant G, Grivegnée AR, Autier P. Toepassing van voedingsinterventie in de niet-farmacologische behandeling van hyperlipidemie. *Tijdschrift voor Geneeskunde* 2003;59:215-218.

115. Mullie P, Muls E, Vansant G, Grivegnée AR, Autier P. Efficiëntie van een samenwerkingsprotocol huisarts-diëtist om hyperlipidemieën te behandelen met gebruik van voedingsmiddelen met plantenstanolen / *Tijdschrift Voeding en Diëtetiek* 2002; 76: 243-246.

116. Mullie P, Vansant G, Grivegnée AR, Autier P. Fruit- en groenteconsumptie bij Belgische mannelijke en vrouwelijke adolescenten tussen 12 en 15 jaar. Welke factoren zijn essentieel om doeltreffende campagnes in te richten ter promotie van fruit en groenten bij de jeugd? *Tijdschrift voor Geneeskunde* 2003;59:799-807.

117. Delagardelle C, Feiereisen P, Autier P, et al. Strenght/endurance training versus endurance training in congestive heart failure. *Med Sci Sports Exerc* 2002; 34: 1868-72.

118. De Vries E, Doré JF, Autier P, Eggermont AM, Coebergh JW. Patient's perception of the cause of their melanoma differs from that of epidemiologists. *Br J Dermatol* 2002; 388-9.

119. Haentjens P, Autier P, Boonen S. Clinical risk factors for hip fracture in elderly women: a case-control study. *J Orthop Trauma* 2002; 16:379-85.

120. Geusens P, Autier P, Boonen S, Vanhoof J, Declerk K, Raus J. The relationship among history of falls, osteoporosis, and fractures in postemopausal women. *Arch Phys Med Rehabil* 2002; 83: 903-6.

121. Pedeux R, Boniol M, Autier P, Doré JF. RE : DNA repair, dysplastic nevi, and sunlight sensitivity in the development of cutaneous malignant melanoma. *J Nat Cancer Inst* 2002; 94: 772-3.

122. Severi G, Cattaruzza MS, Baglietto L, Boniol M, Dore JF, Grivegnee AR, Luther H, Autier P. Sun exposure and sun protection in young European children. an EORTC multicentric study. *Eur J Cancer* 2002; 38:820-6.

123. Autier P. [What is the role of sunscreens in the prevention of melanoma?] Quel est le rôle des écrans solaires dans la prévention du mélanome ? *Rev Med Suisse Romande* 2002; 122:13-6. (in French)

124. Autier P. Should organised faecal occult blood test screening be established? *Ann Oncol* 2002; 13:57-60.

125. Eggermont AM, Keilholz U, Autier P, Ruiter DJ, Lehmann F, Liénard D. The EORTC Melanoma Group. a comprehensive melanoma research programme by clinicians and scientists. *Eur J Cancer* 2002 Mar;38 Suppl 4:114-9.

126. Autier P. Issues about solaria, In Hill D, Elwood M, English D (Eds) Skin Cancer Prevention; *Cancer Causes and Control*; Kluwer Academic Publishers: Boston, 2002.

127. Autier P, Shannoun F, Sharpantgen A, Lux C, Back C, Severi G, Hansen-Koeing D. A breast cancer screening programme operating in a liberal health care system: the Luxembourg Mammography Programme, 1992-1997 *Int J Cancer* 2002 ;97:828-32.

128. Autier P. What is the role of currently available sunscreens in the prevention of melanoma? *Photodermatol Photoimmunol Photomed* 2001; 17: 239-40.

129. Autier P. Response to MA Weinstock:"Sunscreen use can reduce the risk of melanoma". *Photodermatol Photimmunol Photomed* 2001; 17: 236-7.

130. Boyle P, Leon M, Autier P. Epidemiology of osteoporosis. *J Epidemiol Biostat*. 2001;6(2):185-92.

131. Barette M, Renard F, Peltier A, van Velthoven R, Huet F, Grivegnée AR, Autier P. Evaluation of a low invasive strategy for prostate cancer screening with prostate-specific antigen (PSA). *Urology* 2001; 57: 712-6.

132. Haentjens P, Autier P, Barette M, Boonen S. The economic cost of hip fractures among elderly women. A one-year, prospective, observational cohort study with matched pair analysis. *J Bone Joint Surg Am* 2001; 83 (A4): 493-500.

133. Expert participant to : IARC Handbooks of Cancer Prevention. Volume 5: Sunscreens. International Agency for Research on Cancer, Lyon, 2001.

134. Doré JF, Pedeux R, Boniol M, Chignol MC, Autier P. Intermediate-effect biomarkers in prevention of skin cancer. In: Biomarkers in Cancer Prevention. Miller AB, Bartsch H, Boffetta P, Gragsted L, Vainio H (eds). IARC Scientific Publications No 154, International Agency for Research on Cancer, Lyon, 2001.

135. Autier P, Boniol M, Severi G, Doré JF. Quantity of sunscreens used by European students. *Br J Dermatol*, 2001; 144: 288-91.

136. Autier P, Boniol M , Severi G, Giles G, Cattaruzza MS, Luther H, Renard F, Grivegnée AR, Pedeux R, Doré JF. The body-site distribution of melanocytic nevi in 6 to 7 year old European children. *Melanoma Research*, 2001: 11: 123-31.

137. Autier P, Doré JF, Conde Reis A, Trechutet F, Olivaud L, Chamoun E, Rotmencz N, Severi G, Grivegnée A, Césarini JP. Sunscreen use and recreational exposure to ultraviolet A and B radiation: A double blind randomized trial using personal dosimeters. *Br J Cancer* 2000; 9:1243-1248.

138. Autier P, Severi G, Boyle P, Doré JF. RESPONSE More About: Sunscreen Use and Duration of Sun Exposure: a Double-Blind, Randomized Trial. *J Natl Cancer Inst* 2000 ;92: 1532-1533.

139. Boyle P, Maisonneuve P, Autier P. Update on cancer control in women. *Int J Gynaecol Obstet* 2000; 70: 263-303.

140. Autier P. Do high risk factor sunscreens offer protection from melanoma? *Western Journal of Medicine* 2000; 173: 58.

141. Bredart A, Didier F, Robertson C, Scaffidi E, Fonzo D, Costa A, Goldhirsch A, Autier P. Related Articles Pychological distress in cancer patients attending the European Institute of Oncology in Milan. *Oncology* 1999; 57:297-302.

142. Autier P, Severi G, Doré JF, Boniol M. Information on sunscreens should warn against excessive sun exposure. *Br Med J* 2000; 320: 1274-1275.

143. Autier P, Haentjens P, Bentin J, Baillon JM, Grivegnée AR, Closon MC, Boonen S. Costs Induced by Hip Fractures : A Prospective Controlled Study in Belgium. *Ost Int* 2000; 11: 373-380.

144. Severi G, Giles G, Robertson C, Boyle P, Autier P. Trends in mortality from cutaneous melanoma: why are there differences between fair-skinned populations? *Br J Cancer* 2000; 82: 1887-1891.

145. Autier P. Sunscreen and melanoma revisited. *Arch Dermatol* 2000; 136:423.

146. Autier P, Severi G, Doré JF. Betacarotene and sunscreen use. *Lancet* 1999; 354: 2163-4.

147. Autier P, Pedeux R, Doré JF. Re: Sunscreen use and duration of sun exposure. Response to Hemmiki et al. *J Nat Cancer Inst*, 1999; 91: 2047.

148. Autier P, Doré JF, Négrier S, Liénard D, Panizzon R, Lejeune FJ, Guggisberg D, Eggermont AMM. Sunscreen use and duration of sun exposure : A double blind randomized trial. *J Natl Cancer Inst* 1999; 15 : 1304-9.

149. Member of Clinical Synthesis Panel on HRT. Hormone replacement therapy (HRT). *Lancet* 1999; 354: 152-5.

150. Autier P, Coibion M, De Sutter P, Wayenberg M for the European Society for Oncological Research. Cytology alone versus cytology and cervicography for cervical cancer screening : A randomized study. *Obst Gynecol* 1999; 93: 353-8.

151. Autier P, Doré JF. Re: Sunscreen use, wearing clothes and nevi number in 6- to 7-year-old European children. Response to Elwood JM and Gallagher RP *J Natl Cancer Inst* 1999; 13: 1065-66.

152. Autier P, Doré JF. Re: Sunscreen use, wearing clothes and nevi number in 6- to 7-year-old European children. Response to Berwick M. *J Natl Cancer Inst* 1999; 12: 1079-80.

153. Autier P, Doré JF, Cattaruzza MS, Renard F, Luther H, Gentiloni-Silverj F, et al. for the EORTC Melanoma Group. Sunscreen use, wearing clothes and nevi number in 6- to 7-year-old European children. *J Nat Cancer Inst* 1998; 90: 1873-81.

154. Autier P, Boyle P, Doré JF. Sorting the hype from the facts in melanoma. *Lancet* 1998; 352: 738-739.

155. Aoun M, Crokaert F, Paesmans M, Autier P, Klastersky J. Imipenem versus targeted therapy in cancer patients. *Int J Antimicrob Agents* 1998; 10: 263-70.

156. Bredart A, Autier P, Audisio RA, Gerathy J. Psycho-social aspects of breast cancer susceptibility: a literature review. *Eur J Cancer Care* (Engl) 1998; 7: 174-80.

157. Boyle P, Maisonneuve P, Autier P. Towards cancer control in women. *J Epid Biost* 1998; 3: 137-168.

158. Boyle P, Autier P. Colorectal cancer screening: Health policy or a continuing research issue? *Ann Oncol* 1998; 9: 581-584.

159. Autier P. Should there be mass screening using faecal occult blood test for colorectal cancer? *Eur J Cancer* 1998; 6: 773-780.

160. Autier P, Berckmans P, Schmets G. Inappropriate drug donations in Bosnia Herzegovina 1992 to 1996: Reply to the Letters to the Editors (Letter). *New England Journal of Medicine* 1998; 338: 1473-1474.

161. De Sutter P, Coibion M, Vosse M, Huet F, Wesling F, Wayenberg M, Bourdon C, Hertens D, Autier P. A multicenter study comparing cervicography and cytology in the detection of cervical intra-epithelial neoplasia. *Br J Obst Gynaecol* 1998; 105: 613-620.

162. Autier P. Les cancers de la peau et les facteurs d'environnement. *Rev Med Bruxelles* 1998; 19: A346-50.

163. Autier P, Doré JF for *EPIMEL*, EORTC Melanoma Co-operative group. Influence of sun exposures during childhood and during adulthood on melanoma risk. *Int J Cancer*, 1998; 77: 533-537.

164. Autier P, Doré JF, Luther I. The Case for sunscreen revisited. *Arch Dermatol*, 1998; 134: 509-511.

165. Autier P, Doré JF, Geffeler O, et al. Melanoma and residence in sunny areas. *Br J Cancer*, 1997; 76: 1521-1524.

166. Berkmans P, Dawans V, Schmets G, Van den Bergh D, Autier P. Inappropriate drug-donations practices in Bosnia and Herzogovina, 1992 to 1996. *New England Journal of Medicine*, 1997; 337: 1842-1845.

167. Autier P, Doré JF, Cesarini JP, Boyle P. Should subjects who used psoralen suntan activators be screened for melanoma ? *Ann Oncol* 1997; 8: 435-437.

168. Muls E, Autier P, Malbecq W, Vansant G. Coronary heart disease risk factors and LDL-cholesterol-lowering efficacy of fibrates and simvastatin. *J Clin Drug Invest* 1997; 14: 98-108.

169. Muls E, Autier P, Van Gaal N, Vansant G. Effects of initial BMI and on-treatment weight change of the lipid-lowering efficacy of fibrates. *Int J Obesity* 1997; 21: 155-158.

170. Doré JF, Maisonneuve P, Cattaruzza S, Autier P, et al. A molecular epidemiological approach to the study of expression of a metastasis marker in primary melanomas and its correlation with individual patient's risk or recurrence or metastasis. *Melanoma Res* 1997; 7 (suppl 2): S121-S125.

171. Autier P, Doré JF, Renard F, et al. Melanoma and sunscreen use: need for studies representative of actual behaviours. *Melanoma Res* 1997; 7 (suppl 2): S115-S120.

172. Doré JF, Autier P. Facteurs de risque du mélanome. *BEDC, Bureau d'Etude de Dermatologie et Cosmétologie* 1997; 5: 213-223 (in French).

173. Autier P. Epidémiologie des naevi. *Annales de Dermatol. Vénéréol*. 1997; 124: 735-739 (in French).

174. Autier P, Doré JF, Césarini JP, for the Epidemiology and Prevention subgroup, EORTC Melanoma Cooperative Group, and Boyle P, for the EORTC Prevention Research Division. Should subjects who used psoralen suntan activators be screened for melanoma ? *Annals of Oncology*, 1997; 8: 435-437.

175. Autier P. Children and sun. In: Skin Cancer and UV-radiation. Altemeyer et al. (eds). Goldener Schnitt, Sinzheim, 1997; pp 593-598.

176. Autier P, Sancho-Garnier H. Epidemiological bases for dermatologists. In: Epidemiology, Causes and Prevention of Skin Diseases. Grob et al. (eds). Blackwell Science, London, 1997, pp 8-15.

177. Autier P, Huet F, Coibion M, Grivegnée A. Parity and intraepithelial neoplasia of the cervix uteri. Br J Cancer 1996; 74: 488-490.

178. Autier P. Exposure to UV-radiation in sunbeds. In : Internationaler Kongress und kalusurtagung der Strahlensxhutzkommission 6-8 Mai 1996, Hamburg. Gustav Fisher, Stuttgart, 1996; pp 311-315

179. Autier P, Doré JF, Lejeune F, et al, for the EORTC Melanoma Co-operative Group. Sun protection in childhood or early adolescence and reduction of melanoma risk in adults: an EORTC case-control study in Germany, Belgium and France. *J Epid Biost*, 1996; 1: 51-57.

180. Autier P, Doré JF, Schifflers E, et al., for the EORTC Melanoma Cooperative Group. Melanoma and use of sunscreens an EORTC case-control study in Germany, Belgium and France. *Int J Cancer*, 1995; 61: 749-755.

181. Liénard D, Eggermont AM, Schraffordt Koops H, Kroon BB, Rosenkaimer F, Autier P, Lejeune F. Isolated perfusion of the limb with high-dose tumor necrosis factor-alpa (TNF-alpha), Interferon-gamma (IFN-gamma) and melphalan, for melanoma satge III: Results of a multicentre pilot study. *Melanoma Res* 1994; 4 (Suppl.1): 21-6.

182. Autier P, Doré JF, Lejeune F, et al., for the EORTC Melanoma Cooperative Group. Cutaneous malignant melanoma and exposure to sunlamps or sunbeds: An EORTC multicenter case-control study in Belgium, France and Germany. *Int J Cancer*, 1994; 58: 809-813.

183. Autier P, et al. The cost of opportunistic breast cancer screening: the case-study of Belgium. *IBES Briefing No 5*. Belgian Institute for Health Economics, Brussels, June 1994.

