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- Information will be excluded in order to protect the privacy of patients and all named persons associated with the study*
- Patient data listings will be completely removed* to protect patient privacy. Anonymized data from each patient may be made available subject to an approved research proposal. For further information please see the Patient Level Data section of the **GSK Clinical Study Register**.*
- Aggregate data will be included; with any direct reference to individual patients excluded*

**Complete removal of patient data listings may mean that page numbers are no longer consecutively numbered*

PASS information

Title	Risk of solid organ transplant rejection following vaccination with <i>Pandemrix</i> in the United Kingdom
Version identifier of the final study report	Annex Study Report – Final
Date of last version of the final study report	17 March 2014
EU PAS Register Number	Study not registered
Active substance	Purified antigen fractions of inactivated split virion Influenza A/California/7/2009 (H1N1)v-like strain
Medicinal product	Pandemrix™, Pandemic Influenza vaccine (H1N1)v (split virion, inactivated, adjuvanted) A/California/7/2009 (H1N1)v like strain (X-179A)
Product reference	EU/1/08/452/001
Procedure number	EMEA/H/C/0832/
Marketing Authorisation Holder(s)	GlaxoSmithKline Biologicals
Joint PASS	No
Research question and objectives	<p>To assess whether vaccination with <i>Pandemrix</i> (primary and secondary objectives) or with trivalent seasonal influenza vaccines (TIV; tertiary objective) is associated with an increased risk of solid organ transplant rejection of the liver, kidney, lung, heart, or pancreas.</p> <p>The results for the primary and secondary objectives were presented in the main study report.</p> <p>The results for the tertiary objective are provided in this annex report.</p>
Country(-ies) of study	United Kingdom

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1. ABSTRACT

Title

Risk of solid organ transplant rejection following vaccination with Pandemrix in the United Kingdom.

[This report describes the tertiary objectives of the study which investigated trivalent seasonal influenza vaccines (TIV).]

Keywords

Seasonal influenza, TIV, safety, transplantation, rejection, CPRD, HES, SCCS

Rationale and background

Seasonal influenza vaccination is an important public health measure recommended for transplant recipients, due to the elevated risk of complications associated with influenza infection. Safety data on the association between solid organ transplant rejection and vaccination with a trivalent influenza vaccine (TIV) are limited.

Research question and objectives

To assess the risk of solid organ (liver, kidney, lung, heart, pancreas) transplant rejection after vaccination with a TIV.

Study design

Retrospective self-controlled case-series (SCCS) analysis. Analyses were conducted using the SCCS method for perturbed post-event exposure.

Setting

The UK Clinical Practice Research Datalink General Practitioner OnLine database (CPRD GOLD) and its linked component of the Hospital Episodes Statistics (HES).

Subjects and study size, including dropouts

The overall study population included 375 solid organ transplant recipients, of which 156 subjects were exposed to a TIV. A total of 132, 136, and 168 subjects had at least one rejection in seasons 2006/07, 2007/08 and 2008/09, respectively; an overall 45-51% received a TIV. The pooled analysis of the three seasons included 218 subjects, of which 156 (72%) were TIV exposed cases.

Variables and data sources

Data sources consisted of the CPRD/GOLD, HES, and a standardised GP questionnaire. Algorithms were developed to identify rejection events and covariates of interest (time since transplantation, previous rejections, bacterial/viral infections, malignancies). The

endpoint was the occurrence of at least one rejection during any of the three influenza seasons 2006/07, 2007/08 and 2008/09. The risk periods were 30 and 60 days after TIV vaccination.

Results

Relative incidence (RI) of rejection of any of the five organs in the analysis for the pooled influenza seasons, adjusted for time since transplantation, was 1.01 (95%CI: 0.58, 1.76) and 0.88 (95%CI: 0.56, 1.38), 30 and 60 days after vaccination, respectively. Results were mainly driven by kidney, the most commonly transplanted organ, with RIs of 0.91 (95%CI: 0.44, 1.87) and 0.59 (95%CI: 0.32, 1.08), in the 30- and 60-day risk periods, respectively. Risk estimates remained in a range of 0.6 to 1.3 across seasons and various sensitivity analyses, with upper 95% CI limits below 3.0.

Discussion

The study used data from HES, an appropriate source of information for this outcome typically managed in hospital settings. SOT rejection is a complex outcome, affected by several potential risk factors. The SCCS design implicitly controls for fixed confounders, however, except for time since transplantation, risk factors such as infections could not be fully accounted for. The consistent range of risk estimates all in the vicinity of 1.0 (0.6-1.3), with upper 95% confidence limits below 3.0, suggest no evidence of an increased risk of SOT rejection following TIV administration in the UK. These results suggest no increased risk of rejection following TIV administration in solid organ transplant recipients; they inform the benefit-risk assessment for seasonal influenza vaccination and provide additional support to existing recommendations to provide annual seasonal vaccination to this risk group.

Marketing Authorisation Holder(s)

GlaxoSmithKline Biologicals, Rue de l'Institut 89, 1330 Rixensart, Belgium.

Names and affiliations of principal investigators

Not applicable.

2. LIST OF ABBREVIATIONS

CI	Confidence Interval
CPRD GOLD	Clinical Practice Research Datalink General Practitioner OnLine (database)
EMA	European Medicines Agency
EU	European Union
GP	General Practitioner
GSK	GlaxoSmithKline
HES	Hospital Episodes Statistics
ISAC	Independent Scientific Advisory Committee
LL	Lower limit
nvac	Not vaccinated
RI	Relative Incidence
SCCS	Self-Controlled Case-Series
SD	Standard Deviation
SOT	Solid organ transplant
TIV	Trivalent Inactivated Influenza vaccine
UK	United Kingdom
UL	Upper Limit
vac	Vaccinated
VCSP	Vaccine Clinical Safety and Pharmacovigilance

3. MILESTONES

Milestone	Planned date	Actual date	Comments
Approval of protocol by ISAC	Not applicable	13-SEP-2012	Approval of the protocol
Registration in the EU PAS register	Not applicable	Not applicable	Protocol developed before the PASS regulation came into force
Start of data collection	31-AUG-2012	27-SEP-2012	General Practitioner (GP) questionnaires were sent out via CPRD on 31-OCT-2012
Submission of protocol amendment to ISAC	05-JUL-2013	05-JUL-2013	Reasons for protocol amendment explained in Section 9 of the Main study report.
Approval of amendment	Not applicable	15-JUL-2013	None
Database freeze	13-SEP-2013	07-AUG-2013	End of data collection
Statistical analysis complete – Primary and Secondary study objectives	31-OCT-2013	06-DEC-2013	None
Final report of Main study results – Primary and Secondary study objectives	13-DEC-2013	12-DEC-2013	None
Statistical analysis complete – Tertiary objectives	30-JAN-2014	10-MAR-2014	None
Annex report to Main report – Tertiary study objectives	End of MAR-2014	17-MAR-2014	None

4. RATIONALE AND BACKGROUND

During the 2009 H1N1 influenza pandemic, mass vaccination with GSK's inactivated adjuvanted (AS03) A/H1N1 pandemic influenza vaccines *Pandemrix*® and *Arepanrix*™ was initiated in 47 countries worldwide, with large vaccine coverage and/or single use in several countries (e.g., Finland, Sweden, Canada). According to data from the UK Department of Health based on the ImmForm national survey, *Pandemrix* was used widely and in the majority of target groups in the UK, with less than 0.1% of individuals having received vaccines from other manufacturers (mainly Celvapan®) [Department of Health, 2010].

After the pandemic, cases of solid organ transplant (SOT) rejection following vaccination with *Pandemrix* and *Arepanrix* were spontaneously reported in the EU and Canada, respectively. Published reports also described cases temporally associated with vaccination, in kidney and heart transplant recipients immunised with a GSK A/H1N1 pandemic influenza vaccine [Schaffer, 2011] and in one pancreas transplant recipient immunised with a non-GSK adjuvanted vaccine [Vistoli, 2011]. Other studies on the safety of pandemic vaccines (adjuvanted and non-adjuvanted; from GSK and from other manufacturers) in patients with lung, kidney, liver and heart transplants showed no events of acute rejection [Schuermans, 2011; Duesberg, 2010; Hauser, 2011; Fairhead, 2011a; Fairhead, 2011b; Goldschmidt, 2011; Altamirano-Diaz, 2011; Torii, 2011; Crespo, 2011; Esposito, 2011; Vazquez-Alvarez, 2010]. All studies were descriptive and based on relatively small sample sizes. The association between vaccination and clinical rejection has been difficult to assess due to the multiple risk factors for rejection, including

infections, co-morbidities, and lack of compliance with immunosuppressive treatments. A cohort study of 216 SOT recipients and 138 controls concluded that *Pandemrix* was safe in SOT recipients; the prospective nature of the study accounted for some of the difficulties of retrospectively collecting transplantation/rejection data as was done in the majority of studies conducted after the pandemic [Siegrist, 2012].

It has been postulated that seasonal trivalent inactivated influenza vaccine (TIV) administration might increase the risk of SOT rejection. Although generally administered from 3-6 months post-transplantation [Kumar, 2011], once baseline immune-suppression levels are attained, little data is available on the appropriate timing for influenza immunisation following transplantation. On the other hand, influenza viruses cause a spectrum of illness in transplant recipients with a high rate of lower respiratory disease and have been associated with higher morbidity and mortality, graft rejection and prolonged viral shedding [Kumar, 2010; Kunisaki, 2009].

The EPI-FLU-H1N1-012 study (eTrack: 116602) that was a European Medicine Agency (EMA) PASS commitment study intended to assess whether vaccination with *Pandemrix* (primary and secondary objectives) was associated with an increased risk of solid organ transplant rejection of the liver, kidney, lung, heart, or pancreas. A tertiary objective was added to assess the impact of seasonal TIVs, which are recommended in transplant recipients and for which safety data is limited in this population. The study design was a retrospective self-controlled case-series (SCCS) analysis using the UK Clinical Practice Research Datalink GP Online Database (CPRD GOLD) and Hospital Episodes Statistics (HES). The Main study report describing the results of the primary and secondary objectives which related to *Pandemrix* vaccination, was submitted to the EMA in December 2013 [see Section 5; EPI-FLU H1N1-012 Main study report, 2013]. The purpose of this annex report is to describe the results of the first and second tertiary study objectives, which were not part of the EMA PASS commitment, but were designed to ascertain if there was evidence of increased SOT rejection following TIV vaccination (Section 5).

Please refer to the Main study report for full details of: rationale and background for the study, the protocol amendment, and research methods including statistical data analysis. For clarity, the research objectives have been provided in this annex report together with selected sections of text from the main report Methods section, which were most important for the analysis of the seasonal influenza data.

5. RESEARCH QUESTION AND OBJECTIVES

The study intended to assess whether vaccination with *Pandemrix* (primary and secondary objectives) or with TIV (tertiary objective) was associated with an increased risk of solid organ transplant rejection of the liver, kidney, lung, heart, or pancreas.

5.1. Primary objective

- To assess the risk of SOT rejection (liver, kidney, lung, heart, pancreas) within one month after vaccination with *Pandemrix*.

5.2. Secondary objective

- To assess the risk of SOT rejection (liver, kidney, lung, heart, pancreas) within two months after vaccination with *Pandemrix*.

5.3. Tertiary objectives

- To assess the risk of SOT rejection (liver, kidney, lung, heart, pancreas) within one month after seasonal influenza vaccination, during influenza seasons 2006/2007, 2007/2008 and 2008/2009.
- To assess the risk of SOT rejection (liver, kidney, lung, heart, pancreas) within two months after seasonal influenza vaccination, during influenza seasons 2006/2007, 2007/2008 and 2008/2009.

6. METHODS

6.1. Study design

This study was a post-authorisation safety study (PASS), addressing an EMA commitment.

This was a retrospective, observational study using the UK Clinical Practice Research Datalink General Practitioner OnLine database (CPRD GOLD) and the Hospital Episode Statistics (HES) database in the UK.

The self-controlled case-series (SCCS) method was used to assess the association between rejection of solid organ transplant and vaccination.

The SCCS relies on the observation of individuals with the outcome of interest (cases) for both a risk period and control period(s). Since the SCCS analysis relies on case data only, these studies can be performed without the challenges associated with comparison group selection and confounding [Farrington, 1995]. An important feature of this design is that it controls implicitly [Whitaker, 2006] for potential confounders which do not vary with time (e.g. socio-economic status, gender). Additionally, fewer cases are usually required, as compared to a case-control design.

In the present study, the SCCS design required data on transplant rejection events and on cases' history of pandemic and trivalent influenza vaccine (TIV) administration. The risk estimates were derived from a Poisson model by conditioning on the occurrence of rejection.

The study period for the tertiary objective ranged from 01 September 2006 to 31 August 2009 (including the three consecutive influenza seasons 2006/07, 2007/08, and 2008/09).

6.2. Setting

The study was conducted in the UK Clinical Practice Research Datalink General Practitioner OnLine database (CPRD GOLD) and its linked component of the Hospital Episodes Statistics (HES) database.

6.3. Subjects

Subjects enrolled in the study were solid organ transplant recipients with at least one episode of rejection of solid organ transplant between 01 September 2006 and 31 October 2010. See Main report and Protocol Amendment Appendix A for details of identification of cases in HES and CPRD GOLD.

Inclusion criteria

- Subject defined as acceptable in the CPRD GOLD;
- Subject with at least one solid organ transplant rejection reported in the CPRD GOLD and/or HES during the study periods (01 September 2006 to 31 August 2009).

Exclusion criteria

- Subject from HES ("hesid") matched to more than one subject in the CPRD GOLD ("patid").

6.4. Variables

The endpoint for the tertiary objective was the occurrence of at least one SOT rejection in any of the three influenza seasons 2006/07, 2007/08, and 2008/09, within the overall study period from 01 September 2006 to 31 August 2009.

Similarly to the Main report, two data sources were used: CPRD GOLD/HES (primary data source) and CPRD GOLD/HES and the GP questionnaire (secondary data source).

The study design assumed that the large majority of transplanted patients are followed in hospital settings. In order to confirm data from the CPRD GOLD and obtain additional quantitative and qualitative information, a standard questionnaire was sent to the GPs via the CPRD Research Group. Based on the information received from the questionnaires, transplant rejection events appeared to be under-reported and under-documented, with GPs reporting less than 40% of the number of rejections initially identified in CPRD-HES. Therefore, HES was used as the sole data source for the primary analyses for all study objectives and the subpopulation of subjects identified through the GP feedbacks was used to define the subset for the secondary analyses, taking into account linked data from CPRD-HES and complementary information from the GP questionnaires (see Section 6.5.2 of this annex report).

See the Main report for details on the data sources: CPRD GOLD, Hospital Episode Statistics (HES), and the GP questionnaire. Also refer to the Main study report (Section 10.7) for the study size calculation.

6.5. Data transformation

6.5.1. Subject follow-up

For each subject, the follow-up was defined separately for each season. The beginning of the follow-up was 01 September of each season for the influenza seasons 2006/2007, 2007/2008, and 2008/2009. The end of follow-up corresponded to whichever of the following dates/events came first:

- 31 August 2007, 2008, or 2009;
- A new transplantation event as defined in the protocol (see Appendix A of the protocol);
- Subject death;
- Last collection date of the GP practice the subject was registered with;
- Transfer out date of the subject: the subject was included up to the “transfer out date”, in order to ensure continuous follow-up during a given season.
- Last date of collection of HES data in the CPRD-GOLD release used for the analyses.

6.5.2. Subsets of the study population

The tertiary objective was defined to assess the risk of SOT rejection following TIV administration, using two analytical subsets:

Seasonal influenza study period (01 September 2006 – 31 August 2009):

Subset 2a. The primary seasonal influenza subset was to include subjects:

- with a follow-up during at least one of the influenza seasons (2006/2007, 2007/2008 or 2008/2009) in the CPRD GOLD and in HES. The subject follow-up must have included:
 - 01 September and the preceding 180 days period (from 05 March) in the CPRD GOLD and in HES,
- AND
- at least one rejection reported in HES in at least one of the 3 influenza seasons.

Subset 2b. The secondary seasonal influenza subset was to include subjects:

- with a completed GP questionnaire returned and containing all information needed for the analyses,

AND

- with a follow-up during at least one of the influenza seasons (2006/2007, 2007/2008 or 2008/2009) in the CPRD GOLD and in HES. The subject follow-up must have included:
 - 01 September and the preceding 180 days period (from 05 March) in the CPRD GOLD and in HES,

AND

- at least one rejection reported in HES, or in the CPRD GOLD or in the GP questionnaire, in at least one of the 3 influenza seasons.

This annex report describes the results from the primary seasonal influenza subset (Subset 2a) which is based on data from CPRD/HES, and the secondary seasonal influenza subset (Subset 2b) which is based on data from CPRD/HES and from the GP questionnaire.

See the main report for details on: Covariates; hypothesis; and descriptive statistics.

- Covariates included time since transplantation, previous rejections, bacterial/viral infections, malignancies, and chemotherapy.
- Null hypothesis (H0): the incidence rate of solid organ transplant rejection in exposed subjects is the same during the risk period and the control period.
- Alternative hypothesis (H1): the incidence rate of solid organ transplant rejection in exposed subjects is different during the risk period and during the control period.

6.6. Statistical Analyses – Tertiary objectives

Assuming that rejection events are not independent across the three seasons, data from influenza seasons 2006/2007, 2007/2008 and 2008/2009 were analysed separately. However, additional analyses were also carried out combining all seasons (pooled seasonal data).

For each season, only subjects with follow-up starting at least 180 days before 01 September were considered for the analyses. The risk periods spanned from day 0 to day 30, or from day 0 to day 60, after each TIV administration; the control period corresponded to any period of the follow-up, excluding the risk period.

The primary analysis was based on Subset 2a (primary seasonal influenza subset). Only rejection events reported in HES were taken into account. The approach to identify rejection(s) was detailed in the protocol (see protocol: Appendix A). Only the first rejection after 01 September was considered. If several rejections occurred during the follow-up, the subject was censored at the second rejection.

In the analysis for the pooled influenza seasons, each subject contributed to only one season, the first one for which there was informative data (i.e., exposure to a TIV or effect of time since transplantation). With this approach, only one season was considered per subject throughout the analyses in order to avoid subjects being over-represented across several seasons (some subjects with data for one season and others with data for several seasons). This approach also ensured consistency in the analyses because the same season was considered for each subject throughout the analyses for the pooled seasons (main analyses, further adjustments, sensitivity analyses). Indeed, if for each analysis the first season with any covariate was to be considered for each subject, a different season could have been considered according to the covariates used for the adjustments. It was assumed that the baseline was constant across the different seasons and that the effect of TIV was homogeneous across the three seasons.

Primary analyses for the tertiary objectives:

- Number of cases and person-time in the risk period and control periods;
- RI estimates associated with TIV administration adjusted for time since transplantation;
- RI estimates associated with TIV administration adjusted for time since transplantation and for each infection/chronic condition and malignancy/cancer in separate models;
- RI estimates associated with TIV administration adjusted for time since transplantation and for all infections/ chronic conditions and malignancy/cancer.

Secondary analyses for the tertiary objectives:

All the above analyses for separate seasons were repeated for Subset 2b (secondary seasonal influenza subset). Data from the CPRD GOLD/HES and from the GP questionnaires were considered. In addition to the adjustment for time since transplantation and for each infection/ chronic condition and malignancy/cancer, RI estimates were adjusted for chemotherapy, which was derived from the questionnaire. The approach to identify the rejections was described in the protocol (see protocol: Appendix A).

Exploratory analyses for the tertiary objectives:

The potential modifying effect of a previous rejection was to be tested for each season, and pooled seasons, by introducing an interaction term between the fixed effect of a previous rejection and the time-varying effect of TIV administration in the model. The fixed effect was a binary variable: at least one rejection during the 180-day period before the beginning of the influenza season, or no rejection during this period. The interaction was tested in the model with adjustment for time since transplantation.

Stratified analyses (number of cases allowing):

- Subjects with no rejection episode before the beginning of the influenza season, or with rejection episode(s) that occurred >180 days before the beginning of the influenza season. RI estimate associated with vaccination adjusted for time since transplantation.
- Subjects with at least one rejection episode during the 180-day period prior to the influenza season. RI estimate associated with vaccination adjusted for time since transplantation and adjusted for the risk period associated with previous rejections.

These analyses were based on Subset 2a (primary seasonal influenza subset). Only the first rejection reported in HES was considered and subjects were censored at any subsequent rejection.

Planned analyses were conducted pooling all organs. In addition, despite limited statistical power associated with the analyses based on 10 exposed cases, additional analyses by organ were to be conducted only if a minimum of 10 rejections were observed for a given organ.

Refer to the Main report for details of: Statistical models; missing values.

6.6.1. Sensitivity analyses

Sensitivity analyses for the tertiary objectives:

- RI estimates associated with the TIV administration exposure adjusted for time since transplantation using the standard SCCS method [Farrington, 1995]. All rejection events (first and subsequent) were considered.

7. RESULTS

Two tertiary objectives were defined to assess the risk of SOT rejection following TIV administration, using two analytical subsets (Subset 2a and Subset 2b, see Section 6.5.2). Subset 2a is based on data from CPRD/HES, whereas subset 2b is based on data from CPRD/HES and from the GP questionnaire.

7.1. Participants

The total number of subjects with a SOT rejection identifier in the overall study period (2006-2010), including also the pandemic study period, in either CPRD GOLD and/or HES was 587 subjects and the majority of these subjects (545 subjects; 92.8%) had a HES link (Table 1).

With regards to the TIV component of the analysis, the primary seasonal influenza subset (Subset 2a; see Section 6.5.2) contained 375 eligible subjects (63.9% of all 587 subjects identified; Table 1). The secondary seasonal influenza subset (Subset 2b; see Section 6.5.2), which was further restricted to subjects with returned GP questionnaires that had valid/usable information, contained 140 subjects (23.9%).

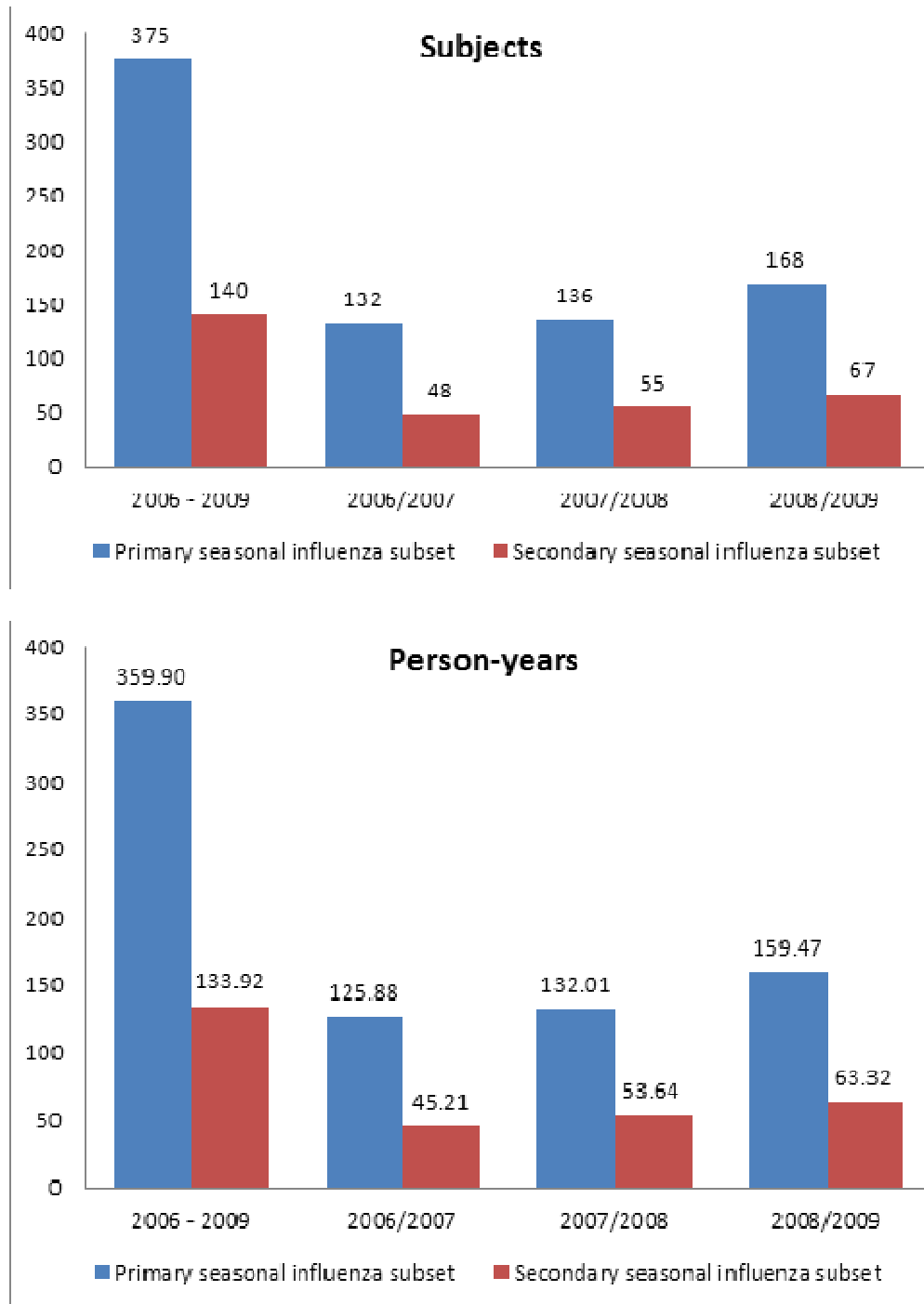
Details of the response rate for the GP questionnaires are provided below:

- From the 587 identified cases in CPRD GOLD or HES for the overall study period (2006-2010), 502 (85.5%) questionnaires were sent to the GPs; the remaining 85 subjects belonged to practices that were no longer active in the CPRD.
- From the 502 questionnaires sent, 359 (71.5%) were returned by the GPs.
- From the 359 returned questionnaires, 226 subjects (63%) were eligible for inclusion, i.e. subjects for whom the GPs addressed the question regarding occurrence of rejection for any of the seasons between 2006 and 2010 (see Protocol Amendment Appendix B: GP questionnaire). A total of 172 subjects (47.9%) were eligible for the pandemic influenza part of the study (2009-2010) and 203 subjects (56.5%) were eligible for the seasonal influenza part (2006-2009). Of these 203, 185 had a HES link (Table 1).
- For 140 subjects, there was a follow-up in CPRD GOLD and/or HES for at least one of the seasons 2006-2007, 2007-2008 or 2008-2009 and at least one SOT rejection in either the CPRD GOLD, HES or the GP questionnaire in one of these seasons (between 01-September and 31-August of next year) (subset 1b).

7.2. Descriptive data

Person-years of follow-up in the study are described in Table 2 and Table 3, by season and by subset; the majority of subjects were followed for the whole duration of the seasons, and this applied to all four subsets. The majority of subjects of subset 2a (363/375 subjects; Table 3) had record(s) of transplantation or rejection for one single organ. This observation is similar for other subsets. Figure 1 presents the distribution of subjects and person time in each influenza study person (season) for each subset.

Figure 1 Distribution of subjects and person-time into each influenza study period for each subset (Total cohort)



7.2.1. Vaccine exposure

In season 2006-07, 45.45% (60/132) of subjects were vaccinated with TIV (Table 4). One subject received two doses of TIV in this season. Considering that this patient could present a specific profile, he was excluded from the analyses of this season. In season 2007-08, 49.26% (67/136) of subjects were vaccinated with TIV. In season 2008-09,

50.6% (85/168) of subjects were vaccinated with TIV (Table 4 and Figure 2). Figure 3, Figure 4, Figure 5 show the distribution of SOT rejections and TIV vaccinations per 15-day periods for each season and Figure 6 displays the data for the three seasons pooled. In the CPRD GOLD, seasonal influenza vaccination appears to be mostly administered between September and December, as per recommendations.

Figure 2 Vaccine exposure

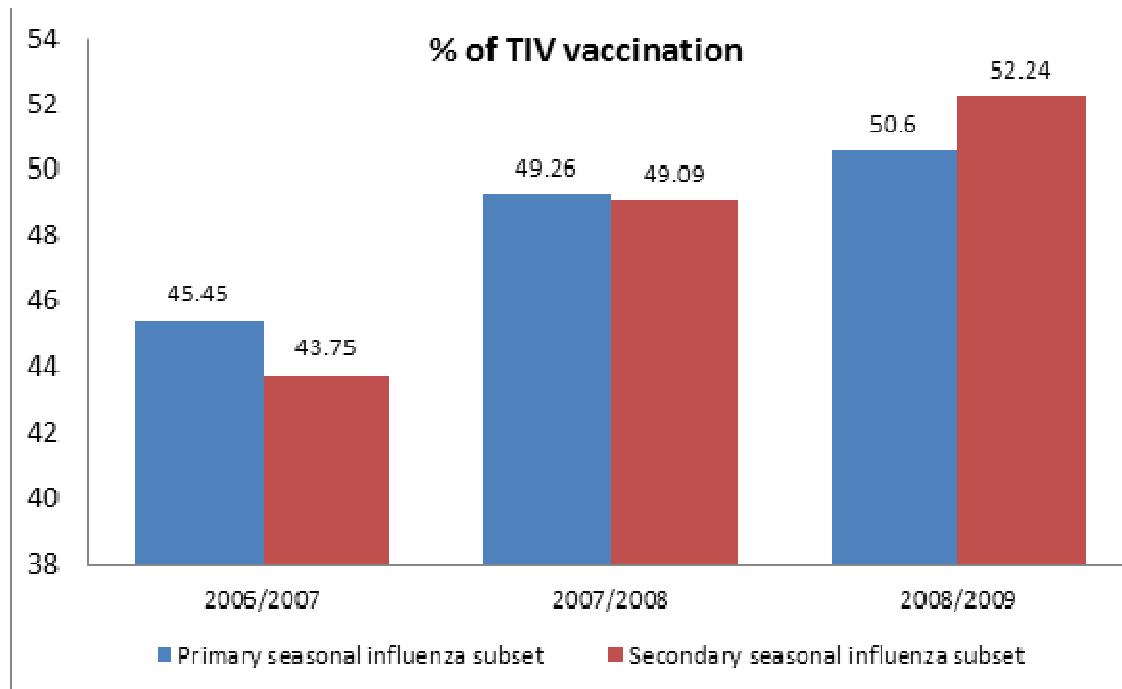


Figure 3 Distribution of SOT rejections and TIV vaccinations per 15-day periods during the period from 01 September 2006 to 31 August 2007 (Subset 1a)

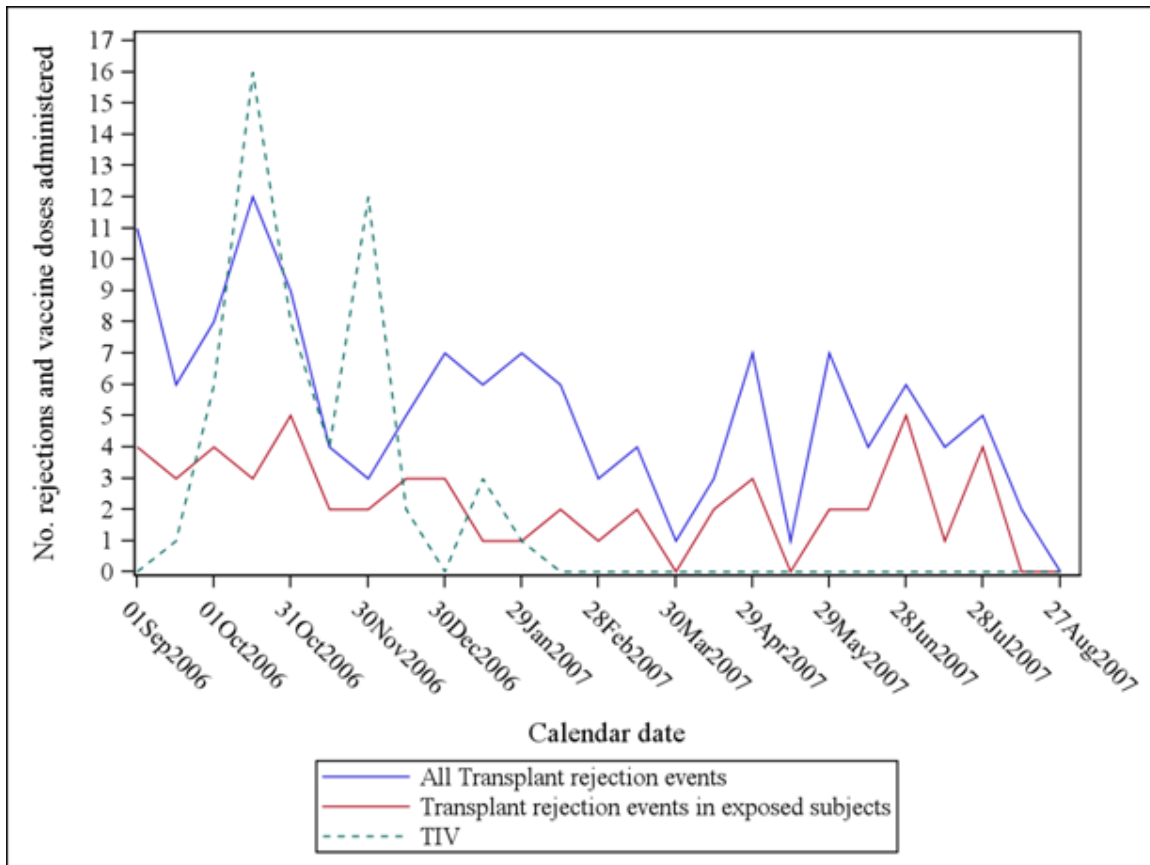


Figure 4 **Distribution of SOT rejections and TIV vaccinations per 15-day periods during the period from 01 September 2007 to 31 August 2008 (Subset 1a)**

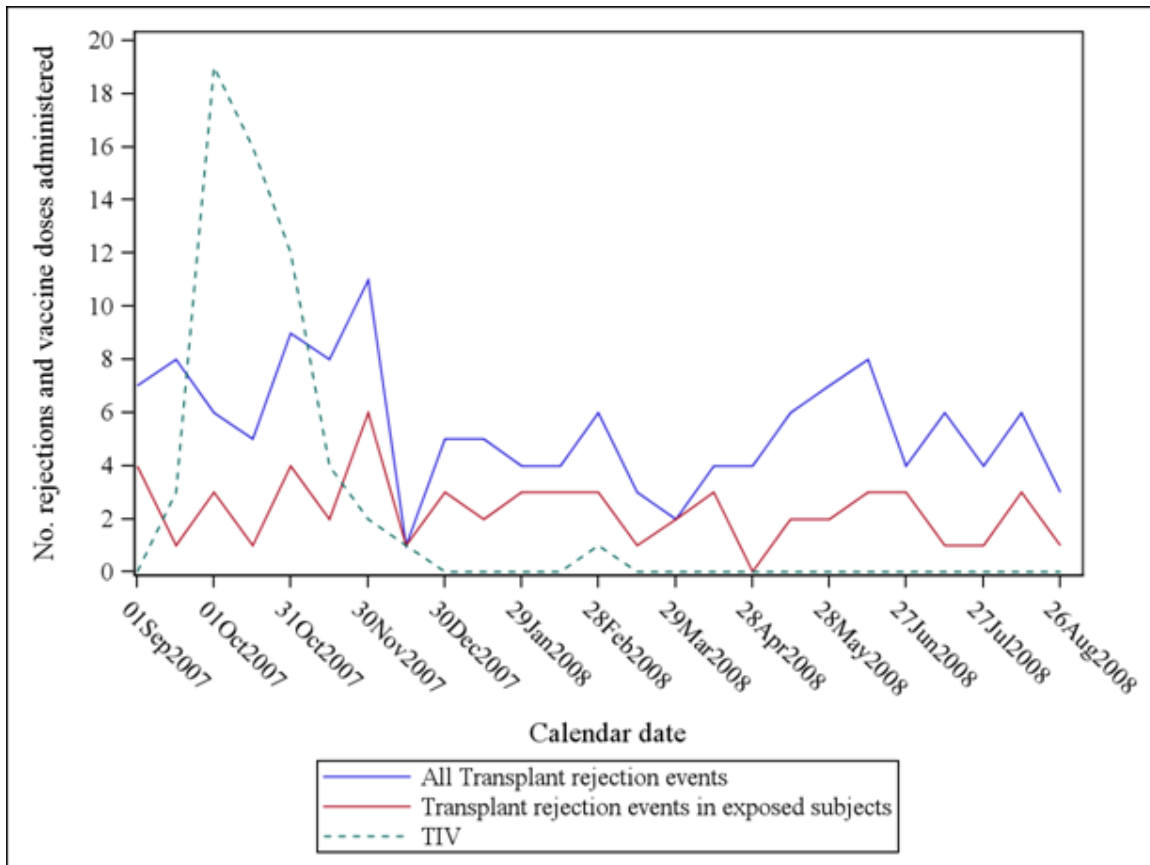


Figure 5 Distribution of SOT rejections and TIV vaccinations per 15-day periods during the period from 01 September 2008 to 31 August 2009 (Subset 1a)

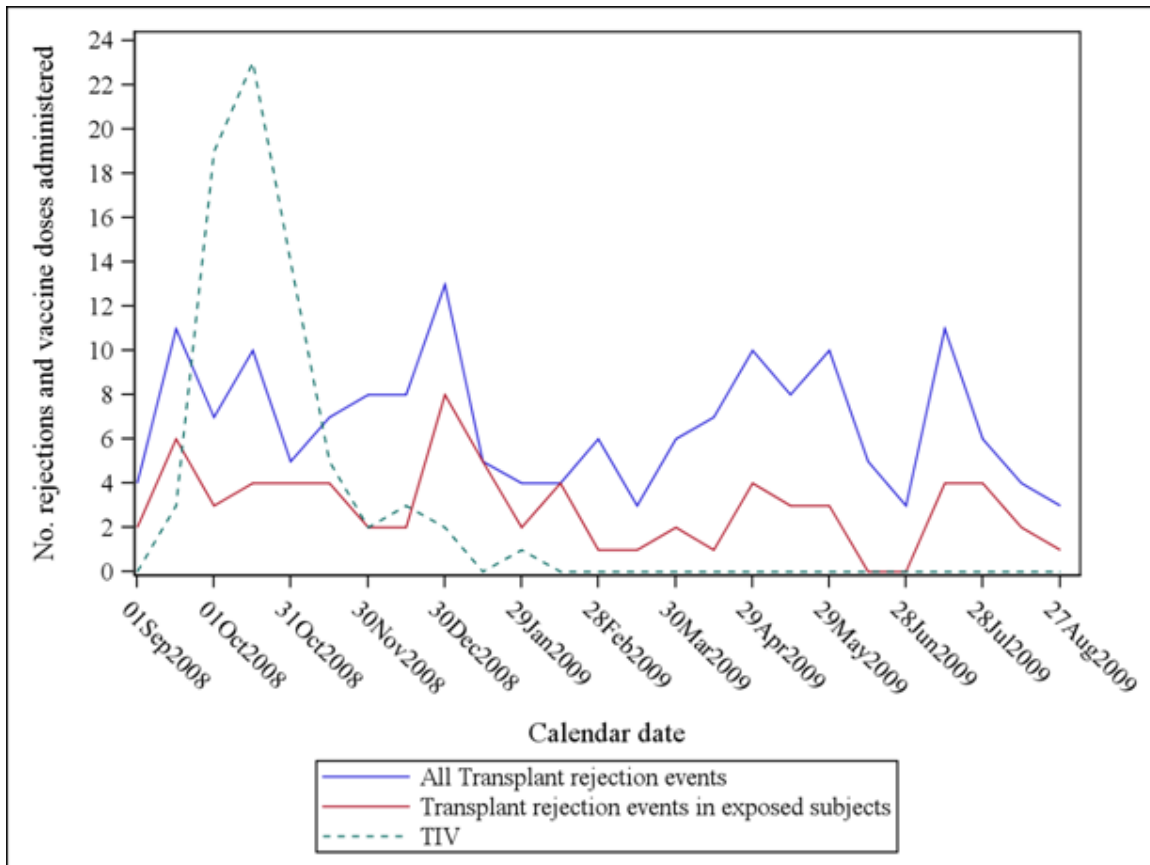
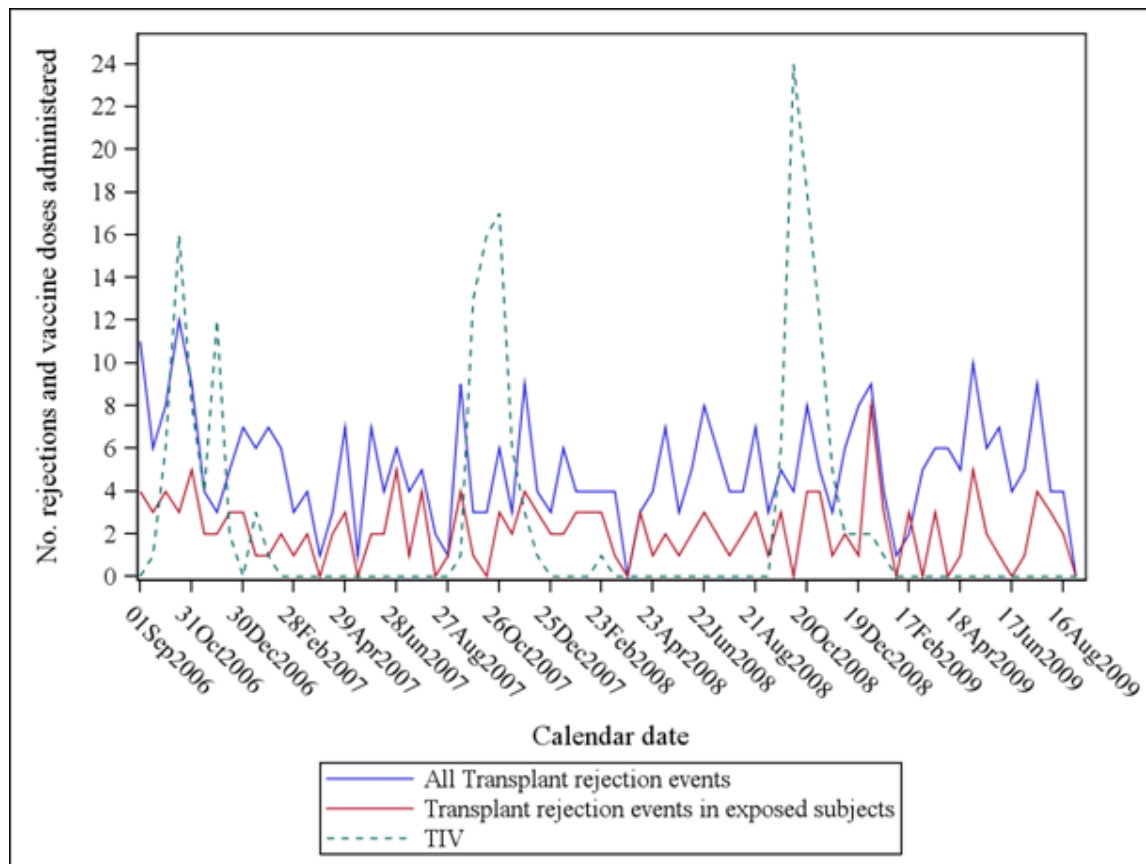


Figure 6 Distribution of SOT rejections and TIV vaccinations per 15-day periods during the period from 01 September 2006 to 31 August 2009 (Subset 1a)



7.2.2. Demographic characteristics

7.2.2.1. Influenza Season 2006-2007

Baseline characteristics of the subjects from the primary seasonal influenza subset eligible for the analyses of season 2006-2007 are given in Table 6 and Table 7.

Among 132 subjects, 130 subjects had only one record of transplantation or rejection for a single organ (Table 7).

Figure 3 shows the distribution of SOT rejection events throughout the 2006-07 influenza season.

Subjects had a mean age of 48.1 years at 01 September 2006, 37.9% were female and 6.8% were noted to have died from any cause during the analysis period (Table 6).

The majority of transplantations (127/132 subjects; 96.2%) were performed prior to the 180 day period before the start of the study period (i.e. before 05 March 2006) or during the 2006-2007 study period (after 01 September 2006; Table 6), while a small proportion

of the transplantations (3.8%; 5/132) occurred within the 180 days prior to the start of the study period (between 05 March and 01 September 2006). For 98 subjects (74.2%; Table 6), there was no record of transplantation in CPRD or HES between 05 March 2006 and 31 August 2007. Among the 34 subjects with a transplantation record, kidney was the most frequently transplanted organ (22 subjects; 16.7%) followed by liver (6 subjects; 4.5%). Information was available on malignancies/cancers in 9 subjects (6.8%). Although transplant recipients are at increased risk of infectious diseases, events relating to infections were reported for only a very small number of subjects.

Most of the subjects (119 subjects; 90.2%; Table 6) were followed over the whole analysis period for season 01-SEP-2006 to 31-AUG-2007. The remaining subjects either died (9 subjects; 6.8%) or were no longer followed in the CPRD GOLD (4 subjects; 3.0%) at 31 August 2007 because e.g. the subject had left the GP practice, or the GP practice was no longer active in CPRD GOLD.

Secondary seasonal influenza subset (HES/CPRD GOLD + GP questionnaire data)

Baseline characteristics of the subjects from the secondary seasonal influenza subset eligible for the analyses of season 2006-2007 are given in Table 14 and Table 15. This secondary subset was further restricted to subjects with available data from the GP questionnaire (N=48 subjects). These subjects had a mean age of 50.9 years with 25% being female, and 5 subjects (10.4%) were noted to have died from any cause during the analysis period (Table 14).

The majority of transplantations (47/48 subjects; 97.9%) were performed prior to the 180-day period before the start of the study period (i.e. before 05 March 2006) or during the 2006-2007 study period (after 01 September 2006; Table 14), while a small proportion of the transplantations (2.1%; 1/48) occurred within the 180 days prior to the start of the study period (between 05 March and 01 September 2006). For 35 subjects (72.9%), there was no record of transplantation in CPRD or HES between 05 March 2006 and 31 August 2007. Among the 13 subjects with a transplantation record, kidney was the most frequently transplanted organ (7 subjects; 14.6%) followed by liver (3 subjects; 6.3%). Although transplant recipients are at high risk of infectious diseases, events relating to infections were reported for only a very small number of subjects.

The demographic characteristics were very similar in the population of subjects with questionnaire information available, with transplantation or rejection involving only one organ (Table 15).

7.2.2.2. Influenza Season 2007-2008

Baseline characteristics of the subjects from the primary seasonal influenza subset eligible for the analyses of season 2007-2008 are given in Table 8 and Table 9.

Among 136 subjects, 128 subjects had only one record of transplantation or rejection for a single organ (Table 9). Subjects had a mean age of 47.4 years at 01 September 2007, 39.0% were female and 8.1% were noted to have died from any cause during the analysis period (Table 8).

Figure 4 shows the distribution of SOT rejection events throughout the 2007-08 influenza season.

The majority of transplantations (126/136 subjects; 92.6%) were performed prior to the 180-day period before the start of the study period (i.e. before 05 March 2007) or during the 2007-2008 study period (after 01 September 2007; Table 8), while a small proportion of the transplantations (7.4%; 10/136) occurred within the 180 days prior to the start of the study period (between 05 March and 01 September 2007). For 101 subjects (74.3%; Table 8), there was no record of transplantation in CPRD or HES between 05 March 2007 and 31 August 2008. Among the 35 subjects with a transplantation record, kidney was the most frequently transplanted organ (22 subjects; 16.2%) followed by heart (4 subjects; 2.9%). Information was available on concomitant medical conditions for malignancies/cancers in 10 subjects (7.4%). Although transplant recipients are at high risk of infectious diseases, events relating to infections were reported for only a very small number of subjects.

Most of the subjects (122 subjects; 89.7%) were followed over the whole analysis period for season 01-SEP-2007 to 31-AUG-2008. The remaining subjects either died (11 subjects; 8.1%) or were no longer followed in the CPRD GOLD (3 subjects; 2.2%) at 31 August 2008, because e.g. the subject had left the GP practice, or the GP practice was no longer active in CPRD GOLD.

Baseline characteristics of the subjects from the secondary seasonal influenza subset eligible for the analyses of season 2007-2008 are given in Table 16 and Table 17. This secondary subset was further restricted to subjects with available data from the GP questionnaire (N=55 subjects; Table 16). These subjects had a mean age of 52.0 years with 30.9% being female, and 4 subjects (7.3%) were noted to have died from any cause during the analysis period (Table 16).

The majority of transplantations (52/55 subjects; 94.5%) were performed prior to the 180-day period before the start of the study period (i.e. before 05 March 2007) or during the 2007-2008 study period (after 01 September 2007; Table 16), while a small proportion of the transplantations (5.5%; 3/55) occurred within the 180 days prior to the start of the study period (between 05 March and 01 September 2007). For 41 subjects (74.5%; Table 16), there was no record of transplantation in CPRD or HES between 05 March 2007 and 31 August 2008. Among the 14 subjects with a transplantation record, kidney was the most frequently transplanted organ (8 subjects; 14.5%) followed by liver (3 subjects; 5.5%). Although transplant recipients are at high risk of infectious diseases, events relating to infections were reported for only a very small number of subjects.

The demographic characteristics were very similar in the population of subjects with questionnaire information available, with transplantation or rejection involving only one organ (Table 17).

7.2.2.3. Influenza Season 2008-2009

Baseline characteristics of the subjects from the primary seasonal influenza subset eligible for the analyses of season 2008-2009 are given in Table 10 and Table 11.

Among 168 subjects, 163 subjects had only one record of transplantation or rejection for a single organ (Table 11).

Figure 5 shows the distribution of SOT rejection events throughout the 2008-09 influenza season.

Subjects had a mean age of 48.4 years at 01 September 2008, 42.3% were female and 7.1% were noted to have died from any cause during the analysis period (Table 10).

The majority of transplantations (161/168 subjects; 95.8%) were performed prior to the 180 day period before the start of the study period (i.e. before 05 March 2008) or during the 2008-2009 study period (after 01 September 2008;; Table 10), while a small proportion of the transplantations (4.2%; 7/168) occurred within the 180 days prior to the start of the study period (between 05 March and 01 September 2008). For 130 subjects (77.4%; Table 10), there was no record of transplantation in CPRD or HES between 05 March 2008 and 31 August 2009. Among the 38 subjects with a transplantation record, kidney was the most frequently transplanted organ (27 subjects; 16.1%) followed by liver (4 subjects; 2.4%). Information was available on concomitant medical conditions for malignancies/cancers in 10 subjects (6.0%). Although this patient population is at high risk of infectious diseases, events relating to infections were reported for only a very small number of subjects.

Most of the subjects (152 subjects; 90.5%; Table 10) were followed over the whole analysis period for season 01-SEP-2008 to 31-AUG-2009. The remaining subjects either died (12 subjects; 7.1%) or were no longer followed in the CPRD GOLD (4 subjects; 2.4%) at 31 August 2009 because e.g. the subject had left the GP practice , or the GP practice was no longer active in CPRD GOLD.

Baseline characteristics of the subjects from the secondary seasonal influenza subset eligible for the analyses of season 2008-2009 are given in Table 18 and Table 19. This secondary subset was further restricted to subjects with available data from the GP questionnaire (N=67 subjects; Table 18). These subjects had a mean age of 50.0 years with 41.8% being female, and 5 subjects (7.5%) were noted to have died from any cause during the analysis period (Table 18).

The majority of transplantations (66/67 subjects; 98.5%) were performed prior to the 180-day period before the start of the study period (i.e. before 05 March 2008) or during the 2008-2009 study period (after 01 September 2008; Table 18), while one transplantation (1.5%) occurred within the 180 days prior to the start of the study period (between 05 March and 01 September 2008). For 52 subjects (77.6%; Table 18), there was no record of transplantation in CPRD or HES between 05 March 2008 and 31 August 2009. Among the 15 subjects with a transplantation record, kidney was the most frequently transplanted organ (9 subjects; 13.4%) followed by liver (2 subjects; 3.0%). Seven subjects (10.4%) had Chemotherapy between 01 September 2007 and 31 August 2009. Although transplant recipients are at high risk of infectious diseases, events relating to infections were reported for only a very small number of subjects.

The demographic characteristics were very similar in the population of subjects with questionnaire information available, with transplantation or rejection involving only one organ (Table 19).

7.2.2.4. Analyses based on pooled influenza seasons

Baseline characteristics of the subjects from the primary seasonal influenza subset eligible for the analyses of the three seasons pooled are given in Table 12 and Table 13. The data of the three seasons were combined as described in Section 6.6.

Among 375 subjects, 363 subjects had only one record of transplantation or rejection for a single organ (Table 13).

Figure 6 shows the distribution of SOT rejection events throughout the pooled 2006-2009 influenza seasonal data.

Subjects had a mean age of 48.1 years at 01 September, 38.4% were female and 6.7% were noted to have died from any cause during the analysis period (Table 12).

The majority of transplantations (355/375 subjects; 94.7%) were performed prior to the 180-day period before the start of the study period (i.e. before 05 March) or during the 2006-2007 study period (after 01 September ;), while a small proportion of the transplantations (5.3%; 20/375) occurred within the 180 days prior to the start of the study period (between 05 March and 01 September). For 275 subjects (73.3%; Table 12), there was no record of transplantation in CPRD or HES between 05 March and 31 August. Among the 100 subjects with a transplantation record, kidney was the most frequently transplanted organ (66 subjects; 17.6%) followed by liver (12 subjects; 3.2%). Information was available on concomitant medical conditions for malignancies/cancers in 25 subjects (6.7%). Although transplant recipients are at high risk of infectious diseases, events relating to infections were reported for only a very small number of subjects.

Most of the subjects (340 subjects; 90.7%; Table 12) were followed over the whole analysis period of the seasons. The remaining subjects either died (25 subjects; 6.7%) or were no longer followed in the CPRD GOLD (10 subjects; 2.7%) at 31 August 2007 because e.g. the subject had left the GP practice, or the GP practice was no longer active in CPRD GOLD.

Secondary seasonal influenza subset (HES/CPRD GOLD + GP questionnaire data)

Baseline characteristics of the subjects from the secondary seasonal influenza subset eligible for the analyses of the three seasons pooled are given in Table 20 and Table 21. This secondary subset was further restricted to subjects with available data from the GP questionnaire (N=140 subjects). These subjects had a mean age of 50.8 years with 32.9% being female, and 12 subjects (8.6%) were noted to have died from any cause during the analysis period (Table 20).

The majority of transplantations (135/140 subjects; 96.4%) were performed prior to the 180-day period before the start of the study period (i.e. before 05 March 2006) or during the 2006-2007 study period (after 01 September 2006), while a small proportion of the

transplantations (3.6%; 5/140) occurred within the 180 days prior to the start of the study period (between 05 March and 01 September 2006). For 101 subjects (72.1%; Table 20), there was no record of transplantation in CPRD or HES between 05 March 2006 and 31 August 2007. Among the 39 subjects with a transplantation record, kidney was the most frequently transplanted organ (22 subjects; 15.7%) followed by liver (8 subjects; 5.7%). Information was available on concomitant medical conditions for malignancies/cancers in 11 subjects (7.9%) and also for chemotherapy in 11 subjects (7.9%). Although transplant recipients are at high risk of infectious diseases, events relating to infections were reported for only a very small number of subjects.

The demographic characteristics were very similar in the population of subjects with questionnaire information available, with transplantation or rejection involving only one organ (Table 21).

7.3. Outcome data

The main outcome of the study was the occurrence of SOT rejection(s) after vaccination with a TIV. The overall study population for the pooled seasonal influenza analysis consisted of 375 subjects who had experienced a SOT rejection between 01 September 2006 and 31 August 2009. The main analyses adjusted for time since transplantation included 218 subjects, of which 156 had been exposed to TIV. In other words, 156 cases were considered to estimate the risk of SOT rejection following vaccination with TIV; 62 additional unexposed cases were also included to better account for time since transplantation, yielding a population of analysis of 218 subjects. The remaining subjects (157 of 375 subjects) for the pooled seasonal analysis had no risk period associated with TIV administration and no risk period associated with time since transplantation in the seasonal influenza study period, and these subjects were excluded from the pooled seasonal analysis (Subset 2a; Table 105).

A total of 46 subjects contributed to the primary analysis (30-day risk period) using data from the GP questionnaire (Subset 2b; Table 134).

7.4. Main results

7.4.1. Primary analysis for the first tertiary objective – 30-day risk period after TIV administration

7.4.1.1. Number of rejections and person-time in each risk and control period associated with TIV and time since transplantation for the pooled influenza seasons

When considering the pooled influenza seasons, a total of 375 subjects with at least one rejection were noted for the primary seasonal influenza subset (Subset 2a; Table 1).

A total of 218 SOT rejections were noted in 218 subjects for the primary seasonal influenza subset (Subset 2a) indicating that no multiple transplant rejections occurred as described in Table 105.

A total of 156 cases were considered to estimate the risk of SOT rejection following vaccination with TIV; 62 additional unexposed cases were also included to better account for time since transplantation, yielding a population of analysis of 218 subjects.

Eighteen out of 156 rejections in exposed subjects occurred in the 0-30 day risk period after TIV vaccination (See seasonal vaccination pooled risk periods row of Table 105).

A total of 146 out of 218 rejections occurred in the control period of >180 days after transplantation. Of the 72 cases occurring in one of the three risk periods post-transplantation (38 subjects / 21 subjects / 13 subjects in the 3 risk periods – see bottom part of Table 105), 38 rejections were noted in the 0-30-day risk period.

7.4.1.2. Number of rejections and person-time in each risk and control period associated with TIV and time since transplantation for individual influenza seasons

Corresponding results for the individual influenza seasons are provided in the following tables:

- For the 2006-2007 influenza season: Table 22;

A total of 159 SOT rejections were noted in 131 subjects for the primary seasonal influenza subset (Subset 2a) as described in Table 22.

A total of 55 cases were considered to estimate the risk of SOT rejection following vaccination with TIV; 19 additional unexposed cases were also included to better account for time since transplantation, yielding a population of analysis of 74 subjects.

5 out of 55 rejections in exposed subjects occurred in the 0-30 day risk period after TIV vaccination (See seasonal vaccination pooled risk periods row of Table 22)

A total of 52 out of 74 rejections occurred in the control period of >90 days after transplantation. Of the 22 cases occurring in one of the 2 risk periods post-transplantation (16 subjects / 6 subjects in the 2 risk periods – see bottom part of Table 22), 16 rejections were noted in the 0-30-day risk period.

- For the 2007-2008 influenza season: Table 49;

A total of 169 SOT rejections were noted in 136 subjects for the primary seasonal influenza subset (Subset 2a) as described in Table 49.

A total of 58 cases were considered to estimate the risk of SOT rejection following vaccination with TIV; 23 additional unexposed cases were also included to better account for time since transplantation, yielding a population of analysis of 81 subjects.

7 out of 58 rejections in exposed subjects occurred in the 0-30 day risk period after TIV vaccination (See seasonal vaccination pooled risk periods row of Table 49).

A total of 57 out of 81 rejections occurred in the control period of >180 days after transplantation. Of the 24 cases occurring in one of the 3 risk periods

post-transplantation (11 subjects / 7 subjects/6 subjects in the 3 risk periods – see bottom part of Table 49.), 11 rejections were noted in the 0-30-day risk period.

- For the 2008-2009 influenza season: Table 77.

A total of 216 SOT rejections were noted in 168 subjects for the primary seasonal influenza subset (Subset 2a) as described in Table 77.

A total of 72 cases were considered to estimate the risk of SOT rejection following vaccination with TIV; 20 additional unexposed cases were also included to better account for time since transplantation, yielding a population of analysis of 92 subjects.

9 out of 72 rejections in exposed subjects occurred in the 0-30 day risk period after TIV vaccination (See seasonal vaccination pooled risk periods row of Table 77.

A total of 70 out of 92 rejections occurred in the control period of >180 days after transplantation. Of the 22 cases occurring in one of the 3 risk periods post-transplantation (11 subjects / 8 subjects/3 subjects in the 3 risk periods – see bottom part of Table 77), 11 rejections were noted in the 0-30-day risk period.

7.4.1.3. Relative incidence of SOT rejection 30 days after receiving a TIV, for the pooled influenza seasons

The relative incidence (RI) of SOT rejection within 30 days of TIV administration, compared to the control period, and adjusted for time since transplantation, is described in Table 106. No difference was detected between the incidence rate of SOT rejection within 30 days after any TIV dose and the incidence rate during the control period: RI = 1.01 (95% CI: 0.58, 1.76).

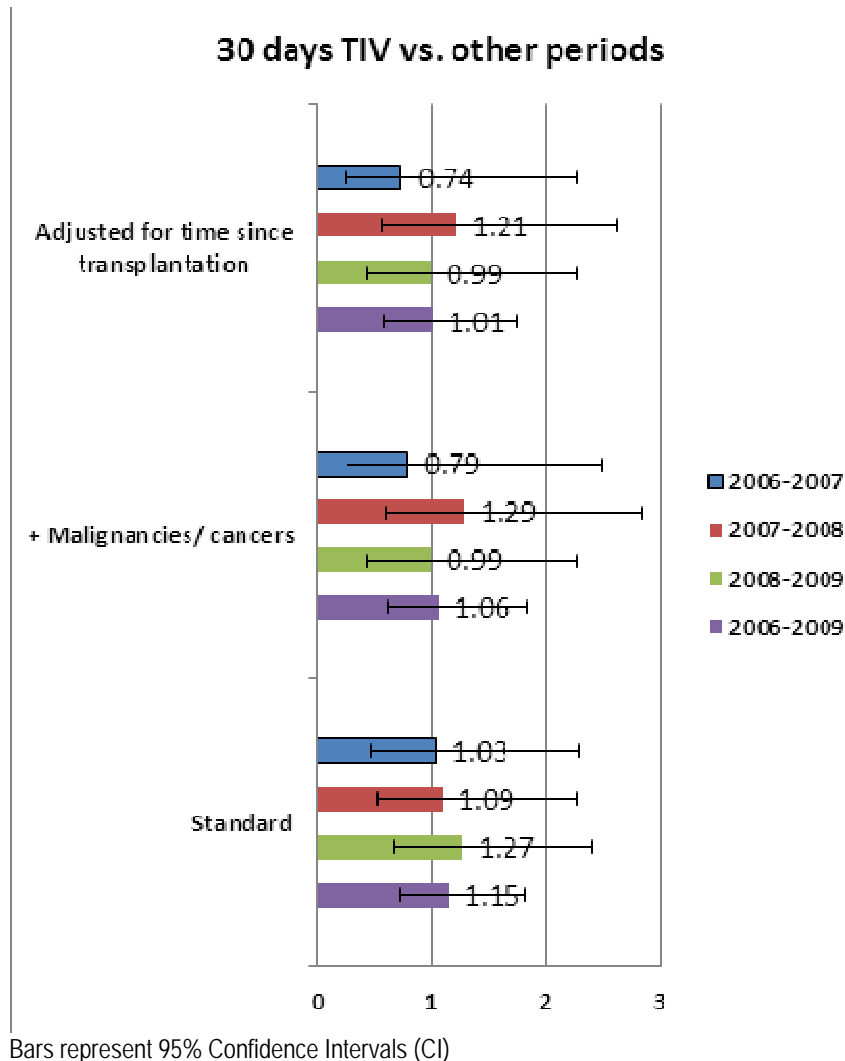
The RI of SOT rejection tended to decrease as time since transplantation increased: RI = 16.41 (95% CI: 5.89, 45.72) in the period 0-30 days post-transplantation; RI = 5.59 (95% CI: 2.14, 14.65) 31-90 days post-transplantation; and RI = 1.94 (95% CI: 0.72, 5.25) 91-180 days post-transplantation, compared to the period “more than 180 days after transplantation”.

7.4.1.4. Relative incidence of SOT rejection 30 days after receiving a TIV, for individual influenza seasons

Data are also provided by individual influenza season. The calculated RI values for SOT rejection within 30 days of any TIV dose compared to control periods were similar but some variation was noted from season to season compared to the pooled RI value of 1.01; see Figure 7:

- For the 2006-2007 influenza season: Table 23; RI = 0.74 (95% CI: 0.24, 2.28)
- For the 2007-2008 influenza season: Table 50; RI = 1.21 (95% CI: 0.55, 2.64)
- For the 2008-2009 influenza season: Table 78; RI = 0.99 (95% CI: 0.43, 2.28)

Figure 7 Relative incidence of SOT rejection 30 days after receiving a TIV: Pooled vs. Individual season



7.4.1.5. Further adjusted analyses for the pooled influenza seasons

Additional covariates, considered as risk factors for SOT rejection (independently of TIV) were added to the main model provided information was available, i.e. for ≥ 5 subjects (see Section 10.8.1.1 of the Main study report): see descriptive tables for all covariates (Table 107); opportunistic infections (Table 109); and malignancies/cancers (Table 111).

Analyses adjusted for time since transplantation and some of the covariates were not conducted because there were less than 5 subjects exposed per covariate; in addition, despite there were more than 5 subjects for some covariates (e.g. opportunistic infections $N=7$, malignancies/cancers, $N=14$), the iterative process to estimate the parameters of the models including seasonal influenza vaccination, time since transplantation, opportunistic infections, and malignancies/cancers, did not converge and no RI could be computed.

However, the model adjusted for time since transplantation and malignancies/cancers yielded a RI of 1.06 (95% CI: 0.61, 1.84) (Table 112).

7.4.1.6. Further adjusted analyses for the individual influenza seasons

Data for covariates by individual season are described in the following descriptive tables:

- For the 2006-2007 influenza season: All covariates (Table 24);
Malignancies/cancers (Table 26)
- For the 2007-2008 influenza season: All covariates (Table 51);
Malignancies/cancers (Table 53)
- For the 2008-2009 influenza season: All covariates (Table 79);
Malignancies/cancers (Table 81).

When malignancies/cancers (only covariate for which information was ≥ 5 subjects) was included in the model, the RI of SOT rejection within 30 days of TIV administration was:

- In the 2006-07 influenza season: 0.79 (95% CI: 0.25, 2.49) (Table 25);
- In the 2007-08 influenza season: 1.29 (95% CI: 0.59, 2.85) (Table 52);
- In the 2008-09 influenza season: 0.99 (95% CI: 0.43, 2.28) (Table 80).

Similar trends in RI of SOT rejection post-transplantation were observed in all analyses.

7.4.1.7. Sensitivity analyses for the first tertiary objective for the pooled influenza seasons

Since independence between a rejection event and administration of a TIV cannot be assumed, the case-series analysis for perturbed post-event exposure was used (see the Main study report: Section 10.9.2.3). However, the standard SCCS method was used in sensitivity analyses to assess the consistency in risk estimates between the two methods.

In this analysis based on the pooled seasons for Subset 2a (primary seasonal influenza subset), 156 subjects were exposed to TIV and 21 subjects had a rejection in the 0-30 day risk period after TIV administration (Table 113). Note three extra rejections in the day 0-30 risk period compared to the main primary analysis (Table 105), which can be explained by the standard method not requiring censoring at a subsequent rejection, thus potentially allowing for multiple events to be included in the analysis.

The observed RI estimate for TIV administration in the main analysis of pooled seasonal data (RI = 1.01, 95% CI: 0.58, 1.76; Table 106) remained in the same range when using the standard SCCS method (not accounting for perturbed post-event exposure): RI = 1.15 (95% CI: 0.73, 1.83; Table 114).

7.4.1.8. Sensitivity analyses for the first tertiary objective for the individual influenza seasons

In this analysis for the individual influenza season for Subset 2a primary seasonal influenza subset:

- 2006-07: 55 subjects were exposed to TIV and a total of 7 subjects had a rejection in the day 0-30 risk period after TIV administration (Table 28).
- 2007-08: 60 subjects were exposed to TIV and a total of 8 subjects had a rejection in the day 0-30 risk period after TIV administration (Table 55).
- 2008-09: 72 subjects were exposed to TIV and a total of 11 subjects had a rejection in day 0-30 risk period (Table 83).

Note that there were a total of $7 + 8 + 11$ subjects = 26 subjects (Table 28, Table 55, Table 83), which is 5 more than the 21 listed for the pooled seasonal data (Table 113). Hence 5 subjects actually provided data for more than one season and only the first season was considered for each subject (see Section 6.6 for the pooling process of the seasonal data). Of note, it was the first season with data on exposure to TIV OR time since transplantation that was considered for each subject.

The observed RI estimate for TIV administration in the main analysis of pooled seasonal data (RI = 1.01, 95% CI: 0.58, 1.76; Table 106) was little affected when using the standard SCCS method for each individual influenza season (not accounting for perturbed post-event exposure):

- 2006-07: 1.03 (95% CI: 0.46, 2.30; Table 29).
- 2007-08: 1.09 (95% CI: 0.52, 2.28; Table 56).
- 2008-09: 1.27 (95% CI: 0.67, 2.41; Table 84).

7.4.1.9. Summary of primary analysis for the first tertiary objective – 30-day risk period associated with TIV

A summary of key results for the primary analysis of risk of SOT rejection within 30 days of TIV administration is provided in Summary Table 1 (see Section 5.3 and 6.5.2).