184. Andry G, Autier P, for the Belgian Thyroid Cancer Study Group. The Belgian and European thyroid cancer registry. *Acta Chir Belgica* 1994; 94: 33-5.

185. Coibion M, Autier P, et al. Is there a role for cervicography in the detection of the pre-malignant lesions of the cervix uteri? *Br J Cancer* 1994; 70: 125-8.

186. Bleiberg H, Autier P, Michaud D. Cost-effectiveness analysis of antiemetic treatment. *Supportive Care in Cancer*, 1994; 2: 145-9.

187. Meunier F, Paesmans M, Autier P. Value of antifungal prophylaxis with antifungal drugs against oropharyngeal candidiasis in cancer patients. *Eur.J.Cancer*, 1994; 30B: 196-199.

188. Autier P, Doré JF, Lejeune F., et al., for the EORTC Melanoma Cooperative Group. Risk factors of the cutaneous melanoma: Results from an EORTC case-control study. *Melanoma Research*, 1994; 4: 79-85.

189. Razavi D, Delvaux N, Brédart A, Autier P, et al. Professional rehabilitation of lymphoma patients: a study of psychosocial factors associated with return to work. *Supportive Care in Cancer*, 1993; 1: 276-8.

190. Autier P. Epidemiology of Melanoma. *In* Malignant Melanoma: The Approach of the Surgical Oncologist. Lejeune F, Chaudhuri P, Gupta TD, Eds. McGraw-Hill, New-York, 1992; PP 1-7.

191. Delvenne CG, Winkler-Gol RA, Piccart MJ, Hustin J, Michaux D, Leclerq G, Nogaret JM, Autier P. Expression of c-erbB2, TGF-b1 and pS2 genes in primary human breast cancers. *Eur J Cancer*, 1992; 28: 700-5.

192. Liénard D, Lejeune F, Autier P, Sales F, Ghanem Ghanem. Physiological and Pharmacokinetics in isolation perfusion of the limbs. *In* Malignant Melanoma: The Approach of the Surgical Oncologist. Lejeune F, Chaudhuri P, Gupta TD, Eds. McGraw-Hill, New-York, 1992; PP 241-9.

193. Autier P, et al. Economic aspects of breast cancer screening (in French). *In* Livre blanc du dépistage du cancer du sein, Gordenne W. et al, Editeurs. Publications Interuniversitaires, 1992.

194. Autier P et al. Cutaneous malignant melanoma and exposure to sunlamps and sunbeds: a descriptive study in Belgium. *Melanoma Research*, 1991 ; 1: 69-74.

195. Buysse M, Autier P, Piedbois P. Clinical trials in cancer prevention. In "Reducing the Risk of cancer". Open University ed., 1991, Cambridge, UK.

196. Autier P & al. Drug supply in the aftermath of the 1988 Armenian earthquake. *The Lancet* 1990; i:1388-90.

197. Autier P et al. Etudes sérologiques et cliniques sur la tréponématose endémique en République du Mali. *Ann Soc Belge Méd Trop*, 1989; 69: 319-329.

198. Autier, P. & al. Migrations and Nutritional Status in the Sahel. *Disasters*, 1989; 13: 144-154.

199. Autier, P. & al. The Food and Nutrition Surveillance Systems of Chad and Mali: the "SAP" After Two Years. *Disasters*, 1989; 13: 9-33.

200. Tollet, D., Autier, P. & Lechat, M.F. (1988). Manuel de Prise en Charge des Camps de Personnes Deplacées: Guide pour la Phase d'Urgence (Manual for the Management of Refugee camps: Guide for the Emergency Phase). Edited by the Center for Research in the Epidemiology of Disasters of the Catholic University of Louvain (Belgium), Brussels. (600 pages, 4 volumes).

201. Autier, P. Nutrition Assessment Through the Use of a Nutritional Scoring System. *Disasters*, 1988; 12: 70-80.

202. Gigase, P.L., Mangelschots, E., Bockaert, R., Autier, P. & Kestens, L. Indicateurs Simples de la Prévalence et de l'Intensité de la Bilharziose Urinaire au Tchad. *Ann Soc Belge Méd Trop*, 1989; 68: 123-132.

203. Autier P. Monitoring Socio-Economic, Health and Nutritional Indicators for Early Detection of Food Emergencies: Experience of Médecins Sans Frontières-Belgium and of the European Association for Health and Development. Food and Agriculture Organization of the United Nations, publication No ESC/CILSS/WNES/8/July 1987, Rome.

204. Autier P, D'Altilia, J.P. & Delamalle J.P. Présentation des Projets "Systèmes d'Alerte Précoce" au Tchad et au Mali. Texte des Conferences du Groupe d'Etude et de Recherche sur la Malnutrition (GERM), Dakar & Paris, 1987.

OFFICIAL REPORTS

Von Karsa L,……, Autier P (last author). Cancer screening in Europe. General Directorate Health and Consumers, Luxembourg, 2008 (available on web site of DG Health and Consumers).

Writer (with JA Lindencrona of Karolinska Institute) of the **Summary Report of the Eurocan+Plus Project**, IARC, March 2008 (available at www.eurocanplus.eu and at www.iarc.fr).

Autier P, Govindaraj R, Gray R, Lakshminarayanan R, Nassery HG, Schmets G. Drug donations in post-ermergency situations. HNP Discussion Paper. **The World Bank**, Washington, June 2002.

Autier P. Evaluation Epidémiologique du Programme de Dépistage du cancer du Sein au Grand Duché de Luxembourg. Juillet 2000. Ministère de la santé, Direction de la Santé, Villa Louvigny, Luxembourg.

Autier P, Renard F. Evaluation épidémiologique et économique du programme de dépistage du cancer du sein au Grand Duché de Luxembourg: proposition d'un cahier des charges. Milan, 2 mars 1998.

Christiane Y & Autier P. Les risques de l'exposition *in utero* au Diethylstilbestrol (DES). Centre National de Pharmacovigilance, Publication No D/1995/2200/1; Ministère de la Santé et des Affaires Sociales, Bruxelles, 1995.

Autier P, et al. Creation of a Protontherapy Centre: Analysis of the epidemiologic, economic and technical implications. Project ULB-UCL-ULg. Funded and published with support of the Belgian National Fund for Scientific Research, Bruxelles, 1993.

Autier P, et al. Survey on breast cancer screening in the Brussels area. Report to the European Communities, Brussels, 1992.

WEBSITE

Initiation and development, with Jacques Ferlay of the European Cancer Observatory launched in April 2009, available at http://www.iarc.fr

CV Chris Robertson

International Prevention Research Institute

Curriculum Vitae

Chris Robertson

Personal Details

Full name	Charles Christopher Robertson
Date of Birth	21 February 1954
Place of Birth	Montrose, Scotland
Marital Status	Married, 3 children
Home Address	15 Moncrieff Avenue, Lenzie, Glasgow G66 4NL
Work Address	Department of Mathematics and Statistics University of Strathclyde Livingstone Tower 26 Richmond Street GlasgowG1 1XH Scotland Health Protection Scotland Clifton House Clifton Place, Glasgow G3 7LN Scotland
Telephone	+44 141 548 3215
Fax:	+44 141 552 2079
email	chris.robertson@strath.ac.uk

Occupations and Education

1966-72	Royal High School, Edinburgh
1972-76	Edinburgh University. B.Sc. Honours (I) Mathematics and Statistics.
1976-77	Kent University, Canterbury. M.Sc. Statistics.
1977-80	Kent University, Canterbury. Ph.D. Statistics. Statistical applications in memory studies.
1980-89	Department of Mathematics, University of Strathclyde, Glasgow.

	Lecturer.
1989-93	Department of Statistics and Modelling Science, University of Strathclyde, Glasgow. Lecturer
1993-96	Department of Statistics and Modelling Science, University of Strathclyde, Glasgow. Senior Lecturer.
1995-2001	Division of Epidemiology and Biostatistics, European Institute of Oncology, Milano. Vice Director of Division and Head of Biostatistics
2002 -	Professor of Public Health Epidemiology, Department of Mathematics and Statistics, University of Strathclyde, Glasgow. and Head of Statistics, Health Protection Scotland, Glasgow

Current Employment

Since 2002 I have been Professor of Public Health Epidemiology at the University of Strathclyde, initially in the Department of Statistics and Modelling Science and, since 2009, in the Department of Mathematics and Statistics, and also Head of Statistics at Health Protection Scotland (HPS), formerly the Scottish Centre for Infection and Environmental Health. I have a joint appointment in the two institutes and my main duties are to lead a team of researchers in public health epidemiology and to manage the statistical research and consultancy service at HPS. In 2009-10 the university group linked with HPS has 1 professor, 2 senior lecturers, 1 principal research assistant, 3 research assistants, 6 PhD students and 1 MPhil student. Since 2010 I am also a senior research fellow with the International Prevention Research Institute, Lyon, France (http://www.i-pri.org/)

Research

I am an applied statistician with interests in the application of Statistics over a wide variety of disciplines. Presently my main research interest is in statistical modelling of infectious diseases and in epidemiological studies. The most important research at present is in statistical modelling and analysis associated with the H1N1 pandemic.Other recent work has focussed on the design of the HPV surveillance system in Scotland for the monitoring of the impact of the HPV vaccination programme and modelling the consequence of vaccination on cervical cancer and cervical screening. The potential for an outbreak of measles, mumps or rubella in Scotland as a consequence of the falling rates of vaccination uptake in the period 2004-06 has also been investigated through modelling. Linked to this work has been the development of a population simulation model for pneumococcal carriage. A second major thrust of my current research is concerned with an investigation of time trends in disease incidence and mortality and in regional variation in these trends which may be associated with environmental effects.

Significant achievements in the recent past include (a) Publication of the National Scottish Prevalence survey of hospital acquired infection. This is a very important piece of work and demonstrated for the first time the level of HAI in Scotland and is a benchmark for efforts to reduce HAI. My role in this study was to design it, supervise the statistical analysis and assist with the writing. (b) Publication of the Handbook of Cancer Prevention, Tobacco Control, Volume 11: Reversal of Risk after Quitting Smoking by the International Agency for Research in Cancer, Lyon, I was part of the working group and contributed one chapter directly. (c) Working in conjunction with colleagues at HPS on the national prevalence survey of HPV infection among children in Scotland aged 12-18. This is a vital piece of research required to assess the level of HPV infection in Scotland before the introduction of the HPV vaccine in September 2007 (d) Developing studies for the assessment of

the effectiveness of the Pneumococcal Conjugate vaccine which was introduced into the immunisation schedule in September 2006. (e) Development and implementation of an Exception Reporting System for flu like illnesses in Scotland using data routinely collected through the NHS24 telephone helpline. This forms part of Health Protection Scotland's surveillance systems for detecting outbreaks of flu and was funded in conjunction with work on preparing Scotland for pandemic flu. (www.stams.strath.ac.uk/~ian/hps/login.php)

I am also been responsible for the management of all phases of epidemiological studies, from design to analysis and day to day management. Examples include a case control study to investigate the causes of the cryptosporidium outbreak in Aberdeen in 2002, campylobacter in Grampian 2005-2007 and a prevalence survey of Healthcare Associated Infection in hospitals in Scotland.

Teaching, Education and Training

At university I am heavily involved in teaching statistics to business students. This has been a long term interest of mine and in 2002 I published a textbook in this area using relevant examples and multimedia technology. I have continued to develop the use of new technologies in teaching elementary statistical concepts and have helped to develop a virtual learning environment (https://vle.stams.strath.ac.uk). In the current year about 500 business students will use this resource which guides them through elementary concepts, practice examples with instant feedback and tests their abilities.

In the past I have taught Statistics at all levels from introductory service courses through to final honours classes and post-graduate lectures. The main thrust of my teaching is to teach Statistics as a practical subject and I place a great deal of emphasis on the applications of Statistics. I am particularly keen to introduce students to the use of Statistics through practical analysis of data which is relevant to their particular interests.

In all my courses, computer laboratories played an important part in teaching Statistics. This is an area in which I take great care and for a number of years I have been involved in using different computer-oriented approaches to teaching statistics. I have made use of the laboratories to experiment with a variety of techniques with the aim of improving the quality and educational content of the courses. These experiences were the principal motivation behind the successful bid to the UFC for support in the research and development of computer based tutorial materials in Statistics and Modelling Science.

Currently I am supervising 4 PhD students in the following areas: parameter estimation for infectious disease models, statistical models for the transmission of pneumococcal carriage, and simultaneous investigation of quality of life and survival in clinical trials, statistical analysis of metabonomic data.

Statistical Consultancy
There are over 150 staff atHealth Protection Scotland and I have organised a statistical consultancy service for them. This service involves all statisticians in the statistics section at SCIEH under my guidance. The main functions include the design of epidemiological studies, including writing the statistical sections of the protocols for these studies and monitoring their progress through the ethical committees and funding bodies. The major task is the analysis of epidemiological studies, providing reports for the investigators and collaborating on the manuscript for publication.

Administration
The main administrative duties I have are related to the management of a team of 9 researchers. I am also a member of the HPS Data Strategy Group. Both of these are management advisory groups.

At various times I have been Undergraduate Director, Advisor of Studies, a member of the Liaison Committee of the Departments of Mathematics and Statistics and Modelling Science. I have been active in organising Open Days and demonstrations for school pupils who have been invited to the university in an effort to publicise our degrees. I also organised the Staff-Student committee for the Mathematics and Statistics Students. I have been on the board of the StrathclydeBusinessSchool as representative of the Mathematics and the Statistics and Modelling Science department. I have also been on the Science Faculty Resource and Planning Committee.

Previous Experience
From 1995 until 2001 I worked as Head of Biostatistics and Deputy Director in the Division of Epidemiology and Biostatistics at the European Institute of Oncology. This Division is a World Health Organisation Collaborating Centre for Statistical Modelling in Chronic Diseases. There were three major aspects to my work – Research, Statistical Consultancy, and Education and Training. My main duties were to engage in and oversee the statistical research of the Division, to manage epidemiological research projects, to publish academic papers, to establish and maintain a statistical consultancy service within the European Institute of Oncology. Much of my current research stems from collaborations which were established during the 6 years I worked in Italy. There was much more emphasis on the design and analysis of clinical studies whereas at present I am mainly involved in epidemiological studies.

Prior to working at the European Institute of Oncology I was a lecturer at StrathclydeUniversity where I participated fully in the three broad areas of academic life – Research, Teaching and Administration.