Summary Table 1 Relative incidence (RI) estimates for primary analysis of risk of SOT rejection within 30 days of TIV administration

Season	Model	All cases	Exposed cases*	RI	95% CI (LL; UL)	Source Data (Table No.)
2006-2007	Main Model **	74	55	0.74	0.24; 2.28	Table 22, Table 23
	Model further adjusted for malignancies/ cancers	75	54	0.79	0.25; 2.49	Table 26, Table 27
	Sensitivity analysis†	74	55	1.03	0.46; 2.3	Table 28, Table 29
2007-2008	Main model**	81	58	1.21	0.55; 2.64	Table 49, Table 50
	Model further adjusted for malignancies/ cancers	81	55	1.29	0.59; 2.85	Table 53, Table 54
	Sensitivity analysis†	83	60	1.09	0.52; 2.28	Table 55, Table 56
2008-2009	Main model**	92	72	0.99	0.43; 2.28	Table 77, Table 78
	Model further adjusted for malignancies/ cancers	93	72	0.99	0.43; 2.28	Table 81, Table 82
	Sensitivity analysis†	92	72	1.27	0.67; 2.41	Table 83, Table 84
Pooled	Main model**	218	156	1.01	0.58; 1.76	Table 105, Table 106
	Model further adjusted for malignancies/ cancers	210	152	1.06	0.61; 1.84	Table 111, Table 112
	Sensitivity analysis†	218	156	1.15	0.73; 1.83	Table 113, Table 114

* Exposed to TIV

** Adjusted for time since transplantation

† Adjusted for time since transplantation using the standard SCCS method

7.4.2. Secondary analyses for the first tertiary objective

Subset 2b encompasses subjects with combined information from the returned GP questionnaires, CPRD GOLD and HES is available - see Section 6.5.2.

7.4.2.1. Number of rejections and person-time in each risk and control period associated with TIV and time since transplantation for the 2006-2007 season

These results describe the individual influenza season, 2006-07, 2007-08 and 2008-09, data for Subset 2b - Secondary seasonal influenza subset. Analyses for the pooled influenza seasons for Subset 2b were not planned (see Section 6.6).

A total of 53 SOT rejections were noted in 46 subjects for the secondary seasonal influenza subset (Subset 2b) for the season 2006-07 as described in Table 134.

A total of 20 cases were considered to estimate the risk of SOT rejection following TIV administration; 6 additional unexposed cases were also included to better account for time since transplantation, yielding a population of analysis of 26 subjects (Table 134).

Four out of 20 rejections in exposed subjects occurred in the 0-30 day risk period after TIV administration (See seasonal vaccination pooled risk periods row of Table 134).

A total of 72 SOT rejections were noted in 51 subjects for the secondary seasonal influenza subset (Subset 2b) for the season 2007-08 as described in Table 148.

A total of 21 cases were considered to estimate the risk of SOT rejection following TIV administration; 11 additional unexposed cases were also included to better account for time since transplantation, yielding a population of analysis of 32 subjects (Table 148).

Four out of 21 rejections in exposed subjects occurred in the 0-30 day risk period after TIV administration (See seasonal vaccination pooled risk periods row of Table 148).

A total of 73 SOT rejections were noted in 58 subjects for the secondary seasonal influenza subset (Subset 2b) for the season 2008-09 as described in Table 171.

A total of 23 cases were considered to estimate the risk of SOT rejection following TIV administration; 9 additional unexposed cases were also included to better account for time since transplantation, yielding a population of analysis of 32 subjects (Table 171).

Four out of 23 rejections in exposed subjects occurred in the 0-30 day risk period after TIV administration (See seasonal vaccination pooled risk periods row of Table 171).

7.4.2.2. Main analysis: relative incidence of SOT rejection 30 days after receiving TIV and time since transplantation for the 2006-2007 season

The RI of SOT rejection within 30 days of TIV administration, compared to the control period, and adjusted for time since transplantation, is described in Table 135. The relative incidence of SOT rejection within 30 days after vaccination with a TIV was 1.93 (95% CI: 0.50, 7.46) (Table 135). Results for the other two influenza seasons are as follows:

- 2007-08: 1.90 (95% CI: 0.68, 5.34; Table 149);
- 2008-09: 1.40 (95% CI: 0.36, 5.48; Table 172).

7.4.2.3. Further adjusted analyses for the individual influenza seasons

Additional covariates, considered as risk factors for SOT rejection (independently of TIV) were added to the main model provided information was available, i.e. for ≥ 5 subjects (see Section 10.8.1.1 of the Main study report): see descriptive tables for all covariates, season 2006/07 (Table 136), 2007-08 (Table 150) and 2008-09 (Table 173).

For 2006/07 influenza season, as there were less than 5 subjects exposed per covariate, RI from models including seasonal influenza vaccination, time since transplantation and other covariates could not be computed.

For the 2007-08 influenza season, despite the fact there were more than 5 subjects for some covariates (e.g. respiratory infections N=7, malignancies/cancers, N=5), the iterative process to estimate the parameters of the models including seasonal influenza vaccination, time since transplantation, respiratory infections, and malignancies/cancers, did not converge and no RI could be computed.

However, the model adjusted for time since transplantation and respiratory infections yielded a RI of 1.92 (95% CI: 0.70, 5.26) (Table 153).

A total of 21 cases were considered to estimate the risk of SOT rejection following vaccination with TIV in this analysis, and 8 of these subjects qualified for the Day 0-30 risk period after a respiratory infection (Table 152).

In models expected to include all covariates, only subjects with a sufficient follow-up (365 days before the start of each season i.e. 01 September) contributed to the analyses. In some of these models, only one covariate was sufficiently represented and therefore the resulting analysis was the same as the analysis with this covariate only (here respiratory infection), but with less subjects and, as a consequence, slightly different results.

A summary of key results for the secondary analysis (Subset 2b) of risk of SOT rejection within 30 days of TIV administration is provided in Summary Table 2 (see Section 5.3 and 6.5.2).

Summary Table 2 Relative incidence (RI) estimates for secondary analysis of risk of SOT rejection within 30 days of TIV administration (Subset 2b)

Season	Model	All cases	Exposed cases*	RI	95% CI (LL; UL)	Source Data (Table No.)
2006-2007	Main Model **	26	20	1.93	(0.50; 7.46)	Table 134, Table 135
	Sensitivity analysis†	26	20	1.72	(0.56; 5.25)	Table 137, Table 138
2007-2008	Main Model **	32	21	1.90	(0.68; 5.34)	Table 148, Table 149
	Model further adjusted for respiratory infection	35	21	1.92	(0.70; 5.26)	Table 152, Table 153
	Sensitivity analysis†	33	22	1.18	(0.41; 3.41)	Table 158, Table 159
2008-2009	Main Model **	32	23	1.40	(0.36; 5.48)	Table 171, Table 172
	Sensitivity analysis†	32	23	1.54	(0.56; 4.28)	Table 174 Table 175

* Exposed to TIV

** Adjusted for time since transplantation

† Adjusted for time since transplantation using the standard SCCS method

7.4.3. Exploratory analyses of the first tertiary objective for pooled influenza seasons - effect of previous rejections

7.4.3.1. Subjects with previous rejection(s)

A previous SOT rejection might influence the risk of a subsequent rejection. Therefore it can be assumed that the risk of rejection might differ between subjects having already experienced a rejection and those who haven't. The effect of a previous rejection could also be time-dependent – see Section 6.6.

A total of 14 SOT rejections were noted in 14 subjects with at least one exposure of interest (previous rejection, TIV, transplantation) for this analysis (Subset 2a) (Table 118). Only four subjects were exposed to one of the risk periods post-transplantation and therefore the RI estimates could not be computed (Table 119).

Descriptive data on previous rejections for the individual influenza seasons are provided in the following tables:

- For the 2006-2007 influenza season: Table 33;
- For the 2007-2008 influenza season: Table 60;

- For the 2008-2009 influenza season: Table 88.

Given the small number of previous rejections (≤ 3) for each season, no RIs were computed (Table 34; Table 61; Table 89).

7.4.3.2. Subjects without previous rejection(s)

Separate analyses only including subjects without previous rejections (N=204) for the pooled seasonal data are presented in Table 116 and Table 117; these sub-analyses are important to more finely estimate the effect of exposure to TIV, limiting the potential confounding effect of previous rejection(s). The relative incidence of SOT rejection within 30 days after any TIV dose in subjects with no previous rejection was: RI = 1.04 (95% CI: 0.59, 1.84).

RI data for the individual seasons are provided below:

- 2006-07: 0.66 (95% CI: 0.19, 2.33; Table 32).
- 2007-08: 1.10 (95% CI: 0.47, 2.55; Table 59).
- 2008-09: 1.01 (95% CI: 0.41, 2.49; Table 87).

7.4.4. Exploratory analyses for the first tertiary objective by organ

7.4.4.1. Subset 2a – primary seasonal influenza subset

There were insufficient subjects identified to calculate the RIs for all individual organs but kidney in the individual and pooled influenza seasons:

- Heart: Season 2006-07: N=7 including 3 exposed cases; Table 35;
Season 2007-08: N= 8 including 4 exposed cases; Table 62
Season 2008-09: N= 7 including 4 exposed cases; Table 90
Pooled seasons: N= 15 including 10 exposed cases; Table 120
- Liver: Season 2006-07: N= 12 including 3 exposed cases; Table 46
Season 2007-08: N= 6 including 1 exposed case; Table 74
Season 2008-09: N= 16 including 7 exposed cases; Table 102
Pooled seasons: N= 16 including 10 exposed cases; Table 131
- Lung: Season 2006-07: N= 6 including 3 exposed cases; Table 47
Season 2007-08: N= 1 including 1 exposed case; Table 75
Season 2008-09: N= 5 including 2 exposed cases; Table 103
Pooled seasons: N= 9 including 5 exposed cases; Table 132

- Pancreas: Season 2006-07: N= 0 cases; Table 48
 Season 2007-08: N= 1 including 0 exposed case; Table 76
 Season 2008-09: N= 0 cases; Table 104
 Pooled seasons: N= 1 including 0 exposed cases; Table 133

Overall results of the analyses including all organs were mainly driven by kidney:

- Kidney: Season 2006-07: N= 67 including 36 exposed cases; Table 36;
 Season 2007-08: N= 84 including 40 exposed cases; Table 63
 Season 2008-09: N= 98 including 47 exposed cases; Table 91
 Pooled seasons: N= 144 including 98 exposed cases; Table 121

In the pooled seasonal analysis for kidney, the RI of SOT rejection within 30 days of TIV administration, compared to the control period, and adjusted for time since transplantation, was 0.91 (95% CI: 0.44, 1.87; Table 122).

Analyses of pooled influenza seasons for kidney only, adjusted for time since transplantation and covariates of interest, were not conducted; despite there were 5 subjects with opportunistic infections reported, the model further adjusted for opportunistic infections did not converge and no RI could be computed – see Table 123 for data on covariates.

Using the standard SCCS method in the analysis of pooled influenza seasons for kidney only, the RI was 1.01 (95%CI: 0.56, 1.82) (Table 125).

Restricting the analysis to subjects without previous rejections (N=134 including 88 exposed cases; Table 127), the RI was 0.91 (95%CI: 0.43, 1.94) (Table 128).

7.4.4.2. Subset 2b – secondary seasonal influenza subset

Similarly to Subset 2a, only analyses for kidney could be conducted for the individual influenza seasons:

- Kidney: Season 2006-07: N= 22 including 13 exposed cases; Table 140;
 Season 2007-08: N= 34 including 15 exposed cases; Table 161
 Season 2008-09: N= 33 including 14 exposed cases; Table 177

A summary of RIs for kidney only, by influenza season, is provided in Summary Table 3.

Summary Table 3 Relative Incidence (RI) estimates for secondary analysis of risk of SOT rejection within 30 days of TIV administration, for kidney only, by individual influenza season

Season	Model	All cases	Exposed cases*	RI	95% CI (LL; UL)	Table
2006-2007	Main model**	16	13	1.04	0.17, 6.56	Table 140, Table 141
	Sensitivity analysis†	16	13	1.06	0.23, 4.96	Table 143, Table 144
2007-2008	Main model**	23	15	1.92	0.60, 6.14	Table 161, Table 162
	Model further adjusted for respiratory infections	25	15	1.88	0.61, 5.75	Table 164, Table 165
	Sensitivity analysis†	24	16	1.01	0.30, 3.42	Table 166, Table 167
2008-2009	Main model**	22	14	1.86	0.36, 9.55	Table 177, Table 178
	Sensitivity analysis†	22	14	2.10	0.68, 6.45	Table 180, Table 181

* Exposed to TIV

** Adjusted for time since transplantation

† Adjusted for time since transplantation using the standard SCCS method

7.4.5. Second tertiary objective (60-day risk period) - Subset 2a

Overall, results of analyses using a 60-day risk period remained in the same range as those with a 30-day risk period (see Section 5.3).

A total of 218 cases with at least one exposure of interest (TIV or time since transplantation) were considered for the analysis of the pooled influenza seasons, which was the same number included in the primary analysis – see Section 7.4.1.1 and Table 268. As for the 30-day risk period, 156 cases were considered to estimate the risk of SOT rejection following vaccination with TIV.

The relative incidence (RI) of SOT rejection within 60 days of TIV administration, compared to the control period, and adjusted for time since transplantation, is described in Table 269. No difference was detected between the incidence rate of SOT rejection within 60 days after any TIV dose and the incidence rate during the control period: RI = 0.88 (95% CI: 0.56, 1.38; see Section 7.4.1.3 for corresponding main primary analysis result using 30 day risk period).

Analyses adjusted for time since transplantation and some of the covariates were not conducted because there were less than 5 subjects exposed per covariate. Despite the fact that there were more than 5 subjects for opportunistic infections (N=7) and

malignancies/cancers (N=14), the iterative process to estimate the parameters of the models including both covariates did not converge and no RI could be computed. However, in the model further adjusted for malignancies/cancers, the RI for the pooled influenza seasons was 0.92 (95% CI: 0.59, 1.45) (Table 270; Table 271; Table 272; Table 273; Table 275).

When applying the standard SCCS method for the pooled influenza seasons, the RI was 0.95 (95% CI: 0.65, 1.39; Table 277).

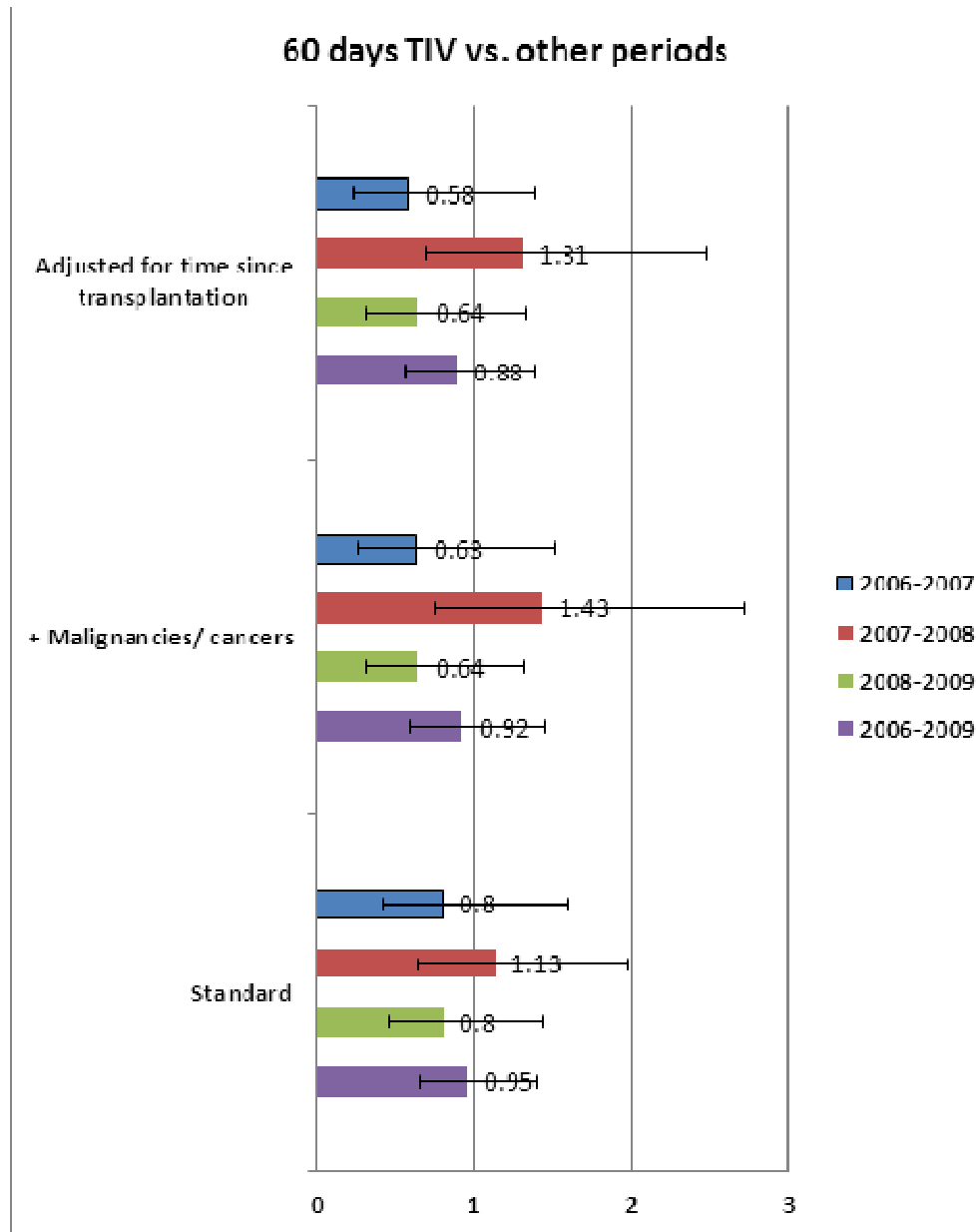
Restricting the analysis to subjects without previous rejections (N=204 including 143 exposed cases; Table 279, the RI was 0.90 (95%CI: 0.57, 1.44; Table 280).

7.4.5.1. Summary of primary analysis for second tertiary objective – 60-day risk period associated with TIV

A summary of key results for the primary analysis of risk of SOT rejection within 60 days of TIV administration is provided in Summary Table 4, including data for individual influenza seasons (see Section 5.3 and 6.5.2).

The calculated RI values for SOT rejection within 60 days of any TIV dose compared to control periods were similar but some variation was noted from season to season compared to the pooled RI value of 0.88; see Figure 8:

Figure 8 **Relative incidence of SOT rejection 60 days after receiving a TIV:**
Pooled vs. Individual season



Bars represent 95% Confidence Intervals (CI)

Another summary table for the 60-day risk period, summarising results for kidney which was the only transplant organ which was sufficiently represented is provided in Summary Table 5.

Summary Table 4 Relative incidence (RI) estimates for primary analysis of risk of SOT rejection within 60 days of TIV administration

Season	Model	All cases	Exposed cases*	RI	95% CI (LL; UL)	Source data (Table No.)
2006-2007	Main Model **	74	55	0.58	(0.24; 1.38)	Table 185, Table 186
	Model further adjusted for malignancies/cancers	75	54	0.63	(0.26; 1.51)	Table 189, Table 190
	Sensitivity analysis†	74	55	0.80	(0.41; 1.59)	Table 191, Table 192
2007-2008	Main Model **	81	58	1.31	(0.69; 2.48)	Table 212, Table 213
	Model further adjusted for malignancies/cancers	81	55	1.43	(0.75; 2.72)	Table 216, Table 217
	Sensitivity analysis†	83	60	1.13	(0.64; 1.98)	Table 218, Table 219
2008-2009	Main Model **	92	72	0.64	(0.31; 1.33)	Table 240, Table 241
	Model further adjusted for malignancies/cancers	93	72	0.64	(0.31; 1.32)	Table 244, Table 245
	Sensitivity analysis†	92	72	0.80	(0.45; 1.43)	Table 246, Table 247
Pooled	Main Model **	218	156	0.88	(0.56; 1.38)	Table 268, Table 269
	Model further adjusted for malignancies/cancers	210	152	0.92	(0.59; 1.45)	Table 274, Table 275
	Sensitivity analysis†	218	156	0.95	(0.65; 1.39)	Table 276, Table 277

* Exposed to TIV

** Adjusted for time since transplantation

† Adjusted for time since transplantation using the standard SCCS method

Summary Table 5 Relative incidence (RI) estimates for primary analysis of risk of SOT rejection within 60 days of TIV administration, kidney only, by individual influenza season

Season	Model	All cases	Exposed cases*	RI	95% CI (LL; UL)	Table
2006-2007	Main Model **	49	36	0.50	0.16, 1.60	Table 199, Table 200,
	Sensitivity analysis†	49	36	0.71	0.30, 1.67	Table 202, Table 203
	Restricting to subjects without previous rejections	43	30	0.27	0.05, 1.45	Table 205, Table 206
2007-2008	Main Model **	57	40	0.82	0.36, 1.86	Table 226, Table 227,
	Sensitivity analysis†	58	41	0.78	0.37, 1.62	Table 230, Table 231
	Restricting to subjects without previous rejections	52	35	0.74	0.30, 1.79	Table 233, Table 234
2008-2009	Main Model **	63	47	0.42	0.15, 1.21	Table 254, Table 255,
	Sensitivity analysis†	63	47	0.64	0.30, 1.35	Table 258, Table 259
	Restricting to subjects without previous rejections	50	34	0.42	0.12, 1.38	Table 261, Table 262
Pooled	Main Model **	144	98	0.59	0.32, 1.08	Table 284, Table 285
	Sensitivity analysis†	144	98	0.68	0.41, 1.14	Table 287, Table 288
	Restricting to subjects without previous rejections	134	88	0.56	0.29, 1.08	Table 290, Table 291

* Exposed to TIV

** Adjusted for time since transplantation

† Adjusted for time since transplantation using the standard SCCS method

7.4.6. Second tertiary objective (60-day risk period) - Subset 2b

Overall, results of analyses using a 60-day risk period in Subset 2b (including data from the GP questionnaire) remain in the same range as those with a 30-day risk period.

A summary of key results for the secondary analysis of risk of SOT rejection within 60 days of TIV administration is provided in Summary Table 6, for the three individual influenza seasons (see Section 5.3 and 6.5.2).

Summary Table 6 Relative incidence (RI) estimates for secondary analysis of risk of SOT rejection within 60-days of TIV administration (subset 2b)

Season	Model	All cases	Exposed cases*	RI	95% CI (LL; UL)	Source Data (Table No.)
2006-2007	Main Model **	26	20	2.13	(0.72; 6.25)	Table 297, Table 298
	Sensitivity analysis†	26	20	1.66	(0.65; 4.21)	Table 300, Table 301
2007-2008	Main Model **	32	21	1.07	(0.38; 3.05)	Table 311, Table 312
	Model further adjusted for respiratory infection	35	21	1.03	(0.35; 3.01)	Table 315, Table 316
	Sensitivity analysis†	33	22	1.03	(0.43; 2.44)	Table 321, Table 322
2008-2009	Main Model **	32	23	1.18	(0.40; 3.47)	Table 334, Table 335
	Sensitivity analysis†	32	23	1.21	(0.51; 2.89)	Table 337, Table 338

* Exposed to TIV

** Adjusted for time since transplantation

† Adjusted for time since transplantation using the standard SCCS method

Summary Table 7 Relative incidence (RI) estimates for secondary analysis of risk of SOT rejection within 60 days of TIV administration for kidney only, by individual season

Season	Model	All cases	Exposed cases*	RI	95% CI (LL; UL)	Source Data (Table No.)
2006-2007	Main Model **	16	13	2.13	0.53, 8.53	Table 303, Table 304
	Sensitivity analysis†	16	13	1.63	0.53, 5.01	Table 306, Table 307
2007-2008	Main Model **	23	15	0.72	0.21, 2.50	Table 324, Table 325
	Model further adjusted for respiratory infections	25	15	0.62	0.20, 1.97	Table 327, Table 328
	Sensitivity analysis†	24	16	0.81	0.29, 2.21	Table 329, Table 330
2008-2009	Main Model **	33	14	0.82	0.16, 4.26	Table 340, Table 341
	Sensitivity analysis†	33	14	1.03	0.34, 3.09	Table 343, Table 344

* Exposed to TIV

** Adjusted for time since transplantation

† Adjusted for time since transplantation using the standard SCCS method

7.5. Other analyses

Not applicable.

7.6. Adverse events/adverse reactions

Not applicable.

8. DISCUSSION

The present exploratory analysis was designed to assess the risk of SOT rejection following vaccination with a TIV. To our knowledge, this is the first formal pharmaco-epidemiological study designed to address this question.

8.1. Key results

The overall study population in this exploratory analysis consisted of 375 eligible subjects in CPRD-HES who had experienced a SOT rejection in any of the three influenza seasons 2006/07, 2008/08, and 2008/09 (Subset 2a, primary seasonal influenza subset).

In the main analysis, a total of 132, 136, and 168 subjects had at least one rejection in seasons 2006/07, 2007/08 and 2008/09, respectively; an overall 45-51% received a TIV. The analysis included 218 subjects, of which 156 (72%) were exposed cases. Relative incidence (RI) of rejection of any of the five organs, adjusted for time since transplantation, was 1.01 (95%CI: 0.58, 1.76) and 0.88 (95%CI: 0.56, 1.38), 30 and 60 days after vaccination, respectively. Results were mainly driven by kidney, the most commonly transplanted organ, with RIs of 0.91 (95%CI: 0.44, 1.87) and 0.59 (95%CI: 0.32, 1.08), in the 30- and 60-day risk periods, respectively.

In the analysis subset that incorporated subjects for which GP questionnaire information was available and valid, the risk estimates remained in the same range.

Considerations related to the assumed confounding effect of time since transplantation and of previous rejection(s) are similar to those discussed in the pandemic analysis (see Section 12.1 of the Main report).

8.2. Strengths and limitations

8.2.1. Strengths

Strengths related to the use of the CPRD GOLD and HES and the choice of the SCCS are those described in the pandemic analysis (see Section 12.2.1 of the Main report).

With 30 expected exposed cases, the study was designed to have 80% statistical power to detect a RI of 3.0 or higher (see Section 10.7 of the Main report). Considering that 156 exposed cases were included in the main analyses, it is assumed that the study was powered to reliably address the research question.

Given that influenza virus circulation is variable from season to season (both in terms of type/subtype strain distribution and in terms of levels of virus circulation) and because vaccine strain composition can also vary from season to season, three seasons were considered to:

- Assess the consistency of the safety profile from one season to another;
- Assess the overall effect of TIV across three seasons, in other words evaluating:
 - The “average” safety profile over time given the underlying year to year variability in strain circulation and vaccine strain composition.

Risk estimates were computed for individual seasons and for the three seasons pooled. The approach for the pooled analyses included only the first season with an exposure to TIV or with an effect of the time since transplantation in the analyses. This approach discarded the data from the following season(s) of each subject to limit potential residual confounding associated with prior exposure or rejection events.

8.2.2. Limitations

Limitations discussed in the main report for the pandemic analysis apply to the analysis of the association between vaccination with a TIV and SOT rejection (see Section 12.2.2 of the Main report), except for the considerations of multiple vaccine doses, which are not applicable here. In summary:

- Challenges/inability to obtain additional qualitative and quantitative information about other risk factors/confounders through the standardised GP questionnaire; this finding highlighted that this patient population is more prone to be managed in highly specialized care settings rather than in the general practice setting;
- Challenges/inability to account for all risk factors/confounders potentially affecting the association. Although information on time since transplantation was available in the study, the effect of this covariate could not be tested due to the fact that for most subjects, the transplantation had occurred more than 6 months before the beginning of the study period; other important established risk factors such as infections could not be fully accounted for, because this information was reported for only a very small number of subjects;
- Although, year to year risk estimates slightly varied within a limited range around a RI of 1.0, the present analysis cannot disentangle whether this variability was a reflection of random error and therefore statistical uncertainty or reflects potential differential effect of year-to-year strain circulation and vaccine virus composition. Nonetheless, these differences do not substantially change the overall inferences;
- For the analysis of the pooled influenza seasons, subjects had to have informative data on seasonal vaccination status or time since transplantation, and contributed only to the first season in which this information was available. Even if additional information on other covariates (e.g. infections) were available for the other seasons, subjects were discarded from the analyses for these other seasons.

8.3. Interpretation

Risk estimates remained in a range of 0.6 to 1.3 across seasons and various sensitivity analyses, with upper 95%CI limits below 3.0. These results suggest no evidence of an increased risk of SOT rejection 30 and 60 days following vaccination with a TIV in the UK.

8.4. Generalisability

Given the representativeness of the CPRD and HES, results from this study could be extrapolated to the overall population of SOT recipients in the UK. Although standards of care of transplanted patients might vary within the UK, documentation/coding guidelines in HES are standardised, hence limiting the variability in patient level information.

However, although the results appeared to be robust and showed a high degree of consistency across the different analyses, the SCCS design does not allow a direct generalization of the conclusions beyond the population included in the analyses.

While a composite of organs were considered in the present study, a substantial proportion of subjects who contributed to calculate the risk estimates received kidney transplantation, resulting in risk estimates mainly accounting for this organ and limiting the possibility of organ-specific risk estimates for other types of SOT.

9. OTHER INFORMATION

The study results are to be reported both internally within GSK and externally to EMA for information, and a manuscript will be submitted to a peer-reviewed journal for publication. A result summary will be posted to the GSK Clinical Study Register.

10. CONCLUSION

Results of these exploratory analyses suggest no increased risk of rejection following vaccination with a TIV in solid organ transplant recipients; in addition, these data do not change the conclusions of the main report (primary and secondary objectives on the association between Pandemrix™ vaccination and SOT rejection).

These data inform the benefit-risk assessment for seasonal influenza vaccination and provide additional support to existing recommendations to provide annual seasonal vaccination to this risk group.

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12. APPENDICES

12.1. Demographic and baseline characteristics

Table 1 Selection of the study population for the seasonal influenza study period (Total cohort)

Title	Total	Percent
Subjects with SOT rejection identifier(s) in the CPRD GOLD or HES during the study period (2006-2010)	587	-
Subjects with HES link	545	92.84
Subjects with at least one SOT rejection reported in HES during one of the seasons between 2006 and 2009 (subset 2a)	375	63.88
Subjects with GP questionnaire returned and usable	185	31.52
Subjects with at least one SOT rejection reported in CPRD GOLD, HES or GP questionnaire during one of the seasons between 2006 and 2009 (subset 2b)	140	23.85

Notes: for each subject, only seasons with 01 September and the preceding 180 days period included in the subject's follow-up are considered. Each season begins on 01 September and ends on 31 August.