Research Funding

Current Research Grants

Research Grants

[updated February 2011]

No	Lead Investigator	All grantholders	Title	Period	Source of funding	Recipient of funding	Funding	
							Total (£1000)	SU share (£1000)
Funded Grants (new, in 2010)								
	C Robertson	C Robertson	Health Protection Scotland Chair	2010-2015	HPS	Strathclyde	209	209
	C Robertson	C Robertson	Collaborative Research in Public Health Epidemiology	2010-2013	IPRI	Strathclyde	155	155
	Simpson C.	Simpson CR, Lone, N, Ritchie LD, Robertson C, Sheikh A, McMenamin J	Seasonal Influenza Vaccine Effectiveness (SIVE)	2010-2011	NIHR	Edinburgh Univeristy	95	41
	Robertson C.	McMemamin, J. Kavanagh, K.	Influenza Vaccine Effectiveness in Scotland using the PIPeR Cohort 2010-11	20010-11	ECDC EpiConcept	Strathclyde	43	23
	Robertson C.	Robertson, C.	Statistical analysis and modelling for MRSA Screening Programme - Continuation	2010-10	HPS	Strathclyde	24	24
	Guthrie, B	Guthrie, B., Bennie, M., Petrie, D., Robertson, C., Ritchie, L., Treweek, S.	Effective Feedback to Improve Primary Care Prescribing Safety (EFIPPS): a randomised controlled trial using ePrescribing data	2011-2014	CSO	Dundee University	225	64
				TOTAL NEW GRANTS			**£751**	**£516**

CSO	Chief Scientist Office, Scottish Government
DoH	Department of Health, England
GGPCT	Greater Glasgow Primary Care Trust
HPS	Health Protection Scotland, NHS Scotland
SG	Scottish Government
WP	Wyeth Pharmaceuticals
UWoS	University of West of Scotland
SUEFRDF	Strathclyde University Education Faculty Research Development Fund
SEHD	Scottish Executive Health Department
LAHT	Lanarkshire Acute Hospital Trust
IPRI	International Prevention Research Institute
ECDC	European Centre for Disease Control

Research Grants

[updated February 2011]

No	Lead Investigator	All grantholders	Title	Period	Source of funding	Recipient of funding	Funding	
							Total (£1000)	SU share (£1000)
Previously Funded Grants (ongoing during 2010)								
1	Cubie, HA	Cubie, H., Cushieri, K, Donaghy, M., Robertson, C., Cruickshank, M., Imrie, J., Williams, A., Howie, Sullivan, F., Harrison, D., Sinka, K.	Scottish Cervical Cancer Prevention Programme: Establishing an HPV Clinical Research Centre	2009-2014	CSO	NHS Lothian/Edinburgh	450	0
2	Cruikshank, M	Cruickshank, M.Campbell, C., Choi, Y., Cubie, H., Cushieri, K., Donaghy, M., Imrie, J., Robertson, C., Sullivan, F., Weller, D.	The Scottish Cervical Cancer Prevention Programme: Assessing And Modelling The Impact Of HPV 16/18 Immunisation .	2010-2015	CSO	Aberdeen University	450	209
3	Robertson C.	Robertson, C.	HPV Surveillance	2008-12	HPS	Strathclyde	42	42
4	Robertson C.	Robertson, C. Ramsay, C., Pollock, K.	Serological Study of Markers of Cryptosporidium associated with changes in water supply	2009-10	HPS	Strathclyde	29	29
5	Robertson C.	Robertson, C.	Statistical analysis and modelling for MRSA Screening Programme	2009-10	HPS	Strathclyde	17	17
6	Farrington, CP	Farrington, CP, Andrews, N., Robertson, C. Garthwaite, P.	Methodological Development of Syndromic and Laboratory Statistical Surveillance Systems in England	2009-10	NIHR	Open University	28	6
7	Woolhouse, MEJ	Woolhouse, MEJ, Leigh-Brown A, Simmonds, P., Robertson, C., Mcmenamin,J., Carman, W	Enhanced Influenza Surveillance In Scotland From Autumn 2009.	2009-10	CSO	Edinburgh Univeristy	131	5
8	Simpson C.	Simpson CR, Ritchie LD, Robertson C, Sheikh A, McMenamin J	Vaccine effectiveness In Pandemic influenza - primary carE Reporting (VIPER)	2009-10	NIHR	Edinburgh Univeristy	87	7
9	Robertson C.	McMemamin, J. Kavanagh, K.	Influenza Vaccine Effectiveness in Scotland using the PIPeR Cohort	2009-10	ECDC EpiConcept	Strathclyde	35	13
10	Robertson C.	McMemamin, J. Kavanagh, K.	Influenza Vaccine Effectiveness in Scotland using the PIPeR Cohort	2009-10	EU EpiConcept	Strathclyde	40	15
1	Robertson C.	Robertson C, Choi, Y., Edmunds, J.	Developing serotype-specific models of the transmission of pneumococcal carriage in UK	2008-12	HPA	Strathclyde	66	66
2	Hewitt A.	Hewitt, A., Wilson, A.; Smith, I., Robertson, C..	School, Neighbourhood and Local Authority Effects on Uptake and Attainment in Music – A Multilevel Analysis.	2008-10	SUEFRDF	Strathclyde	4	0
6	Robertson C.	Robertson C, McKenzie E.	Statistical Research Support for Lanarkshire Acute Trusts	2005-10	LAHT	Strathclyde	25	25
1	Robertson, C	Robertson C	Statistical Research Support for Health Protection Scotland	2005-10	HPS	Strathclyde	709	709
				TOTAL FUNDING ON ACTIVE GRANTS			**£2,113**	**£1,143**

International Prevention Research Institute

Publications

Books

1. McCloskey, M., Blythe S., Robertson C. (1997). Quercus: Statistics for Bioscientists. A Student Guidebook. London: Edward Arnold.

2. Robertson C. and McCloskey, M. (2003). Statistical Concepts and Applications for Business Students .London: Edward Arnold.

Chapters in Books

1. Robertson, C. (1991). Computationally intensive statistics. In New Developments in Statistics for Psychology and the Social Sciences Volume 2. Edited by P. Lovie and A. D. Lovie. London: British Psychological Society and Routledge.

2. Robertson, A. G., Wheldon, T. E. and Robertson, C. (1996). Applying sound radiobilogical principles to the management of carcinoma of the larynx. In Current Radiation Oncology Volume 2. Edited by J. S. Tobias and P. R. M. Thomas. London: Arnold.

3. **Robertson C** (2007) Prediction of Lung Cancer Mortality Rates in Selected Countries in IARC Handbooks of Cancer Prevention, Tobacco Control, Volume 11: Reversal of Risk after Quitting Smoking, Editors: David Burns, Carolyn Dressler. International Agency for Research in Cancer, Lyon France.

4. Robertson, C, Mazzetta, C, D'Onofrio A Chapter 5: Regional variation and spatial correlation. In Atlas of Cancer Mortality in the European Union and the European Economic Area 1993-1997 (2008) Edited by P. Boyle and M. Smans, IARC Scientific Publication No. 159, Lyon France

Papers published in assessed journals (since 2000)

64 published papers from 1980 to 1999.

.

1. Boyle, P., **Robertson, C.**, Lowe, F., Roehrborn, C. (2000) Meta Analysis of clinical trials of Permixon® in the treatment of symptomatic benign prostatic hyperplasia. Urology. 55, 533-539.

2. Andrea Decensi, Bernardo Bonanni, AlianaGuerrieri-Gonzaga, RosalbaTorrisi, LapoManetti, **Chris Robertson**, Giuseppe De Palo, Franca Formelli, Alberto

Costa and Umberto Veronesi. (2000). Chemoprevention of Breast Cancer: The Italian Experience. Journal of Cellular Biochemistry (Supplement) 34, 84-96.

3. Zurrida, S., Galimberti, V., Orvieto, E., **Robertson, C.,** Ballinardi, B., Cremonesi, M., De Cicco, C., Luini, A., (2000), Radioguided sentinel node biopsy to avoid axillary dissection in breast cancer. Annals of Surgical Oncology. 7, 28-31.

4. Preti, M., Mezzetti, M., **Robertson, C.**, Sideri, M. (2000). Interobserver Variation in Vulvar Intraepithelial Neoplasia Histopathological Diagnosis and Grading. British Journal of Obstetrics and Gynaecology an International Journal of Obstetrics & Gynaecology. 107(5):594-9.

5. Gandini, S., Merzenich, H., **Robertson, C.**, Boyle, P. (2000) Meta-analysis of diet and breast cancer risk: The role of vegetable and fruit consumption and related vitamins. European Journal of Cancer 36, 636-646

6. Severi, G., Giles, G., **Robertson, C.**, Autier, P., Boyle, P. (2000) Mortality from cutaneous melanoma: evidence for contrasting trends between populations British Journal of Cancer. 82(11):1887-91.

7. Baglietto, L., Torrisi, R; Arena, G., Francesca Tosetti, F., Guerrieri Gonzaga, A., Pasquetti, W., **Robertson, C.**, Decensi, A. (2000) Ocular Effects of Fenretinide, a vitamin A analogue, in a chemo prevention trial of bladder cancer. Cancer Detection and Prevention. 24, 369-75

8. Torrisi, R ,Mezzetti, M., Johansson, H., Barreca, A., **Robertson, C.**, Costa, A., Decensi, A. (2000). Time Course of Fenretinide: Modulation of Circulating IGF-1, IGF-2 and IGFBP-3 in a Bladder Cancer Trial. International Journal of Cancer. 87, 601-605

9. **Robertson, C.**, Perone C., Primic-Zakel, M., PompeKirn, V., Boyle, P. (2000) Breast Cancer Incidence Rates in Slovenia 1971-1993. International Journal of Epidemiology. 29, 969-974.

10. Audisio, R. and **Robertson, C**. (2000) Colorectal Cancer Follow Up – Perspectives for future studies. European Journal of Surgical Oncology. 26, 329-337.

11. Boyle, P., Gandini, S., **Robertson, C**., Zatonski, W., Fagerstrom, K., Slama, K., Kunze, M., Gray, N. and International Smokers Survey Group (2000). Characteristics of smokers' attitudes towards stopping: survey of 10,295 smokers in representative samples from 17 European countries. European Journal of Public Health, 10 (3, supplement), 5-14

12. Decensi A, Bonanni B, Rotmensz N, **Robertson C**, Guerrieri-Gonzaga A, Mora S, Diani S, Cazzaniga M, Costa A. (2000) Update on tamoxifen to prevent breast cancer. The Italian Tamoxifen Prevention Study. Eur J Cancer. 36 Suppl 4:50-51

13. Bonanni B, Guerrieri-Gonzaga A, Rotmensz N, Torrisi R, Pigatto F, Cazzaniga M, Mora S, Diani S, **Robertson C**, Decensi A. (2000) Hormonal Therapy and Chemoprevention. Breast J. 6, 317-323.

14. Colleoni, M., Mandala M., Peruzzotti, G., **Robertson, C.**, Goldhirsch, A. (2000) Depression and degree of acceptance of adjuvant cytotoxics in patients in Italy. Lancet, 356, 1326-1327.

15. Boyle, P., Bellanti, J. A., **Robertson, C**. (2000) Meta-analysis of Published Clinical Trials of Ribomunyl in Prevention of Respiratory Infections., Biodrugs. 14, 389-408.

16. Kubik A, Zatloukal P, Boyle P, **Robertson C**, Gandini S, Tomasek L, Gray N, Havel L. (2001) A case-control study of lung cancer among Czech women. Lung Cancer. 31:111-122.

17. Veronesi U, Galimberti V, Zurrida S, Pigatto F, Veronesi P, **Robertson C,** Paganelli G, Sciascia V, Viale G. (2001) Sentinel lymph node biopsy as an indicator for axillary dissection in early breast cancer. Eur J Cancer.37:454-8

18. Meuleman, E.J.H., Donkers, L.H.C., **Robertson, C**., Keech, M., Boyle, P., Kiemeney, L.A.L.M. (2001) Erectile dysfunction: prevalence and effect on the quality of life; Boxmeer study. NederlandsTijdschriftGeneeskunde 145.,576-81. (in Dutch).

19. Bredart A, Razavi D, **Robertson C,** Batel-Copel L, Larsson G, Lichosik D, Meyza J, Schraub S, von Essen L, de Haes JC.(2001) A comprehensive assessment of satisfaction with care: preliminary psychometric analysis in French, Polish, Swedish and Italian oncology patients. Patient Education and Counselling. 43(3):243-53.

20. **Robertson, C.**, Van Den Donk, M., Primic-Zakelj, M., Macfarlane, T., Boyle, P (2001). The association between induced and spontaneous abortion and risk of breast cancer in Slovenian women aged 25 to 54. The Breast 10, 291-298.

21. Baglietto, L., Severi, G., **Robertson, C.** Hopper, J.L. (2001) A combination of analytical and graphical methods to model the association between family

history and disease estimated from a case-control study. Methods of Information in Medicine. 40,112-6

22. Brédart, A., **Robertson, C.** (2001) Assessment of quality of care using patients' satisfaction information -the study on the IEO sample analysing predictors of satisfaction. Oncology. 61, 120-128.

23. Guerrieri-Gonzaga A, Baglietto L, Johansson H, Bonanni B, **Robertson C**, Sandri MT, Canigiula L, Lampreda C, Diani S, Lien EA, Decensi A. (2001) Correlation between Tamoxifen Elimination and Biomarker Recovery in a Primary Prevention Trial. Cancer Epidemiol Biomarkers Prev 10(9):967-70.

24. **Robertson, C.** and Ecob, R. (2001) Age Period Cohort Analysis of Time Trends in Regional Mortality Rates in England, Wales and Scotland. Journal of Evaluation in Clinical Practice 7, 299-309

25. Bartsch, G., Horninger, W., Klocker, H., Reissigl, A., Oberaigner, W., Severi, G., **Robertson, C.**, Boyle, P. (2001) Prostate cancer mortality following introduction of prostate specific antigen (PSA) mass screening in the federal state of Tyrol, Austria. Urology, 58, 417-24.

26. Stenzl, A., Jarolim, L., Coloby, P., Golia, S., Bartsch, G., Babjuk, M., **Robertson, C**. (2001) Urethra sparing cystectomy and orthotopic urinary diversion in women with malignant pelvic tumours. Cancer (*in press*)

27. Brédart, A., Razavi, D., **Robertson, C.**, Brignone, S., Fonzo, D., de Haes, J.C.J.M. (2001) Effects of patient assessment timing on questionnaire acceptability, completeness of data, reliability and variability of scores. Patient Education and Counselling. (*in press*)

28. Boyle, P, **Robertson, C.**, Manski, R., Paddley, R, Roehrborn, C. (2001) Meta-analysis of randomised trials of Terazosin in the treatment of Benign Prostatic Hyperplasia. Urology *(in press).*

29. Bonanni, B., Johansson, H., Gandini, S., Guerrieri-Gonzaga A., Torrisi, R., Sandri, M.T., Cazzaniga, M., **Robertson, C.**, Lien, E.A., Decensi, A. (2001). Effect of low dose tamoxifen on the insulin-like growth factor system in healthy women. Breast Cancer Research and Treatment. (*in press*)

30. Biffi, R., De Braud, F., Orsi, F., Pozzi, S., Arnaldi, P., Goldhirsch, A., Rotmensz, N., **Robertson, C.**, Bellomi, M., Andreoni, B. (2001) A randomised prospective trial of central venous ports connected to standard open ended or groshong catheter in adult oncology patients. Cancer (*in press*)

31. Robertson, A.G., **Robertson, C**., Soutar, D. S., Burns, H. Hole, D., McCarron, P. (2001) Treatment of oral cancer. The need for defined protocols and specialised centres. Clinical Oncology (*in press*)
32. Bredart,A., D.Razavi, **C.Robertson**, S.Brignone, D.Fonzo, J.Y.Petit, and J.C.de Haes. 2002. "Timing of patient satisfaction assessment: effect on questionnaire acceptability, completeness of data, reliability and variability of scores." *Patient.Educ.Couns.* 46:131-136.

33. Colleoni,M., N.Rotmensz, **C.Robertson**, L.Orlando, G.Viale, G.Renne, A.Luini, P.Veronesi, M.Intra, R.Orecchia, G.Catalano, V.Galimberti, F.Nole, G.Martinelli, and A.Goldhirsch. 2002. "Very young women (<35 years) with operable breast cancer: features of disease at presentation." *Ann.Oncol.* 13:273-279.

34. Colleoni,M., A.Rocca, M.T.Sandri, L.Zorzino, G.Masci, F.Nole, G.Peruzzotti, **C.Robertson**, L.Orlando, S.Cinieri, B.F.de, G.Viale, and A.Goldhirsch. 2002. "Low-dose oral methotrexate and cyclophosphamide in metastatic breast cancer: antitumor activity and correlation with vascular endothelial growth factor levels." *Ann.Oncol.* 13:73-80.

35. Curigliano,G., M.Colleoni, G.Renne, G.Mazzarol, R.Gennari, G.Peruzzotti, E.de Braud, **C.Robertson**, E.Maiorano, P.Veronesi, F.Nole, M.Mandala, G.Ferretti, G.Viale, and A.Goldhirsch. 2002. "Recognizing features that are dissimilar in male and female breast cancer: expression of p21Waf1 and p27Kip1 using an immunohistochemical assay." *Ann.Oncol.* 13:895-902.

36. De Pas,T., U.Pastorino, L.Spaggiari, G.Curigliano, F.DeBraud, and **C.Robertson**. 2002. "Preoperative chemotherapy in non-small-cell lung cancer: nothing new in N2 disease." *J.Clin.Oncol.* 20:2603-2604.

37. Decensi,A., U.Omodei, **C.Robertson**, B.Bonanni, A.Guerrieri-Gonzaga, F.Ramazzotto, H.Johansson, S.Mora, M.T.Sandri, M.Cazzaniga, M.Franchi, and S.Pecorelli. 2002. "Effect of transdermal estradiol and oral conjugated estrogen on C-reactive protein in retinoid-placebo trial in healthy women." *Circulation*. 106:1224-1228.

38. Fourcade,R.O., A.F.Gaudin, C.Mazzetta, **C.Robertson**, and P.Boyle. 2002. "[Prevalence of lower urinary tract disorders and incontinence in Auxerre. French segment of the UrEpik study]." *Presse Med.* 31:202-210.

39. Grana,C., M.Chinol, **C.Robertson**, C.Mazzetta, M.Bartolomei, C.DeCicco, M.Fiorenza, M.Gatti, P.Caliceti, and G.Paganelli. 2002. "Pretargeted adjuvant radioimmunotherapy with yttrium-90-biotin in malignant glioma patients: a pilot study." *Br.J.Cancer*. 86:207-212.

40. Orecchia,R., B.A.Jereczek-Fossa, G.Catalano, F.Chiesa, T.De Pas, G.Masci, M.Krengli, A.Vavassori, F.De Paoli, **C.Robertson**, E.Marrocco, F.DeBraud, and T.DePas. 2002. "Phase II trial of vinorelbine, cisplatin and continuous infusion of 5-fluorouracil followed by hyperfractionated radiotherapy in locally advanced head and neck cancer." *Oncology*. 63:115-123.

41. Rotmensz,N., A.Decensi, P.Maisonneuve, A.Costa, V.Sacchini, R.Travaglini, G.D'Aiuto, F.Lovison, G.Gucciardo, M.G.Muraca, M.A.Pizzichetta, S.Conforti, **C.Robertson**, P.Boyle, and U.Veronesi. 2002. "Rationale for a study adding tamoxifen to HRT." *Eur.J.Cancer*. 38 Suppl 6:22-3.:22-23.

42. Sonke,G.S., **C.Robertson**, A.L.Verbeek, W.P.Witjes, J.J.de la Rosette, and L.A.Kiemeney. 2002. "A method for estimating within-patient variability in maximal urinary flow rate adjusted for voided volume." *Urology*. 59:368-372.

43. Boyle P, **Robertson C**, Mazzetta C, Keech M, Hobbs R, Fourcade R, KiemeneyL,Lee C; The UrEpik Study Group. The association between lower urinary tract symptoms and erectile dysfunction in four centres: the UrEpik study. BJU Int. 2003 Nov;92(7):719-725.

44. Boyle P, Diehm C, **Robertson C**. Meta-analysis of clinical trials of Cyclo 3 Fort in the treatment of chronic venous insufficiency. IntAngiol. 2003 Sep;22(3):250-62.

45. Boyle P, **Robertson C,** Mazzetta C, Keech M, Hobbs R, Fourcade R, Kiemeney L, Lee C; UrEpik Study Group. The relationship between lower urinary tract symptoms and health status: the UREPIK study. BJU Int. 2003 Oct;92(6):575-80.

46. Calais da Silva F, Bono A, Whelan P, Brausi M, Queimadelos M, Portillo J, Kirkali Z, **Robertson C.** Intermittent androgen deprivation for locally advanced prostate cancer. Preliminary experience from an ongoing randomized controlled study of the South European urooncological group. Oncology. 2003;65Suppl 1:24-8.

47. Boyle P, **Robertson C**, Mazzetta C, Keech M, Hobbs FD, Fourcade R, Kiemeney L, Lee C; TheUrEpik Study Group. The prevalence of lower urinary tract symptoms in men and women in four centres. The UrEpik study. BJU Int. 2003 Sep;92(4):409-414.

48. Veronesi U, Paganelli G, Viale G, Luini A, Zurrida S, Galimberti V, Intra M, Veronesi P, **Robertson C**, Maisonneuve P, Renne G, De Cicco C, De Lucia F,

Gennari R. A randomized comparison of sentinel-node biopsy with routine axillary dissection in breast cancer. N Engl J Med. 2003 Aug 7;349(6):546-53.

49. Boyle P, d'Onofrio A, Maisonneuve P, Severi G, **Robertson C**, Tubiana M, Veronesi U. Measuring progress against cancer in Europe: has the 15% decline targeted for 2000 come about? Ann Oncol. 2003 Aug;14(8):1312-25.

50. Quinn MJ, d'Onofrio A, Moller B, Black R, Martinez-Garcia C, Moller H, Rahu M, Robertson C, Schouten LJ, La Vecchia C, Boyle P. Cancer mortality trends in the EU and acceding countries up to 2015. Ann Oncol. 2003 Jul;14(7):1148-52.

51. Decensi A, **Robertson C**, Viale G, Pigatto F, Johansson H, Kisanga ER, Veronesi P, Torrisi R, Cazzaniga M, Mora S, Sandri MT, Pelosi G, Luini A, Goldhirsch A, Lien EA, Veronesi U. A randomized trial of low-dose tamoxifen on breast cancer proliferation and blood estrogenic biomarkers. J Natl Cancer Inst. 2003 Jun 4;95(11):779-90.

52. Leonardi MC, Brambilla MG, Zurrida S, Intra M, Frasson A, Severi G, **Robertson C**, Orecchia R. Analysis of irradiated lung and heart volumes using virtual simulation in postoperative treatment of stage I breast carcinoma. Tumori. 2003 Jan-Feb;89(1):60-7.

53. Boyle P, Golia S, Daly P, Johnston PG, **Robertson C.** Cancer mortality in Ireland, 1926-1995. Ann Oncol. 2003 Feb;14(2):323-32.

54. Bredart A, **Robertson C**, Razavi D, Batel-Copel L, Larsson G, Lichosik D, Meyza J, Schraub S, von Essen L, de Haes JC. Patients' satisfaction ratings and their desire for care improvement across oncology settings from France, Italy, Poland and Sweden. Psychooncology. 2003 Jan-Feb;12(1):68-77.

55. Veronesi U, Maisonneuve P, Rotmensz N, Costa A, Sacchini V, Travaglini R, D'Aiuto G, Lovison F, Gucciardo G, Muraca MG, Pizzichetta MA, Conforti S, Decensi A, **Robertson C,** Boyle P; Italian Tamoxifen Study Group. Italian randomized trial among women with hysterectomy: tamoxifen and hormone-dependent breast cancer in high-risk women. J Natl Cancer Inst. 2003 Jan 15;95(2):160-5.

56. Trabattoni D, Bartorelli AL, Montorsi P, Fabbiocchi F, Loaldi A, Galli S, Ravagnani P, Cozzi S, Grancini L, Liverani A, Leon ME, **Robertson C,** Boyle P. Comparison of outcomes in women and men treated with coronary stent implantation. Catheter CardiovascInterv. 2003 Jan;58(1):20-8.

57. Gennari,R., Curigliano,G., Rotmensz,N., **Robertson,C.**, Colleoni,M., Zurrida,S., Nole,F., Braud,F.F., Orlando,L., Leonardi,M.C., Galimberti,V., Intra,M.,

Veronesi,P., Renne,G., Cinieri,S., Audisio,R.A., Luini,A., Orecchia,R., Viale,G., and Goldhirsch,A. (2004). Breast carcinoma in elderly women. Cancer *:NA.*, NA.

58. Mooney,J.D., Christie,P., **Robertson,C.**, and Clarke,S.C. (2004). The impact of meningococcal serogroup C conjugate vaccine in Scotland. Clin. Infect. Dis. *39*, 349-356.

59. Evans,C.J., Christie,P., **Robertson,C.**, Smith,A., and Mooney,J. (2004). Do real time 'flu spotter rates warn us about impending emergency admissions and deaths? Commun. Dis. Public Health *7*, 120-122.

60. Decensi,A., Bonanni,B., Baglietto,L., Guerrieri-Gonzaga,A., Ramazzotto,F., Johansson,H., **Robertson,C.**, Marinucci,I., Mariette,F., Sandri,M.T., Daldoss,C., Bianco,V., Buttarelli,M., Cazzaniga,M., Franchi,D., Cassano,E., and Omodei,U. (2004). A two-by-two factorial trial comparing oral with transdermal estrogen therapy and fenretinide with placebo on breast cancer biomarkers. Clin. Cancer Res. *10*, 4389-4397.

61. Boyle,P., **Robertson,C.**, Vaughan,E.D., and Fitzpatrick,J.M. (2004). A meta-analysis of trials of transurethral needle ablation for treating symptomatic benign prostatic hyperplasia. BJU. Int. *94*, 83-88.

62. Boyle,P., Mezzetti,M., La Vecchia,C., Franceschi,S., Decarli,A., and **Robertson,C.** (2004). Contribution of three components to individual cancer risk predicting breast cancer risk in Italy. Eur. J. Cancer Prev. *13*, 183-191.

63. Horninger,W., Berger,A., Pelzer,A., Klocker,H., Oberaigner,W., Schonitzer,D., Severi,G., **Robertson,C.**, Boyle,P., and Bartsch,G. (2004). Screening for prostate cancer: updated experience from the Tyrol study. Curr. Urol. Rep. *5*, 220-225.

64. Kisanga,E.R., Gjerde,J., Guerrieri-Gonzaga,A., Pigatto,F., Pesci-Feltri,A., **Robertson,C.**, Serrano,D., Pelosi,G., Decensi,A., and Lien,E.A. (2004). Tamoxifen and metabolite concentrations in serum and breast cancer tissue during three dose regimens in a randomized preoperative trial. Clin. Cancer Res. *10*, 2336-2343.

65. Boyle,P., **Robertson,C.**, Lowe,F., and Roehrborn,C. (2004). Updated meta-analysis of clinical trials of Serenoarepens extract in the treatment of symptomatic benign prostatic hyperplasia. BJU. Int. *93*, 751-756.

66. Nicoletti,G., Soutar,D.S., Jackson,M.S., Wrench,A.A., Robertson,G., and **Robertson,C**. (2004). Objective assessment of speech after surgical treatment for oral cancer: experience from 196 selected cases. Plast. Reconstr. Surg. *113*, 114-125.

67. **Robertson C**, Idris NR, Boyle P (2004), Beyond classical meta-analysis: can inadequately reported studies be included?, Drug Discov.Today 9: 924-931

68. Vandoninck V, Bemelmans BL, Mazzetta C, **Robertson C**, Keech M, Boyle P, Kiemeney LA. (2004) The prevalence of urinary incontinence in community-dwelling married women: a matter of definition. BJU Int. 94(9):1291-5.

69. Gennari R, Curigliano G, Rotmensz N, **Robertson C**, Colleoni M, Zurrida S, Nole F, de Braud F, Orlando L, Leonardi MC, Galimberti V, Intra M, Veronesi P, Renne G, Cinieri S, Audisio RA, Luini A, Orecchia R, Viale G, Goldhirsch A. (2004) Breast carcinoma in elderly women: features of disease presentation, choice of local and systemic treatments compared with younger postmenopausal patients. Cancer. 101(6):1302-10.

70. Horninger W, Berger A, Pelzer A, Klocker H, Oberaigner W, Schonitzer D, Severi G, **Robertson C**, Boyle P, Bartsch G. Screening for prostate cancer: updated experience from the Tyrol study. Can J Urol. 2005 Feb;12Suppl 1:7-13; discussion 92-3.

71. Guerrieri-Gonzaga A, **Robertson C**, Bonanni B, Serrano D, Cazzaniga M, Mora S, Gulisano M, Johansson H, Intra M, Latronico A, Franchi D, Pelosi G, Johnson K, Decensi A. (2006) Preliminary results on safety and activity of a randomized, double-blind, 2 x 2 trial of low-dose tamoxifen and fenretinide for breast cancer prevention in premenopausal women. J ClinOncol. 2006 Jan 1;24(1):129-3

72. Dancer SJ, Coyne M, **Robertson C**, Thomson A, Guleri A, Alcock S. Antibiotic use is associated with resistance of environmental organisms in a teaching hospital. J Hosp Infect. 2006;62:200-206.

73. Friederichs V, Cameron JC, **Robertson C** (2006) Impact of adverse publicity on MMR vaccine uptake: a population based analysis of vaccine uptake records for one million children, born 1987-2004. Arch Dis Child 91: 465-468

74. Alzweiri M, Watson DG, **Robertson C**, Sills GJ, Parkinson P (2007) Comparison of different water-miscible solvents for the preparation of plasma and urine samples in metabolic profiling studies *Talanta* 74, 1060-1065.