Table 2 Distribution of subjects and person-time into each influenza study period for each subset (Total cohort)

Subset	Influenza season	N	%	Person-years
Primary pandemic influenza subset	2009/2010	184	-	192.82
Secondary pandemic influenza subset	2009/2010	67	-	70.38
Primary seasonal influenza subset	2006 - 2009	375	-	359.90
	2006/2007	132	35.20	125.88
	2007/2008	136	36.27	132.01
	2008/2009	168	44.80	159.47
Secondary seasonal influenza subset	2006 - 2009	140	-	133.92
	2006/2007	48	34.29	45.21
	2007/2008	55	39.29	53.64
	2008/2009	67	47.86	63.32

N: Number of subjects considered in the influenza season

?: Percentage of subjects considered in the influenza season in the corresponding subset

Table 3 Distribution of subjects and person-time into each influenza study period for each subset (Total cohort, subjects with transplantation or rejection for only one organ)

Subset	Influenza season	N	%	Person-years
Primary pandemic influenza subset	2009/2010	179	-	187.91
Secondary pandemic influenza subset	2009/2010	63	-	66.55
Primary seasonal influenza subset	2006 - 2009	363	-	347.88
	2006/2007	130	35.81	123.88
	2007/2008	128	35.26	123.99
	2008/2009	163	44.90	154.47
Secondary seasonal influenza subset	2006 - 2009	133	-	126.91
	2006/2007	45	33.83	42.21
	2007/2008	52	39.10	50.63
	2008/2009	63	47.37	59.32

N: Number of subjects considered in the influenza season

?: Percentage of subjects considered in the influenza season in the corresponding subset

Table 4 Description of vaccine exposure in the seasonal influenza study period (Total cohort)

Subset	Influenza season	Vaccination	N	n	%
Primary seasonal influenza subset	2006/2007	Not vaccinated	132	72	54.55
		Vaccinated	132	60	45.45
	2007/2008	Not vaccinated	136	69	50.74
		Vaccinated	136	67	49.26
	2008/2009	Not vaccinated	168	83	49.40
		Vaccinated	168	85	50.60
Secondary seasonal influenza subset	2006/2007	Not vaccinated	48	27	56.25
		Vaccinated	48	21	43.75
	2007/2008	Not vaccinated	55	28	50.91
		Vaccinated	55	27	49.09
	2008/2009	Not vaccinated	67	32	47.76
		Vaccinated	67	35	52.24

N: Number of subjects in the considered subset and season

n/%: Number/Percentage of subjects in each category

Table 5 Description of vaccine exposure in the seasonal influenza study period (Total cohort, subjects with transplanted or rejection for only one organ)

Subset	Influenza season	Vaccination	N	n	%
Primary seasonal influenza subset	2006/2007	Not vaccinated	130	71	54.62
		Vaccinated	130	59	45.38
	2007/2008	Not vaccinated	128	69	53.91
		Vaccinated	128	59	46.09
	2008/2009	Not vaccinated	163	81	49.69
		Vaccinated	163	82	50.31
Secondary seasonal influenza subset	2006/2007	Not vaccinated	45	26	57.78
		Vaccinated	45	19	42.22
	2007/2008	Not vaccinated	52	28	53.85
		Vaccinated	52	24	46.15
	2008/2009	Not vaccinated	63	30	47.62
		Vaccinated	63	33	52.38

N: Number of subjects in the considered subset and season

n/%: Number/Percentage of subjects in each category

Table 6 Demographic and baseline characteristics of subjects with data for season 2006-2007 (Primary seasonal influenza subset)

		nvac N = 72		vac N = 60		Total N = 132	
Characteristics	Parameters or Categories	Value or n	%	Value or n	%	Value or n	%
Age at 01-Sep-2006 [years]	N	72	-	60	-	132	-
	Mean	43.0	-	54.2	-	48.1	-
	SD	16.73	-	18.83	-	18.50	-
	Median	43.5	-	53.5	-	47.0	-
	Minimum	5	-	6	-	5	-
	Maximum	77	-	90	-	90	-
Age group at 01-Sep-2006 [years]	[0-17]	5	6.9	2	3.3	7	5.3
	[18-44]	32	44.4	17	28.3	49	37.1
	[45-60]	26	36.1	19	31.7	45	34.1
	61+	9	12.5	22	36.7	31	23.5
Gender	Female	28	38.9	22	36.7	50	37.9
	Male	44	61.1	38	63.3	82	62.1
Died between 01-Sep-2006 and 31-Aug-2007	No	69	95.8	54	90.0	123	93.2
	Yes	3	4.2	6	10.0	9	6.8
Time since transplantation at 01-Sep-2006 [days]	Before transplantation or more than 180 days after transplantation	69	95.8	58	96.7	127	96.2
	0-30	1	1.4	0	0.0	1	0.8
	31-90	2	2.8	2	3.3	4	3.0
	91-180	0	0.0	0	0.0	0	0.0
Organ transplanted before or during the season**	Heart	1	1.4	1	1.7	2	1.5
	Heart+Lung	1	1.4	0	0.0	1	0.8
	Kidney	11	15.3	11	18.3	22	16.7
	Liver	3	4.2	3	5.0	6	4.5
	Lung	2	2.8	1	1.7	3	2.3
	No transplantation recorded	54	75.0	44	73.3	98	74.2
Number of rejections between 05-Mar-2006 and 01-Sep-2006	None	67	93.1	51	85.0	118	89.4
	At least one	5	6.9	9	15.0	14	10.6
Number of transplantation events between 01-Sep-2006 and 31-Aug-2007	0	57	79.2	46	76.7	103	78.0
	1	11	15.3	13	21.7	24	18.2
	2	4	5.6	1	1.7	5	3.8

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Characteristics	Parameters or Categories	nvac N = 72		vac N = 60		Total N = 132	
		Value or n	%	Value or n	%	Value or n	%
Respiratory infection[s] between 02-Aug-2006 and 31-Aug-2007	No	72	100	59	98.3	131	99.2
	Yes	0	0.0	1	1.7	1	0.8
Acute bacterial infection[s] between 02-Aug-2006 and 31-Aug-2007	No	72	100	60	100	132	100
	Yes	0	0.0	0	0.0	0	0.0
Opportunistic infection[s] between 02-Aug-2006 and 31-Aug-2007	No	71	98.6	58	96.7	129	97.7
	Yes	1	1.4	2	3.3	3	2.3
Chronic viral infection[s] between 05-Mar-2006 and 31-Aug-2007	No	72	100	60	100	132	100
	Yes	0	0.0	0	0.0	0	0.0
Malignancy/cancer[s] between 05-Mar-2006 and 31-Aug-2007	No	68	94.4	55	91.7	123	93.2
	Yes	4	5.6	5	8.3	9	6.8
Reasons for end of follow-up	End of season [31 August]	66	91.7	53	88.3	119	90.2
	Death	3	4.2	6	10.0	9	6.8
	End of CRPD GOLD follow-up	3	4.2	1	1.7	4	3.0

nvac = not_vaccinated

vac = vaccinated

*Transplantations could happen after 01-September 2006

**Each subject is classified in one category. All combinations are possible. All transplantations between 05-Mar-2006 and 31-Aug-2007 are considered.

n = number of subjects in a given category

Value = value of the considered parameter

% = n / Number of subjects with available results x 100

SD = Standard deviation

Table 7 Demographic and baseline characteristics of subjects with data for season 2006-2007 (Primary seasonal influenza subset, subjects with transplantation or rejection for only one organ)

		nvac N = 71		vac N = 59		Total N = 130	
Characteristics	Parameters or Categories	Value or n	%	Value or n	%	Value or n	%
Age at 01-Sep-2006 [years]	N	71	-	59	-	130	-
	Mean	42.9	-	54.6	-	48.2	-
	SD	16.79	-	18.70	-	18.56	-
	Median	43.0	-	55.0	-	47.0	-
	Minimum	5	-	6	-	5	-
	Maximum	77	-	90	-	90	-
Age group at 01-Sep-2006 [years]	[0-17]	5	7.0	2	3.4	7	5.4
	[18-44]	32	45.1	16	27.1	48	36.9
	[45-60]	25	35.2	19	32.2	44	33.8
	61+	9	12.7	22	37.3	31	23.8
Gender	Female	28	39.4	21	35.6	49	37.7
	Male	43	60.6	38	64.4	81	62.3
Died between 01-Sep-2006 and 31-Aug-2007	No	68	95.8	53	89.8	121	93.1
	Yes	3	4.2	6	10.2	9	6.9
Time since transplantation at 01-Sep-2006 [days]	Before transplantation or more than 180 days after transplantation	68	95.8	57	96.6	125	96.2
	0-30	1	1.4	0	0.0	1	0.8
	31-90	2	2.8	2	3.4	4	3.1
	91-180	0	0.0	0	0.0	0	0.0
Organ transplanted before or during the season**	Heart	1	1.4	1	1.7	2	1.5
	Kidney	11	15.5	11	18.6	22	16.9
	Liver	3	4.2	3	5.1	6	4.6
	Lung	2	2.8	1	1.7	3	2.3
	No transplantation recorded	54	76.1	43	72.9	97	74.6
Number of rejections between 05-Mar-2006 and 01-Sep-2006	None	66	93.0	50	84.7	116	89.2
	At least one	5	7.0	9	15.3	14	10.8
Number of transplantation events between 01-Sep-2006 and 31-Aug-2007	0	57	80.3	45	76.3	102	78.5
	1	11	15.5	13	22.0	24	18.5
	2	3	4.2	1	1.7	4	3.1

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Characteristics	Parameters or Categories	nvac N = 71		vac N = 59		Total N = 130	
		Value or n	%	Value or n	%	Value or n	%
Respiratory infection[s] between 02-Aug-2006 and 31-Aug-2007	No	71	100	58	98.3	129	99.2
	Yes	0	0.0	1	1.7	1	0.8
Acute bacterial infection[s] between 02-Aug-2006 and 31-Aug-2007	No	71	100	59	100	130	100
	Yes	0	0.0	0	0.0	0	0.0
Opportunistic infection[s] between 02-Aug-2006 and 31-Aug-2007	No	70	98.6	57	96.6	127	97.7
	Yes	1	1.4	2	3.4	3	2.3
Chronic viral infection[s] between 05-Mar-2006 and 31-Aug-2007	No	71	100	59	100	130	100
	Yes	0	0.0	0	0.0	0	0.0
Malignancy/cancer[s] between 05-Mar-2006 and 31-Aug-2007	No	67	94.4	54	91.5	121	93.1
	Yes	4	5.6	5	8.5	9	6.9
Reasons for end of follow-up	End of season [31 August]	65	91.5	52	88.1	117	90.0
	Death	3	4.2	6	10.2	9	6.9
	End of CRPD GOLD follow-up	3	4.2	1	1.7	4	3.1

nvac = not_vaccinated

vac = vaccinated

*Transplantations could happen after 01-September 2006

**Each subject is classified in one category. All combinations are possible. All transplantations between 05-Mar-2006 and 31-Aug-2007 are considered.

n = number of subjects in a given category

Value = value of the considered parameter

% = n / Number of subjects with available results x 100

SD = Standard deviation

Table 8 Demographic and baseline characteristics of subjects with data for season 2007-2008 (Primary seasonal influenza subset)

Characteristics	Parameters or Categories	nvac N = 69		vac N = 67		Total N = 136	
		Value or n	%	Value or n	%	Value or n	%
Age at 01-Sep-2007 [years]	N	69	-	67	-	136	-
	Mean	42.4	-	52.6	-	47.4	-
	SD	18.03	-	17.27	-	18.31	-
	Median	44.0	-	51.0	-	46.0	-
	Minimum	1	-	9	-	1	-
	Maximum	75	-	87	-	87	-
Age group at 01-Sep-2007 [years]	[0-17]	7	10.1	2	3.0	9	6.6
	[18-44]	28	40.6	18	26.9	46	33.8
	[45-60]	24	34.8	23	34.3	47	34.6
	61+	10	14.5	24	35.8	34	25.0
Gender	Female	22	31.9	31	46.3	53	39.0
	Male	47	68.1	36	53.7	83	61.0
Died between 01-Sep-2007 and 31-Aug-2008	No	66	95.7	59	88.1	125	91.9
	Yes	3	4.3	8	11.9	11	8.1
Time since transplantation at 01-Sep-2007 [days]	Before transplantation or more than 180 days after transplantation	65	94.2	61	91.0	126	92.6
	0-30	1	1.4	0	0.0	1	0.7
	31-90	2	2.9	4	6.0	6	4.4
	91-180	1	1.4	2	3.0	3	2.2
Organ transplanted before or during the season**	Heart	2	2.9	2	3.0	4	2.9
	Kidney	16	23.2	6	9.0	22	16.2
	Kidney+Pancreas	0	0.0	4	6.0	4	2.9
	Liver	1	1.4	1	1.5	2	1.5
	Lung	0	0.0	1	1.5	1	0.7
	Pancreas	0	0.0	2	3.0	2	1.5
	No transplantation recorded	50	72.5	51	76.1	101	74.3
Number of rejections between 05-Mar-2007 and 01-Sep-2007	None	60	87.0	61	91.0	121	89.0
	At least one	9	13.0	6	9.0	15	11.0

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Characteristics	Parameters or Categories	nvac N = 69		vac N = 67		Total N = 136	
		Value or n	%	Value or n	%	Value or n	%
Number of transplantation events between 01-Sep-2007 and 31-Aug-2008	0	54	78.3	56	83.6	110	80.9
	1	14	20.3	9	13.4	23	16.9
	2	1	1.4	2	3.0	3	2.2
Respiratory infection[s] between 02-Aug-2007 and 31-Aug-2008	No	69	100	67	100	136	100
	Yes	0	0.0	0	0.0	0	0.0
Acute bacterial infection[s] between 02-Aug-2007 and 31-Aug-2008	No	69	100	67	100	136	100
	Yes	0	0.0	0	0.0	0	0.0
Opportunistic infection[s] between 02-Aug-2007 and 31-Aug-2008	No	67	97.1	65	97.0	132	97.1
	Yes	2	2.9	2	3.0	4	2.9
Chronic viral infection[s] between 01-Sep-2006 and 31-Aug-2008	No	69	100	67	100	136	100
	Yes	0	0.0	0	0.0	0	0.0
Malignancy/cancer[s] between 01-Sep-2006 and 31-Aug-2008	No	65	94.2	61	91.0	126	92.6
	Yes	4	5.8	6	9.0	10	7.4
Reasons for end of follow-up	End of season [31 August]	64	92.8	58	86.6	122	89.7
	Death	3	4.3	8	11.9	11	8.1
	End of CRPD GOLD follow-up	2	2.9	1	1.5	3	2.2

nvac = not_vaccinated

vac = vaccinated

*Transplantations could happen after 01-September 2007

**Each subject is classified in one category. All combinations are possible. All transplantations between 05-Mar-2007 and 31-Aug-2008 are considered.

N = number of subjects

n = number of subjects in a given category

Value = value of the considered parameter

% = n / Number of subjects with available results x 100

SD = Standard deviation

Table 9 Demographic and baseline characteristics of subjects with data for season 2007-2008 (Primary seasonal influenza subset, subjects with transplantation or rejection for only one organ)

Characteristics	Parameters or Categories	nvac N = 69		vac N = 59		Total N = 128	
		Value or n	%	Value or n	%	Value or n	%
Age at 01-Sep-2007 [years]	N	69	-	59	-	128	-
	Mean	42.4	-	53.8	-	47.7	-
	SD	18.03	-	17.62	-	18.66	-
	Median	44.0	-	57.0	-	46.0	-
	Minimum	1	-	9	-	1	-
	Maximum	75	-	87	-	87	-
Age group at 01-Sep-2007 [years]	[0-17]	7	10.1	2	3.4	9	7.0
	[18-44]	28	40.6	13	22.0	41	32.0
	[45-60]	24	34.8	21	35.6	45	35.2
	61+	10	14.5	23	39.0	33	25.8
Gender	Female	22	31.9	27	45.8	49	38.3
	Male	47	68.1	32	54.2	79	61.7
Died between 01-Sep-2007 and 31-Aug-2008	No	66	95.7	51	86.4	117	91.4
	Yes	3	4.3	8	13.6	11	8.6
Time since transplantation at 01-Sep-2007 [days]	Before transplantation or more than 180 days after transplantation	65	94.2	56	94.9	121	94.5
	0-30	1	1.4	0	0.0	1	0.8
	31-90	2	2.9	2	3.4	4	3.1
	91-180	1	1.4	1	1.7	2	1.6
Organ transplanted before or during the season**	Heart	2	2.9	2	3.4	4	3.1
	Kidney	16	23.2	6	10.2	22	17.2
	Liver	1	1.4	1	1.7	2	1.6
	Lung	0	0.0	1	1.7	1	0.8
	No transplantation recorded	50	72.5	49	83.1	99	77.3
Number of rejections between 05-Mar-2007 and 01-Sep-2007	None	60	87.0	54	91.5	114	89.1
	At least one	9	13.0	5	8.5	14	10.9
Number of transplantation events between 01-Sep-2007 and 31-Aug-2008	0	54	78.3	52	88.1	106	82.8
	1	14	20.3	6	10.2	20	15.6
	2	1	1.4	1	1.7	2	1.6

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Characteristics	Parameters or Categories	nvac N = 69		vac N = 59		Total N = 128	
		Value or n	%	Value or n	%	Value or n	%
Respiratory infection[s] between 02-Aug-2007 and 31-Aug-2008	No	69	100	59	100	128	100
	Yes	0	0.0	0	0.0	0	0.0
Acute bacterial infection[s] between 02-Aug-2007 and 31-Aug-2008	No	69	100	59	100	128	100
	Yes	0	0.0	0	0.0	0	0.0
Opportunistic infection[s] between 02-Aug-2007 and 31-Aug-2008	No	67	97.1	59	100	126	98.4
	Yes	2	2.9	0	0.0	2	1.6
Chronic viral infection[s] between 01-Sep-2006 and 31-Aug-2008	No	69	100	59	100	128	100
	Yes	0	0.0	0	0.0	0	0.0
Malignancy/cancer[s] between 01-Sep-2006 and 31-Aug-2008	No	65	94.2	53	89.8	118	92.2
	Yes	4	5.8	6	10.2	10	7.8
Reasons for end of follow-up	End of season [31 August]	64	92.8	50	84.7	114	89.1
	Death	3	4.3	8	13.6	11	8.6
	End of CRPD GOLD follow-up	2	2.9	1	1.7	3	2.3

nvac = not_vaccinated

vac = vaccinated

*Transplantations could happen after 01-September 2007

**Each subject is classified in one category. All combinations are possible. All transplantations between 05-Mar-2007 and 31-Aug-2008 are considered.

N = number of subjects

n = number of subjects in a given category

Value = value of the considered parameter

% = n / Number of subjects with available results x 100

SD = Standard deviation

Table 10 Demographic and baseline characteristics of subjects with data for season 2008-2009 (Primary seasonal influenza subset)

		nvac N = 83		vac N = 85		Total N = 168	
Characteristics	Parameters or Categories	Value or n	%	Value or n	%	Value or n	%
Age at 01-Sep-2008 [years]	N	83	-	85	-	168	-
	Mean	45.2	-	51.6	-	48.4	-
	SD	17.85	-	17.38	-	17.86	-
	Median	45.0	-	53.0	-	48.0	-
	Minimum	1	-	6	-	1	-
	Maximum	82	-	88	-	88	-
Age group at 01-Sep-2008 [years]	[0-17]	5	6.0	3	3.5	8	4.8
	[18-44]	36	43.4	26	30.6	62	36.9
	[45-60]	24	28.9	25	29.4	49	29.2
	61+	18	21.7	31	36.5	49	29.2
Gender	Female	36	43.4	35	41.2	71	42.3
	Male	47	56.6	50	58.8	97	57.7
Died between 01-Sep-2008 and 31-Aug-2009	No	77	92.8	79	92.9	156	92.9
	Yes	6	7.2	6	7.1	12	7.1
Time since transplantation at 01-Sep-2008 [days]	Before transplantation or more than 180 days after transplantation	82	98.8	79	92.9	161	95.8
	0-30	0	0.0	0	0.0	0	0.0
	31-90	1	1.2	0	0.0	1	0.6
	91-180	0	0.0	6	7.1	6	3.6
Organ transplanted before or during the season**	Kidney	11	13.3	16	18.8	27	16.1
	Kidney+Pancreas	1	1.2	2	2.4	3	1.8
	Liver	3	3.6	1	1.2	4	2.4
	Lung	0	0.0	3	3.5	3	1.8
	Pancreas	1	1.2	0	0.0	1	0.6
	No transplantation recorded	67	80.7	63	74.1	130	77.4
Number of rejections between 05-Mar-2008 and 01-Sep-2008	None	75	90.4	71	83.5	146	86.9
	At least one	8	9.6	14	16.5	22	13.1

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		nvac N = 83		vac N = 85		Total N = 168	
Characteristics	Parameters or Categories	Value or n	%	Value or n	%	Value or n	%
Number of transplantation events between 01-Sep-2008 and 31-Aug-2009	0	67	80.7	68	80.0	135	80.4
	1	15	18.1	13	15.3	28	16.7
	2	1	1.2	4	4.7	5	3.0
Respiratory infection[s] between 02-Aug-2008 and 31-Aug-2009	No	82	98.8	85	100	167	99.4
	Yes	1	1.2	0	0.0	1	0.6
Acute bacterial infection[s] between 02-Aug-2008 and 31-Aug-2009	No	83	100	85	100	168	100
	Yes	0	0.0	0	0.0	0	0.0
Opportunistic infection[s] between 02-Aug-2008 and 31-Aug-2009	No	83	100	81	95.3	164	97.6
	Yes	0	0.0	4	4.7	4	2.4
Chronic viral infection[s] between 01-Sep-2007 and 31-Aug-2009	No	83	100	85	100	168	100
	Yes	0	0.0	0	0.0	0	0.0
Malignancy/cancer[s] between 01-Sep-2007 and 31-Aug-2009	No	79	95.2	79	92.9	158	94.0
	Yes	4	4.8	6	7.1	10	6.0
Reasons for end of follow-up	End of season [31 August]	74	89.2	78	91.8	152	90.5
	Death	6	7.2	6	7.1	12	7.1
	End of CRPD GOLD follow-up	3	3.6	1	1.2	4	2.4

nvac = not_vaccinated

vac = vaccinated

*Transplantations could happen after 01-September 2008

**Each subject is classified in one category. All combinations are possible. All transplantations between 05-Mar-2008 and 31-Aug-2009 are considered.

N = number of subjects

n = number of subjects in a given category

Value = value of the considered parameter

% = n / Number of subjects with available results x 100

SD = Standard deviation

Table 11 Demographic and baseline characteristics of subjects with data for season 2008-2009 (Primary seasonal influenza subset, subjects with transplantation or rejection for only one organ)

		nvac N = 81		vac N = 82		Total N = 163	
Characteristics	Parameters or Categories	Value or n	%	Value or n	%	Value or n	%
Age at 01-Sep-2008 [years]	N	81	-	82	-	163	-
	Mean	45.3	-	52.2	-	48.8	-
	SD	18.05	-	17.35	-	17.99	-
	Median	45.0	-	54.0	-	49.0	-
	Minimum	1	-	6	-	1	-
	Maximum	82	-	88	-	88	-
Age group at 01-Sep-2008 [years]	[0-17]	5	6.2	3	3.7	8	4.9
	[18-44]	34	42.0	23	28.0	57	35.0
	[45-60]	24	29.6	25	30.5	49	30.1
	61+	18	22.2	31	37.8	49	30.1
Gender	Female	35	43.2	34	41.5	69	42.3
	Male	46	56.8	48	58.5	94	57.7
Died between 01-Sep-2008 and 31-Aug-2009	No	75	92.6	76	92.7	151	92.6
	Yes	6	7.4	6	7.3	12	7.4
Time since transplantation at 01-Sep-2008 [days]	Before transplantation or more than 180 days after transplantation	80	98.8	78	95.1	158	96.9
	0-30	0	0.0	0	0.0	0	0.0
	31-90	1	1.2	0	0.0	1	0.6
	91-180	0	0.0	4	4.9	4	2.5
Organ transplanted before or during the season**	Kidney	11	13.6	16	19.5	27	16.6
	Liver	3	3.7	1	1.2	4	2.5
	Lung	0	0.0	2	2.4	2	1.2
	No transplantation recorded	67	82.7	63	76.8	130	79.8
Number of rejections between 05-Mar-2008 and 01-Sep-2008	None	73	90.1	69	84.1	142	87.1
	At least one	8	9.9	13	15.9	21	12.9
Number of transplantation events between 01-Sep-2008 and 31-Aug-2009	0	67	82.7	67	81.7	134	82.2
	1	14	17.3	12	14.6	26	16.0
	2	0	0.0	3	3.7	3	1.8
Respiratory infection[s] between 02-Aug-2008 and 31-Aug-2009	No	80	98.8	82	100	162	99.4
	Yes	1	1.2	0	0.0	1	0.6

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Characteristics	Parameters or Categories	nvac N = 81		vac N = 82		Total N = 163	
		Value or n	%	Value or n	%	Value or n	%
Acute bacterial infection[s] between 02-Aug-2008 and 31-Aug-2009	No	81	100	82	100	163	100
	Yes	0	0.0	0	0.0	0	0.0
Opportunistic infection[s] between 02-Aug-2008 and 31-Aug-2009	No	81	100	78	95.1	159	97.5
	Yes	0	0.0	4	4.9	4	2.5
Chronic viral infection[s] between 01-Sep-2007 and 31-Aug-2009	No	81	100	82	100	163	100
	Yes	0	0.0	0	0.0	0	0.0
Malignancy/cancer[s] between 01-Sep-2007 and 31-Aug-2009	No	77	95.1	76	92.7	153	93.9
	Yes	4	4.9	6	7.3	10	6.1
Reasons for end of follow-up	End of season [31 August]	72	88.9	75	91.5	147	90.2
	Death	6	7.4	6	7.3	12	7.4
	End of CRPD GOLD follow-up	3	3.7	1	1.2	4	2.5

nvac = not_vaccinated

vac = vaccinated

*Transplantations could happen after 01-September 2008

**Each subject is classified in one category. All combinations are possible. All transplantations between 05-Mar-2008 and 31-Aug-2009 are considered.

N = number of subjects

n = number of subjects in a given category

Value = value of the considered parameter

% = n / Number of subjects with available results x 100

SD = Standard deviation

Table 12 Demographic and baseline characteristics of subjects with data for pooled seasonal analysis (Primary seasonal influenza subset)

		nvac N = 200		vac N = 175		Total N = 375	
Characteristics	Parameters or Categories	Value or n	%	Value or n	%	Value or n	%
Age at the beginning of the analysed season [years]	N	200	-	175	-	375	-
	Mean	43.7	-	53.1	-	48.1	-
	SD	17.75	-	18.18	-	18.53	-
	Median	45.0	-	53.0	-	48.0	-
	Minimum	1	-	6	-	1	-
	Maximum	82	-	90	-	90	-
Age group at the beginning of the analysable season	[0-17]	16	8.0	7	4.0	23	6.1
	[18-44]	82	41.0	48	27.4	130	34.7
	[45-60]	70	35.0	54	30.9	124	33.1
	61+	32	16.0	66	37.7	98	26.1
Gender	Female	74	37.0	70	40.0	144	38.4
	Male	126	63.0	105	60.0	231	61.6
Died during the analysed season	No	190	95.0	160	91.4	350	93.3
	Yes	10	5.0	15	8.6	25	6.7
Time since transplantation at the beginning of the analysed season [days]	Before transplantation or more than 180 days after transplantation	192	96.0	163	93.1	355	94.7
	0-30	2	1.0	0	0.0	2	0.5
	31-90	5	2.5	6	3.4	11	2.9
	91-180	1	0.5	6	3.4	7	1.9
Organ transplanted before or during the season**	Heart	3	1.5	3	1.7	6	1.6
	Heart+Lung	1	0.5	0	0.0	1	0.3
	Kidney	34	17.0	32	18.3	66	17.6
	Kidney+Pancreas	1	0.5	5	2.9	6	1.6
	Liver	7	3.5	5	2.9	12	3.2
	Lung	2	1.0	4	2.3	6	1.6
	Pancreas	1	0.5	2	1.1	3	0.8
	No transplantation recorded	151	75.5	124	70.9	275	73.3
Number of rejections	None	195	97.5	164	93.7	359	95.7
	At least one	5	2.5	11	6.3	16	4.3

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		nvac N = 200		vac N = 175		Total N = 375	
Characteristics	Parameters or Categories	Value or n	%	Value or n	%	Value or n	%
Number of transplantation events	0	158	79.0	135	77.1	293	78.1
	1	36	18.0	33	18.9	69	18.4
	2	6	3.0	7	4.0	13	3.5
Respiratory infection[s]	No	199	99.5	174	99.4	373	99.5
	Yes	1	0.5	1	0.6	2	0.5
Acute bacterial infection[s]	No	200	100	175	100	375	100
	Yes	0	0.0	0	0.0	0	0.0
Opportunistic infection[s]	No	197	98.5	169	96.6	366	97.6
	Yes	3	1.5	6	3.4	9	2.4
Chronic viral infection[s]	No	200	100	175	100	375	100
	Yes	0	0.0	0	0.0	0	0.0
Malignancy/cancer[s]	No	188	94.0	162	92.6	350	93.3
	Yes	12	6.0	13	7.4	25	6.7
Reasons for end of follow-up	End of season [31 August]	183	91.5	157	89.7	340	90.7
	Death	10	5.0	15	8.6	25	6.7
	End of CRPD GOLD follow-up	7	3.5	3	1.7	10	2.7

nvac = not_vaccinated

vac = vaccinated

*Transplantations could happen after 01-September

**Each subject is classified in one category. All combinations are possible. All transplantations between 05-March and 31-August of next year are considered.

N = number of subjects

n = number of subjects in a given category

Value = value of the considered parameter

% = n / Number of subjects with available results x 100

SD = Standard deviation

Note: For each subject, data used for pooled analysis was data of the first season analysed

Table 13 Demographic and baseline characteristics of subjects with data for pooled seasonal analysis (Primary seasonal influenza subset, subjects with transplantation or rejection for only one organ)

Characteristics	Parameters or Categories	nvac N = 197		vac N = 166		Total N = 363	
		Value or n	%	Value or n	%	Value or n	%
Age at the beginning of the analysed season [years]	N	197	-	166	-	363	-
	Mean	43.7	-	53.7	-	48.2	-
	SD	17.86	-	18.34	-	18.73	-
	Median	45.0	-	55.0	-	48.0	-
	Minimum	1	-	6	-	1	-
	Maximum	82	-	90	-	90	-
Age group at the beginning of the analysed season	[0-17]	16	8.1	7	4.2	23	6.3
	[18-44]	80	40.6	42	25.3	122	33.6
	[45-60]	69	35.0	52	31.3	121	33.3
	61+	32	16.2	65	39.2	97	26.7
Gender	Female	73	37.1	66	39.8	139	38.3
	Male	124	62.9	100	60.2	224	61.7
Died during the analysed season	No	187	94.9	151	91.0	338	93.1
	Yes	10	5.1	15	9.0	25	6.9
Time since transplantation at the beginning of the analysed season [days]	Before transplantation or more than 180 days after transplantation	189	95.9	157	94.6	346	95.3
	0-30	2	1.0	0	0.0	2	0.6
	31-90	5	2.5	4	2.4	9	2.5
	91-180	1	0.5	5	3.0	6	1.7
Organ transplanted before or during the season**	Heart	3	1.5	3	1.8	6	1.7
	Kidney	34	17.3	32	19.3	66	18.2
	Liver	7	3.6	5	3.0	12	3.3
	Lung	2	1.0	4	2.4	6	1.7
	No transplantation recorded	151	76.6	122	73.5	273	75.2
Number of rejections	None	192	97.5	155	93.4	347	95.6
	At least one	5	2.5	11	6.6	16	4.4
Number of transplantation events	0	158	80.2	131	78.9	289	79.6
	1	35	17.8	30	18.1	65	17.9
	2	4	2.0	5	3.0	9	2.5

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		nvac N = 197		vac N = 166		Total N = 363	
Characteristics	Parameters or Categories	Value or n	%	Value or n	%	Value or n	%
Respiratory infection[s]	No	196	99.5	165	99.4	361	99.4
	Yes	1	0.5	1	0.6	2	0.6
Acute bacterial infection[s]	No	197	100	166	100	363	100
	Yes	0	0.0	0	0.0	0	0.0
Opportunistic infection[s]	No	194	98.5	162	97.6	356	98.1
	Yes	3	1.5	4	2.4	7	1.9
Chronic viral infection[s]	No	197	100	166	100	363	100
	Yes	0	0.0	0	0.0	0	0.0
Malignancy/cancer[s]	No	185	93.9	153	92.2	338	93.1
	Yes	12	6.1	13	7.8	25	6.9
Reasons for end of follow-up	End of season [31 August]	180	91.4	148	89.2	328	90.4
	Death	10	5.1	15	9.0	25	6.9
	End of CRPD GOLD follow-up	7	3.6	3	1.8	10	2.8

nvac = not_vaccinated

vac = vaccinated

*Transplantations could happen after 01-September

**Each subject is classified in one category. All combinations are possible. All transplantations between 05-March and 31-August of next year are considered.

N = number of subjects

n = number of subjects in a given category

Value = value of the considered parameter

% = n / Number of subjects with available results x 100

SD = Standard deviation

Note: For each subject, data used for pooled analysis was data of the first season analysed

Table 14 Demographic and baseline characteristics of subjects with data for season 2006-2007 (Secondary seasonal influenza subset)

		nvac N = 27		vac N = 21		Total N = 48	
Characteristics	Parameters or Categories	Value or n	%	Value or n	%	Value or n	%
Age at 01-Sep-2006 [years]	N	27	-	21	-	48	-
	Mean	47.3	-	55.6	-	50.9	-
	SD	13.15	-	21.70	-	17.71	-
	Median	47.0	-	55.0	-	50.0	-
	Minimum	26	-	15	-	15	-
	Maximum	74	-	88	-	88	-
Age group at 01-Sep-2006 [years]	[0-17]	0	0.0	1	4.8	1	2.1
	[18-44]	12	44.4	5	23.8	17	35.4
	[45-60]	11	40.7	6	28.6	17	35.4
	61+	4	14.8	9	42.9	13	27.1
Gender	Female	6	22.2	6	28.6	12	25.0
	Male	21	77.8	15	71.4	36	75.0
Died between 01-Sep-2006 and 31-Aug-2007	No	25	92.6	18	85.7	43	89.6
	Yes	2	7.4	3	14.3	5	10.4
Time since transplantation at 01-Sep-2006 [days]	Before transplantation or more than 180 days after transplantation	26	96.3	21	100	47	97.9
	0-30	0	0.0	0	0.0	0	0.0
	31-90	1	3.7	0	0.0	1	2.1
	91-180	0	0.0	0	0.0	0	0.0
Organ transplanted before or during the season**	Heart	1	3.7	1	4.8	2	4.2
	Heart+Lung	1	3.7	0	0.0	1	2.1
	Kidney	4	14.8	3	14.3	7	14.6
	Liver	2	7.4	1	4.8	3	6.3
	No transplantation recorded	19	70.4	16	76.2	35	72.9
Number of rejections between 05-Mar-2006 and 01-Sep-2006	None	25	92.6	19	90.5	44	91.7
	At least one	2	7.4	2	9.5	4	8.3
Number of transplantation events between 01-Sep-2006 and 31-Aug-2007	0	20	74.1	16	76.2	36	75.0
	1	4	14.8	5	23.8	9	18.8
	2	3	11.1	0	0.0	3	6.3

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Characteristics	Parameters or Categories	nvac N = 27		vac N = 21		Total N = 48	
		Value or n	%	Value or n	%	Value or n	%
Respiratory infection[s] between 02-Aug-2006 and 31-Aug-2007	No	27	100	20	95.2	47	97.9
	Yes	0	0.0	1	4.8	1	2.1
Acute bacterial infection[s] between 02-Aug-2006 and 31-Aug-2007	No	27	100	21	100	48	100
	Yes	0	0.0	0	0.0	0	0.0
Opportunistic infection[s] between 02-Aug-2006 and 31-Aug-2007	No	25	92.6	20	95.2	45	93.8
	Yes	2	7.4	1	4.8	3	6.3
Chronic viral infection[s] between 05-Mar-2006 and 31-Aug-2007	No	27	100	21	100	48	100
	Yes	0	0.0	0	0.0	0	0.0
Malignancy/cancer[s] between 05-Mar-2006 and 31-Aug-2007	No	26	96.3	18	85.7	44	91.7
	Yes	1	3.7	3	14.3	4	8.3
Chemotherapy between 01-Sep-2005 and 31-Aug-2007	No	26	96.3	21	100	47	97.9
	Yes	1	3.7	0	0.0	1	2.1
Reasons for end of follow-up	End of season [31 August]	24	88.9	18	85.7	42	87.5
	Death	2	7.4	3	14.3	5	10.4
	End of CRPD GOLD follow-up	1	3.7	0	0.0	1	2.1

nvac = not_vaccinated

vac = vaccinated

*Transplantations could happen after 01-September 2006

**Each subject is classified in one category. All combinations are possible. All transplantations between 05-Mar-2006 and 31-Aug-2007 are considered.

N = number of subjects

n = number of subjects in a given category

Value = value of the considered parameter

% = n / Number of subjects with available results x 100

SD = Standard deviation

Table 15 Demographic and baseline characteristics of subjects with data for season 2006-2007 (Secondary seasonal influenza subset, subjects with transplantation or rejection for only one organ)

		nvac N = 26		vac N = 19		Total N = 45	
Characteristics	Parameters or Categories	Value or n	%	Value or n	%	Value or n	%
Age at 01-Sep-2006 [years]	N	26	-	19	-	45	-
	Mean	47.0	-	57.3	-	51.3	-
	SD	13.31	-	21.91	-	17.99	-
	Median	46.0	-	60.0	-	49.0	-
	Minimum	26	-	15	-	15	-
	Maximum	74	-	88	-	88	-
Age group at 01-Sep-2006 [years]	[0-17]	0	0.0	1	5.3	1	2.2
	[18-44]	12	46.2	4	21.1	16	35.6
	[45-60]	10	38.5	5	26.3	15	33.3
	61+	4	15.4	9	47.4	13	28.9
Gender	Female	6	23.1	6	31.6	12	26.7
	Male	20	76.9	13	68.4	33	73.3
Died between 01-Sep-2006 and 31-Aug-2007	No	24	92.3	16	84.2	40	88.9
	Yes	2	7.7	3	15.8	5	11.1
Time since transplantation at 01-Sep-2006 [days]	Before transplantation or more than 180 days after transplantation	25	96.2	19	100	44	97.8
	0-30	0	0.0	0	0.0	0	0.0
	31-90	1	3.8	0	0.0	1	2.2
	91-180	0	0.0	0	0.0	0	0.0
Organ transplanted before or during the season**	Heart	1	3.8	1	5.3	2	4.4
	Kidney	4	15.4	3	15.8	7	15.6
	Liver	2	7.7	1	5.3	3	6.7
	No transplantation recorded	19	73.1	14	73.7	33	73.3
Number of rejections between 05-Mar-2006 and 01-Sep-2006	None	24	92.3	18	94.7	42	93.3
	At least one	2	7.7	1	5.3	3	6.7
Number of transplantation events between 01-Sep-2006 and 31-Aug-2007	0	20	76.9	14	73.7	34	75.6
	1	4	15.4	5	26.3	9	20.0
	2	2	7.7	0	0.0	2	4.4
Respiratory infection[s] between 02-Aug-2006 and 31-Aug-2007	No	26	100	18	94.7	44	97.8
	Yes	0	0.0	1	5.3	1	2.2

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Characteristics	Parameters or Categories	nvac N = 26		vac N = 19		Total N = 45	
		Value or n	%	Value or n	%	Value or n	%
Acute bacterial infection[s] between 02-Aug-2006 and 31-Aug-2007	No	26	100	19	100	45	100
	Yes	0	0.0	0	0.0	0	0.0
Opportunistic infection[s] between 02-Aug-2006 and 31-Aug-2007	No	24	92.3	18	94.7	42	93.3
	Yes	2	7.7	1	5.3	3	6.7
Chronic viral infection[s] between 05-Mar-2006 and 31-Aug-2007	No	26	100	19	100	45	100
	Yes	0	0.0	0	0.0	0	0.0
Malignancy/cancer[s] between 05-Mar-2006 and 31-Aug-2007	No	25	96.2	16	84.2	41	91.1
	Yes	1	3.8	3	15.8	4	8.9
Chemotherapy between 01-Sep-2005 and 31-Aug-2007	No	25	96.2	19	100	44	97.8
	Yes	1	3.8	0	0.0	1	2.2
Reasons for end of follow-up	End of season [31 August]	23	88.5	16	84.2	39	86.7
	Death	2	7.7	3	15.8	5	11.1
	End of CRPD GOLD follow-up	1	3.8	0	0.0	1	2.2

nvac = not_vaccinated

vac = vaccinated

*Transplantations could happen after 01-September 2006

**Each subject is classified in one category. All combinations are possible. All transplantations between 05-Mar-2006 and 31-Aug-2007 are considered.