75. Cameron JC, Friederichs V, **Robertson C** (2007) Vaccine uptake: new tools for investigating changes in age distribution and predicting final values. *Vaccine* 25: 6078-6085

76. **Robertson C**, Link CL, Onel E, Mazzetta C, Keech M, Hobbs R, Fourcade R, Kiemeney L, Lee C, Boyle P, McKinlay JB (2007) The impact of lower urinary tract symptoms and comorbidities on quality of life: the BACH and UREPIK studies. *BJU Int* 99: 347-354

77. White LF, Dancer SJ, **Robertson C** (2007) A microbiological evaluation of hospital cleaning methods. *Int J Environ Health Res* 17: 285-295

78. Alzweiri M, Watson DG, **Robertson C**, Sills GJ, Parkinson JA (2008) Comparison of different water-miscible solvents for the preparation of plasma and urine samples in metabolic profiling studies. *Talanta* 74: 1060-1065

79. Bartsch G, Horninger W, Klocker H, Pelzer A, Bektic J, Oberaigner W, Schennach H, Schafer G, Frauscher F, Boniol M, Severi G, **Robertson C**, Boyle P (2008) Tyrol Prostate Cancer Demonstration Project: early detection, treatment, outcome, incidence and mortality. *BJU Int* 101: 809-816

80. McDonald SA, Donaghy M, Goldberg DJ, Hutchinson S, **Robertson C**, Bird S, Mills P, Dillon J, Bloor M, Hayes P, Graham L (2008) A population-based record linkage study of mortality in hepatitis C-diagnosed persons with or without HIV coinfection in Scotland. *Stat Methods Med Res*

81. McDonald SA, Hutchinson SJ, Bird SM, **Robertson C**, Mills PR, Dillon JF, Goldberg DJ (2008) A record-linkage study of the development of hepatocellular carcinoma in persons with hepatitis C infection in Scotland. *Br J Cancer* 99: 805-810

82. Meyer N, McMenamin J, **Robertson C**, Donaghy M, Allardice G, Cooper D (2008) A multi-data source surveillance system to detect a bioterrorism attack during the G8 Summit in Scotland. *Epidemiol Infect* 136: 876-885

83. Mooney JD, Weir A, McMenamin J, Ritchie LD, Macfarlane TV, Simpson CR, Ahmed S, **Robertson C**, Clarke SC (2008) The impact and effectiveness of pneumococcal vaccination in Scotland for those aged 65 and over during winter 2003/2004. *BMC Infect Dis* 8:53.: 53

84. Reilly J, Stewart S, Allardice GA, Noone A, **Robertson C**, Walker A, Coubrough S (2008) Results from the Scottish National HAI Prevalence Survey. *J Hosp Infect* 69: 62-68

85. White LF, Dancer SJ, **Robertson C**, McDonald J (2008) Are hygiene standards useful in assessing infection risk? *Am J Infect Control* 36: 381-384

86. McDonald,S.A., Hutchinson,S.J., Mills,P.R., Bird,S.M., **Robertson,C.**, Dillon,J.F., Springbett,A., and Goldberg,D.J. (2010). Diagnosis of hepatitis C virus infection in Scotland's injecting drug user population. Epidemiol. Infect. 138, 393-402.

87. Calais da Silva,F.E., Bono,A.V., Whelan,P., Brausi,M., Marques,Q.A., Martin,J.A., Kirkali,Z., Calais da Silva,F.M., and **Robertson,C.** (2009). Intermittent androgen deprivation for locally advanced and metastatic prostate cancer: results from a randomised phase 3 study of the South European Uroncological Group. Eur. Urol. 55, 1269-1277.

88. Dancer,S.J., White,L.F., Lamb,J., Girvan,E.K., and **Robertson,C.** (2009). Measuring the effect of enhanced cleaning in a UK hospital: a prospective cross-over study. BMC. Med. 7:28., 28.

89. Decensi,A., **Robertson,C.**, Guerrieri-Gonzaga,A., Serrano,D., Cazzaniga,M., Mora,S., Gulisano,M., Johansson,H., Galimberti,V., Cassano,E., Moroni,S.M., Formelli,F., Lien,E.A., Pelosi,G., Johnson,K.A., and Bonanni,B. (2009). Randomized double-blind 2 x 2 trial of low-dose tamoxifen and fenretinide for breast cancer prevention in high-risk premenopausal women. J. Clin. Oncol. 27, 3749-3756.

90. Ellaway,A., Morris,G., Curtice,J., **Robertson,C.**, Allardice,G., and Robertson,R. (2009). Associations between health and different types of environmental incivility: a Scotland-wide study. Public Health. 123, 708-713.

91. Ghani,A.C., Baguelin,M., Griffin,J., Flasche,S., Pebody,R., van Hoek,A.J., Cauchemez,S., Hall,I.M., Donnelly,C., **Robertson,C.**, White,M.T., Barrass,I., Fraser,C., Bermingham,A., Truscott,J., Ellis,J., Jenkins,H., Kafatos,G., Garske,T., Harris,R., McMenamin,J., Hawkins,C., Phin,N., Charlett,A., Zambon,M., Edmonds,W.J., Catchpole,M., Leach,S., White,P., Ferguson,N.M., and Cooper,B. (2009). The Early Transmission Dynamics of H1N1 Pandemic Influenza in the United Kingdom. PLoS. Curr. Influenza. RRN1130.

92. Idris,N.R.N. and **Robertson,C.** (2009). The Effects of Imputing the Missing Standard Deviations on the Standard Error of Meta Analysis Estimates. Communications in Statistics - Simulation and Computation 38, 513-526.

93. McDonald,S.A., Hutchinson,S.J., Mills,P.R., Bird,S.M., **Robertson,C.**, Dillon,J.F., Springbett,A., and Goldberg,D.J. (2009). Diagnosis of hepatitis C virus infection in Scotland's injecting drug user population. Epidemiol. Infect. 1-10.

94. McDonald,S.A., Hutchinson,S.J., Bird,S.M., Graham,L., **Robertson,C.**, Mills,P.R., Hayes,P., Dillon,J.F., and Goldberg,D.J. (2009). Association of self-reported alcohol use and hospitalization for an alcohol-related cause in Scotland: a record-linkage study of 23,183 individuals. Addiction. 104, 593-602.

95. McDonald,S.A., Hutchinson,S.J., Bird,S.M., Mills,P.R., Dillon,J., Bloor,M., **Robertson,C.**, Donaghy,M., Hayes,P., Graham,L., and Goldberg,D.J. (2009). A population-based record linkage study of mortality in hepatitis C-diagnosed persons with or without HIV coinfection in Scotland. Stat. Methods Med. Res. 18, 271-283.

96. Singh BK, SavillNJ, FergusonNM, **Robertson C**, Woolhouse ME. Rapid detection of pandemic influenza in the presence of seasonal influenza.BMC Public Health. 2010 Nov 24;10:726.

97. Tom BD, VAN Hoek AJ, Pebody R, McMenamin J, **Robertson C**, Catchpole M, DE Angelis D.Estimating time to onset of swine influenza symptoms after initial novel A(H1N1v) viral infection.Epidemiol Infect. 2010 Nov 19:1-7. [Epub ahead of print]

98. Boyle P, Chapman CJ, Holdenrieder S, Murray A, **Robertson C,** Wood WC, Maddison P, Healey G, Fairley GH, Barnes AC, Robertson JF.Clinical validation of an autoantibody test for lung cancer.Ann Oncol. 2011 Feb;22(2):383-9. Epub 2010 Jul 30.

99. Cooke B, Smith A, Diggle M, Lamb K, **Robertson C**, Inverarity D, Jefferies J, Edwards G, Mitchell T, Clarke S, McMenamin J.Antibiotic resistance in invasive Streptococcus pneumoniae isolates identified in Scotland between 1999 and 2007. J Med Microbiol. 2010 Oct;59(Pt 10):1212-8. Epub 2010 Jul 22.

100. Simpson CR, Ritchie LD, **Robertson C,** Sheikh A, McMenamin J.Vaccine effectiveness in pandemic influenza - primary care reporting (VIPER): an observational study to assess the effectiveness of the pandemic influenza A (H1N1)v vaccine. Health Technol Assess. 2010 Jul;14(34):313-46.

101. Adamson WE, Maddi S, **Robertson C**, McDonagh S, Molyneaux PJ, Templeton KE, Carman WF.2009 pandemic influenza A(H1N1) virus in Scotland: geographically variable immunity in Spring 2010, following the winter outbreak. Euro Surveill. 2010 Jun 17;15(24). pii: 19590.

102. Elliot AJ, Singh N, Loveridge P, Harcourt S, Smith S, Pnaiser R, Kavanagh K, **Robertson C**, Ramsay CN, McMenamin J, Kibble A, Murray V, Ibbotson S, Catchpole M, McCloskey B, Smith GE.Syndromic surveillance to assess the potential public health impact of the Icelandic volcanic ash plume across the United Kingdom, April 2010.Euro Surveill. 2010 Jun 10;15(23). pii: 19583.

103. McDonald SA, Hutchinson SJ, Bird SM, **Robertson C**, Mills PR, Dillon JF, Goldberg DJ.Hospitalisation for an alcohol-related cause among injecting drug users in Scotland: Increased risk following diagnosis with hepatitis C infection.Int J Drug Policy. 2011 Jan;22(1):63-9. Epub 2010 May 15.

104. McDonald SA, Hutchinson SJ, Bird SM, **Robertson C**, Mills PR, Graham L, Dillon JF, Goldberg DJ.The growing contribution of hepatitis C virus infection to liver-related mortality in Scotland.Euro Surveill. 2010 May 6;15(18). pii: 19562.

105. Al Zweiri M, Sills GJ, Leach JP, Brodie MJ, **Robertson C**, Watson DG, Parkinson JA. Response to drug treatment in newly diagnosed epilepsy: a pilot study of (1)H NMR- and MS-based metabonomic analysis.Epilepsy Res. 2010 Feb;88(2-3):189-95. Epub 2009 Dec 11.

106. McDonald SA, Hutchinson SJ, Bird SM, Mills PR, **Robertson C**, Dillon JF, Williams T, Goldberg DJ.Hospitalization of hepatitis C-diagnosed individuals in Scotland for decompensated cirrhosis: a population-based record-linkage study.Eur J GastroenterolHepatol. 2010 Jan;22(1):49-57.

107. McDonald SA, Hutchinson SJ, Mills PR, Bird SM, **Robertson C**, Dillon JF, Springbett A, Goldberg DJ. Diagnosis of hepatitis C virus infection in Scotland's injecting drug user population.Epidemiol Infect. 2010 Mar;138(3):393-402. Epub 2009 Sep 2.

108. Greenhalgh, D., Lamb, K. and **Robertson, C**. (2011) A mathematical model for the spread of Streptococcus Pneumoniae with transmission due to sequence type. Discrete and Continuous Dynamical Systems, Supplement 2011: Dynamical Systems, Differential Equations and Applications. (American Institute of Mathematical Sciences) ed. W. Feng, Z. Feng, M. Grasselli, X. Lu, S. Sigmund and J. Voight. 553-567.

109. Sinka K, Lacey M, **Robertson C,** Kavanagh K, Cuschieri K, Nicholson D, Donaghy M. Acceptability and response to a postal survey using self-taken samples for HPV vaccine impact monitoring. Sex Transm Infect. 2011 Dec;87(7):548-52. Epub 2011 Oct 11. PubMed PMID: 21990427.

110. Cuschieri K, Nandwani R, McGough P, Cook F, Hogg L, **Robertson C**, Cubie H.Urine testing as a surveillance tool to monitor the impact of HPV immunization programs. J Med Virol. 2011 Nov;83(11):1983-7. doi: 10.1002/jmv.22183. Epub2011 Aug 23. PubMed PMID: 21915874.

111. McLeish NJ, Simmonds P, **Robertson C**, Handel I, McGilchrist M, Singh BK, KerrS, Chase-Topping ME, Sinka K, Bronsvoort M, Porteous DJ, Carman W, McMenamin J,Leigh-Brown A, Woolhouse ME. Sero-prevalence and incidence of A/H1N1 2009influenza infection in Scotland in winter 2009-2010. PLoS One. 2011;6(6):e20358. Epub 2011 Jun 8. PubMed PMID: 21687661; PubMed Central PMCID: PMC3110753.

112. Anderson RE, Young V, Stewart M, **Robertson C**, Dancer SJ. Cleanliness audit of clinical surfaces and equipment: who cleans what? J Hosp Infect. 2011Jul;78(3):178-81. Epub 2011 Apr 16. PubMed PMID: 21497943.

113. Inverarity D, Lamb K, Diggle M, **Robertson C**, Greenhalgh D, Mitchell TJ, Smith A, Jefferies JM, Clarke SC, McMenamin J, Edwards GF. Death or survival frominvasive pneumococcal disease in Scotland: associations with serogroups andmultilocus sequence types. J Med Microbiol. 2011 Jun;60(Pt 6):793-802. Epub2011 Mar 10. PubMed PMID: 21393453; PubMed Central PMCID: PMC3167921.

114. O'Leary MC, Sinka K, **Robertson C**, Cuschieri K, Lyman R, Lacey M, Potts A,Cubie HA, Donaghy M. HPV type-specific prevalence using a urine assay inunvaccinated male and female 11- to 18-year olds in Scotland. Br J Cancer. 2011Mar 29;104(7):1221-6. Epub 2011 Feb 22. PubMed PMID: 21343934; PubMed CentralPMCID: PMC3068489.

115. Pebody R, Hardelid P, Fleming D, McMenamin J, Andrews N, **Robertson C**, ThomasD, Sebastianpillai P, Ellis J, Carman W, Wreghitt T, Zambon M, Watson J.Effectiveness of seasonal 2010/11 and pandemic influenza A(H1N1)2009 vaccines in preventing influenza infection in the United Kingdom: mid-season analysis2010/11. Euro Surveill. 2011 Feb 10;16(6). pii: 19791. PubMed PMID: 21329644.

116. Hardelid P, Fleming DM, McMenamin J, Andrews N, **Robertson C**, SebastianPillaiP, Ellis J, Carman W, Wreghitt T, Watson JM, Pebody RG. Effectiveness of pandemicand seasonal influenza vaccine in preventing pandemic influenza A(H1N1)2009infection in England and Scotland 2009-2010. Euro Surveill. 2011 Jan 13;16(2).pii: 19763. PubMed PMID: 21251487.

117. Mulvey D, Redding P, **Robertson C**, Woodall C, Kingsmore P, Bedwell D, DancerSJ. Finding a benchmark for monitoring hospital cleanliness. J Hosp Infect. 2011 Jan;77(1):25-30. Epub 2010 Dec 3. PubMed PMID: 21129820.

118. Kavanagh K, **Robertson C**, McMenamin J (2011) Assessment of the Variability in Influenza A(H1N1) Vaccine Effectiveness Estimates Dependent on Outcome and Methodological Approach. PLoS ONE 6(12): e28743. doi:10.1371/journal.pone.0028743

119. Greenhalgh, D., Lamb, K. and **Robertson, C**. (2012) A mathematical model for the spread of Streptococcus Pneumoniae with transmission due to serotype type. To Appear. Journal of Biological Dynamics. 6 Suppl 1:72-87 Published online http://dx.doi.org/10.1080/17513758.2011.592548.

120. Lone NI, Simpson C, Kavanagh K, **Robertson C**, McMenamin J, Ritchie L, Sheikh A.Seasonal Influenza Vaccine Effectiveness in the community (SIVE): protocol for a cohort study exploiting a unique national linked data set. BMJ Open. 2012 Mar 15;2(2):e001019. Print 2012.PMID: 22422920 [PubMed - in process]

121. Lycett S, McLeish NJ, **Robertson C**, Carman W, Baillie G, McMenamin J, Rambaut A, Simmonds P, Woolhouse M, Leigh Brown AJ.Origin and Fate of A/H1N1 Influenza in Scotland during 2009.J Gen Virol. 2012 Feb 15. [Epub ahead of print]PMID: 22337637 [PubMed - as supplied by publisher]

122. Smith SJ, Young V, **Robertson C**, Dancer SJ.Where do hands go? An audit of sequential hand-touch events on a hospital ward.J Hosp Infect. 2012 Mar;80(3):206-11. Epub 2012 Jan 30.PMID: 22297169 [PubMed - in process]

123. Simpson CR, Ritchie LD, **Robertson C**, Sheikh A, McMenamin J. Effectiveness of H1N1 vaccine for the prevention of pandemic influenza in Scotland, UK: a retrospective observational cohort study. Lancet Infect Dis. 2012 Sep;12(9):696-702. Epub 2012 Jun 26.

124. Reilly J, Cairns S, Fleming S, Hewitt D, Lawder R, **Robertson C**, Malcolm W,Nathwani D, Williams C. Results from the second Scottish national prevalence survey: the changing epidemiology of healthcare-associated infection in Scotland. J Hosp Infect. 2012 Sep 27. pii: S0195-6701(12)00277-0. doi:10.1016/j.jhin.2012.07.024. [Epub ahead of print] PubMed PMID: 23022370.

125. Boyle P, Boniol M, Koechlin A, **Robertson C**, Valentini F, Coppens K, Fairley LL, Boniol M, Zheng T, Zhang Y, Pasterk M, Smans M, Curado MP, Mullie P, Gandini S, Bota M, Bolli GB, Rosenstock J, Autier P. Diabetes and breast cancer risk: a meta-analysis. Br J Cancer. 2012 Sep 20. doi: 10.1038/bjc.2012.414. [Epub ahead of print] PubMed PMID: 22996614.

126. Pebody RG, Andrews N, Fleming DM, McMenamin J, Cottrell S, Smyth B, Durnall H, **Robertson C**, Carman W, Ellis J, Sebastian-Pillai P, Zambon M, Kearns C, Moore C, Thomas DR, Watson JM. Age-specific vaccine effectiveness of seasonal 2010/2011 and pandemic influenza A(H1N1) 2009 vaccines in preventing influenza in the United Kingdom. Epidemiol Infect. 2012 Jun 13:1-11. [Epub ahead of print] PubMed PMID: 22691710.

127. Beverland IJ, Cohen GR, Heal MR, Carder M, Yap C, **Robertson C**, Hart CL, Agius RM. A Comparison of Short-term and Long-term Air Pollution Exposure Associations with Mortality in Two Cohorts in Scotland. Environ Health Perspect. 2012 Sep;120(9):1280-5. Epub 2012 Jun 6. PubMed PMID: 22674867.

128. Chapman CJ, Healey GF, Murray A, Boyle P, **Robertson C**, Peek LJ, Allen J, Thorpe AJ, Hamilton-Fairley G, Parsy-Kowalska CB, Macdonald IK, Jewell W, Maddison P, Robertson JF. EarlyCDT®-Lung test: improved clinical utility through additional autoantibody assays. Tumour Biol. 2012 Apr 11. [Epub ahead of print] PubMed PMID: 22492236; PubMed Central PMCID: PMC3460172.

129. Innes HA, Hutchinson SJ, Allen S, Bhattacharyya D, Bramley P, Carman B, Delahooke TE, Dillon JF, Goldberg DJ, Kennedy N, Mills PR, Morris J, Morris J, **Robertson C**, Stanley AJ, Hayes P; Hepatitis C Clinical Database Monitoring Committee. Ranking predictors of a sustained viral response for patients with chronic hepatitis C treated with pegylated interferon and ribavirin in Scotland. Eur J Gastroenterol Hepatol. 2012 Jun;24(6):646-55. Review. PubMed PMID:22433796.

130. Kavanagh K, **Robertson C**, Murdoch H et al. (2012) Syndromic surveillance of influenza-like illness in Scotland during the Influenza A H1N1v pandemic and beyond. Journal of the Royal Statistical Society Series A: Statistics in Society. 175 (4) pp.939-958

Papers published in non refereed journals, communications, reports and reviews (since 2000)

35 published communications such as letters, conference papers, research grant reports (from 1980 to 1999)

1. Gray, N., Zaridze, D. Robertson, C. Krivosheeva, L., Sigacheva, N., Boyle, P. and the International Cigarette Variation Group. (2000) Variation within global cigarette brands in tar, nicotine and certain nitrosamines: analytic study. Tobacco Control. Letter to the Editor, 9, 351.

2. Robertson, C., Boyle, P., Mazzetta, C., Keech, M., Hobbs,R., Fourcade,R., Kiemeney, L.A.M., Lee, C. and the UrEpik Study Group. (2000). Response Bias and Sampling Weights for the UrEpiK Study: The UREPIK study. Technical Report of Project supported by a research grant from GlaxoWellcome (24pp). Milan: European Institute of Oncology, Division of Epidemiology and Biostatistics: Statistics and Data Analysis Centre.

3. Robertson, C. (2000) Neural Networks: An Introductory Guide for Social Scientists. The Statistician. 49, 123-124. (Book review)

4. Robertson, C. (2000) Statistics and Problem Solving: Computer based modules from the STEPS project. International Society for Clinical Biostatistics Newsletter, December Issue 30, 25. (Book review)

5. Boyle, P., Gandini, S., Baglietto, L., Severi, G., Robertson, C. (2001) Epidemiology of Prostate cancer. European Urology 39 (4S) 2-3.

6. Robertson, C. (2001) Modelling Survival Data. Extending the Cox Model by Terry Therneau and Patricia Grambsch, Journal of Epidemiology and Biostatistics 6 (5). (Book review)

7. Robertson, C. (2002). Report of the Analysis of the Case Control Study associated with the outbreak of Cryptospiridium in Aberdeen in 2002. Published by Scottish Centre for Infection and Environmental Health and Grampian Health Board. 20pp.

8. Robertson, C. (2003) Quantitative Methods for the Evaluation of Cancer Screening. Statistical Methods in Medical Research (Book review)

9. Robertson, C. and Bramley C. (2003). A Simulation model for Pneumococcal Carriage in Scotland.. Published by Scottish Centre for Infection and Environmental Health. 60pp.

10. Cree, L., Robertson, C., House, R. (2004). Food Surveillance System for Scotland. Scottish Centre for Infection and Environmental Health Weekly Report 38 (2004/31) 186-187.

11. Martin Donaghy, Claire Cameron Health Protection Scotland, Vera Friederichs, Chris Robertson University of Strathclyde, Elaine Strange, Jim Chalmers, Information Services Division. (2004) Therisk of transmission of Measles in Scotland. A report for the Chief Medical Officer of Scotland Dec 18 2004

12. Cree, L., **Robertson, C**., Michie, N. House, R. (2005). Food Surveillance System for Scotland. Health Protection Scotland Weekly Report 38 (2005/35) 194-195.

13. John Curtice, Anne Ellaway, **Chris Robertson**, George Morris, Gwen Allardice, Ruth Robertson (2005) Public Attitudes and Environmental Justice in Scotland. Scottish Executive Social Research (pp 83)

14. Cree, L., **Robertson, C**., Michie, N. (2006). Food Surveillance System for Scotland – 2005 Data. Health Protection Scotland Weekly Report 40.

15. **Robertson, C.** (2007) Protecting the leaders—syndromic surveillance for the G8 summit in Scotland. Significance, 3: 69-72

16. Dr. J. A. Parkinson, Dr. G. J. Sills, Prof. M. J. Brodie, Dr. D. G. Watson, **Prof. C. Robertson**, Dr. J.-P. Leach (2006) Metabolic Profiling in the identification of drug-resistant epilepsy. Final Report to Chief Scientist Office, Scottish Executive. (pp13 + Appendix 22pp)

17. Beverland, I, Yap, C., **Robertson, C**., Agius, R., Hole, D., Cohen, G., Heal, M., Carder, M., Henderson, D., Ferguson, N., Lee, A., Fowkes, G., Morris, G. (2006). Final Report for Department of Health research project (Ref: 0020015): Health effects of long-term exposure to air pollution in Scotland (54pp)

18. Robertson, C., Cameron. J.C., Friederichs, V. (2006) Final Report for Modelling the Epidemic process for Measles Mumps and Rubella. Scottish Executive Health Department.

19. Reilly J., Stewart S., Allardice, G., Noone A., **Robertson, C**., Walker A., and Coubrough S. NHS Scotland national HAI prevalence survey. (2007). Glasgow, Health Protection Scotland. Report 239pp http://www.hps.scot.nhs.uk/haiic/publicationsdetail.aspx?id=34832

20. Cree, L., **Robertson, C**., Michie, N. (2007). Food Surveillance System for Scotland – 2006 Data. Health Protection Scotland Weekly Report 46, 392-394.

21. Cree, L., Reid, M., **Robertson, C**., Dryburgh, L. (2008). The UK Food Surveillance System(FSS UK) – 2007 Scotland Data. Health Protection Scotland Weekly Report 47, 400-2.

22. Sinka, K,Scoular, A, **Robertson, C** , Donaghy, M(2008) HPV immunisation in ScotlandPlanning for equity. A report prepared for the HPV Service Delivery Group. Health Protection Scotland, Glasgow.

23. Cree, L., Reid, M., Robertson, C., Dryburgh, L. (2009). The UK Food Surveillance System (FSS UK) – 2008 Scotland Data. Health Protection Scotland Weekly Report 47, 440-2. http://www.documents.hps.scot.nhs.uk/ewr/pdf2009/0947.pdf

24. Lamb, K., Greenhalgh, D., Robertson, C. (2009) Mathematical Modelling of Genetic Effects in the Transmission of Pneumococcal Carriage and Infection. Proceedings of the 9th international conference computational and mathematical methods in science and engineering. ISBN: 978-84-612-9727-6

Invited conference papers since 2000.

1. Diet, Nutrition and Colorectal Cancer Risk. Scottish Cancer Foundation. Perth, November 2000
2. Meta Analysis of Clinical Trials, BIOSS Conference, Glasgow May 2002
3. Modelling Regional Variation. Napier/Edinburgh University, June 2002.
4. Modelling Trends in Regional Variation, LeedsUniversity, July 2002
5. Meta Analysis, Scottish Centre for Infection and Environmental Health, March 2003
6. Analysis of clinical trial results on intermittent therapy in the treatment of prostate cancer, South European Urology Group, Lisbon, May 2003
7. Beyond Meta Analysis. International Conference for Clinical Biostatistics, Society for Clinical Trials, London. July 2003
8. A Simulation Model Pneumococcal Carriage and Transmission. Wyeth Pneumococcal Workshop, Manchester, December 2003
9. Analysis of clinical trial results on intermittent therapy in the treatment of prostate cancer, South European Urology Group, Lisbon, Feb 2004
10. Modelling the impact of vaccination on pneumococcal carriage, infection and disease (With A Weir), Pneumococcal Disease Workshop, Royal College of Physicians, Glasgow June 2004
11. Mathematical Modelling of Infectious Diseases, Pan Celtic Microbiological Forum, Greenock , Sept 2004.
12. Statistical Methods for Monitoring Performance. Decontamination Conference, Glasgow, Sept 2004.

13. Regional Variation in Epidemiology, International Agency for Research in Cancer, Lyon. January, 2005
14. Analysis of clinical trial results on intermittent therapy in the treatment of prostate cancer, South European Urology Group, Lisbon, Feb 2005
15. Intermittent Hormone Therapy in Advanced Prostate Cancer. Presentation of Trial Results. Intermittent Therapy Research Group. St Barts'sLondon March 2005
16. Invited Discussant on Clinical Trials in Cancer Treatment. Frontier Science Meeting. Edinburgh 2005
17. Effects of Long term Exposure to Air Pollution in Scotland. Royal Statistical Society Medical Section Meeting. Leeds, October 2005.
18. Analysis of clinical trial results on intermittent therapy in the treatment of prostate cancer, South European Urology Group, Lisbon, Feb 2006
19. Statistics and Health Protection Scotland, Research Day, Lanarkshire Hospitals Trust, June 2006
20. Effects of Long term Exposure to Air Pollution in Scotland. ManchesterUniversity, October 2006.
21. An investigation of the effects of the fall in MMR vaccination rates on the likelihood of a Measles Epidemic in Scotland. LancasterUniversity 19 January 2007
22. Syndromic Surveillance at Health Protection Scotland. Health Care Commission Workshop on Statistical Methods in Syndromic Surveillance, London 20 June, 2007
23. Modelling Infections Diseases at Health Protection Scotland, Health Protection Scotland, 7 November 2007
24. Syndromic Surveillance Systems at Health Protection Scotland. Open University Conference on Surveillance Systems, Milton Keynes21 May, 2008
25. Assessing the impact of pneumococcal vaccination in Scotland. Wyeth ATENEA Study Group, Madrid, 26/27 May, 2008
26. Epidemiological Issues in developing a national vaccination programme and surveillance system in Scotland. Workshop on the impact of HPV vaccination on cervical screening Workshop organised by WHO/IARC, Milan 3-5 Dec 2008.
27. Syndromic Surveillance at Health Protection Scotland, ICHAIR, Centre for Modelling Infectious Diseases, Edinburgh University, 10 December 2008
28. Statistics at Health Protection Scotland, Glasgow Group, Royal Statistical Society, 11 December 2008
29. Royal Statistical Society Conference, Edinburgh, Sept 2009
30. ScotStat Conference, Edinburgh, Edinburgh, Oct 2009
31. Management of H1N1 Influenza, Glasgow, November, 2009
32. Institute of Advanced Studies Workshop on preparing for pandemics, Strathclyde, Nov 2009
33. Applications of Statistics in Health Protection, Glasgow University, 02/02/11
34. Statistical Aspects of Syndromic Surveillance in Scotland, Stirling University, March 8, 2011

35. Introduction to Medical Statistics, Monklands Hospital, March 11, 2011

PhD Students.