N = number of subjects

n = number of subjects in a given category

Value = value of the considered parameter

% = n / Number of subjects with available results x 100

SD = Standard deviation

Table 16 Demographic and baseline characteristics of subjects with data for season 2007-2008 (Secondary seasonal influenza subset)

		nvac N = 28		vac N = 27		Total N = 55	
Characteristics	Parameters or Categories	Value or n	%	Value or n	%	Value or n	%
Age at 01-Sep-2007 [years]	N	28	-	27	-	55	-
	Mean	49.9	-	54.2	-	52.0	-
	SD	17.48	-	16.20	-	16.85	-
	Median	51.5	-	49.0	-	51.0	-
	Minimum	13	-	25	-	13	-
	Maximum	75	-	87	-	87	-
Age group at 01-Sep-2007 [years]	[0-17]	2	7.1	0	0.0	2	3.6
	[18-44]	7	25.0	7	25.9	14	25.5
	[45-60]	11	39.3	10	37.0	21	38.2
	61+	8	28.6	10	37.0	18	32.7
Gender	Female	10	35.7	7	25.9	17	30.9
	Male	18	64.3	20	74.1	38	69.1
Died between 01-Sep-2007 and 31-Aug-2008	No	27	96.4	24	88.9	51	92.7
	Yes	1	3.6	3	11.1	4	7.3
Time since transplantation at 01-Sep-2007 [days]	Before transplantation or more than 180 days after transplantation	26	92.9	26	96.3	52	94.5
	0-30	0	0.0	0	0.0	0	0.0
	31-90	2	7.1	0	0.0	2	3.6
	91-180	0	0.0	1	3.7	1	1.8
Organ transplanted before or during the season**	Heart	1	3.6	0	0.0	1	1.8
	Kidney	6	21.4	2	7.4	8	14.5
	Kidney+Pancreas	0	0.0	2	7.4	2	3.6
	Liver	2	7.1	1	3.7	3	5.5
	No transplantation recorded	19	67.9	22	81.5	41	74.5
Number of rejections between 05-Mar-2007 and 01-Sep-2007	None	24	85.7	22	81.5	46	83.6
	At least one	4	14.3	5	18.5	9	16.4
Number of transplantation events between 01-Sep-2007 and 31-Aug-2008	0	21	75.0	23	85.2	44	80.0
	1	6	21.4	3	11.1	9	16.4
	2	1	3.6	1	3.7	2	3.6

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Characteristics	Parameters or Categories	nvac N = 28		vac N = 27		Total N = 55	
		Value or n	%	Value or n	%	Value or n	%
Respiratory infection[s] between 02-Aug-2007 and 31-Aug-2008	No	23	82.1	23	85.2	46	83.6
	Yes	5	17.9	4	14.8	9	16.4
Acute bacterial infection[s] between 02-Aug-2007 and 31-Aug-2008	No	28	100	27	100	55	100
	Yes	0	0.0	0	0.0	0	0.0
Opportunistic infection[s] between 02-Aug-2007 and 31-Aug-2008	No	27	96.4	25	92.6	52	94.5
	Yes	1	3.6	2	7.4	3	5.5
Chronic viral infection[s] between 01-Sep-2006 and 31-Aug-2008	No	28	100	27	100	55	100
	Yes	0	0.0	0	0.0	0	0.0
Malignancy/cancer[s] between 01-Sep-2006 and 31-Aug-2008	No	26	92.9	24	88.9	50	90.9
	Yes	2	7.1	3	11.1	5	9.1
Chemotherapy between 01-Sep-2006 and 31-Aug-2008	No	25	89.3	25	92.6	50	90.9
	Yes	3	10.7	2	7.4	5	9.1
Reasons for end of follow-up	End of season [31 August]	27	96.4	23	85.2	50	90.9
	Death	1	3.6	3	11.1	4	7.3
	End of CRPD GOLD follow-up	0	0.0	1	3.7	1	1.8

nvac = not_vaccinated

vac = vaccinated

*Transplantations could happen after 01-September 2007

**Each subject is classified in one category. All combinations are possible. All transplantations between 05-Mar-2007 and 31-Aug-2008 are considered.

N = number of subjects

n = number of subjects in a given category

Value = value of the considered parameter

% = n / Number of subjects with available results x 100

SD = Standard deviation

Table 17 Demographic and baseline characteristics of subjects with data for season 2007-2008 (Secondary seasonal influenza subset, subjects with transplantation or rejection for only one organ)

		nvac N = 28		vac N = 24		Total N = 52	
Characteristics	Parameters or Categories	Value or n	%	Value or n	%	Value or n	%
Age at 01-Sep-2007 [years]	N	28	-	24	-	52	-
	Mean	49.9	-	55.2	-	52.3	-
	SD	17.48	-	16.86	-	17.23	-
	Median	51.5	-	51.5	-	51.5	-
	Minimum	13	-	25	-	13	-
	Maximum	75	-	87	-	87	-
Age group at 01-Sep-2007 [years]	[0-17]	2	7.1	0	0.0	2	3.8
	[18-44]	7	25.0	6	25.0	13	25.0
	[45-60]	11	39.3	8	33.3	19	36.5
	61+	8	28.6	10	41.7	18	34.6
Gender	Female	10	35.7	7	29.2	17	32.7
	Male	18	64.3	17	70.8	35	67.3
Died between 01-Sep-2007 and 31-Aug-2008	No	27	96.4	21	87.5	48	92.3
	Yes	1	3.6	3	12.5	4	7.7
Time since transplantation at 01-Sep-2007 [days]	Before transplantation or more than 180 days after transplantation	26	92.9	24	100	50	96.2
	0-30	0	0.0	0	0.0	0	0.0
	31-90	2	7.1	0	0.0	2	3.8
	91-180	0	0.0	0	0.0	0	0.0
Organ transplanted before or during the season**	Heart	1	3.6	0	0.0	1	1.9
	Kidney	6	21.4	2	8.3	8	15.4
	Liver	2	7.1	1	4.2	3	5.8
	No transplantation recorded	19	67.9	21	87.5	40	76.9
Number of rejections between 05-Mar-2007 and 01-Sep-2007	None	24	85.7	20	83.3	44	84.6
	At least one	4	14.3	4	16.7	8	15.4
Number of transplantation events between 01-Sep-2007 and 31-Aug-2008	0	21	75.0	21	87.5	42	80.8
	1	6	21.4	3	12.5	9	17.3
	2	1	3.6	0	0.0	1	1.9
Respiratory infection[s] between 02-Aug-2007 and 31-Aug-2008	No	23	82.1	20	83.3	43	82.7
	Yes	5	17.9	4	16.7	9	17.3

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		nvac N = 28		vac N = 24		Total N = 52	
Characteristics	Parameters or Categories	Value or n	%	Value or n	%	Value or n	%
Acute bacterial infection[s] between 02-Aug-2007 and 31-Aug-2008	No	28	100	24	100	52	100
	Yes	0	0.0	0	0.0	0	0.0
Opportunistic infection[s] between 02-Aug-2007 and 31-Aug-2008	No	27	96.4	23	95.8	50	96.2
	Yes	1	3.6	1	4.2	2	3.8
Chronic viral infection[s] between 01-Sep-2006 and 31-Aug-2008	No	28	100	24	100	52	100
	Yes	0	0.0	0	0.0	0	0.0
Malignancy/cancer[s] between 01-Sep-2006 and 31-Aug-2008	No	26	92.9	21	87.5	47	90.4
	Yes	2	7.1	3	12.5	5	9.6
Chemotherapy between 01-Sep-2006 and 31-Aug-2008	No	25	89.3	22	91.7	47	90.4
	Yes	3	10.7	2	8.3	5	9.6
Reasons for end of follow-up	End of season [31 August]	27	96.4	20	83.3	47	90.4
	Death	1	3.6	3	12.5	4	7.7
	End of CRPD GOLD follow-up	0	0.0	1	4.2	1	1.9

nvac = not_vaccinated

vac = vaccinated

*Transplantations could happen after 01-September 2007

**Each subject is classified in one category. All combinations are possible. All transplantations between 05-Mar-2007 and 31-Aug-2008 are considered.

N = number of subjects

n = number of subjects in a given category

Value = value of the considered parameter

% = n / Number of subjects with available results x 100

SD = Standard deviation

Table 18 Demographic and baseline characteristics of subjects with data for season 2008-2009 (Secondary seasonal influenza subset)

		nvac N = 32		vac N = 35		Total N = 67	
Characteristics	Parameters or Categories	Value or n	%	Value or n	%	Value or n	%
Age at 01-Sep-2008 [years]	N	32	-	35	-	67	-
	Mean	47.9	-	51.9	-	50.0	-
	SD	18.37	-	19.79	-	19.09	-
	Median	47.0	-	60.0	-	51.0	-
	Minimum	5	-	6	-	5	-
	Maximum	77	-	84	-	84	-
Age group at 01-Sep-2008 [years]	[0-17]	2	6.3	2	5.7	4	6.0
	[18-44]	12	37.5	11	31.4	23	34.3
	[45-60]	9	28.1	5	14.3	14	20.9
	61+	9	28.1	17	48.6	26	38.8
Gender	Female	12	37.5	16	45.7	28	41.8
	Male	20	62.5	19	54.3	39	58.2
Died between 01-Sep-2008 and 31-Aug-2009	No	28	87.5	34	97.1	62	92.5
	Yes	4	12.5	1	2.9	5	7.5
Time since transplantation at 01-Sep-2008 [days]	Before transplantation or more than 180 days after transplantation	32	100	34	97.1	66	98.5
	0-30	0	0.0	0	0.0	0	0.0
	31-90	0	0.0	0	0.0	0	0.0
	91-180	0	0.0	1	2.9	1	1.5
Organ transplanted before or during the season**	Kidney	2	6.3	7	20.0	9	13.4
	Kidney+Pancreas	1	3.1	2	5.7	3	4.5
	Liver	2	6.3	0	0.0	2	3.0
	Pancreas	1	3.1	0	0.0	1	1.5
	No transplantation recorded	26	81.3	26	74.3	52	77.6
Number of rejections between 05-Mar-2008 and 01-Sep-2008	None	28	87.5	27	77.1	55	82.1
	At least one	4	12.5	8	22.9	12	17.9

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		nvac N = 32		vac N = 35		Total N = 67	
Characteristics	Parameters or Categories	Value or n	%	Value or n	%	Value or n	%
Number of transplantation events between 01-Sep-2008 and 31-Aug-2009	0	26	81.3	27	77.1	53	79.1
	1	5	15.6	5	14.3	10	14.9
	2	1	3.1	2	5.7	3	4.5
	3	0	0.0	1	2.9	1	1.5
Respiratory infection[s] between 02-Aug-2008 and 31-Aug-2009	No	30	93.8	34	97.1	64	95.5
	Yes	2	6.3	1	2.9	3	4.5
Acute bacterial infection[s] between 02-Aug-2008 and 31-Aug-2009	No	32	100	35	100	67	100
	Yes	0	0.0	0	0.0	0	0.0
Opportunistic infection[s] between 02-Aug-2008 and 31-Aug-2009	No	31	96.9	31	88.6	62	92.5
	Yes	1	3.1	4	11.4	5	7.5
Chronic viral infection[s] between 01-Sep-2007 and 31-Aug-2009	No	32	100	35	100	67	100
	Yes	0	0.0	0	0.0	0	0.0
Malignancy/cancer[s] between 01-Sep-2007 and 31-Aug-2009	No	31	96.9	33	94.3	64	95.5
	Yes	1	3.1	2	5.7	3	4.5
Chemotherapy between 01-Sep-2007 and 31-Aug-2009	No	28	87.5	32	91.4	60	89.6
	Yes	4	12.5	3	8.6	7	10.4
Reasons for end of follow-up	End of season [31 August]	28	87.5	34	97.1	62	92.5
	Death	4	12.5	1	2.9	5	7.5
	End of CRPD GOLD follow-up	0	0.0	0	0.0	0	0.0

nvac = not_vaccinated

vac = vaccinated

*Transplantations could happen after 01-September 2008

**Each subject is classified in one category. All combinations are possible. All transplantations between 05-Mar-2008 and 31-Aug-2009 are considered.

N = number of subjects

n = number of subjects in a given category

Value = value of the considered parameter

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% = n / Number of subjects with available results x 100
SD = Standard deviation

Table 19 Demographic and baseline characteristics of subjects with data for season 2008-2009 (Secondary seasonal influenza subset, subjects with transplantation or rejection for only one organ)

		nvac N = 30		vac N = 33		Total N = 63	
Characteristics	Parameters or Categories	Value or n	%	Value or n	%	Value or n	%
Age at 01-Sep-2008 [years]	N	30	-	33	-	63	-
	Mean	48.5	-	52.8	-	50.7	-
	SD	18.86	-	20.10	-	19.48	-
	Median	47.5	-	61.0	-	53.0	-
	Minimum	5	-	6	-	5	-
	Maximum	77	-	84	-	84	-
Age group at 01-Sep-2009 [years]	[0-17]	2	6.7	2	6.1	4	6.3
	[18-44]	10	33.3	9	27.3	19	30.2
	[45-60]	9	30.0	5	15.2	14	22.2
	61+	9	30.0	17	51.5	26	41.3
Gender	Female	11	36.7	15	45.5	26	41.3
	Male	19	63.3	18	54.5	37	58.7
Died between 01-Sep-2008 and 31-Aug-2009	No	26	86.7	32	97.0	58	92.1
	Yes	4	13.3	1	3.0	5	7.9
Time since transplantation at 01-Sep-2008 [days]	Before transplantation or more than 180 days after transplantation	30	100	32	97.0	62	98.4
	0-30	0	0.0	0	0.0	0	0.0
	31-90	0	0.0	0	0.0	0	0.0
	91-180	0	0.0	1	3.0	1	1.6
Organ transplanted before or during the season**	Kidney	2	6.7	7	21.2	9	14.3
	Liver	2	6.7	0	0.0	2	3.2
	No transplantation recorded	26	86.7	26	78.8	52	82.5
Number of rejections between 05-Mar-2008 and 01-Sep-2008	None	26	86.7	25	75.8	51	81.0
	At least one	4	13.3	8	24.2	12	19.0
Number of transplantation events between 01-Sep-2008 and 31-Aug-2009	0	26	86.7	27	81.8	53	84.1
	1	4	13.3	5	15.2	9	14.3
	2	0	0.0	1	3.0	1	1.6

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Characteristics	Parameters or Categories	nvac N = 30		vac N = 33		Total N = 63	
		Value or n	%	Value or n	%	Value or n	%
Respiratory infection[s] between 02-Aug-2008 and 31-Aug-2009	No	28	93.3	32	97.0	60	95.2
	Yes	2	6.7	1	3.0	3	4.8
Acute bacterial infection[s] between 02-Aug-2008 and 31-Aug-2009	No	30	100	33	100	63	100
	Yes	0	0.0	0	0.0	0	0.0
Opportunistic infection[s] between 02-Aug-2008 and 31-Aug-2009	No	29	96.7	29	87.9	58	92.1
	Yes	1	3.3	4	12.1	5	7.9
Chronic viral infection[s] between 01-Sep-2007 and 31-Aug-2009	No	30	100	33	100	63	100
	Yes	0	0.0	0	0.0	0	0.0
Malignancy/cancer[s] between 01-Sep-2007 and 31-Aug-2009	No	29	96.7	31	93.9	60	95.2
	Yes	1	3.3	2	6.1	3	4.8
Chemotherapy between 01-Sep-2007 and 31-Aug-2009	No	26	86.7	30	90.9	56	88.9
	Yes	4	13.3	3	9.1	7	11.1
Reasons for end of follow-up	End of season [31 August]	26	86.7	32	97.0	58	92.1
	Death	4	13.3	1	3.0	5	7.9
	End of CRPD GOLD follow-up	0	0.0	0	0.0	0	0.0

nvac = not_vaccinated

vac = vaccinated

*Transplantations could happen after 01-September 2008

**Each subject is classified in one category. All combinations are possible. All transplantations between 05-Mar-2008 and 31-Aug-2009 are considered.

N = number of subjects

n = number of subjects in a given category

Value = value of the considered parameter

% = n / Number of subjects with available results x 100

SD = Standard deviation

Table 20 Demographic and baseline characteristics of subjects with data for pooled seasonal analysis (Secondary seasonal influenza subset)

		nvac N = 76		vac N = 64		Total N = 140	
Characteristics	Parameters or Categories	Value or n	%	Value or n	%	Value or n	%
Age at the beginning of the analysed season [years]	N	76	-	64	-	140	-
	Mean	48.0	-	54.1	-	50.8	-
	SD	15.91	-	19.82	-	18.00	-
	Median	48.0	-	55.0	-	51.0	-
	Minimum	5	-	6	-	5	-
	Maximum	77	-	88	-	88	-
Age group at the beginning of the analysed season	[0-17]	3	3.9	3	4.7	6	4.3
	[18-44]	28	36.8	16	25.0	44	31.4
	[45-60]	29	38.2	16	25.0	45	32.1
	61+	16	21.1	29	45.3	45	32.1
Gender	Female	24	31.6	22	34.4	46	32.9
	Male	52	68.4	42	65.6	94	67.1
Died during the analysed season	No	70	92.1	58	90.6	128	91.4
	Yes	6	7.9	6	9.4	12	8.6
Time since transplantation at the beginning of the analysed season [days]	Before transplantation or more than 180 days after transplantation	73	96.1	62	96.9	135	96.4
	0-30	0	0.0	0	0.0	0	0.0
	31-90	3	3.9	0	0.0	3	2.1
	91-180	0	0.0	2	3.1	2	1.4
Organ transplanted before or during the season**	Heart	2	2.6	1	1.6	3	2.1
	Heart+Lung	1	1.3	0	0.0	1	0.7
	Kidney	11	14.5	11	17.2	22	15.7
	Kidney+Pancreas	1	1.3	4	6.3	5	3.6
	Liver	6	7.9	2	3.1	8	5.7
	No transplantation recorded	55	72.4	46	71.9	101	72.1
Number of rejections	None	74	97.4	61	95.3	135	96.4
	At least one	2	2.6	3	4.7	5	3.6

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		nvac N = 76		vac N = 64		Total N = 140	
Characteristics	Parameters or Categories	Value or n	%	Value or n	%	Value or n	%
Number of transplantation events	0	58	76.3	48	75.0	106	75.7
	1	13	17.1	12	18.8	25	17.9
	2	5	6.6	3	4.7	8	5.7
	3	0	0.0	1	1.6	1	0.7
Respiratory infection[s]	No	70	92.1	59	92.2	129	92.1
	Yes	6	7.9	5	7.8	11	7.9
Acute bacterial infection[s]	No	76	100	64	100	140	100
	Yes	0	0.0	0	0.0	0	0.0
Opportunistic infection[s]	No	72	94.7	59	92.2	131	93.6
	Yes	4	5.3	5	7.8	9	6.4
Chronic viral infection[s]	No	76	100	64	100	140	100
	Yes	0	0.0	0	0.0	0	0.0
Malignancy/cancer[s]	No	72	94.7	57	89.1	129	92.1
	Yes	4	5.3	7	10.9	11	7.9
Chemotherapy	No	69	90.8	60	93.8	129	92.1
	Yes	7	9.2	4	6.3	11	7.9
Reasons for end of follow-up	End of season [31 August]	69	90.8	57	89.1	126	90.0
	Death	6	7.9	6	9.4	12	8.6
	End of CRPD GOLD follow-up	1	1.3	1	1.6	2	1.4

nvac = not_vaccinated

vac = vaccinated

*Transplantations could happen after 01-September

**Each subject is classified in one category. All combinations are possible. All transplantations between 05-March and 31-August of next year are considered.

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N = number of subjects

n = number of subjects in a given category

Value = value of the considered parameter

% = n / Number of subjects with available results x 100

SD = Standard deviation

Note: For each subject, data used for pooled analysis was data of the first season analysed

Table 21 Demographic and baseline characteristics of subjects with data for pooled seasonal analysis (Secondary seasonal influenza subset, subjects with transplantation or rejection for only one organ)

		nvac N = 74		vac N = 59		Total N = 133	
Characteristics	Parameters or Categories	Value or n	%	Value or n	%	Value or n	%
Age at the beginning of the analysed season [years]	N	74	-	59	-	133	-
	Mean	48.0	-	55.0	-	51.1	-
	SD	16.08	-	20.28	-	18.33	-
	Median	48.0	-	60.0	-	52.0	-
	Minimum	5	-	6	-	5	-
	Maximum	77	-	88	-	88	-
Age group at the beginning of the analysed season	[0-17]	3	4.1	3	5.1	6	4.5
	[18-44]	27	36.5	13	22.0	40	30.1
	[45-60]	28	37.8	14	23.7	42	31.6
	61+	16	21.6	29	49.2	45	33.8
Gender	Female	23	31.1	21	35.6	44	33.1
	Male	51	68.9	38	64.4	89	66.9
Died during the analysed season	No	68	91.9	53	89.8	121	91.0
	Yes	6	8.1	6	10.2	12	9.0
Time since transplantation at the beginning of the analysed season [days]	Before transplantation or more than 180 days after transplantation	71	95.9	58	98.3	129	97.0
	0-30	0	0.0	0	0.0	0	0.0
	31-90	3	4.1	0	0.0	3	2.3
	91-180	0	0.0	1	1.7	1	0.8
Organ transplanted before or during the season**	Heart	2	2.7	1	1.7	3	2.3
	Kidney	11	14.9	11	18.6	22	16.5
	Liver	6	8.1	2	3.4	8	6.0
	No transplantation recorded	55	74.3	45	76.3	100	75.2

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		nvac N = 74		vac N = 59		Total N = 133	
Characteristics	Parameters or Categories	Value or n	%	Value or n	%	Value or n	%
Number of rejections	None	72	97.3	57	96.6	129	97.0
	At least one	2	2.7	2	3.4	4	3.0
Number of transplantation events	0	58	78.4	46	78.0	104	78.2
	1	13	17.6	12	20.3	25	18.8
	2	3	4.1	1	1.7	4	3.0
Respiratory infection[s]	No	68	91.9	54	91.5	122	91.7
	Yes	6	8.1	5	8.5	11	8.3
Acute bacterial infection[s]	No	74	100	59	100	133	100
	Yes	0	0.0	0	0.0	0	0.0
Opportunistic infection[s]	No	70	94.6	55	93.2	125	94.0
	Yes	4	5.4	4	6.8	8	6.0
Chronic viral infection[s]	No	74	100	59	100	133	100
	Yes	0	0.0	0	0.0	0	0.0
Malignancy/cancer[s]	No	70	94.6	52	88.1	122	91.7
	Yes	4	5.4	7	11.9	11	8.3
Chemotherapy	No	67	90.5	55	93.2	122	91.7
	Yes	7	9.5	4	6.8	11	8.3
Reasons for end of follow-up	End of season [31 August]	67	90.5	52	88.1	119	89.5
	Death	6	8.1	6	10.2	12	9.0
	End of CRPD GOLD follow-up	1	1.4	1	1.7	2	1.5

nvac = not_vaccinated

vac = vaccinated

*Transplantations could happen after 01-September

**Each subject is classified in one category. All combinations are possible. All transplantations between 05-March and 31-August of next year are considered.

N = number of subjects

n = number of subjects in a given category

Value = value of the considered parameter

% = n / Number of subjects with available results x 100

SD = Standard deviation

Note: For each subject, data used for pooled analysis was data of the first season analysed

12.2. TIV risk period of 30 days**12.2.1. Subset 2a****12.2.1.1. Season 2006-2007****Table 22 SOT rejections from 01-SEP-2006 to 31-AUG-2007 according to the 30-days risk periods of seasonal vaccination and the time since transplantation (Subset 2a)**

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	131	100.0	159	45581
Data after censoring according to transplantations	131	100.0	153	40721
Data after censoring according to second rejection	131	100.0	131	37815
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	74	56.5	74	20560
Seasonal vaccination - Control period before first dose	72	55.0	37	7264
Seasonal vaccination - Risk period after any dose	55	42.0	5	1662
Seasonal vaccination - Control period after any dose	53	40.5	32	11634
Seasonal vaccination - Pooled risk periods	55	42.0	5	1662
Seasonal vaccination - Pooled control periods	74	56.5	69	18898
Day0 to Day30 after transplantation	22	16.8	16	630
Day31 to Day90 after transplantation	22	16.8	6	1127
> 90 days after transplantation	68	51.9	52	18803

Table 23 **Relative incidence of SOT rejection within 30 days after seasonal vaccination in season 2006-2007 adjusted for the time since transplantation (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	0.74	0.24	2.28
Time since transplantation	0-30 vs. >90 days	24.81	4.59	134.18
	31-90 vs. >90 days	4.65	0.94	22.91

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

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Table 24 SOT rejections from 01-SEP-2006 to 31-AUG-2007 according to the 30-days risk periods of seasonal vaccination, the time since transplantation and all covariates (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	128	100.0	156	44486
Data after censoring according to transplantations	128	100.0	150	39787
Data after censoring according to second rejection	128	100.0	128	36881
Subjects with at least one exposure of interest (Acute bacterial infection, Cancer, Chronic viral infection, Opportunistic infection, Respiratory infection, Seasonal vaccination, transplantation)	75	58.6	75	21086
Seasonal vaccination - Control period before first dose	73	57.0	39	8009
Seasonal vaccination - Risk period after any dose	54	42.2	5	1631
Seasonal vaccination - Control period after any dose	52	40.6	31	11446
Seasonal vaccination - Pooled risk periods	54	42.2	5	1631
Seasonal vaccination - Pooled control periods	75	58.6	70	19455
Day0 to Day30 after transplantation	21	16.4	15	599
Day31 to Day90 after transplantation	20	15.6	5	1026
> 90 days after transplantation	69	53.9	55	19461
> 30 days after Respiratory infection	75	58.6	75	21086
Day0 to Day30 after Opportunistic infection	2	1.6	0	60
> 30 days after Opportunistic infection	75	58.6	75	21026
> 30 days after Acute bacterial infection	75	58.6	75	21086
> 365 days after Chronic viral infection	75	58.6	75	21086
Day0 to Day365 after Cancer	9	7.0	8	2252
> 365 days after Cancer	73	57.0	67	18834

Table 25 **Relative incidence of SOT rejection within 30 days after seasonal vaccination in season 2006-2007 adjusted for all covariates (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	0.79	0.25	2.49
Time since transplantation	0-30 vs. >90 days	18.87	3.90	91.34
	31-90 vs. >90 days	3.49	0.74	16.43
Malignancies/ cancers	365 days after any record vs. other periods	4.84	0.35	66.11

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

Note: only subjects with one year of follow-up before the beginning of the season were considered

Table 26 SOT rejections from 01-SEP-2006 to 31-AUG-2007 according to the 30-days risk periods of seasonal vaccination, the time since transplantation and malignancies/cancers (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	128	100.0	156	44486
Data after censoring according to transplantations	128	100.0	150	39787
Data after censoring according to second rejection	128	100.0	128	36881
Subjects with at least one exposure of interest (Cancer, Seasonal vaccination, transplantation)	75	58.6	75	21086
Seasonal vaccination - Control period before first dose	73	57.0	39	8009
Seasonal vaccination - Risk period after any dose	54	42.2	5	1631
Seasonal vaccination - Control period after any dose	52	40.6	31	11446
Seasonal vaccination - Pooled risk periods	54	42.2	5	1631
Seasonal vaccination - Pooled control periods	75	58.6	70	19455
Day0 to Day30 after transplantation	21	16.4	15	599
Day31 to Day90 after transplantation	20	15.6	5	1026
> 90 days after transplantation	69	53.9	55	19461
Day0 to Day365 after Cancer	9	7.0	8	2252
> 365 days after Cancer	73	57.0	67	18834

Table 27 **Relative incidence of SOT rejection within 30 days after seasonal vaccination in season 2006-2007 adjusted for the time since transplantation and malignancies/cancers (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	0.79	0.25	2.49
Time since transplantation	0-30 vs. >90 days	18.87	3.90	91.34
	31-90 vs. >90 days	3.49	0.74	16.43
Malignancies/ cancers	365 days after any record vs. other periods	4.84	0.35	66.11

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

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Table 28 SOT rejections from 01-SEP-2006 to 31-AUG-2007 according to the 30-days risk periods of seasonal vaccination and the time since transplantation – with subsequent rejections (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	131	100.0	159	45581
Data after censoring according to transplantations	131	100.0	153	40721
Subjects with at least one exposure of interest (seasonal vaccination, transplantation)	74	56.5	83	21781
seasonal vaccination - Control period before first dose	72	55.0	39	7453
seasonal vaccination - Risk period after any dose	55	42.0	7	1682
seasonal vaccination - Control period after any dose	55	42.0	37	12646
seasonal vaccination - Pooled risk periods	55	42.0	7	1682
seasonal vaccination - Pooled control periods	74	56.5	76	20099
Day0 to Day30 after transplantation	22	16.8	16	630
Day31 to Day90 after transplantation	22	16.8	6	1127
> 90 days after transplantation	68	51.9	61	20024

Table 29 **Relative incidence of SOT rejection within 30 days after seasonal vaccination in season 2006-2007 adjusted for the time since transplantation - not accounting for perturbed post-event exposure (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	1.03	0.46	2.30
Time since transplantation	0-30 vs. >90 days	18.22	5.55	59.87
	31-90 vs. >90 days	4.20	1.25	14.18

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Table 30 **Relative incidence of SOT rejection within 30 days after seasonal vaccination in season 2006-2007 adjusted for the time since transplantation and conditioned to previous rejections (Subset 2a)**

No records exist in this table

Table 31 SOT rejections from 01-SEP-2006 to 31-AUG-2007 according to the 30-days risk periods of seasonal vaccination and the time since transplantation - Subjects without previous rejections (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	65	100.0	74	22811
Data after censoring according to transplantations	65	100.0	71	18802
Data after censoring according to second rejection	65	100.0	65	18290
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	65	100.0	65	18290
Seasonal vaccination - Control period before first dose	63	96.9	33	6496
Seasonal vaccination - Risk period after any dose	47	72.3	4	1434
Seasonal vaccination - Control period after any dose	47	72.3	28	10360
Seasonal vaccination - Pooled risk periods	47	72.3	4	1434
Seasonal vaccination - Pooled control periods	65	100.0	61	16856
Day0 to Day30 after transplantation	22	33.8	16	630
Day31 to Day90 after transplantation	20	30.8	4	1072
> 90 days after transplantation	59	90.8	45	16588

Table 32 Relative incidence of SOT rejection within 30 days after seasonal vaccination in season 2006-2007 adjusted for the time since transplantation - Subjects without previous rejections (Subset 2a)

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	0.66	0.19	2.33
Time since transplantation	0-30 vs. >90 days	18.13	4.20	78.24
	31-90 vs. >90 days	2.67	0.54	13.17

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

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Table 33 SOT rejections from 01-SEP-2006 to 31-AUG-2007 according to the 30-days risk periods of seasonal vaccination, the time since transplantation and previous rejection (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	13	100.0	19	4242
Data after censoring according to transplantations	13	100.0	18	4120
Data after censoring according to second rejection	13	100.0	13	3180
Subjects with at least one exposure of interest (Previous rejection, Seasonal vaccination, transplantation)	13	100.0	13	3180
Seasonal vaccination - Control period before first dose	13	100.0	8	1678
Seasonal vaccination - Risk period after any dose	8	61.5	1	228
Seasonal vaccination - Control period after any dose	6	46.2	4	1274
Seasonal vaccination - Pooled risk periods	8	61.5	1	228
Seasonal vaccination - Pooled control periods	13	100.0	12	2952
Day31 to Day90 after transplantation	2	15.4	2	55
> 90 days after transplantation	13	100.0	11	3125
Day0 to Day180 after Previous rejection	13	100.0	6	898
> 180 days after Previous rejection	11	84.6	7	2282

Table 34 **Relative incidence of SOT rejection within 30 days after seasonal vaccination in season 2006-2007 adjusted for the time since transplantation and previous rejection - Subjects with previous rejections (Subset 2a)**

No records exist in this table

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Table 35 Heart transplant rejection from 01-SEP-2006 to 31-AUG-2007 according to the 30-days risk periods of seasonal vaccination and the time since transplantation (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	7	100.0	10	2013
Data after censoring according to transplantations	7	100.0	10	1701
Data after censoring according to second rejection	7	100.0	7	1408
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	5	71.4	5	933
Seasonal vaccination - Control period before first dose	5	71.4	3	183
Seasonal vaccination - Risk period after any dose	3	42.9	0	93
Seasonal vaccination - Control period after any dose	3	42.9	2	657
Seasonal vaccination - Pooled risk periods	3	42.9	0	93
Seasonal vaccination - Pooled control periods	5	71.4	5	840
Day0 to Day30 after transplantation	2	28.6	2	17
> 90 days after transplantation	3	42.9	3	916

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Table 36 Kidney transplant rejection from 01-SEP-2006 to 31-AUG-2007 according to the 30-days risk periods of seasonal vaccination and the time since transplantation (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	67	100.0	83	23398
Data after censoring according to transplantations	67	100.0	79	20320
Data after censoring according to second rejection	67	100.0	67	18761
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	49	73.1	49	13686
Seasonal vaccination - Control period before first dose	47	70.1	26	5048
Seasonal vaccination - Risk period after any dose	36	53.7	3	1077
Seasonal vaccination - Control period after any dose	35	52.2	20	7561
Seasonal vaccination - Pooled risk periods	36	53.7	3	1077
Seasonal vaccination - Pooled control periods	49	73.1	46	12609
Day0 to Day30 after transplantation	16	23.9	11	489
Day31 to Day90 after transplantation	15	22.4	3	835
> 90 days after transplantation	46	68.7	35	12362