Naeem Al Rehman.A statistical investigation of methods for the comparison of vaginal bleeding patterns in contracepting women. Awarded 1992
Professor Economics Department, University of Peshawar, Pakistan

SuliemanKhattak. A study of staying on rates of pupils in schools using logistic regression : multinomial and multilevel models to analyse data from the Scottish Young People's Surveys of 1985-87 and 1987-89. Awarded 1993
Lecturer, University of Peshawar, Pakistan

Khudadad Khan. Statistical models in incidence and treatment of cancer of the larynx. Awarded 1995
Assistant Professor, Institute of Statistics , University of the Punjab, Lahore, Pakistan

Zamalia Mahud. A study on teaching statistical concepts at the introductory level: the development and testing of a teaching model and an investigation into the methodological techniques
Professor Madja, Centre for Statistical Studies, Faculty of Computer and Mathematical Sciences, UniversitiTeknologiMARA, MALAYSIA

Nik.Ruzni.NikIdris, Estimating meta analysis parameters in non-standard data. Awarded 2006
Lecturer, Statistics

Amanda Weir. Statistical Modelling of Pneumococcal Carriage and Infection, Awarded 2009
Statistician, Health Economic Modeller Health Protection Scotland

Oarabile Molaodi. Analysis of Disease Maps. Awarded 2009
Statistician, MRC Public Health Unit, Glasgow University

Karen Lamb. Modelling Serotype and Sequence Type Information in the Carriage of Pneumocaccal Infection. Awarded 2010
Statistician, MRC Public Health Unit, Glasgow University

Adam Wagner. Statistical Analysis of Spatially Linked Time Series.Awarded 2010.
Statistician, MRC Public Health Unit, Cambridge University

Stefan Flasche. Developing serotype-specific models of the transmission of pneumococcal carriage and the effect of pneumococcal conjugate vaccines on disease in the UK .Awarded 2012.
Modeller, LSHTM, London

Other Related Activities

External Links, Invited visits (since 1995).

ESRC Survey Link Fellow attached to the Centre for Educational Sociology, EdinburghUniversity. June 1987-1996
European Institute of Oncology, Division of Biostatistics and Epidemiology, Milan, Italy. Honorary Senior Research Associate 1994-1995
Statistical Assessor for British Journal of General Practise. July 1992-2000
Editorial Board, Journal of Epidemiology and Biostatistics. 1995- , Associate Editor 1997 – 1998, Executive Editor 1999 -2002
External Examiner, UndergraduateClassesNapierUniversity, Edinburgh. 1995-1996
External Examiner, PhDThesesKeeleUniversity. 1990, 1995
Statistical Assessor on Data Monitoring Committee for EORTC Trial MAB Intermittent PGU P9401 1996-
Abbot Laboratories, Waukegan, Michigan, United States.Invited Statistical Consultant, June 9-13, 1997.
Merck Research Laboratories, Bluebell, Pennsylvania, United States.Invited Statistical Consultant, Sept 15-19, 1997.
Statistical Assessor on Data Monitoring Committee for Trial CAB Intermittent SEUG9901 1999-
Pierre Fabre Pharmaceutics, Castres France. Statistical Consultant 1999-2001.
External Examiner, PhDThesisCardiffUniversity. 2003
External Examiner, PhDThesisManchesterUniversity. 2004.
External Examiner, PhDThesisUniversity of Dijon. 2004

Royal Statistical Society, Medical Section Committee Member 2002-.06
Director of Frontier Science (Scotland) a charity conducting clinical trials in Scotland 2002-
Western Infirmary, Glasgow, Ethics Committee 2003-
Scientific Advisory Committee Meeting, *Boston Area Community Health Survey* 2001-*5*
Scientific Advisory Committee for the European Code Against Cancer Projections Sub-Group 2002-03
Scientific Advisory Committee for the European Cancer Mortality Atlas 2002-09
Scientific Advisory Committee for the Department of Health Project: Health effects of long-term exposure to air pollutants in Scotland 2002-
Data Safety Monitoring Committee for

a. HRT and Low Dose Tamoxifen Study for the prevention of Breast Cancer (Italy) 2002-08
b. Trials of intermittent therapy in advanced prostate cancer patients (Southern European Urology Group) 1997-2010
c. Trials IEO007, IEO183 and IEO167. Chemoprevention studies in Italy, sponsored by the European Institute of Oncology 2002-08

Ethics Committee for International Breast Cancer Study Group 2006-
Scottish Government SCOTSTAT Committee for Health and Care 2004-
External Assessor for Information Services Division, NHS, Senior Promotions Panel (April 2008)
Home Office Surveys, Design and Statistics Workshop, July 2008
Scientific Advisory Board for the Interdisciplinary Centre for Human and Avian Influenza Research, Edinburgh University 2008-
Member of Data Safety Monitoring Committee for International Breast Cancer Study Group Trials 2009-
Scientific Advisory Board for the MRSA Screening Programme, Health Protection Scotland 2008-
SPI-M Department of Health Committee to inform on policy regarding H1N1 pandemic June 2009-Jan 2010

Professional Bodies
Fellow of the Royal Statistical Society (1978 -)

Awards
2000. Bruno Martinetto Prize for Contributions to Research in Chemoprevention in Italy

International Prevention Research Institute

Appendix III

Statistical analysis plan for the Northern European Database study of glargine insulin use and risk of cancer

Diabetes treatment and risk of cancer

Proposed analysis plan

(Condensed version)

Authors :
Paolo Boffetta, Mathieu Boniol, Maria Bota, Peter Boyle, Chris Robertson(IPRI Lyon, France)

Henrik Sorensen; Sinna Pilgaard Ulrichsen'; Timothy Lee Lash; Jacob Bonde Jacobson

Tuomilehto Jaakko; Reijo Sund;

Lars Vatten; Bjorn. O.Asvold

Helen Colhoun; Shona Livingstone; Daniel Levin;

Anders Ekbom; Helle Kieler; Rickard Ljung; Bengt Haglund

Table of Contents

Objectives

The aim of this study is to compare the risk of cancer (primarily: breast, colorectal and prostate cancer; secondarily: lung, pancreatic and all cancers) in diabetic patients exposed to insulin glargine with that of patients prescribed other types of insulin.

The suggested analysis plan is a Two stage process with an Individual Level Analysis within each centre using the same statistical methodology followed by a combination of the within study estimated effects using meta – regression methods (Thompson et al 2010).

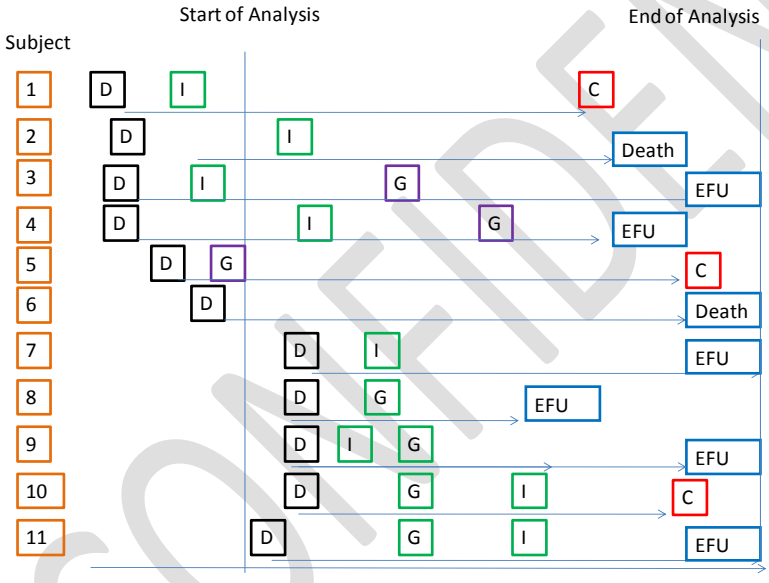
To make use of all the data from the opening of the registry until the end of the follow-up a survival model with time dependent covariates is an appropriate statistical model. This assumes that the hazards of a cancer during follow up are proportional and this would need to be checked.

Description of the data

Sources: prescription database, cancer registry, mortality registry, diabetes registry, confounding data from various other sources.

Two separate data sets will be used for the analyses: one for all patients included in the prescription registry and a second analysis is intended, as far as possible, to isolate newly diagnosed patients. The second analysis data set will be referred to as patients with no history of insulin in the preceding 6 months (PNHIP6M) and are presumed new initiators of any type of insulin (example patients 7-11 on Figure 1).

Figure 1: Illustration of different patient trajectories



In the trajectories **D** is date of diagnosis of Diabetes (which may not be known), **I** date of initiation of Non Glargine Insulin, **G** date of beginning Glargine, **C** Date of diagnosis of cancer, **Death** date of death and **EFU** date of end of follow up. Once a patient has entered the database of the treatment registry it will be assumed that the patient' therapy is known.

Patient	Ever Insulin	Ever Glargine	Start	End	Cancer
1	1	0	t0	tc	1
2	1	0	ti	tc	0
3	1	0	t0	tg	0
3	1	1	tg	tc	0
4	1	0	ti	tg	0
4	1	1	tg	tc	0
5	0	1	t0	tc	1
7	1	0	ti	tc	0
8	0	1	tg	tc	0
9	1	0	ti	tg	0
9	1	1	tg	tc	0
10	0	1	tg	ti	0
10	1	1	ti	tc	1
11	0	1	tg	ti	0
11	1	1	ti	tc	0

Table 3: Coding for survival model (see also Appendix 4 for data management example)

← Ever/never analysis

↓ Dose response analysis

Patient	Glargine Dose Gp	start	end	Cancer
A	1	tg	tg+x	0
A	2	tg+x	tg+2x	0
A	3	tg+2x	tc	1
B	1	tg	tc	0
C	1	tg	tg+x	0
C	2	tg+x	tc	0

Exclusion criteria

Any patient with no record of any prescription of any type of insulin will be excluded. Patients in the Prescription Registry with a cancer prior to their start date (or within 3 months of their start date) will not be included in the analysis as it is not feasible to associate the cancer with the insulin treatment.

An additional reason to exclude the first 3 months from beginning of insulin treatment is the possibility that diabetes was caused by (or diagnosed following clinical workout for) cancer (reverse causality).

Gestational diabetes patients (when we can identify them via a diabetes registry) will be excluded.

Person time at risk

All analyses will exclude the first 3 months from the numerator and denominator and there will be no built in 'immorality'

The 3 month exclusion will be applied to initiations of all new insulins (glargine/non glargine long acting/non long acting insulins). This will effectively be done by shifting all prescription dates by 3 months.

Contrasts

The primary objective of this study is to assess the risk of cancer for the glargine users in comparison with all other insulin users.

Nevertheless it would be particularly interesting to consider a contrast between comparable insulin users: we have identified that users of long acting insulin have common characteristics, which is the reason why we will also run analyses where we separate non glargine users into: long acting on glargine (LANG) and non long acting insulin (NLA).

Table 4: All possible covariate patterns when considering non glargine long acting insulins separately from non long acting insulins and coding each as ever/never

Pattern	Sequence	E-NLA	E-LA	E-G	Start	End	Group
A	1	1	0	0			1
B	1	0	1	0			2
C	2	1	1	0			3
D	1	0	0	1			4
E	2	1	0	1			5
F	2	0	1	1			6
G	3	1	1	1			7

Group1: non long acting insulin (NLA)
Group2: LANG
Group3: LANG + NLA
Group4: G
Group5: G+NLA
Group 6: G+LANG
Group7: G+LANG+NLA
Proposed comparison
Groups 4 and 5 combined compared with groups 2 and 3 combined and group 4 compared to group 2. This will be a direct comparison of glargine users with patients who have received another long acting insulin (not Glargine - LANG).

2 types of analysis:

1) Ever/never analysis - ever exposed to glargine (or detemir) compared to never exposed to glargine(or detemir)
2) Dose response analysis - dose of glargine (or detemir) compared to non glargine (or non detemir)
Dose = cumulative exposure time to glargine – adding up durations between prescriptions; if duration > 6 months (181 days) then this is not counted in the cumulative time.
Proposed dose groups are <1 year, 1 - <2 years, 2 - <2 years, 3+ years**.**
Some countries have enough data for a 5th dose group, which will be accepted: <1 year, 1 - <2 years, 2 - <3 years, 3 - <4 years, 4+ years. Make sure that there are enough events in the 4+ years category though.
Patients who cease glargine/detemir will remain in their highest attained dose group for the duration of follow up.
*Dose response will be calculated for glargine and detemir; it will not be calculated for non long acting insulins.

Stratification

- Age Group at the beginning of the Patient Prescription Registry opening in 10 year age bands (<34, 35-44, …, 65-74, 75+.). The follow up is not so long that it is necessary to have age group as a time dependent effect.
- Sex.
- Type of Diabetes, Type I and Type II separately.

Allocation bias

Allocation bias is the big problem and to control this (partly) Type 1 and Type 2 patients will be analysed separately. Adjustment for differences between Type 1 and Type 2 diabetics are likely to lead to more complex interaction models and it is simpler to fit separate models for each type and use a meta regression model to investigate if the effect of ever taking glargine on cancer risk is the same in type 1 patients compared to type 2.
Patients who take glargine on its own must be Type 2.

Type 1 patients can be of any age though age at first insulin below 35 is a good proxy for type 1

Type 1 patients more likely to have glargine are the relatively healthy and active.

Type 2 patients more likely to be on glargine are elderly, frail, and not coping on other insulins.

Confounders (most measured on study)

These will not be the same in all centres though if it is possible to identify a minimal set which are available then the following model will be used.

There will be missing values for the covariates. Imputations will be used.

But we have to make sure that multiple imputation should be conducted only if missing values represent a small proportion of the dataset. We should not apply it for variables missing in 50-90% of individuals.

Within each centre there will require to be the assessment of whether or not a potential confounder variable does require being in the model. Possible confounders are smoking status, deprivation etc,

Type of insulin regimen is associated with unmeasured confounders.

Age at the birth of the first (live?) child might be used for breast cancer over and above the variables used in the previous analysis.

Metformin will be included as a time dependent confounder among incident insulin users, coded as Ever/Never. This will result in a split in a follow up record for patients who are first prescribed during the follow up period.
Metformin is the only time dependent confounder – all others will be considered fixed at baseline.

Data and Estimates to be used for the meta-analysis

- Frequency table of the variables with the categorisation used.

For each variable entered in the model:

a) For categorical variables provide a cross tabulation of this variable with the insulin groupings used in the model.

b) For continuous variables provide summary statistics (n, min, max, mean, median, quartile 1, and quartile 3) for each insulin group.

- Results from each Cox model with the minimum following details:

-Number of subjects included in the analysis.
-Number of events.
-For each parameter included in the model, the estimate and the corresponding standard error.
-The covariance matrix estimated from the model.
-A graph of the Schoenfeld residuals vs log of time (including if possible a smoothing curve).

Models

The basic model which can be fitted in all centres will be a **time dependent Cox proportional hazards** with time measured in days from the date at which the Prescription Registry opens. Stratification is on the basis of the combination of Age Group and Sex (strata). The main explanatory variable is the indicator variable denoting that the patient has ever taken Glargine (g) or the dose group variable.

Example for the ever/never analysis:

The data will be arranged in the 'long format' with up to two records for each patient with the start and end date of each episode and an indicator (cancer) denoting if the endpoint has occurred. Annex 4 present an example of database format. In *R* terminology the model can be written, using the *coxph()* function, as:

Surv(date.start,date.end,cancer) ~ strata(strata)+g

Ever/Never Glarine

Model: Ever/Never

Surv(date.start,date.end,cancer) ~ strata(strata)+g

Model 1 in Summary_AllCancers_May15.xlsx Sheet EverNever+Dose

Model: Ever/Never by Period

Surv(date.start,date.end,cancer) ~ strata(strata)+g + fu.period:g

Model 3 in Summary_AllCancers_May15.xlsx Sheet EverNever+Dose (slight modification for period to have 3 groups <1 year, 1-2 years 2+ years

Glargine/non Glargine Long Acting/non long acting (GLANLA)

Model: GLANLA_Group

Surv(date.start,date.end,cancer) ~ strata(strata)+GLANLA_group)

Cox Model	1		RR	LCL	UCL
		NLA	1.000		
		LA	0.000	0.000	Inf
		NLA+LA	0.961	0.697	1.325
		G	1.247	0.402	3.873
		NLA+G	0.824	0.637	1.066
		LA+G	0.000	0.000	Inf
		NLA+LA+G	1.451	0.689	3.055

Model 1 in Summary_AllCancers_May15.xlsx Sheet G+LA+NLA

Model: GLANLA_Contrast

Surv(date.start,date.end,cancer) ~ strata(strata)+ Ever Any LA + Any.Long.Alone+ G.comp.LA.Con)

4	NLA	1.000			
	Ever Any LA	0.910	0.741	1.117	LA, NLA+LA, G, NLA+G, LA+G, NLA+LA+G (1) NLA (0)
	Any.Long.Alone	1.003	0.318	3.165	LA, G, LA+G (1) , Anything involving NLA (0)
	G.comp.LA.Con	0.937	0.771	1.140	G, NLA+G (1) VS LA, NLA+LA (-1) - Contrast

Model 4 in Summary_AllCancers_May15.xlsx Sheet G+LA+NLA

Model: GvsLA_Subset

analysis using only periods LA, G, NLA+LA, NLA+G

Surv(date.start,date.end,cancer) ~ strata(strata)+ G.comp.L.)

G.comp.LA is an indicator variable with G, NLA+G (1) VS LA, NLA+LA (0)

Model 5 in Summary_AllCancers_May15.xlsx Sheet G+LA+NLA

Dose Response

Model: G_DoseGp

Surv(date.start,date.end,cancer) ~ strata(strata)+ dose.gp)

	RR	LCL	UCL	
7	Never G	1.000		
	<1 year	0.964	0.595	1.564
	1-2	0.397	0.128	1.238
	2+	1.390	0.616	3.134

Model 7 in Summary_AllCancers_May15.xlsx Sheet EverNever+Dose

Model: G_DoseGp_Linear

Surv(date.start,date.end,cancer) ~ strata(strata)+ G + Linear.Trend)

8	Never G	1.000		
	Any G	0.811	0.492	1.336
	Linear	1.201	0.752	1.918

Any G is dose groups <1, 1-2, 2+ (1) compared to Never G (0); Linear is the linear trend 2+ (1), 1-2 (0), <1 (-1) Never G (0).

Model 8 in Summary_AllCancers_May15.xlsx Sheet EverNever+Dose

Model: LA_DoseGp

Surv(date.start,date.end,cancer) ~ strata(strata)+ la.dose.gp)

La.dose.gp is dose groups for non glargine long acting and have levels <1 year , 1-2 years, 2+ years

Model: G_LA_DoseGp

Surv(date.start,date.end,cancer) ~ strata(strata)+ dose.gp + la.dose.gp)

Summary

	Dataset	
	All Insulin Users	PNHIP6M
Model: Ever/Never		
Model: Ever/Never by Period		
Model: GLANLA_Group		
Model: GLANLA_Contrast		
Model: GvsLA_Subset		
Model: G_DoseGp		
Model: G_DoseGp_Linear		
Model: LA_DoseGp		
Model: G_LA_DoseGp		

Most Important
Desirable to Fit
Don't Fit

All models to be fitted with and without the indicator for Metformin

Where possible
All models to be fitted with and without the indicator for Metformin + Confounders
Confounders - BMI, Smoking and there may be others

All models to be fitted on all data and the subset of Type 2 diabetes only
In some centres Type 2 diabetes will only be presumed from
date of first prescription and so only for the PNHIP6M dataset

The above analysis will be applied to each cancer site defined in Appendix 2: ICD codes.
The comparison of glargine against all other insulin will represent the main analysis since it is defined as the main endpoint in the operational protocol. Further analysis in order to identify if an increase risk of cancer is observed for long acting insulin separating glargine from long acting non glargine insulin will be conducted. An analysis will be conducted to compare glargine to other LANG, which is the most equivalent group to glargine (same indication for treatment).

Common steps:

- Starting date: first use of insulin following the introduction of Glargine in the country
- Follow-up: until either (1) date of cancer, (2)date of death (right censoring, only if death occurs before the last date of available data in cancer registry), (3) last date

of available data in cancer registry (right censoring, this date will be similar to most individuals in the study)
- Eligible insulin prescription: only those occurring 3 month or more before the censoring date (cancer, death, and last date in registry).
- All prescription dates should be shifted by 3 months for each individual, then usual data management should be conducted to classify individuals (i.e. a cancer occurring before the first prescription is not included). This will avoid including an immortal time bias since both events and person-years are removed from the 3 month period.
- Method: Cox proportional hazard model with time dependent variable for exposure variable
- Analysis stratified on gender and age group* => allowing different underlying hazard functions for each stratum.
- Analysis is also adjusted systematically for metformin use included in the model as a time dependent variable. The metformin variable will be entered as an ever/never variable.
*Age groups: <35, 35-44, .., 65-74, 75+.

Sensibility analysis

s – 1– Latency **
s – 1– 1: Analysis restricted to Patients with No History of Insulin in the Previous 8 Months (PNHIP8M)
s – 2– 2: Analysis restricted to Patients with No History of Insulin in the Previous 12 Months (PNHIP12M)

s – 2– Restricted **to type II diabetes****
s – 3– Adjusted for covariates**

IPRI International Prevention Research Institute

Suggestion for the evaluation of the association between glargine use and potential confounders

To evaluate the potential impact of confounding factors, descriptive tables will be conducted to compare glargine users according to different covariates. Statistical analysis will also be conducted.

This would provide some information on the likely size of bias even in countries with data available on a limited subset and for which a fully adjusted analysis will not be possible.

For example, in the subset of individual with available data on BMI, a table in the following format would be useful

	BMI <25	BMI 25-29	BMI30+
Glargine users			
Other Long Acting insulin users			
Non long actin users (Intermediate acting + short acting)			

Such tables should be conducted for each available confounder; also produced stratified on age and sex and type I vs type II diabetes.

Then we could envisage a logistic regression investigating the predicting factors for being under glargine:
Proba(glargine/non glargine) = BMI (30+/25-29/<25 [ref]) + Age (categories) + sex + Smoking (Current/Former/Never[ref]) _____ analysis stratified on type I vs II diabetes

Same could then be conducted with a comparison to other long acting (essentially determir).
Proba(glargine/other long acting) = BMI (30+/25-29/<25 [ref]) + Age (categories) + sex + Smoking (Current/Former/Never[ref]) _____ analysis stratified on type I vs II diabetes

Appendix1: Dates – definition

Terminology and source of dates

Patient Prescription Registry. This has records and dates of all insulin and metformin prescriptions.

Cancer Registry. This is assumed to have complete cancer registrations up to a certain date – Date Cancer Registry closed.

Date of cancer incidence

Mortality Registry. This is assumed to have complete death registrations up to a certain date – Date Mortality Registry closed.

Date of Death

Diabetes registry: In addition, some centres may have a diabetes registry of patients diagnosed with diabetes and from this the *date of diagnosis* of diabetes and type of diabetes will be available.

Study period: The study will be conducted between the first recorded date of glargine use in the country, until the last date available from cancer registry data.

Centre	Reason	Start Date	End Date
Denmark	Glargine first used	1 May 2004	31 Dec 2009
Finland	Glargine first used	1 July 2003	31 Dec 2009
Norway	Prescription Database Start Glargine first used on	1 January 2004	31 Dec 2008
Scotland	Glargine first used	23 Aug 2002	31 Dec 2007
Sweden	Prescription Database Start Glargine first used on	1 July 2005	31 Dec 2009

End Date

For patients with an event (cancer) their last time on study is the date of cancer.

For patients who died without/with an event (cancer) their last time on study is the date of death or date the cancer registry closed (whichever is the earliest).

For patients with no event (cancer) and no entry in the Mortality Registry their last time on study is the date the cancer registry closed.

Start Date

The beginning of the study period will correspond to the first record of Glargine prescription in the country.

Glargine was first licensed in 2002 and there is merit in beginning the study in each centre at some time after this point as then the exposures to the different types of insulin will be relatively balanced over time. If a country has data prior to 2002 then this could be used to increase precision of the estimated effect of non glargine insulin by using a longer follow up time but would not have much impact on the estimated effect of Glargine use and the comparison of Glargine use with non Glargine use. Furthermore a bias may be introduced if there is a change to the detection of cancers – for example by screening effects which change over time.

For patients already in the Patient Prescription Registry at the beginning of the study period their start date will be the beginning of the study date.

For patients who are first recorded in the Patient Prescription Registry after the beginning of the study period their start date will be their date of first prescription.

Appendix 2: ICD codes

Codification of cancer cases in cancer registries for Glagine study - based on ICD codes

Site	Code			
	ICD7	ICD8	ICD9	ICD10
All cancers (but non-melanoma skin cancers)	140-205 but 191	140-209 but 173	140-208 but 173	C00-C96 but C44
Breast *	170	174	174	C50
Colorectal **	153-154 **	153-154 **	153-154	C18-C21
Prostate	177	185	185	C61
Lung ***	162-163 ***	162	162	C33-C34
Pancreas	157	157	157	C25

** Only to be used for women*

*** Includes intestinal tract NOS => ICD7-8 no perfectly comparable to ICD 9-10*

**** Includes trachea, bronchus and pleura => ICD7 no perfectly comparable to ICD 8-10*

Appendix 3: ATC codes

A10A Insulins and analogues

A10AB Insulins and analogues for injection, fast-acting
- A10AB01 Insulin (human)
- A10AB02 Insulin (beef)
- A10AB03 Insulin (pork)
- A10AB04 Insulin lispro
- A10AB05 Insulin aspart
- A10AB06 Insulin glulisine
- A10AB30 Combinations

A10AC Insulins and analogues for injection, intermediate-acting
- A10AC01 Insulin (human)
- A10AC02 Insulin (beef)
- A10AC03 Insulin (pork)
- A10AC04 Insulin lispro
- A10AC30 Combinations

A10AD Insulins and analogues for injection, intermediate-acting combined with fast-acting
- A10AD01 Insulin (human)
- A10AD02 Insulin (beef)
- A10AD03 Insulin (pork)
- A10AD04 Insulin lispro
- A10AD05 Insulin aspart
- A10AD30 Combinations

A10AE Insulins and analogues for injection, long-acting
- A10AE01 Insulin (human)
- A10AE02 Insulin (beef)
- A10AE03 Insulin (pork)
- A10AE04 Insulin glargine
- A10AE05 Insulin detemir
- A10AE30 Combinations
- A10AF Insulins and analogues for inhalation
- A10AF01 Insulin (human)

To summarize:

We will use the following ATC codes:

Glargine = A10AE04.

Long acting non glargine = A10A01, A10A02, A10A03, A10A05, A10A30.

Non long acting insulin = A10AB (all subcategories), A10AC (all subcategories), A10AD (all subcategories).

Metformin = A10BA02

Appendix IV

Scientific Steering Committee

An independent **Scientific Steering Committee** will be appointed to oversee the study and advise on treatment, methodological and biostatistical issues. This group will meet regularly throughout the duration of the study and incorporate a **Biostatistical Advisory Group**, to advise on all aspects of the design and data analysis.

The international **Scientific Steering Committee** will comprise:

Professor Geremia Bolli
University of Perugia
Perugia, Italy

Professor Stuart Pocock
University College London
London, United Kingdom

Professor Ian Ford
Robertson centre for Biostatistics
University of Glasgow,
Glasgow, United Kingdom

Professor Theodore Holford
Department of Biostatistics
Yale University School of Public Health
New Haven, United States of America

Professor Hertzel Gerstein
McMaster University,
Hamilton, Canada

Professor Derek LeRoith
Mount Sinai Hospital
New York, United States of America.

Appendix V

ATC List of Anti-Diabetic Drugs

A10 - Drugs used in diabetes*

A10A - Insulins and analogues

A10AB - Insulins and analogues for injection, fast-acting

A10AB01 - Insulin (human)

A10AB02 - Insulin (beef)

A10AB03 - Insulin (pork)

A10AB04 - Insulin lispro

A10AB05 - Insulin aspart

A10AB06 - Insulin glulisine

A10AB30 - Combinations

A10AC - Insulins and analogues for injection, intermediate-acting

A10AC01 - Insulin (human)

A10AC02 - Insulin (beef)

A10AC03 - Insulin (pork)

A10AC04 - Insulin lispro

A10AC30 - Combinations

A10AD - Insulins and analogues for injection, intermediate-acting combined with fast-acting

A10AD01 - Insulin (human)

A10AD02 - Insulin (beef)

A10AD03 - Insulin (pork)

A10AD04 - Insulin lispro

A10AD05 - Insulin aspart

A10AD30 - Combinations

A10AE - Insulins and analogues for injection, long-acting

A10AE01 - Insulin (human)

A10AE02 - Insulin (beef)

A10AE03 - Insulin (pork)

A10AE04 - Insulin glargine

A10AE05 - Insulin detemir

A10AE30 - Combinations

A10AF - Insulins and analogues, for inhalation

A10AF01 - Insulin (human)

A10B - Blood glucose lowering drugs, excluding insulins

A10BA - Biguanides

A10BA02 - Metformin

A10BB - Sulfonamides, urea derivatives

A10BB12 - Glimepiride

A10BD - Combinations of oral blood glucose lowering drugs

A10BD03 - Metformin and rosiglitazone

A10BD04 - Glimepiride and rosiglitazone

A10BD05 - Metformin and pioglitazone

A10BD06 - Glimepiride and pioglitazone

A10BD07 - Metformin and sitagliptin

A10BD08 - Metformin and vildagliptin

A10BD11 - Metformin and linagliptin

A10BG - Thiazolidinediones

A10BG02 - Rosiglitazone

A10BG03 - Pioglitazone

A10BH - Dipeptidyl peptidase 4 (dpp-4) inhibitors

A10BH01 - Sitagliptin

A10BH02 - Vildagliptin

A10BH03 - Saxagliptin

A10BH05 - Linagliptin

A10BX - Other oral blood glucose lowering drugs

A10BX02 - Repaglinide

A10BX03 - Nateglinide

A10BX04 - Exenatide

A10BX06 - Benfluorex

A10BX07 - Liraglutide

*Source: http://ec.europa.eu/health/documents/community-register/html/atc.htm