Table 37 **Relative incidence of kidney transplant rejection within 30 days after seasonal vaccination in season 2006-2007 adjusted for the time since transplantation (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	0.59	0.13	2.63
Time since transplantation	0-30 vs. >90 days	16.35	3.60	74.31
	31-90 vs. >90 days	2.26	0.40	12.87

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

Table 38 Kidney transplant rejection from 01-SEP-2006 to 31-AUG-2007 according to the 30-days risk periods of seasonal vaccination, the time since transplantation and all covariates (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	65	100.0	81	22668
Data after censoring according to transplantations	65	100.0	77	19751
Data after censoring according to second rejection	65	100.0	65	18192
Subjects with at least one exposure of interest (Acute bacterial infection, Cancer, Chronic viral infection, Opportunistic infection, Respiratory infection, Seasonal vaccination, transplantation)	47	72.3	47	13117
Seasonal vaccination - Control period before first dose	45	69.2	25	4698
Seasonal vaccination - Risk period after any dose	35	53.8	3	1046
Seasonal vaccination - Control period after any dose	34	52.3	19	7373
Seasonal vaccination - Pooled risk periods	35	53.8	3	1046
Seasonal vaccination - Pooled control periods	47	72.3	44	12071
Day0 to Day30 after transplantation	15	23.1	10	458
Day31 to Day90 after transplantation	14	21.5	3	775
> 90 days after transplantation	44	67.7	34	11884
> 30 days after Respiratory infection	47	72.3	47	13117
Day0 to Day30 after Opportunistic infection	1	1.5	0	29
> 30 days after Opportunistic infection	47	72.3	47	13088
> 30 days after Acute bacterial infection	47	72.3	47	13117
> 365 days after Chronic viral infection	47	72.3	47	13117
Day0 to Day365 after Cancer	1	1.5	1	221
> 365 days after Cancer	46	70.8	46	12896

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Table 39 Kidney transplant rejections from 01-SEP-2006 to 31-AUG-2007 according to the 30-days risk periods of seasonal vaccination and the time since transplantation – with subsequent rejections (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	67	100.0	83	23398
Data after censoring according to transplantations	67	100.0	79	20320
Subjects with at least one exposure of interest (seasonal vaccination, transplantation)	49	73.1	55	14426
seasonal vaccination - Control period before first dose	47	70.1	28	5237
seasonal vaccination - Risk period after any dose	36	53.7	4	1093
seasonal vaccination - Control period after any dose	36	53.7	23	8096
seasonal vaccination - Pooled risk periods	36	53.7	4	1093
seasonal vaccination - Pooled control periods	49	73.1	51	13333
Day0 to Day30 after transplantation	16	23.9	11	489
Day31 to Day90 after transplantation	15	22.4	3	835
> 90 days after transplantation	46	68.7	41	13102

Table 40 **Relative incidence of kidney transplant rejection within 30 days after seasonal vaccination in season 2006-2007 adjusted for the time since transplantation - not accounting for perturbed post-event exposure (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	0.80	0.27	2.31
Time since transplantation	0-30 vs. >90 days	11.16	3.46	36.05
	31-90 vs. >90 days	1.95	0.46	8.28

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Table 41 **Relative incidence of kidney transplant rejection within 30 days after seasonal vaccination in season 2006-2007 adjusted for the time since transplantation and conditioned to previous rejections (Subset 2a)**

No records exist in this table

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Table 42 Kidney transplant rejection from 01-SEP-2006 to 31-AUG-2007 according to the 30-days risk periods of seasonal vaccination and the time since transplantation - Subjects without previous rejections (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	43	100.0	50	15498
Data after censoring according to transplantations	43	100.0	47	12542
Data after censoring according to second rejection	43	100.0	43	12209
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	43	100.0	43	12209
Seasonal vaccination - Control period before first dose	41	95.3	24	4724
Seasonal vaccination - Risk period after any dose	30	69.8	2	907
Seasonal vaccination - Control period after any dose	30	69.8	17	6578
Seasonal vaccination - Pooled risk periods	30	69.8	2	907
Seasonal vaccination - Pooled control periods	43	100.0	41	11302
Day0 to Day30 after transplantation	16	37.2	11	489
Day31 to Day90 after transplantation	15	34.9	3	835
> 90 days after transplantation	40	93.0	29	10885

Table 43 **Relative incidence of kidney transplant rejection within 30 days after seasonal vaccination in season 2006-2007 adjusted for the time since transplantation - Subjects without previous rejections (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	0.44	0.07	2.55
Time since transplantation	0-30 vs. >90 days	17.72	4.04	77.81
	31-90 vs. >90 days	2.26	0.40	12.86

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

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Table 44 **Kidney transplant rejection from 01-SEP-2006 to 31-AUG-2007 according to the 30-days risk periods of seasonal vaccination, the time since transplantation and previous rejection - Subjects with previous rejections (Subset 2a)**

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	9	100.0	14	3101
Data after censoring according to transplantations	9	100.0	13	2979
Data after censoring according to second rejection	9	100.0	9	2341
Subjects with at least one exposure of interest (Previous rejection, Seasonal vaccination, transplantation)	9	100.0	9	2341
Seasonal vaccination - Control period before first dose	9	100.0	5	1188
Seasonal vaccination - Risk period after any dose	6	66.7	1	170
Seasonal vaccination - Control period after any dose	5	55.6	3	983
Seasonal vaccination - Pooled risk periods	6	66.7	1	170
Seasonal vaccination - Pooled control periods	9	100.0	8	2171
> 90 days after transplantation	9	100.0	9	2341
Day0 to Day180 after Previous rejection	9	100.0	3	600
> 180 days after Previous rejection	9	100.0	6	1741

Table 45 **Relative incidence of kidney transplant rejection within 30 days after seasonal vaccination in season 2006-2007 adjusted for the time since transplantation and previous rejection - Subjects with previous rejections (Subset 2a)**

No records exist in this table

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Table 46 Liver transplant rejection from 01-SEP-2006 to 31-AUG-2007 according to the 30-days risk periods of seasonal vaccination and the time since transplantation (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	12	100.0	14	4061
Data after censoring according to transplantations	12	100.0	13	3473
Data after censoring according to second rejection	12	100.0	12	3337
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	5	41.7	5	1604
Seasonal vaccination - Control period before first dose	5	41.7	4	867
Seasonal vaccination - Risk period after any dose	3	25.0	0	93
Seasonal vaccination - Control period after any dose	3	25.0	1	644
Seasonal vaccination - Pooled risk periods	3	25.0	0	93
Seasonal vaccination - Pooled control periods	5	41.7	5	1511
Day0 to Day30 after transplantation	2	16.7	2	62
Day31 to Day90 after transplantation	4	33.3	1	164
> 90 days after transplantation	5	41.7	2	1378

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Table 47 Lung transplant rejection from 01-SEP-2006 to 31-AUG-2007 according to the 30-days risk periods of seasonal vaccination and the time since transplantation (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	6	100.0	8	2190
Data after censoring according to transplantations	6	100.0	7	1308
Data after censoring according to second rejection	6	100.0	6	1006
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	5	83.3	5	1003
Seasonal vaccination - Control period before first dose	5	83.3	3	346
Seasonal vaccination - Risk period after any dose	3	50.0	0	89
Seasonal vaccination - Control period after any dose	2	33.3	2	568
Seasonal vaccination - Pooled risk periods	3	50.0	0	89
Seasonal vaccination - Pooled control periods	5	83.3	5	914
Day0 to Day30 after transplantation	2	33.3	1	62
Day31 to Day90 after transplantation	3	50.0	2	128
> 90 days after transplantation	4	66.7	2	813

Table 48 Pancreas transplant rejection from 01-SEP-2006 to 31-AUG-2007 according to the 30-days risk periods of seasonal vaccination and the time since transplantation (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	0			
Data after censoring according to transplantations	0			
Data after censoring according to second rejection	0			
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	0			

12.2.1.2. Season 2007-2008**Table 49 SOT rejections from 01-SEP-2007 to 31-AUG-2008 according to the 30-days risk periods of seasonal vaccine and the time since transplantation (Subset 2a)**

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	136	100.0	169	48185
Data after censoring according to transplantations	136	100.0	167	43886
Data after censoring according to second rejection	136	100.0	136	40848
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	81	59.6	81	23406
Seasonal vaccination - Control period before first dose	81	59.6	32	7730
Seasonal vaccination - Risk period after any dose	58	42.6	7	1776
Seasonal vaccination - Control period after any dose	57	41.9	42	13900
Seasonal vaccination - Pooled risk periods	58	42.6	7	1776
Seasonal vaccination - Pooled control periods	81	59.6	74	21630
Day0 to Day30 after transplantation	22	16.2	11	588
Day31 to Day90 after transplantation	23	16.9	7	1266
Day91 to Day180 after transplantation	24	17.6	6	2009
> 180 days after transplantation	71	52.2	57	19543

Table 50 **Relative incidence of SOT rejection within 30 days after seasonal vaccination in season 2007-2008 adjusted for the time since transplantation (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	1.21	0.55	2.64
Time since transplantation	0-30 vs. >180 days	5.51	1.13	26.97
	31-90 vs. >180 days	2.35	0.62	8.84
	91-180 vs. >180 days	1.19	0.30	4.71

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

Table 51 SOT rejections from 01-SEP-2007 to 31-AUG-2008 according to the 30-days risk periods of seasonal vaccination, the time since transplantation and all covariates (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	130	100.0	161	45994
Data after censoring according to transplantations	130	100.0	160	41839
Data after censoring according to second rejection	130	100.0	130	38826
Subjects with at least one exposure of interest (Acute bacterial infection, Cancer, Chronic viral infection, Opportunistic infection, Respiratory infection, Seasonal vaccination, transplantation)	82	63.1	82	23814
Seasonal vaccination - Control period before first dose	82	63.1	36	9093
Seasonal vaccination - Risk period after any dose	55	42.3	7	1683
Seasonal vaccination - Control period after any dose	54	41.5	39	13038
Seasonal vaccination - Pooled risk periods	55	42.3	7	1683
Seasonal vaccination - Pooled control periods	82	63.1	75	22131
Day0 to Day30 after transplantation	21	16.2	11	557
Day31 to Day90 after transplantation	22	16.9	7	1206
Day91 to Day180 after transplantation	23	17.7	5	1919
> 180 days after transplantation	72	55.4	59	20132
> 30 days after Respiratory infection	82	63.1	82	23814
Day0 to Day30 after Opportunistic infection	3	2.3	0	93
> 30 days after Opportunistic infection	82	63.1	82	23721
> 30 days after Acute bacterial infection	82	63.1	82	23814
> 365 days after Chronic viral infection	82	63.1	82	23814
Day0 to Day365 after Cancer	10	7.7	7	2506
> 365 days after Cancer	81	62.3	75	21308

Table 52 **Relative incidence of SOT rejection within 30 days after seasonal vaccination in season 2007-2008 adjusted for all covariates (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	1.29	0.59	2.85
Time since transplantation	0-30 vs. >180 days	6.25	1.25	31.29
	31-90 vs. >180 days	2.57	0.68	9.67
	91-180 vs. >180 days	1.06	0.25	4.56
Malignancies/ cancers	365 days after any record vs. other periods	0.76	0.11	5.38

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

Note: only subjects with one year of follow-up before the beginning of the season were considered

Table 53 SOT rejections from 01-SEP-2007 to 31-AUG-2008 according to the 30-days risk periods of seasonal vaccination, the time since transplantation and malignancies/cancers (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	130	100.0	161	45994
Data after censoring according to transplantations	130	100.0	160	41839
Data after censoring according to second rejection	130	100.0	130	38826
Subjects with at least one exposure of interest (Cancer, Seasonal vaccination, transplantation)	81	62.3	81	23479
Seasonal vaccination - Control period before first dose	81	62.3	35	8758
Seasonal vaccination - Risk period after any dose	55	42.3	7	1683
Seasonal vaccination - Control period after any dose	54	41.5	39	13038
Seasonal vaccination - Pooled risk periods	55	42.3	7	1683
Seasonal vaccination - Pooled control periods	81	62.3	74	21796
Day0 to Day30 after transplantation	21	16.2	11	557
Day31 to Day90 after transplantation	22	16.9	7	1206
Day91 to Day180 after transplantation	23	17.7	5	1919
> 180 days after transplantation	71	54.6	58	19797
Day0 to Day365 after Cancer	10	7.7	7	2506
> 365 days after Cancer	80	61.5	74	20973

Table 54 Relative incidence of SOT rejection within 30 days after seasonal vaccination in season 2007-2008 adjusted for the time since transplantation and malignancies/cancers (Subset 2a)

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	1.29	0.59	2.85
Time since transplantation	0-30 vs. >180 days	6.25	1.25	31.29
	31-90 vs. >180 days	2.57	0.68	9.67
	91-180 vs. >180 days	1.06	0.25	4.56
Malignancies/ cancers	365 days after any record vs. other periods	0.76	0.11	5.38

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

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Table 55 SOT rejections from 01-SEP-2007 to 31-AUG-2008 according to the 30-days risk periods of seasonal vaccine and the time since transplantation – with subsequent rejections (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	136	100.0	169	48185
Data after censoring according to transplantations	136	100.0	167	43886
Subjects with at least one exposure of interest (seasonal vaccine, transplantation)	83	61.0	104	25581
seasonal vaccine - Control period before first dose	83	61.0	39	8172
seasonal vaccine - Risk period after any dose	60	44.1	8	1860
seasonal vaccine - Control period after any dose	60	44.1	57	15549
seasonal vaccine - Pooled risk periods	60	44.1	8	1860
seasonal vaccine - Pooled control periods	83	61.0	96	23721
Day0 to Day30 after transplantation	22	16.2	11	588
Day31 to Day90 after transplantation	23	16.9	8	1303
Day91 to Day180 after transplantation	25	18.4	6	2099
> 180 days after transplantation	74	54.4	79	21591

Table 56 **Relative incidence of SOT rejection within 30 days after seasonal vaccination in season 2007-2008 adjusted for the time since transplantation - not accounting for perturbed post-event exposure (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	1.09	0.52	2.28
Time since transplantation	0-30 vs. >180 days	3.55	1.10	11.49
	31-90 vs. >180 days	1.74	0.60	5.04
	91-180 vs. >180 days	0.85	0.29	2.49

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Table 57 **Relative incidence of SOT rejection within 30 days after seasonal vaccination in season 2007-2008 adjusted for the time since transplantation and conditioned to previous rejections (Subset 2a)**

No records exist in this table

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Table 58 SOT rejections from 01-SEP-2007 to 31-AUG-2008 according to the 30-days risk periods of seasonal vaccine and the time since transplantation - Subjects without previous rejections (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	75	100.0	86	26654
Data after censoring according to transplantations	75	100.0	85	22803
Data after censoring according to second rejection	75	100.0	75	21910
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	75	100.0	75	21910
Seasonal vaccination - Control period before first dose	75	100.0	29	7273
Seasonal vaccination - Risk period after any dose	52	69.3	6	1612
Seasonal vaccination - Control period after any dose	52	69.3	40	13025
Seasonal vaccination - Pooled risk periods	52	69.3	6	1612
Seasonal vaccination - Pooled control periods	75	100.0	69	20298
Day0 to Day30 after transplantation	22	29.3	11	588
Day31 to Day90 after transplantation	23	30.7	7	1266
Day91 to Day180 after transplantation	24	32.0	6	2009
> 180 days after transplantation	65	86.7	51	18047

Table 59 Relative incidence of SOT rejection within 30 days after seasonal vaccination in season 2007-2008 adjusted for the time since transplantation - Subjects without previous rejections (Subset 2a)

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	1.10	0.47	2.55
Time since transplantation	0-30 vs. >180 days	5.56	1.13	27.28
	31-90 vs. >180 days	2.37	0.63	8.95
	91-180 vs. >180 days	1.21	0.30	4.78

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

Table 60 SOT rejections from 01-SEP-2007 to 31-AUG-2008 according to the 30-days risk periods of seasonal vaccine, the time since transplantation and previous rejection (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	14	100.0	24	4901
Data after censoring according to transplantations	14	100.0	24	4901
Data after censoring according to second rejection	14	100.0	14	3987
Subjects with at least one exposure of interest (Previous rejection, Seasonal vaccination, transplantation)	14	100.0	14	3987
Seasonal vaccination - Control period before first dose	14	100.0	11	2948
Seasonal vaccination - Risk period after any dose	6	42.9	1	164
Seasonal vaccination - Control period after any dose	5	35.7	2	875
Seasonal vaccination - Pooled risk periods	6	42.9	1	164
Seasonal vaccination - Pooled control periods	14	100.0	13	3823
> 180 days after transplantation	14	100.0	14	3987
Day0 to Day180 after Previous rejection	14	100.0	10	1545
> 180 days after Previous rejection	11	78.6	4	2442

Table 61 **Relative incidence of SOT rejection within 30 days after seasonal vaccination in season 2007-2008 adjusted for the time since transplantation and previous rejection - Subjects with previous rejections (Subset 2a)**

No records exist in this table

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Table 62 Heart transplant rejection from 01-SEP-2007 to 31-AUG-2008 according to the 30-days risk periods of seasonal vaccine and the time since transplantation (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	8	100.0	9	2859
Data after censoring according to transplantations	8	100.0	9	2225
Data after censoring according to second rejection	8	100.0	8	2206
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	7	87.5	7	1840
Seasonal vaccination - Control period before first dose	7	87.5	3	651
Seasonal vaccination - Risk period after any dose	4	50.0	0	124
Seasonal vaccination - Control period after any dose	4	50.0	4	1065
Seasonal vaccination - Pooled risk periods	4	50.0	0	124
Seasonal vaccination - Pooled control periods	7	87.5	7	1716
Day0 to Day30 after transplantation	2	25.0	2	29
Day31 to Day90 after transplantation	2	25.0	0	96
Day91 to Day180 after transplantation	2	25.0	1	180
> 180 days after transplantation	5	62.5	4	1535

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Table 63 Kidney transplant rejection from 01-SEP-2007 to 31-AUG-2008 according to the 30-days risk periods of seasonal vaccine and the time since transplantation (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	84	100.0	110	29421
Data after censoring according to transplantations	84	100.0	109	26177
Data after censoring according to second rejection	84	100.0	84	23853
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	57	67.9	57	15815
Seasonal vaccination - Control period before first dose	57	67.9	26	5825
Seasonal vaccination - Risk period after any dose	40	47.6	5	1218
Seasonal vaccination - Control period after any dose	39	46.4	26	8772
Seasonal vaccination - Pooled risk periods	40	47.6	5	1218
Seasonal vaccination - Pooled control periods	57	67.9	52	14597
Day0 to Day30 after transplantation	17	20.2	8	466
Day31 to Day90 after transplantation	18	21.4	7	990
Day91 to Day180 after transplantation	18	21.4	3	1495
> 180 days after transplantation	50	59.5	39	12864

Table 64 **Relative incidence of kidney transplant rejection within 30 days after seasonal vaccination in season 2007-2008 adjusted for the time since transplantation (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	1.28	0.52	3.15
Time since transplantation	0-30 vs. >180 days	5.71	0.99	33.06
	31-90 vs. >180 days	2.91	0.68	12.56
	91-180 vs. >180 days	0.62	0.11	3.55

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

Table 65 Kidney transplant rejection from 01-SEP-2007 to 31-AUG-2008 according to the 30-days risk periods of seasonal vaccine, the time since transplantation and all covariates (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	81	100.0	107	28323
Data after censoring according to transplantations	81	100.0	106	25079
Data after censoring according to second rejection	81	100.0	81	22755
Subjects with at least one exposure of interest (Acute bacterial infection, Cancer, Chronic viral infection, Opportunistic infection, Respiratory infection, Seasonal vaccination, transplantation)	54	66.7	54	14717
Seasonal vaccination - Control period before first dose	54	66.7	26	5688
Seasonal vaccination - Risk period after any dose	37	45.7	5	1125
Seasonal vaccination - Control period after any dose	36	44.4	23	7904
Seasonal vaccination - Pooled risk periods	37	45.7	5	1125
Seasonal vaccination - Pooled control periods	54	66.7	49	13592
Day0 to Day30 after transplantation	17	21.0	8	466
Day31 to Day90 after transplantation	18	22.2	7	990
Day91 to Day180 after transplantation	18	22.2	3	1495
> 180 days after transplantation	47	58.0	36	11766
> 30 days after Respiratory infection	54	66.7	54	14717
Day0 to Day30 after Opportunistic infection	2	2.5	0	62
> 30 days after Opportunistic infection	54	66.7	54	14655
> 30 days after Acute bacterial infection	54	66.7	54	14717
> 365 days after Chronic viral infection	54	66.7	54	14717
Day0 to Day365 after Cancer	3	3.7	2	525
> 365 days after Cancer	53	65.4	52	14192

Table 66 **Relative incidence of kidney transplant rejection within 30 days after seasonal vaccination in season 2007-2008 adjusted for all covariates (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	1.41	0.56	3.50
Time since transplantation	0-30 vs. >180 days	5.66	0.98	32.75
	31-90 vs. >180 days	2.88	0.67	12.43
	91-180 vs. >180 days	0.61	0.10	3.54

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

Note: only subjects with one year of follow-up before the beginning of the season were considered

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Table 67 Kidney transplant rejections from 01-SEP-2007 to 31-AUG-2008 according to the 30-days risk periods of seasonal vaccine and the time since transplantation – with subsequent rejections (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	84	100.0	110	29421
Data after censoring according to transplantations	84	100.0	109	26177
Subjects with at least one exposure of interest (seasonal vaccine, transplantation)	58	69.0	76	17580
seasonal vaccine - Control period before first dose	58	69.0	30	6149
seasonal vaccine - Risk period after any dose	41	48.8	6	1271
seasonal vaccine - Control period after any dose	41	48.8	40	10160
seasonal vaccine - Pooled risk periods	41	48.8	6	1271
seasonal vaccine - Pooled control periods	58	69.0	70	16309
Day0 to Day30 after transplantation	17	20.2	8	466
Day31 to Day90 after transplantation	18	21.4	8	1027
Day91 to Day180 after transplantation	19	22.6	3	1585
> 180 days after transplantation	52	61.9	57	14502

Table 68 **Relative incidence of kidney transplant rejection within 30 days after seasonal vaccination in season 2007-2008 adjusted for the time since transplantation - not accounting for perturbed post-event exposure (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	1.08	0.46	2.54
Time since transplantation	0-30 vs. >180 days	4.55	1.21	17.15
	31-90 vs. >180 days	2.60	0.80	8.41
	91-180 vs. >180 days	0.64	0.15	2.63

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Table 69 **Relative incidence of kidney transplant rejection within 30 days after seasonal vaccination in season 2007-2008 adjusted for the time since transplantation and conditioned to previous rejections (Subset 2a)**

No records exist in this table

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Table 70 Kidney transplant rejection from 01-SEP-2007 to 31-AUG-2008 according to the 30-days risk periods of seasonal vaccine and the time since transplantation - Subjects without previous rejections (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	52	100.0	61	18330
Data after censoring according to transplantations	52	100.0	61	15534
Data after censoring according to second rejection	52	100.0	52	14666
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	52	100.0	52	14666
Seasonal vaccination - Control period before first dose	52	100.0	23	5437
Seasonal vaccination - Risk period after any dose	35	67.3	4	1085
Seasonal vaccination - Control period after any dose	35	67.3	25	8144
Seasonal vaccination - Pooled risk periods	35	67.3	4	1085
Seasonal vaccination - Pooled control periods	52	100.0	48	13581
Day0 to Day30 after transplantation	17	32.7	8	466
Day31 to Day90 after transplantation	18	34.6	7	990
Day91 to Day180 after transplantation	18	34.6	3	1495
> 180 days after transplantation	45	86.5	34	11715

Table 71 **Relative incidence of kidney transplant rejection within 30 days after seasonal vaccination in season 2007-2008 adjusted for the time since transplantation - Subjects without previous rejections (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	1.07	0.39	2.90
Time since transplantation	0-30 vs. >180 days	5.80	1.00	33.61
	31-90 vs. >180 days	2.96	0.69	12.79
	91-180 vs. >180 days	0.63	0.11	3.58

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

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Table 72 Kidney transplant rejection from 01-SEP-2007 to 31-AUG-2008 according to the 30-days risk periods of seasonal vaccine, the time since transplantation and previous rejection - Subjects with previous rejections (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	11	100.0	19	3876
Data after censoring according to transplantations	11	100.0	19	3876
Data after censoring according to second rejection	11	100.0	11	3046
Subjects with at least one exposure of interest (Previous rejection, Seasonal vaccination, transplantation)	11	100.0	11	3046
Seasonal vaccination - Control period before first dose	11	100.0	9	2285
Seasonal vaccination - Risk period after any dose	5	45.5	1	133
Seasonal vaccination - Control period after any dose	4	36.4	1	628
Seasonal vaccination - Pooled risk periods	5	45.5	1	133
Seasonal vaccination - Pooled control periods	11	100.0	10	2913
> 180 days after transplantation	11	100.0	11	3046
Day0 to Day180 after Previous rejection	11	100.0	8	1203
> 180 days after Previous rejection	8	72.7	3	1843

Table 73 **Relative incidence of kidney transplant rejection within 30 days after seasonal vaccination in season 2007-2008 adjusted for the time since transplantation and previous rejection - Subjects with previous rejections (Subset 2a)**

No records exist in this table

Table 74 **Liver transplant rejection from 01-SEP-2007 to 31-AUG-2008 according to the 30-days risk periods of seasonal vaccine and the time since transplantation (Subset 2a)**

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	6	100.0	7	2191
Data after censoring according to transplantations	6	100.0	7	1983
Data after censoring according to second rejection	6	100.0	6	1958
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	3	50.0	3	860
Seasonal vaccination - Control period before first dose	3	50.0	2	536
Seasonal vaccination - Risk period after any dose	1	16.7	0	31
Seasonal vaccination - Control period after any dose	1	16.7	1	293
Seasonal vaccination - Pooled risk periods	1	16.7	0	31
Seasonal vaccination - Pooled control periods	3	50.0	3	829
Day0 to Day30 after transplantation	2	33.3	1	62
Day31 to Day90 after transplantation	2	33.3	0	120
Day91 to Day180 after transplantation	2	33.3	1	180
> 180 days after transplantation	3	50.0	1	498

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Table 75 Lung transplant rejection from 01-SEP-2007 to 31-AUG-2008 according to the 30-days risk periods of seasonal vaccine and the time since transplantation (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	1	100.0	1	366
Data after censoring according to transplantations	1	100.0	1	366
Data after censoring according to second rejection	1	100.0	1	366
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	1	100.0	1	366
Seasonal vaccination - Control period before first dose	1	100.0	0	45
Seasonal vaccination - Risk period after any dose	1	100.0	0	31
Seasonal vaccination - Control period after any dose	1	100.0	1	290
Seasonal vaccination - Pooled risk periods	1	100.0	0	31
Seasonal vaccination - Pooled control periods	1	100.0	1	335
Day91 to Day180 after transplantation	1	100.0	0	86
> 180 days after transplantation	1	100.0	1	280

Table 76 Pancreas transplant rejection from 01-SEP-2007 to 31-AUG-2008 according to the 30-days risk periods of seasonal vaccine and the time since transplantation (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	1	100.0	1	366
Data after censoring according to transplantations	1	100.0	1	6
Data after censoring according to second rejection	1	100.0	1	6
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	1	100.0	1	6
Seasonal vaccination - Control period before first dose	1	100.0	1	6
Seasonal vaccination - Pooled control periods	1	100.0	1	6
Day0 to Day30 after transplantation	1	100.0	1	6

12.2.1.3. Season 2008-2009**Table 77 SOT rejections from 01-SEP-2008 to 31-AUG-2009 according to the 30-days risk periods of seasonal vaccination and the time since transplantation (Subset 2a)**

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	168	100.0	216	58205
Data after censoring according to transplantations	168	100.0	211	52640
Data after censoring according to second rejection	168	100.0	168	48524
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	92	54.8	92	25217
Seasonal vaccination - Control period before first dose	92	54.8	34	7135
Seasonal vaccination - Risk period after any dose	72	42.9	9	2173
Seasonal vaccination - Control period after any dose	68	40.5	49	15909
Seasonal vaccination - Pooled risk periods	72	42.9	9	2173
Seasonal vaccination - Pooled control periods	92	54.8	83	23044
Day0 to Day30 after transplantation	20	11.9	11	593
Day31 to Day90 after transplantation	19	11.3	8	954
Day91 to Day180 after transplantation	19	11.3	3	1174
> 180 days after transplantation	77	45.8	70	22496

Table 78 Relative incidence of SOT rejection within 30 days after seasonal vaccination in season 2008-2009 adjusted for the time since transplantation (Subset 2a)

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	0.99	0.43	2.28
Time since transplantation	0-30 vs. >180 days	25.86	3.22	207.75
	31-90 vs. >180 days	13.88	1.65	117.01
	91-180 vs. >180 days	1.49	0.39	5.70

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

Table 79 SOT rejections from 01-SEP-2008 to 31-AUG-2009 according to the 30-days risk periods of seasonal vaccination, the time since transplantation and all covariates (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	160	100.0	208	55571
Data after censoring according to transplantations	160	100.0	203	50278
Data after censoring according to second rejection	160	100.0	160	46162
Subjects with at least one exposure of interest (Acute bacterial infection, Cancer, Chronic viral infection, Opportunistic infection, Respiratory infection, Seasonal vaccination, transplantation)	94	58.8	94	25969
Seasonal vaccination - Control period before first dose	94	58.8	36	7887
Seasonal vaccination - Risk period after any dose	72	45.0	9	2173
Seasonal vaccination - Control period after any dose	68	42.5	49	15909
Seasonal vaccination - Pooled risk periods	72	45.0	9	2173
Seasonal vaccination - Pooled control periods	94	58.8	85	23796
Day0 to Day30 after transplantation	19	11.9	10	562
Day31 to Day90 after transplantation	18	11.3	8	894
Day91 to Day180 after transplantation	18	11.3	3	1138
> 180 days after transplantation	80	50.0	73	23375
Day0 to Day30 after Respiratory infection	1	0.6	0	31
> 30 days after Respiratory infection	94	58.8	94	25938
Day0 to Day30 after Opportunistic infection	3	1.9	2	93
> 30 days after Opportunistic infection	94	58.8	92	25876
> 30 days after Acute bacterial infection	94	58.8	94	25969
> 365 days after Chronic viral infection	94	58.8	94	25969
Day0 to Day365 after Cancer	8	5.0	5	1565
> 365 days after Cancer	93	58.1	89	24404

Table 80 **Relative incidence of SOT rejection within 30 days after seasonal vaccination in season 2008-2009 adjusted for all covariates (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	0.99	0.43	2.28
Time since transplantation	0-30 vs. >180 days	23.45	2.89	190.50
	31-90 vs. >180 days	14.32	1.71	120.10
	91-180 vs. >180 days	1.50	0.39	5.73
Malignancies/ cancers	365 days after any record vs. other periods	0.98	0.25	3.85

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

Note: only subjects with one year of follow-up before the beginning of the season were considered

Table 81 SOT rejections from 01-SEP-2008 to 31-AUG-2009 according to the 30-days risk periods of seasonal vaccination, the time since transplantation and malignancies/cancers (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	160	100.0	208	55571
Data after censoring according to transplantations	160	100.0	203	50278
Data after censoring according to second rejection	160	100.0	160	46162
Subjects with at least one exposure of interest (Cancer, Seasonal vaccination, transplantation)	93	58.1	93	25604
Seasonal vaccination - Control period before first dose	93	58.1	35	7522
Seasonal vaccination - Risk period after any dose	72	45.0	9	2173
Seasonal vaccination - Control period after any dose	68	42.5	49	15909
Seasonal vaccination - Pooled risk periods	72	45.0	9	2173
Seasonal vaccination - Pooled control periods	93	58.1	84	23431
Day0 to Day30 after transplantation	19	11.9	10	562
Day31 to Day90 after transplantation	18	11.3	8	894
Day91 to Day180 after transplantation	18	11.3	3	1138
> 180 days after transplantation	79	49.4	72	23010
Day0 to Day365 after Cancer	8	5.0	5	1565
> 365 days after Cancer	92	57.5	88	24039

Table 82 Relative incidence of SOT rejection within 30 days after seasonal vaccination in season 2008-2009 adjusted for the time since transplantation and malignancies/cancers (Subset 2a)

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	0.99	0.43	2.28
Time since transplantation	0-30 vs. >180 days	23.45	2.89	190.50
	31-90 vs. >180 days	14.32	1.71	120.10
	91-180 vs. >180 days	1.50	0.39	5.73
Malignancies/ cancers	365 days after any record vs. other periods	0.98	0.25	3.85

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

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Table 83 SOT rejections from 01-SEP-2008 to 31-AUG-2009 according to the 30-days risk periods of seasonal vaccination and the time since transplantation – with subsequent rejections (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	168	100.0	216	58205
Data after censoring according to transplantations	168	100.0	211	52640
Subjects with at least one exposure of interest (seasonal vaccination, transplantation)	92	54.8	114	27710
seasonal vaccination - Control period before first dose	92	54.8	37	7618
seasonal vaccination - Risk period after any dose	72	42.9	11	2214
seasonal vaccination - Control period after any dose	70	41.7	66	17878
seasonal vaccination - Pooled risk periods	72	42.9	11	2214
seasonal vaccination - Pooled control periods	92	54.8	103	25496
Day0 to Day30 after transplantation	20	11.9	11	593
Day31 to Day90 after transplantation	19	11.3	9	968
Day91 to Day180 after transplantation	20	11.9	6	1313
> 180 days after transplantation	80	47.6	88	24836

Table 84 Relative incidence of SOT rejection within 30 days after seasonal vaccination in season 2008-2009 adjusted for the time since transplantation - not accounting for perturbed post-event exposure (Subset 2a)

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	1.27	0.67	2.41
Time since transplantation	0-30 vs. >180 days	23.17	4.18	128.46
	31-90 vs. >180 days	13.68	2.51	74.57
	91-180 vs. >180 days	3.52	0.98	12.62

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

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Table 85 **Relative incidence of SOT rejection within 30 days after seasonal vaccination in season 2008-2009 adjusted for the time since transplantation and conditioned to previous rejections (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
seasonal vaccination in cases without previous rejection	30 days after any dose vs. other periods	1.01	.	.
seasonal vaccination in cases without previous rejection in cases with previous rejection	30 days after any dose vs. other periods	0.90	.	.
Time since transplantation	0-30 vs. >180 days	25.86	.	.
	31-90 vs. >180 days	13.88	.	.
	91-180 vs. >180 days	1.49	.	.

95% CI = 95% percentile bootstrap confidence interval

LL =lower limit

UL =upper limit

Number of bootstrap steps: NA

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Table 86 SOT rejections from 01-SEP-2008 to 31-AUG-2009 according to the 30-days risk periods of seasonal vaccination and the time since transplantation - Subjects without previous rejections (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	78	100.0	95	27316
Data after censoring according to transplantations	78	100.0	95	23124
Data after censoring according to second rejection	78	100.0	78	21091
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	78	100.0	78	21091
Seasonal vaccination - Control period before first dose	78	100.0	30	6251
Seasonal vaccination - Risk period after any dose	58	74.4	7	1762
Seasonal vaccination - Control period after any dose	56	71.8	41	13078
Seasonal vaccination - Pooled risk periods	58	74.4	7	1762
Seasonal vaccination - Pooled control periods	78	100.0	71	19329
Day0 to Day30 after transplantation	20	25.6	11	593
Day31 to Day90 after transplantation	19	24.4	8	954
Day91 to Day180 after transplantation	18	23.1	3	1152
> 180 days after transplantation	63	80.8	56	18392

Table 87 Relative incidence of SOT rejection within 30 days after seasonal vaccination in season 2008-2009 adjusted for the time since transplantation - Subjects without previous rejections (Subset 2a)

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	1.01	0.41	2.49
Time since transplantation	0-30 vs. >180 days	28.89	3.45	242.10
	31-90 vs. >180 days	15.50	1.76	136.34
	91-180 vs. >180 days	1.72	0.40	7.33

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

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Table 88 SOT rejections from 01-SEP-2008 to 31-AUG-2009 according to the 30-days risk periods of seasonal vaccination, the time since transplantation and previous rejection (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	22	100.0	37	7359
Data after censoring according to transplantations	22	100.0	36	7140
Data after censoring according to second rejection	22	100.0	22	5776
Subjects with at least one exposure of interest (Previous rejection, Seasonal vaccination, transplantation)	22	100.0	22	5776
Seasonal vaccination - Control period before first dose	22	100.0	12	2534
Seasonal vaccination - Risk period after any dose	14	63.6	2	411
Seasonal vaccination - Control period after any dose	12	54.5	8	2831
Seasonal vaccination - Pooled risk periods	14	63.6	2	411
Seasonal vaccination - Pooled control periods	22	100.0	20	5365
Day91 to Day180 after transplantation	1	4.5	0	22
> 180 days after transplantation	22	100.0	22	5754
Day0 to Day180 after Previous rejection	22	100.0	14	2410
> 180 days after Previous rejection	19	86.4	8	3366

Table 89 Relative incidence of SOT rejection within 30 days after seasonal vaccination in season 2008-2009 adjusted for the time since transplantation and previous rejection - Subjects with previous rejections (Subset 2a)

No records exist in this table

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Table 90 Heart transplant rejection from 01-SEP-2008 to 31-AUG-2009 according to the 30-days risk periods of seasonal vaccination and the time since transplantation (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	7	100.0	7	2555
Data after censoring according to transplantations	7	100.0	7	2555
Data after censoring according to second rejection	7	100.0	7	2555
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	4	57.1	4	1460
Seasonal vaccination - Control period before first dose	4	57.1	0	219
Seasonal vaccination - Risk period after any dose	4	57.1	1	124
Seasonal vaccination - Control period after any dose	4	57.1	3	1117
Seasonal vaccination - Pooled risk periods	4	57.1	1	124
Seasonal vaccination - Pooled control periods	4	57.1	3	1336
> 180 days after transplantation	4	57.1	4	1460

Table 91 Kidney transplant rejection from 01-SEP-2008 to 31-AUG-2009 according to the 30-days risk periods of seasonal vaccination and the time since transplantation (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	98	100.0	142	34626
Data after censoring according to transplantations	98	100.0	138	30365
Data after censoring according to second rejection	98	100.0	98	26600
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	63	64.3	63	16396
Seasonal vaccination - Control period before first dose	63	64.3	28	5219
Seasonal vaccination - Risk period after any dose	47	48.0	6	1398
Seasonal vaccination - Control period after any dose	43	43.9	29	9779
Seasonal vaccination - Pooled risk periods	47	48.0	6	1398
Seasonal vaccination - Pooled control periods	63	64.3	57	14998
Day0 to Day30 after transplantation	16	16.3	7	469
Day31 to Day90 after transplantation	15	15.3	8	805
Day91 to Day180 after transplantation	15	15.3	3	988
> 180 days after transplantation	51	52.0	45	14134

Table 92 Relative incidence of kidney transplant rejection within 30 days after seasonal vaccination in season 2008-2009 adjusted for the time since transplantation (Subset 2a)

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	0.98	0.34	2.80
Time since transplantation	0-30 vs. >180 days	22.83	2.26	230.30
	31-90 vs. >180 days	18.33	1.76	191.03
	91-180 vs. >180 days	2.12	0.39	11.57

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

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Table 93 Kidney transplant rejection from 01-SEP-2008 to 31-AUG-2009 according to the 30-days risk periods of seasonal vaccination, the time since transplantation and all covariates (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	97	100.0	141	34261
Data after censoring according to transplantations	97	100.0	137	30000
Data after censoring according to second rejection	97	100.0	97	26235
Subjects with at least one exposure of interest (Acute bacterial infection, Cancer, Chronic viral infection, Opportunistic infection, Respiratory infection, Seasonal vaccination, transplantation)	64	66.0	64	16761
Seasonal vaccination - Control period before first dose	64	66.0	29	5584
Seasonal vaccination - Risk period after any dose	47	48.5	6	1398
Seasonal vaccination - Control period after any dose	43	44.3	29	9779
Seasonal vaccination - Pooled risk periods	47	48.5	6	1398
Seasonal vaccination - Pooled control periods	64	66.0	58	15363
Day0 to Day30 after transplantation	16	16.5	7	469
Day31 to Day90 after transplantation	15	15.5	8	805
Day91 to Day180 after transplantation	15	15.5	3	988
> 180 days after transplantation	52	53.6	46	14499
Day0 to Day30 after Respiratory infection	1	1.0	0	31
> 30 days after Respiratory infection	64	66.0	64	16730
Day0 to Day30 after Opportunistic infection	2	2.1	1	62
> 30 days after Opportunistic infection	64	66.0	63	16699
> 30 days after Acute bacterial infection	64	66.0	64	16761
> 365 days after Chronic viral infection	64	66.0	64	16761
Day0 to Day365 after Cancer	3	3.1	0	245
> 365 days after Cancer	64	66.0	64	16516

Table 94 **Relative incidence of kidney transplant rejection within 30 days after seasonal vaccination in season 2008-2009 adjusted for all covariates (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	0.98	0.34	2.80
Time since transplantation	0-30 vs. >180 days	22.83	2.26	230.30
	31-90 vs. >180 days	18.33	1.76	191.03
	91-180 vs. >180 days	2.12	0.39	11.57

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

Note: only subjects with one year of follow-up before the beginning of the season were considered

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Table 95 Kidney transplant rejections from 01-SEP-2008 to 31-AUG-2009 according to the 30-days risk periods of seasonal vaccination and the time since transplantation – with subsequent rejections (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	98	100.0	142	34626
Data after censoring according to transplantations	98	100.0	138	30365
Subjects with at least one exposure of interest (seasonal vaccination, transplantation)	63	64.3	83	18551
seasonal vaccination - Control period before first dose	63	64.3	31	5702
seasonal vaccination - Risk period after any dose	47	48.0	8	1439
seasonal vaccination - Control period after any dose	45	45.9	44	11410
seasonal vaccination - Pooled risk periods	47	48.0	8	1439
seasonal vaccination - Pooled control periods	63	64.3	75	17112
Day0 to Day30 after transplantation	16	16.3	7	469
Day31 to Day90 after transplantation	15	15.3	9	819
Day91 to Day180 after transplantation	16	16.3	6	1127
> 180 days after transplantation	54	55.1	61	16136

Table 96 **Relative incidence of kidney transplant rejection within 30 days after seasonal vaccination in season 2008-2009 adjusted for the time since transplantation - not accounting for perturbed post-event exposure (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	1.30	0.61	2.76
Time since transplantation	0-30 vs. >180 days	20.25	3.10	132.21
	31-90 vs. >180 days	17.82	2.95	107.73
	91-180 vs. >180 days	4.61	1.12	18.91

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

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Table 97 Relative incidence of kidney transplant rejection within 30 days after seasonal vaccination in season 2008-2009 adjusted for the time since transplantation and conditioned to previous rejections (Subset 2a)

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
seasonal vaccination in cases without previous rejection	30 days after any dose vs. other periods	0.97	.	.
seasonal vaccination in cases without previous rejection in cases with previous rejection	30 days after any dose vs. other periods	1.01	.	.
Time since transplantation	0-30 vs. >180 days	22.83	.	.
	31-90 vs. >180 days	18.33	.	.
	91-180 vs. >180 days	2.12	.	.

95% CI = 95% percentile bootstrap confidence interval

LL =lower limit

UL =upper limit

Number of bootstrap steps: NA

Table 98 Kidney transplant rejection from 01-SEP-2008 to 31-AUG-2009 according to the 30-days risk periods of seasonal vaccination and the time since transplantation - Subjects without previous rejections (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	50	100.0	65	17558
Data after censoring according to transplantations	50	100.0	65	14330
Data after censoring according to second rejection	50	100.0	50	12635
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	50	100.0	50	12635
Seasonal vaccination - Control period before first dose	50	100.0	24	4398
Seasonal vaccination - Risk period after any dose	34	68.0	4	1018
Seasonal vaccination - Control period after any dose	32	64.0	22	7219
Seasonal vaccination - Pooled risk periods	34	68.0	4	1018
Seasonal vaccination - Pooled control periods	50	100.0	46	11617
Day0 to Day30 after transplantation	16	32.0	7	469
Day31 to Day90 after transplantation	15	30.0	8	805
Day91 to Day180 after transplantation	15	30.0	3	988
> 180 days after transplantation	38	76.0	32	10373

Table 99 Relative incidence of kidney transplant rejection within 30 days after seasonal vaccination in season 2008-2009 adjusted for the time since transplantation - Subjects without previous rejections (Subset 2a)

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	0.97	0.29	3.22
Time since transplantation	0-30 vs. >180 days	22.83	2.26	230.30
	31-90 vs. >180 days	18.33	1.76	191.03
	91-180 vs. >180 days	2.12	0.39	11.57

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

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Table 100 Kidney transplant rejection from 01-SEP-2008 to 31-AUG-2009 according to the 30-days risk periods of seasonal vaccination, the time since transplantation and previous rejection - Subjects with previous rejections (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	20	100.0	35	6975
Data after censoring according to transplantations	20	100.0	34	6756
Data after censoring according to second rejection	20	100.0	20	5392
Subjects with at least one exposure of interest (Previous rejection, Seasonal vaccination, transplantation)	20	100.0	20	5392
Seasonal vaccination - Control period before first dose	20	100.0	11	2452
Seasonal vaccination - Risk period after any dose	13	65.0	2	380
Seasonal vaccination - Control period after any dose	11	55.0	7	2560
Seasonal vaccination - Pooled risk periods	13	65.0	2	380
Seasonal vaccination - Pooled control periods	20	100.0	18	5012
> 180 days after transplantation	20	100.0	20	5392
Day0 to Day180 after Previous rejection	20	100.0	13	2301
> 180 days after Previous rejection	18	90.0	7	3091

Table 101 **Relative incidence of kidney transplant rejection within 30 days after seasonal vaccination in season 2008-2009 adjusted for the time since transplantation and previous rejection - Subjects with previous rejections (Subset 2a)**

No records exist in this table

Table 102 Liver transplant rejection from 01-SEP-2008 to 31-AUG-2009 according to the 30-days risk periods of seasonal vaccination and the time since transplantation (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	16	100.0	17	4857
Data after censoring according to transplantations	16	100.0	17	4428
Data after censoring according to second rejection	16	100.0	16	4322
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	9	56.3	9	2854
Seasonal vaccination - Control period before first dose	9	56.3	4	889
Seasonal vaccination - Risk period after any dose	7	43.8	0	217
Seasonal vaccination - Control period after any dose	7	43.8	5	1748
Seasonal vaccination - Pooled risk periods	7	43.8	0	217
Seasonal vaccination - Pooled control periods	9	56.3	9	2637
Day0 to Day30 after transplantation	2	12.5	2	62
Day31 to Day90 after transplantation	2	12.5	0	120
Day91 to Day180 after transplantation	2	12.5	0	126
> 180 days after transplantation	8	50.0	7	2546

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Table 103 Lung transplant rejection from 01-SEP-2008 to 31-AUG-2009 according to the 30-days risk periods of seasonal vaccination and the time since transplantation (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	5	100.0	5	1611
Data after censoring according to transplantations	5	100.0	5	972
Data after censoring according to second rejection	5	100.0	5	972
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	4	80.0	4	607
Seasonal vaccination - Control period before first dose	4	80.0	2	169
Seasonal vaccination - Risk period after any dose	2	40.0	0	62
Seasonal vaccination - Control period after any dose	2	40.0	2	376
Seasonal vaccination - Pooled risk periods	2	40.0	0	62
Seasonal vaccination - Pooled control periods	4	80.0	4	545
Day0 to Day30 after transplantation	2	40.0	2	62
Day31 to Day90 after transplantation	2	40.0	0	29
Day91 to Day180 after transplantation	1	20.0	0	38
> 180 days after transplantation	2	40.0	2	478

Table 104 Pancreas transplant rejection from 01-SEP-2008 to 31-AUG-2009 according to the 30-days risk periods of seasonal vaccination and the time since transplantation (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	0			
Data after censoring according to transplantations	0			
Data after censoring according to second rejection	0			
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	0			

12.2.1.4. Pooled seasons**Table 105 SOT rejections according to the 30-days risk periods of seasonal vaccination and the time since transplantation - pooled seasons (Subset 2a)**

	Subjects		Rejections	Person*days
	N	%		
Subjects with at least one exposure of interest (seasonal vaccination, transplantation) in any of the seasons*	218	100.0	218	61162
Subjects with data from season 06-07	74	33.9	74	20560
Subjects with data from season 07-08	74	33.9	74	21441
Subjects with data from season 08-09	70	32.1	70	19161
seasonal vaccination - Control period before first dose	216	99.1	93	20299
seasonal vaccination - Risk period after any dose	156	71.6	18	4757
seasonal vaccination - Control period after any dose	152	69.7	107	36106
seasonal vaccination - Pooled risk periods	156	71.6	18	4757
seasonal vaccination - Pooled control periods	218	100.0	200	56405
Day0 to Day30 after transplantation	64	29.4	38	1811
Day31 to Day90 after transplantation	64	29.4	21	3347
Day91 to Day180 after transplantation	62	28.4	13	4831
> 180 days after transplantation	182	83.5	146	51173

*Only the first season with data on exposures of interest is considered for each patient

Table 106 **Relative incidence of SOT rejection within 30 days after seasonal vaccination in seasons 2006-2009 adjusted for the time since transplantation (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	1.01	0.58	1.76
Time since transplantation	0-30 vs. >180 days	16.41	5.89	45.72
	31-90 vs. >180 days	5.59	2.14	14.65
	91-180 vs. >180 days	1.94	0.72	5.25

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

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Table 107 SOT rejections according to the 30-days risk periods of seasonal vaccination, the time since transplantation and all covariates - pooled seasons (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subjects with at least one exposure of interest (Acute bacterial infection, Cancer, Chronic viral infection, Opportunistic infection, Respiratory infection, Seasonal vaccination, transplantation) in any of the seasons*	210	100.0	210	58815
Subjects with data from season 06-07	71	33.8	71	19626
Subjects with data from season 07-08	70	33.3	70	20155
Subjects with data from season 08-09	69	32.9	69	19034
Seasonal vaccination - Control period before first dose	208	99.0	89	19123
Seasonal vaccination - Risk period after any dose	152	72.4	18	4633
Seasonal vaccination - Control period after any dose	148	70.5	103	35059
Seasonal vaccination - Pooled risk periods	152	72.4	18	4633
Seasonal vaccination - Pooled control periods	210	100.0	192	54182
Day0 to Day30 after transplantation	61	29.0	36	1718
Day31 to Day90 after transplantation	60	28.6	20	3126
Day91 to Day180 after transplantation	58	27.6	12	4525
> 180 days after transplantation	175	83.3	142	49446
> 30 days after Respiratory infection	210	100.0	210	58815
Day0 to Day30 after Opportunistic infection	7	3.3	2	215
> 30 days after Opportunistic infection	210	100.0	208	58600
> 30 days after Acute bacterial infection	210	100.0	210	58815
> 365 days after Chronic viral infection	210	100.0	210	58815
Day0 to Day365 after Cancer	14	6.7	12	3366
> 365 days after Cancer	207	98.6	198	55449

*Only the first season with data on exposures of interest is considered for each patient

Table 108 **Relative incidence of SOT rejection within 30 days after seasonal vaccination in seasons 2006-2009 adjusted for all covariates (Subset 2a)**

No records exist in this table

Table 109 SOT rejections according to the 30-days risk periods of seasonal vaccination, the time since transplantation and opportunistic infections - pooled seasons (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subjects with at least one exposure of interest (Opportunistic infection, seasonal vaccination, transplantation) in any of the seasons*	218	100.0	218	61162
Subjects with data from season 06-07	74	33.9	74	20560
Subjects with data from season 07-08	74	33.9	74	21441
Subjects with data from season 08-09	70	32.1	70	19161
seasonal vaccination - Control period before first dose	216	99.1	93	20299
seasonal vaccination - Risk period after any dose	156	71.6	18	4757
seasonal vaccination - Control period after any dose	152	69.7	107	36106
seasonal vaccination - Pooled risk periods	156	71.6	18	4757
seasonal vaccination - Pooled control periods	218	100.0	200	56405
Day0 to Day30 after transplantation	64	29.4	38	1811
Day31 to Day90 after transplantation	64	29.4	21	3347
Day91 to Day180 after transplantation	62	28.4	13	4831
> 180 days after transplantation	182	83.5	146	51173
Day0 to Day30 after Opportunistic infection	7	3.2	2	215
> 30 days after Opportunistic infection	218	100.0	216	60947

*Only the first season with data on exposures of interest is considered for each patient

Table 110 **Relative incidence of SOT rejection within 30 days after seasonal vaccination in seasons 2006-2009 adjusted for the time since transplantation and opportunistic infections (Subset 2a)**

No records exist in this table

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Table 111 SOT rejections according to the 30-days risk periods of seasonal vaccination, the time since transplantation and malignancies/cancers - pooled seasons (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subjects with at least one exposure of interest (Cancer, seasonal vaccination, transplantation) in any of the seasons*	210	100.0	210	58815
Subjects with data from season 06-07	71	33.8	71	19626
Subjects with data from season 07-08	70	33.3	70	20155
Subjects with data from season 08-09	69	32.9	69	19034
seasonal vaccination - Control period before first dose	208	99.0	89	19123
seasonal vaccination - Risk period after any dose	152	72.4	18	4633
seasonal vaccination - Control period after any dose	148	70.5	103	35059
seasonal vaccination - Pooled risk periods	152	72.4	18	4633
seasonal vaccination - Pooled control periods	210	100.0	192	54182
Day0 to Day30 after transplantation	61	29.0	36	1718
Day31 to Day90 after transplantation	60	28.6	20	3126
Day91 to Day180 after transplantation	58	27.6	12	4525
> 180 days after transplantation	175	83.3	142	49446
Day0 to Day365 after Cancer	14	6.7	12	3366
> 365 days after Cancer	207	98.6	198	55449

*Only the first season with data on exposures of interest is considered for each patient

Table 112 **Relative incidence of SOT rejection within 30 days after seasonal vaccination in seasons 2006-2009 adjusted for the time since transplantation and malignancies/cancers (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	1.06	0.61	1.84
Time since transplantation	0-30 vs. >180 days	15.00	5.33	42.19
	31-90 vs. >180 days	5.34	2.04	14.01
	91-180 vs. >180 days	1.80	0.65	5.00
Malignancies/ cancers	365 days after any record vs. other periods	3.46	0.42	28.21

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

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Table 113 SOT rejections according to the 30-days risk periods of seasonal vaccination and the time since transplantation – with subsequent rejections - pooled seasons (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subjects with at least one exposure of interest (seasonal vaccination, transplantation) in any of the seasons*	218	100.0	250	64659
Subjects with data from season 06-07	74	33.9	83	21781
Subjects with data from season 07-08	74	33.9	85	22374
Subjects with data from season 08-09	70	32.1	82	20504
seasonal vaccination - Control period before first dose	216	99.1	101	21240
seasonal vaccination - Risk period after any dose	156	71.6	21	4801
seasonal vaccination - Control period after any dose	155	71.1	128	38618
seasonal vaccination - Pooled risk periods	156	71.6	21	4801
seasonal vaccination - Pooled control periods	218	100.0	229	59858
Day0 to Day30 after transplantation	64	29.4	38	1811
Day31 to Day90 after transplantation	64	29.4	23	3398
Day91 to Day180 after transplantation	64	29.4	19	5124
> 180 days after transplantation	189	86.7	170	54326

*Only the first season with data on exposures of interest is considered for each patient

Table 114 **Relative incidence of SOT rejection within 30 days after seasonal vaccination in seasons 2006-2009 adjusted for the time since transplantation - not accounting for perturbed post-event exposure (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	1.15	0.73	1.83
Time since transplantation	0-30 vs. >180 days	13.76	6.05	31.27
	31-90 vs. >180 days	5.42	2.44	12.00
	91-180 vs. >180 days	2.50	1.20	5.19

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

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Table 115 Relative incidence of SOT rejection within 30 days after seasonal vaccination in seasons 2006-2009 adjusted for the time since transplantation and conditioned to previous rejections (Subset 2a)

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
seasonal vaccination	30 days after any dose vs. other periods	1.04	.	.
seasonal vaccination in cases with previous rejection	30 days after any dose vs. other periods	0.73	.	.
Time since transplantation	0-30 vs. >180 days	16.35	.	.
	31-90 vs. >180 days	5.58	.	.
	91-180 vs. >180 days	1.94	.	.

95% CI = 95% percentile bootstrap confidence interval

LL =lower limit

UL =upper limit

Number of bootstrap steps: NA

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Table 116 SOT rejections according to the 30-days risk periods of seasonal vaccination and the time since transplantation - Subjects without previous rejections - pooled seasons (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subjects with at least one exposure of interest (seasonal vaccination, transplantation) in any of the seasons*	204	100.0	204	57109
Subjects with data from season 06-07	65	31.9	65	18290
Subjects with data from season 07-08	73	35.8	73	21118
Subjects with data from season 08-09	66	32.4	66	17701
seasonal vaccination - Control period before first dose	202	99.0	88	19162
seasonal vaccination - Risk period after any dose	143	70.1	17	4374
seasonal vaccination - Control period after any dose	141	69.1	99	33573
seasonal vaccination - Pooled risk periods	143	70.1	17	4374
seasonal vaccination - Pooled control periods	204	100.0	187	52735
Day0 to Day30 after transplantation	64	31.4	38	1811
Day31 to Day90 after transplantation	62	30.4	19	3292
Day91 to Day180 after transplantation	60	29.4	13	4692
> 180 days after transplantation	169	82.8	134	47314

*Only the first season with data on exposures of interest is considered for each patient

Table 117 Relative incidence of SOT rejection within 30 days after seasonal vaccination in seasons 2006-2009 adjusted for the time since transplantation - Subjects without previous rejections (Subset 2a)

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	1.04	0.59	1.84
Time since transplantation	0-30 vs. >180 days	14.77	5.39	40.47
	31-90 vs. >180 days	4.78	1.83	12.46
	91-180 vs. >180 days	1.94	0.73	5.20

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

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Table 118 SOT rejections according to the 30-days risk periods of seasonal vaccination, the time since transplantation and previous rejection - pooled seasons (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subjects with at least one exposure of interest (Previous rejection, seasonal vaccination, transplantation) in any of the seasons*	14	100.0	14	4053
Subjects with data from season 06-07	9	64.3	9	2270
Subjects with data from season 07-08	1	7.1	1	323
Subjects with data from season 08-09	4	28.6	4	1460
seasonal vaccination - Control period before first dose	14	100.0	5	1137
seasonal vaccination - Risk period after any dose	13	92.9	1	383
seasonal vaccination - Control period after any dose	11	78.6	8	2533
seasonal vaccination - Pooled risk periods	13	92.9	1	383
seasonal vaccination - Pooled control periods	14	100.0	13	3670
Day31 to Day90 after transplantation	2	14.3	2	55
Day91 to Day180 after transplantation	2	14.3	0	139
> 180 days after transplantation	13	92.9	12	3859
Day0 to Day180 after Previous rejection	14	100.0	6	1187
> 180 days after Previous rejection	13	92.9	8	2866

*Only the first season with data on exposures of interest is considered for each patient

Table 119 **Relative incidence of SOT rejection within 30 days after seasonal vaccination in seasons 2006-2009 adjusted for the time since transplantation and previous rejection - Subjects with previous rejections (Subset 2a)**

No records exist in this table

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Table 120 Heart transplant rejection according to the 30-days risk periods of seasonal vaccination and the time since transplantation - pooled seasons (Subset 2a)

	Subjects			
	N	%	Rejections	Person*days
Subjects with at least one exposure of interest (seasonal vaccination, transplantation) in any of the seasons*	15	100.0	15	3882
Subjects with data from season 06-07	5	33.3	5	933
Subjects with data from season 07-08	6	40.0	6	1489
Subjects with data from season 08-09	4	26.7	4	1460
seasonal vaccination - Control period before first dose	15	100.0	6	983
seasonal vaccination - Risk period after any dose	10	66.7	1	310
seasonal vaccination - Control period after any dose	10	66.7	8	2589
seasonal vaccination - Pooled risk periods	10	66.7	1	310
seasonal vaccination - Pooled control periods	15	100.0	14	3572
Day0 to Day30 after transplantation	4	26.7	4	46
Day31 to Day90 after transplantation	2	13.3	0	96
Day91 to Day180 after transplantation	2	13.3	1	180
> 180 days after transplantation	11	73.3	10	3560

*Only the first season with data on exposures of interest is considered for each patient

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Table 121 Kidney transplant rejection according to the 30-days risk periods of seasonal vaccination and the time since transplantation - pooled seasons (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subjects with at least one exposure of interest (seasonal vaccination, transplantation) in any of the seasons*	144	100.0	144	38892
Subjects with data from season 06-07	49	34.0	49	13686
Subjects with data from season 07-08	51	35.4	51	14217
Subjects with data from season 08-09	44	30.6	44	10989
seasonal vaccination - Control period before first dose	142	98.6	70	14495
seasonal vaccination - Risk period after any dose	98	68.1	11	2963
seasonal vaccination - Control period after any dose	95	66.0	63	21434
seasonal vaccination - Pooled risk periods	98	68.1	11	2963
seasonal vaccination - Pooled control periods	144	100.0	133	35929
Day0 to Day30 after transplantation	49	34.0	26	1424
Day31 to Day90 after transplantation	48	33.3	18	2630
Day91 to Day180 after transplantation	47	32.6	9	3720
> 180 days after transplantation	120	83.3	91	31118

*Only the first season with data on exposures of interest is considered for each patient

Table 122 **Relative incidence of kidney transplant rejection within 30 days after seasonal vaccination in seasons 2006-2009 adjusted for the time since transplantation (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	0.91	0.44	1.87
Time since transplantation	0-30 vs. >180 days	13.07	4.18	40.87
	31-90 vs. >180 days	5.40	1.84	15.82
	91-180 vs. >180 days	1.52	0.47	4.92

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

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Table 123 Kidney transplant rejection according to the 30-days risk periods of seasonal vaccination, the time since transplantation and all covariates - pooled seasons (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subjects with at least one exposure of interest (Acute bacterial infection, Cancer, Chronic viral infection, Opportunistic infection, Respiratory infection, seasonal vaccination, transplantation) in any of the seasons*	139	100.0	139	37228
Subjects with data from season 06-07	47	33.8	47	13117
Subjects with data from season 07-08	48	34.5	48	13122
Subjects with data from season 08-09	44	31.7	44	10989
seasonal vaccination - Control period before first dose	137	98.6	69	14008
seasonal vaccination - Risk period after any dose	94	67.6	11	2839
seasonal vaccination - Control period after any dose	91	65.5	59	20381
seasonal vaccination - Pooled risk periods	94	67.6	11	2839
seasonal vaccination - Pooled control periods	139	100.0	128	34389
Day0 to Day30 after transplantation	48	34.5	25	1393
Day31 to Day90 after transplantation	47	33.8	18	2570
Day91 to Day180 after transplantation	46	33.1	9	3630
> 180 days after transplantation	115	82.7	87	29635
> 30 days after Respiratory infection	139	100.0	139	37228
Day0 to Day30 after Opportunistic infection	5	3.6	1	153
> 30 days after Opportunistic infection	139	100.0	138	37075
> 30 days after Acute bacterial infection	139	100.0	139	37228
> 365 days after Chronic viral infection	139	100.0	139	37228
Day0 to Day365 after Cancer	4	2.9	3	745
> 365 days after Cancer	137	98.6	136	36483

*Only the first season with data on exposures of interest is considered for each patient

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Table 124 Kidney transplant rejections according to the 30-days risk periods of seasonal vaccination and the time since transplantation with subsequent rejections - pooled seasons (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subjects with at least one exposure of interest (seasonal vaccination, transplantation) in any of the seasons*	144	100.0	171	41777
Subjects with data from season 06-07	49	34.0	55	14426
Subjects with data from season 07-08	51	35.4	61	15125
Subjects with data from season 08-09	44	30.6	55	12226
seasonal vaccination - Control period before first dose	142	98.6	77	15411
seasonal vaccination - Risk period after any dose	98	68.1	13	3003
seasonal vaccination - Control period after any dose	97	67.4	81	23363
seasonal vaccination - Pooled risk periods	98	68.1	13	3003
seasonal vaccination - Pooled control periods	144	100.0	158	38774
Day0 to Day30 after transplantation	49	34.0	26	1424
Day31 to Day90 after transplantation	48	33.3	20	2681
Day91 to Day180 after transplantation	49	34.0	14	3972
> 180 days after transplantation	126	87.5	111	33700

*Only the first season with data on exposures of interest is considered for each patient

Table 125 Relative incidence of kidney transplant rejection within 30 days after seasonal vaccination in seasons 2006-2009 adjusted for the time since transplantation - not accounting for perturbed post-event exposure (Subset 2a)

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	1.01	0.56	1.82
Time since transplantation	0-30 vs. >180 days	12.33	4.84	31.38
	31-90 vs. >180 days	5.92	2.40	14.58
	91-180 vs. >180 days	2.39	1.01	5.63

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

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**Table 126 Relative incidence of kidney transplant rejection within 30 days after seasonal vaccination in seasons 2006-2009
adjusted for the time since transplantation and conditioned to previous rejections (Subset 2a)**

		95% CI		
Variable	Compared periods	Relative Incidence	LL	UL
seasonal vaccination	30 days after any dose vs. other periods	0.91	.	.
seasonal vaccination in cases with previous rejection	30 days after any dose vs. other periods	0.88	.	.
Time since transplantation	0-30 vs. >180 days	13.06	.	.
	31-90 vs. >180 days	5.40	.	.
	91-180 vs. >180 days	1.52	.	.

95% CI = 95% percentile bootstrap confidence interval

LL =lower limit

UL =upper limit

Number of bootstrap steps: NA

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Table 127 Kidney transplant rejection according to the 30-days risk periods of seasonal vaccination and the time since transplantation - Subjects without previous rejections - pooled seasons (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subjects with at least one exposure of interest (seasonal vaccination, transplantation) in any of the seasons*	134	100.0	134	35997
Subjects with data from season 06-07	43	32.1	43	12209
Subjects with data from season 07-08	50	37.3	50	13894
Subjects with data from season 08-09	41	30.6	41	9894
seasonal vaccination - Control period before first dose	132	98.5	67	13865
seasonal vaccination - Risk period after any dose	88	65.7	10	2669
seasonal vaccination - Control period after any dose	86	64.2	57	19463
seasonal vaccination - Pooled risk periods	88	65.7	10	2669
seasonal vaccination - Pooled control periods	134	100.0	124	33328
Day0 to Day30 after transplantation	49	36.6	26	1424
Day31 to Day90 after transplantation	48	35.8	18	2630
Day91 to Day180 after transplantation	47	35.1	9	3720
> 180 days after transplantation	110	82.1	81	28223

*Only the first season with data on exposures of interest is considered for each patient

Table 128 **Relative incidence of kidney transplant rejection within 30 days after seasonal vaccination in seasons 2006-2009 adjusted for the time since transplantation - Subjects without previous rejections (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	0.91	0.43	1.94
Time since transplantation	0-30 vs. >180 days	13.06	4.18	40.80
	31-90 vs. >180 days	5.40	1.84	15.81
	91-180 vs. >180 days	1.52	0.47	4.92

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

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Table 129 Kidney transplant rejection according to the 30-days risk periods of seasonal vaccination, the time since transplantation and previous rejection - Subjects with previous rejections - pooled seasons (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subjects with at least one exposure of interest (Previous rejection, seasonal vaccination, transplantation) in any of the seasons*	10	100.0	10	2895
Subjects with data from season 06-07	6	60.0	6	1477
Subjects with data from season 07-08	1	10.0	1	323
Subjects with data from season 08-09	3	30.0	3	1095
seasonal vaccination - Control period before first dose	10	100.0	3	630
seasonal vaccination - Risk period after any dose	10	100.0	1	294
seasonal vaccination - Control period after any dose	9	90.0	6	1971
seasonal vaccination - Pooled risk periods	10	100.0	1	294
seasonal vaccination - Pooled control periods	10	100.0	9	2601
> 180 days after transplantation	10	100.0	10	2895
Day0 to Day180 after Previous rejection	10	100.0	4	845
> 180 days after Previous rejection	10	100.0	6	2050

*Only the first season with data on exposures of interest is considered for each patient

Table 130 **Relative incidence of kidney transplant rejection within 30 days after seasonal vaccination in seasons 2006-2009 adjusted for the time since transplantation and previous rejection - Subjects with previous rejections (Subset 2a)**

No records exist in this table

Table 131 **Liver transplant rejection according to the 30-days risk periods of seasonal vaccination and the time since transplantation - pooled seasons (Subset 2a)**

	Subjects		Rejections	Person*days
	N	%		
Subjects with at least one exposure of interest (seasonal vaccination, transplantation) in any of the seasons*	16	100.0	16	4950
Subjects with data from season 06-07	5	31.3	5	1604
Subjects with data from season 07-08	3	18.8	3	857
Subjects with data from season 08-09	8	50.0	8	2489
seasonal vaccination - Control period before first dose	16	100.0	10	2211
seasonal vaccination - Risk period after any dose	10	62.5	0	310
seasonal vaccination - Control period after any dose	10	62.5	6	2429
seasonal vaccination - Pooled risk periods	10	62.5	0	310
seasonal vaccination - Pooled control periods	16	100.0	16	4640
Day0 to Day30 after transplantation	6	37.5	5	186
Day31 to Day90 after transplantation	8	50.0	1	404
Day91 to Day180 after transplantation	8	50.0	2	656
> 180 days after transplantation	14	87.5	8	3704

*Only the first season with data on exposures of interest is considered for each patient

Table 132 Lung transplant rejection according to the 30-days risk periods of seasonal vaccination and the time since transplantation - pooled seasons (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subjects with at least one exposure of interest (seasonal vaccination, transplantation) in any of the seasons*	9	100.0	9	1824
Subjects with data from season 06-07	5	55.6	5	1003
Subjects with data from season 07-08	1	11.1	1	365
Subjects with data from season 08-09	3	33.3	3	456
seasonal vaccination - Control period before first dose	9	100.0	5	527
seasonal vaccination - Risk period after any dose	5	55.6	0	151
seasonal vaccination - Control period after any dose	4	44.4	4	1146
seasonal vaccination - Pooled risk periods	5	55.6	0	151
seasonal vaccination - Pooled control periods	9	100.0	9	1673
Day0 to Day30 after transplantation	4	44.4	3	124
Day31 to Day90 after transplantation	5	55.6	2	157
Day91 to Day180 after transplantation	4	44.4	0	207
> 180 days after transplantation	4	44.4	4	1336

*Only the first season with data on exposures of interest is considered for each patient

Table 133 Pancreas transplant rejection according to the 30-days risk periods of seasonal vaccination and the time since transplantation - pooled seasons (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subjects with at least one exposure of interest (seasonal vaccination, transplantation) in any of the seasons*	1	100.0	1	6
Subjects with data from season 07-08	1	100.0	1	6
seasonal vaccination - Control period before first dose	1	100.0	1	6
seasonal vaccination - Pooled control periods	1	100.0	1	6
Day0 to Day30 after transplantation	1	100.0	1	6

*Only the first season with data on exposures of interest is considered for each patient

12.2.2. Subset 2B**12.2.2.1. Season 2006-2007****Table 134 SOT rejections from 01-SEP-2006 to 31-AUG-2007 according to the 30-days risk periods of seasonal vaccination and the time since transplantation (Subset 2b)**

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	46	100.0	53	15771
Data after censoring according to transplantations	46	100.0	53	14272
Data after censoring according to second rejection	46	100.0	46	13834
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	26	56.5	26	7227
Seasonal vaccination - Control period before first dose	25	54.3	11	2192
Seasonal vaccination - Risk period after any dose	20	43.5	4	605
Seasonal vaccination - Control period after any dose	20	43.5	11	4430
Seasonal vaccination - Pooled risk periods	20	43.5	4	605
Seasonal vaccination - Pooled control periods	26	56.5	22	6622
Day0 to Day30 after transplantation	9	19.6	8	234
> 30 days after transplantation	24	52.2	18	6993

Table 135 **Relative incidence of SOT rejection within 30 days after seasonal vaccination in season 2006-2007 adjusted for the time since transplantation (Subset 2b)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	1.93	0.50	7.46
Time since transplantation	0-30 vs. >30 days	41.44	5.17	331.84

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

Table 136 SOT rejections from 01-SEP-2006 to 31-AUG-2007 according to the 30-days risk periods of seasonal vaccination, the time since transplantation and all covariates (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	45	100.0	52	15406
Data after censoring according to transplantations	45	100.0	52	13907
Data after censoring according to second rejection	45	100.0	45	13469
Subjects with at least one exposure of interest (Acute bacterial infection, Cancer, Chronic viral infection, Opportunistic infection, Respiratory infection, Seasonal vaccination, chemo, transplantation)	28	62.2	28	7945
Seasonal vaccination - Control period before first dose	27	60.0	13	2910
Seasonal vaccination - Risk period after any dose	20	44.4	4	605
Seasonal vaccination - Control period after any dose	20	44.4	11	4430
Seasonal vaccination - Pooled risk periods	20	44.4	4	605
Seasonal vaccination - Pooled control periods	28	62.2	24	7340
Day0 to Day30 after transplantation	9	20.0	8	234
> 30 days after transplantation	26	57.8	20	7711
Day0 to Day30 after Respiratory infection	1	2.2	0	31
> 30 days after Respiratory infection	28	62.2	28	7914
Day0 to Day30 after Opportunistic infection	2	4.4	0	62
> 30 days after Opportunistic infection	28	62.2	28	7883
> 30 days after Acute bacterial infection	28	62.2	28	7945
> 365 days after Chronic viral infection	28	62.2	28	7945
Day0 to Day365 after Cancer	4	8.9	4	1022
> 365 days after Cancer	26	57.8	24	6923
Day0 to Day365 after chemo	1	2.2	1	264
> 365 days after chemo	28	62.2	27	7681

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Table 137 SOT rejections from 01-SEP-2006 to 31-AUG-2007 according to the 30-days risk periods of seasonal vaccination and the time since transplantation – with subsequent rejections (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	46	100.0	53	15771
Data after censoring according to transplantations	46	100.0	53	14272
Subjects with at least one exposure of interest (seasonal vaccination, transplantation)	26	56.5	31	7539
seasonal vaccination - Control period before first dose	25	54.3	11	2192
seasonal vaccination - Risk period after any dose	20	43.5	4	605
seasonal vaccination - Control period after any dose	20	43.5	16	4742
seasonal vaccination - Pooled risk periods	20	43.5	4	605
seasonal vaccination - Pooled control periods	26	56.5	27	6934
Day0 to Day30 after transplantation	9	19.6	8	234
> 30 days after transplantation	24	52.2	23	7305

Table 138 **Relative incidence of SOT rejection within 30 days after seasonal vaccination in season 2006-2007 adjusted for the time since transplantation - not accounting for perturbed post-event exposure (Subset 2b)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	1.72	0.56	5.25
Time since transplantation	0-30 vs. >30 days	38.84	4.44	339.43

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

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Table 139 Heart transplant rejection from 01-SEP-2006 to 31-AUG-2007 according to the 30-days risk periods of seasonal vaccination and the time since transplantation (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	4	100.0	5	918
Data after censoring according to transplantations	4	100.0	5	606
Data after censoring according to second rejection	4	100.0	4	492
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	2	50.0	2	17
Seasonal vaccination - Control period before first dose	2	50.0	2	17
Seasonal vaccination - Pooled control periods	2	50.0	2	17
Day0 to Day30 after transplantation	2	50.0	2	17

Table 140 Kidney transplant rejection from 01-SEP-2006 to 31-AUG-2007 according to the 30-days risk periods of seasonal vaccination and the time since transplantation (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	22	100.0	27	7694
Data after censoring according to transplantations	22	100.0	27	6864
Data after censoring according to second rejection	22	100.0	22	6632
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	16	72.7	16	4790
Seasonal vaccination - Control period before first dose	15	68.2	6	1488
Seasonal vaccination - Risk period after any dose	13	59.1	2	388
Seasonal vaccination - Control period after any dose	13	59.1	8	2914
Seasonal vaccination - Pooled risk periods	13	59.1	2	388
Seasonal vaccination - Pooled control periods	16	72.7	14	4402
Day0 to Day30 after transplantation	5	22.7	4	155
> 30 days after transplantation	16	72.7	12	4635

Table 141 **Relative incidence of kidney transplant rejection within 30 days after seasonal vaccination in season 2006-2007 adjusted for the time since transplantation (Subset 2b)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	1.04	0.17	6.56
Time since transplantation	0-30 vs. >30 days	34.05	3.75	308.93

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

Table 142 Kidney transplant rejection from 01-SEP-2006 to 31-AUG-2007 according to the 30-days risk periods of seasonal, vaccination the time since transplantation and all covariates (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	22	100.0	27	7694
Data after censoring according to transplantations	22	100.0	27	6864
Data after censoring according to second rejection	22	100.0	22	6632
Subjects with at least one exposure of interest (Acute bacterial infection, Cancer, Chronic viral infection, Opportunistic infection, Respiratory infection, Seasonal vaccination, chemo, transplantation)	17	77.3	17	5143
Seasonal vaccination - Control period before first dose	16	72.7	7	1841
Seasonal vaccination - Risk period after any dose	13	59.1	2	388
Seasonal vaccination - Control period after any dose	13	59.1	8	2914
Seasonal vaccination - Pooled risk periods	13	59.1	2	388
Seasonal vaccination - Pooled control periods	17	77.3	15	4755
Day0 to Day30 after transplantation	5	22.7	4	155
> 30 days after transplantation	17	77.3	13	4988
Day0 to Day30 after Respiratory infection	1	4.5	0	31
> 30 days after Respiratory infection	17	77.3	17	5112
Day0 to Day30 after Opportunistic infection	1	4.5	0	31
> 30 days after Opportunistic infection	17	77.3	17	5112
> 30 days after Acute bacterial infection	17	77.3	17	5143
> 365 days after Chronic viral infection	17	77.3	17	5143
Day0 to Day365 after Cancer	1	4.5	1	221
> 365 days after Cancer	16	72.7	16	4922
Day0 to Day365 after chemo	1	4.5	1	264
> 365 days after chemo	17	77.3	16	4879

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Table 143 Kidney transplant rejections from 01-SEP-2006 to 31-AUG-2007 according to the 30-days risk periods of seasonal vaccination and the time since transplantation – with subsequent rejections (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	22	100.0	27	7694
Data after censoring according to transplantations	22	100.0	27	6864
Subjects with at least one exposure of interest (seasonal vaccination, transplantation)	16	72.7	20	5010
seasonal vaccination - Control period before first dose	15	68.2	6	1488
seasonal vaccination - Risk period after any dose	13	59.1	2	388
seasonal vaccination - Control period after any dose	13	59.1	12	3134
seasonal vaccination - Pooled risk periods	13	59.1	2	388
seasonal vaccination - Pooled control periods	16	72.7	18	4622
Day0 to Day30 after transplantation	5	22.7	4	155
> 30 days after transplantation	16	72.7	16	4855

Table 144 **Relative incidence of kidney transplant rejection within 30 days after seasonal vaccination in season 2006-2007 adjusted for the time since transplantation - not accounting for perturbed post-event exposure (Subset 2b)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	1.06	0.23	4.96
Time since transplantation	0-30 vs. >30 days	26.30	2.72	254.74

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

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Table 145 Liver transplant rejection from 01-SEP-2006 to 31-AUG-2007 according to the 30-days risk periods of seasonal vaccination and the time since transplantation (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	6	100.0	6	2190
Data after censoring according to transplantations	6	100.0	6	2073
Data after censoring according to second rejection	6	100.0	6	2073
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	2	33.3	2	703
Seasonal vaccination - Control period before first dose	2	33.3	1	179
Seasonal vaccination - Risk period after any dose	2	33.3	0	62
Seasonal vaccination - Control period after any dose	2	33.3	1	462
Seasonal vaccination - Pooled risk periods	2	33.3	0	62
Seasonal vaccination - Pooled control periods	2	33.3	2	641
Day0 to Day30 after transplantation	1	16.7	1	31
> 30 days after transplantation	2	33.3	1	672

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Table 146 Lung transplant rejection from 01-SEP-2006 to 31-AUG-2007 according to the 30-days risk periods of seasonal vaccination and the time since transplantation (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	1	100.0	1	365
Data after censoring according to transplantations	1	100.0	1	125
Data after censoring according to second rejection	1	100.0	1	125
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	1	100.0	1	125
Seasonal vaccination - Control period before first dose	1	100.0	1	125
Seasonal vaccination - Pooled control periods	1	100.0	1	125
Day0 to Day30 after transplantation	1	100.0	1	31
> 30 days after transplantation	1	100.0	0	94

Table 147 Pancreas transplant rejection from 01-SEP-2006 to 31-AUG-2007 according to the 30-days risk periods of seasonal vaccination and the time since transplantation (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	1	100.0	1	365
Data after censoring according to transplantations	1	100.0	1	365
Data after censoring according to second rejection	1	100.0	1	365
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	1	100.0	1	365
Seasonal vaccination - Control period before first dose	1	100.0	0	54
Seasonal vaccination - Risk period after any dose	1	100.0	0	31
Seasonal vaccination - Control period after any dose	1	100.0	1	280
Seasonal vaccination - Pooled risk periods	1	100.0	0	31
Seasonal vaccination - Pooled control periods	1	100.0	1	334
> 30 days after transplantation	1	100.0	1	365

12.2.2.2. Season 2007-2008**Table 148 SOT rejections from 01-SEP-2007 to 31-AUG-2008 according to the 30-days risk periods of seasonal vaccination and the time since transplantation (Subset 2b)**

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	51	100.0	72	18114
Data after censoring according to transplantations	51	100.0	72	16291
Data after censoring according to second rejection	51	100.0	51	14639
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	32	62.7	32	8823
Seasonal vaccination - Control period before first dose	32	62.7	14	3482
Seasonal vaccination - Risk period after any dose	21	41.2	4	651
Seasonal vaccination - Control period after any dose	21	41.2	14	4690
Seasonal vaccination - Pooled risk periods	21	41.2	4	651
Seasonal vaccination - Pooled control periods	32	62.7	28	8172
Day0 to Day30 after transplantation	9	17.6	5	271
Day31 to Day90 after transplantation	10	19.6	3	577
Day91 to Day180 after transplantation	10	19.6	2	862
> 180 days after transplantation	28	54.9	22	7113

Table 149 Relative incidence of SOT rejection within 30 days after seasonal vaccination in season 2007-2008 adjusted for the time since transplantation (Subset 2b)

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	1.90	0.68	5.34
Time since transplantation	0-30 vs. >180 days	8.96	1.10	73.24
	31-90 vs. >180 days	2.85	0.45	18.06
	91-180 vs. >180 days	1.15	0.25	5.34

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

Table 150 SOT rejections from 01-SEP-2007 to 31-AUG-2008 according to the 30-days risk periods of seasonal vaccination and the time since transplantation and all covariates (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	49	100.0	69	17387
Data after censoring according to transplantations	49	100.0	69	15702
Data after censoring according to second rejection	49	100.0	49	14075
Subjects with at least one exposure of interest (Acute bacterial infection, Cancer, Chronic viral infection, Opportunistic infection, Respiratory infection, Seasonal vaccination, chemo, transplantation)	37	75.5	37	10488
Seasonal vaccination - Control period before first dose	37	75.5	20	5479
Seasonal vaccination - Risk period after any dose	20	40.8	4	620
Seasonal vaccination - Control period after any dose	20	40.8	13	4389
Seasonal vaccination - Pooled risk periods	20	40.8	4	620
Seasonal vaccination - Pooled control periods	37	75.5	33	9868
Day0 to Day30 after transplantation	8	16.3	5	240
Day31 to Day90 after transplantation	9	18.4	3	517
Day91 to Day180 after transplantation	9	18.4	1	772
> 180 days after transplantation	33	67.3	28	8959
Day0 to Day30 after Respiratory infection	7	14.3	2	248
> 30 days after Respiratory infection	37	75.5	35	10240
Day0 to Day30 after Opportunistic infection	2	4.1	0	44
> 30 days after Opportunistic infection	37	75.5	37	10444
> 30 days after Acute bacterial infection	37	75.5	37	10488
> 365 days after Chronic viral infection	37	75.5	37	10488
Day0 to Day365 after Cancer	5	10.2	5	1420
> 365 days after Cancer	36	73.5	32	9068

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	Subjects		Rejections	Person*days
	N	%		
Day0 to Day365 after chemo	5	10.2	3	802
> 365 days after chemo	36	73.5	34	9686

Table 151 **Relative incidence of SOT rejection within 30 days after seasonal vaccination in season 2007-2008 adjusted for all covariates (Subset 2b)**

No records exist in this table

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Table 152 SOT rejections from 01-SEP-2007 to 31-AUG-2008 according to the risk periods of seasonal vaccination and the time since transplantation and respiratory infections (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	51	100.0	72	18114
Data after censoring according to transplantations	51	100.0	72	16291
Data after censoring according to second rejection	51	100.0	51	14639
Subjects with at least one exposure of interest (Respiratory infection, Seasonal vaccination, transplantation)	35	68.6	35	9901
Seasonal vaccination - Control period before first dose	35	68.6	17	4560
Seasonal vaccination - Risk period after any dose	21	41.2	4	651
Seasonal vaccination - Control period after any dose	21	41.2	14	4690
Seasonal vaccination - Pooled risk periods	21	41.2	4	651
Seasonal vaccination - Pooled control periods	35	68.6	31	9250
Day0 to Day30 after transplantation	9	17.6	5	271
Day31 to Day90 after transplantation	10	19.6	3	577
Day91 to Day180 after transplantation	10	19.6	2	862
> 180 days after transplantation	31	60.8	25	8191
Day0 to Day30 after Respiratory infection	8	15.7	3	292
> 30 days after Respiratory infection	35	68.6	32	9609

Table 153 **Relative incidence of SOT rejection within 30 days after seasonal vaccination in season 2007-2008 adjusted for the time since transplantation and respiratory infections (Subset 2b)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	1.92	0.70	5.26
Time since transplantation	0-30 vs. >180 days	9.91	1.09	90.28
	31-90 vs. >180 days	3.20	0.42	24.27
	91-180 vs. >180 days	1.28	0.25	6.48
Respiratory infections	30 days after infection vs. other periods	5.68	1.48	21.83

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

Table 154 SOT rejections from 01-SEP-2007 to 31-AUG-2008 according to the 30-days risk periods of seasonal vaccination, the time since transplantation and malignancies/cancers (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	49	100.0	69	17387
Data after censoring according to transplantations	49	100.0	69	15702
Data after censoring according to second rejection	49	100.0	49	14075
Subjects with at least one exposure of interest (Cancer, Seasonal vaccination, transplantation)	32	65.3	32	8991
Seasonal vaccination - Control period before first dose	32	65.3	15	3982
Seasonal vaccination - Risk period after any dose	20	40.8	4	620
Seasonal vaccination - Control period after any dose	20	40.8	13	4389
Seasonal vaccination - Pooled risk periods	20	40.8	4	620
Seasonal vaccination - Pooled control periods	32	65.3	28	8371
Day0 to Day30 after transplantation	8	16.3	5	240
Day31 to Day90 after transplantation	9	18.4	3	517
Day91 to Day180 after transplantation	9	18.4	1	772
> 180 days after transplantation	28	57.1	23	7462
Day0 to Day365 after Cancer	5	10.2	5	1420
> 365 days after Cancer	31	63.3	27	7571

Table 155 **Relative incidence of SOT rejection within 30 days after seasonal vaccination in season 2007-2008 adjusted for the time since transplantation and malignancies/cancers (Subset 2b)**

No records exist in this table

Table 156 SOT rejections from 01-SEP-2007 to 31-AUG-2008 according to the risk periods of seasonal vaccination, the time since transplantation and chemotherapy (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	49	100.0	69	17387
Data after censoring according to transplantations	49	100.0	69	15702
Data after censoring according to second rejection	49	100.0	49	14075
Subjects with at least one exposure of interest (Chemotherapy, Seasonal vaccination, transplantation)	32	65.3	32	8991
Seasonal vaccination - Control period before first dose	32	65.3	15	3982
Seasonal vaccination - Risk period after any dose	20	40.8	4	620
Seasonal vaccination - Control period after any dose	20	40.8	13	4389
Seasonal vaccination - Pooled risk periods	20	40.8	4	620
Seasonal vaccination - Pooled control periods	32	65.3	28	8371
Day0 to Day30 after transplantation	8	16.3	5	240
Day31 to Day90 after transplantation	9	18.4	3	517
Day91 to Day180 after transplantation	9	18.4	1	772
> 180 days after transplantation	28	57.1	23	7462
Day0 to Day365 after Chemotherapy	5	10.2	3	802
> 365 days after Chemotherapy	31	63.3	29	8189

Table 157 **Relative incidence of SOT rejection within 30 days after seasonal vaccination in season 2007-2008 adjusted for the time since transplantation and chemotherapy (Subset 2b)**

No records exist in this table

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Table 158 SOT rejections from 01-SEP-2007 to 31-AUG-2008 according to the 30-days risk periods of seasonal vaccination and the time since transplantation – with subsequent rejections (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	51	100.0	72	18114
Data after censoring according to transplantations	51	100.0	72	16291
Subjects with at least one exposure of interest (seasonal vaccination, transplantation)	33	64.7	48	9853
seasonal vaccination - Control period before first dose	33	64.7	19	3614
seasonal vaccination - Risk period after any dose	22	43.1	4	682
seasonal vaccination - Control period after any dose	22	43.1	25	5557
seasonal vaccination - Pooled risk periods	22	43.1	4	682
seasonal vaccination - Pooled control periods	33	64.7	44	9171
Day0 to Day30 after transplantation	9	17.6	5	271
Day31 to Day90 after transplantation	10	19.6	3	577
Day91 to Day180 after transplantation	10	19.6	3	865
> 180 days after transplantation	29	56.9	37	8140

Table 159 Relative incidence of SOT rejection within 30 days after seasonal vaccination in season 2007-2008 adjusted for the time since transplantation - not accounting for perturbed post-event exposure (Subset 2b)

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	1.18	0.41	3.41
Time since transplantation	0-30 vs. >180 days	2.27	0.39	13.07
	31-90 vs. >180 days	0.83	0.14	4.81
	91-180 vs. >180 days	0.61	0.11	3.28

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

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Table 160 Heart transplant rejection from 01-SEP-2007 to 31-AUG-2008 according to the 30-days risk periods of seasonal vaccination and the time since transplantation (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	1	100.0	1	366
Data after censoring according to transplantations	1	100.0	1	366
Data after censoring according to second rejection	1	100.0	1	366
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	1	100.0	1	366
Seasonal vaccination - Control period before first dose	1	100.0	1	366
Seasonal vaccination - Pooled control periods	1	100.0	1	366
Day31 to Day90 after transplantation	1	100.0	0	56
Day91 to Day180 after transplantation	1	100.0	0	90
> 180 days after transplantation	1	100.0	1	220

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Table 161 Kidney transplant rejection from 01-SEP-2007 to 31-AUG-2008 according to the 30-days risk periods of seasonal vaccination and the time since transplantation (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	34	100.0	53	11917
Data after censoring according to transplantations	34	100.0	53	10302
Data after censoring according to second rejection	34	100.0	34	8941
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	23	67.6	23	5787
Seasonal vaccination - Control period before first dose	23	67.6	11	2353
Seasonal vaccination - Risk period after any dose	15	44.1	3	465
Seasonal vaccination - Control period after any dose	15	44.1	9	2969
Seasonal vaccination - Pooled risk periods	15	44.1	3	465
Seasonal vaccination - Pooled control periods	23	67.6	20	5322
Day0 to Day30 after transplantation	7	20.6	4	209
Day31 to Day90 after transplantation	7	20.6	3	401
Day91 to Day180 after transplantation	7	20.6	1	592
> 180 days after transplantation	19	55.9	15	4585

Table 162 **Relative incidence of kidney transplant rejection within 30 days after seasonal vaccination in season 2007-2008 adjusted for the time since transplantation (Subset 2b)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	1.92	0.60	6.14
Time since transplantation	0-30 vs. >180 days	18.47	1.15	296.44
	31-90 vs. >180 days	8.18	0.79	84.68
	91-180 vs. >180 days	1.27	0.18	8.90

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

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Table 163 Kidney transplant rejection from 01-SEP-2007 to 31-AUG-2008 according to the 30-days risk periods of seasonal vaccination, the time since transplantation and all covariates (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	33	100.0	52	11551
Data after censoring according to transplantations	33	100.0	52	9936
Data after censoring according to second rejection	33	100.0	33	8575
Subjects with at least one exposure of interest (Acute bacterial infection, Cancer, Chronic viral infection, Opportunistic infection, Respiratory infection, Seasonal vaccination, chemo, transplantation)	27	81.8	27	6918
Seasonal vaccination - Control period before first dose	27	81.8	16	3816
Seasonal vaccination - Risk period after any dose	14	42.4	3	434
Seasonal vaccination - Control period after any dose	14	42.4	8	2668
Seasonal vaccination - Pooled risk periods	14	42.4	3	434
Seasonal vaccination - Pooled control periods	27	81.8	24	6484
Day0 to Day30 after transplantation	7	21.2	4	209
Day31 to Day90 after transplantation	7	21.2	3	401
Day91 to Day180 after transplantation	7	21.2	1	592
> 180 days after transplantation	23	69.7	19	5716
Day0 to Day30 after Respiratory infection	5	15.2	1	186
> 30 days after Respiratory infection	27	81.8	26	6732
Day0 to Day30 after Opportunistic infection	2	6.1	0	44
> 30 days after Opportunistic infection	27	81.8	27	6874
> 30 days after Acute bacterial infection	27	81.8	27	6918
> 365 days after Chronic viral infection	27	81.8	27	6918
Day0 to Day365 after Cancer	2	6.1	2	568
> 365 days after Cancer	26	78.8	25	6350

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	Subjects			
	N	%	Rejections	Person*days
Day0 to Day365 after chemo	3	9.1	2	423
> 365 days after chemo	27	81.8	25	6495

Table 164 Kidney transplant rejection from 01-SEP-2007 to 31-AUG-2008 according to the risk periods of seasonal vaccination, the time since transplantation and respiratory infections (Subset 2b)

	Subjects			
	N	%	Rejections	Person*days
Subset 2b	34	100.0	53	11917
Data after censoring according to transplantations	34	100.0	53	10302
Data after censoring according to second rejection	34	100.0	34	8941
Subjects with at least one exposure of interest (Respiratory infection, Seasonal vaccination, transplantation)	25	73.5	25	6499
Seasonal vaccination - Control period before first dose	25	73.5	13	3065
Seasonal vaccination - Risk period after any dose	15	44.1	3	465
Seasonal vaccination - Control period after any dose	15	44.1	9	2969
Seasonal vaccination - Pooled risk periods	15	44.1	3	465
Seasonal vaccination - Pooled control periods	25	73.5	22	6034
Day0 to Day30 after transplantation	7	20.6	4	209
Day31 to Day90 after transplantation	7	20.6	3	401
Day91 to Day180 after transplantation	7	20.6	1	592
> 180 days after transplantation	21	61.8	17	5297
Day0 to Day30 after Respiratory infection	6	17.6	2	230
> 30 days after Respiratory infection	25	73.5	23	6269

Table 165 **Relative incidence of kidney transplant rejection within 30 days after seasonal vaccination in season 2007-2008 adjusted for the time since transplantation and respiratory infections (Subset 2b)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	1.88	0.61	5.75
Time since transplantation	0-30 vs. >180 days	22.67	1.17	439.79
	31-90 vs. >180 days	10.25	0.78	134.16
	91-180 vs. >180 days	1.47	0.18	11.68
Respiratory infections	30 days after infection vs. other periods	6.14	1.30	28.96

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

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Table 166 Kidney transplant rejections from 01-SEP-2007 to 31-AUG-2008 according to the 30-days risk periods of seasonal vaccination and the time since transplantation – with subsequent rejections (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	34	100.0	53	11917
Data after censoring according to transplantations	34	100.0	53	10302
Subjects with at least one exposure of interest (seasonal vaccination, transplantation)	24	70.6	38	6792
seasonal vaccination - Control period before first dose	24	70.6	15	2460
seasonal vaccination - Risk period after any dose	16	47.1	3	496
seasonal vaccination - Control period after any dose	16	47.1	20	3836
seasonal vaccination - Pooled risk periods	16	47.1	3	496
seasonal vaccination - Pooled control periods	24	70.6	35	6296
Day0 to Day30 after transplantation	7	20.6	4	209
Day31 to Day90 after transplantation	7	20.6	3	401
Day91 to Day180 after transplantation	7	20.6	2	595
> 180 days after transplantation	20	58.8	29	5587

Table 167 **Relative incidence of kidney transplant rejection within 30 days after seasonal vaccination in season 2007-2008 adjusted for the time since transplantation - not accounting for perturbed post-event exposure (Subset 2b)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	1.01	0.30	3.42
Time since transplantation	0-30 vs. >180 days	3.77	0.35	41.10
	31-90 vs. >180 days	1.89	0.19	18.56
	91-180 vs. >180 days	0.90	0.09	8.89

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Table 168 Liver transplant rejection from 01-SEP-2007 to 31-AUG-2008 according to the 30-days risk periods of seasonal vaccination and the time since transplantation (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	4	100.0	5	1459
Data after censoring according to transplantations	4	100.0	5	1251
Data after censoring according to second rejection	4	100.0	4	1226
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	2	50.0	2	494
Seasonal vaccination - Control period before first dose	2	50.0	2	494
Seasonal vaccination - Pooled control periods	2	50.0	2	494
Day0 to Day30 after transplantation	2	50.0	1	62
Day31 to Day90 after transplantation	2	50.0	0	120
Day91 to Day180 after transplantation	2	50.0	1	180
> 180 days after transplantation	2	50.0	0	132

Table 169 Lung transplant rejection from 01-SEP-2007 to 31-AUG-2008 according to the 30-days risk periods of seasonal vaccination and the time since transplantation (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	0			
Data after censoring according to transplantations	0			
Data after censoring according to second rejection	0			
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	0			

Table 170 Pancreas transplant rejection from 01-SEP-2007 to 31-AUG-2008 according to the 30-days risk periods of seasonal vaccination and the time since transplantation (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	1	100.0	1	366
Data after censoring according to transplantations	1	100.0	1	366
Data after censoring according to second rejection	1	100.0	1	366
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	0	0.0		

12.2.2.3. Season 2008-2009**Table 171 SOT rejections from 01-SEP-2008 to 31-AUG-2009 according to the 30-days risk periods of seasonal vaccination and the time since transplantation (Subset 2b)**

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	58	100.0	73	20171
Data after censoring according to transplantations	58	100.0	70	17923
Data after censoring according to second rejection	58	100.0	58	16576
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	32	55.2	32	8280
Seasonal vaccination - Control period before first dose	32	55.2	13	2842
Seasonal vaccination - Risk period after any dose	23	39.7	4	676
Seasonal vaccination - Control period after any dose	20	34.5	15	4762
Seasonal vaccination - Pooled risk periods	23	39.7	4	676
Seasonal vaccination - Pooled control periods	32	55.2	28	7604
Day0 to Day30 after transplantation	10	17.2	5	283
Day31 to Day90 after transplantation	9	15.5	4	449
> 90 days after transplantation	28	48.3	23	7548

Table 172 **Relative incidence of SOT rejection within 30 days after seasonal vaccination in season 2008-2009 adjusted for the time since transplantation (Subset 2b)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	1.40	0.36	5.48
Time since transplantation	0-30 vs. >90 days	9.30	0.85	101.53
	31-90 vs. >90 days	6.65	0.55	81.16

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

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Table 173 SOT rejections from 01-SEP-2008 to 31-AUG-2009 according to the 30-days risk periods of seasonal vaccination, the time since transplantation and all covariates (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	57	100.0	72	19806
Data after censoring according to transplantations	57	100.0	69	17558
Data after censoring according to second rejection	57	100.0	57	16211
Subjects with at least one exposure of interest (Acute bacterial infection, Cancer, Chronic viral infection, Opportunistic infection, Respiratory infection, Seasonal vaccination, chemo, transplantation)	34	59.6	34	8794
Seasonal vaccination - Control period before first dose	34	59.6	15	3356
Seasonal vaccination - Risk period after any dose	23	40.4	4	676
Seasonal vaccination - Control period after any dose	20	35.1	15	4762
Seasonal vaccination - Pooled risk periods	23	40.4	4	676
Seasonal vaccination - Pooled control periods	34	59.6	30	8118
Day0 to Day30 after transplantation	10	17.5	5	283
Day31 to Day90 after transplantation	9	15.8	4	449
> 90 days after transplantation	30	52.6	25	8062
Day0 to Day30 after Respiratory infection	2	3.5	0	62
> 30 days after Respiratory infection	34	59.6	34	8732
Day0 to Day30 after Opportunistic infection	3	5.3	1	93
> 30 days after Opportunistic infection	34	59.6	33	8701
> 30 days after Acute bacterial infection	34	59.6	34	8794
> 365 days after Chronic viral infection	34	59.6	34	8794
Day0 to Day365 after Cancer	3	5.3	2	460
> 365 days after Cancer	33	57.9	32	8334
Day0 to Day365 after chemo	3	5.3	2	685

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	Subjects			
	N	%	Rejections	Person*days
> 365 days after chemo	32	56.1	32	8109

Table 174 SOT rejections from 01-SEP-2008 to 31-AUG-2009 according to the 30-days risk periods of seasonal vaccination and the time since transplantation – with subsequent rejections (Subset 2b)

	Subjects			
	N	%	Rejections	Person*days
Subset 2b	58	100.0	73	20171
Data after censoring according to transplantations	58	100.0	70	17923
Subjects with at least one exposure of interest (seasonal vaccination, transplantation)	32	55.2	42	9457
seasonal vaccination - Control period before first dose	32	55.2	15	3111
seasonal vaccination - Risk period after any dose	23	39.7	5	700
seasonal vaccination - Control period after any dose	21	36.2	22	5646
seasonal vaccination - Pooled risk periods	23	39.7	5	700
seasonal vaccination - Pooled control periods	32	55.2	37	8757
Day0 to Day30 after transplantation	10	17.2	5	283
Day31 to Day90 after transplantation	9	15.5	5	463
> 90 days after transplantation	29	50.0	32	8711

Table 175 **Relative incidence of SOT rejection within 30 days after seasonal vaccination in season 2008-2009 adjusted for the time since transplantation - not accounting for perturbed post-event exposure (Subset 2b)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	1.54	0.56	4.28
Time since transplantation	0-30 vs. >90 days	6.60	1.08	40.30
	31-90 vs. >90 days	5.56	1.04	29.81

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

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Table 176 Heart transplant rejection from 01-SEP-2008 to 31-AUG-2009 according to the 30-days risk periods of seasonal vaccination and the time since transplantation (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	3	100.0	3	1095
Data after censoring according to transplantations	3	100.0	3	1095
Data after censoring according to second rejection	3	100.0	3	1095
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	2	66.7	2	730
Seasonal vaccination - Control period before first dose	2	66.7	0	136
Seasonal vaccination - Risk period after any dose	2	66.7	1	62
Seasonal vaccination - Control period after any dose	2	66.7	1	532
Seasonal vaccination - Pooled risk periods	2	66.7	1	62
Seasonal vaccination - Pooled control periods	2	66.7	1	668
> 90 days after transplantation	2	66.7	2	730

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Table 177 Kidney transplant rejection from 01-SEP-2008 to 31-AUG-2009 according to the 30-days risk periods of seasonal vaccination and the time since transplantation (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	33	100.0	46	11613
Data after censoring according to transplantations	33	100.0	45	10094
Data after censoring according to second rejection	33	100.0	33	8892
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	22	66.7	22	5277
Seasonal vaccination - Control period before first dose	22	66.7	11	2086
Seasonal vaccination - Risk period after any dose	14	42.4	3	404
Seasonal vaccination - Control period after any dose	12	36.4	8	2787
Seasonal vaccination - Pooled risk periods	14	42.4	3	404
Seasonal vaccination - Pooled control periods	22	66.7	19	4873
Day0 to Day30 after transplantation	8	24.2	3	221
Day31 to Day90 after transplantation	7	21.2	4	383
> 90 days after transplantation	19	57.6	15	4673

Table 178 **Relative incidence of kidney transplant rejection within 30 days after seasonal vaccination in season 2008-2009 adjusted for the time since transplantation (Subset 2b)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	1.86	0.36	9.55
Time since transplantation	0-30 vs. >90 days	5.01	0.45	55.63
	31-90 vs. >90 days	5.90	0.44	79.94

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

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Table 179 Kidney transplant rejection from 01-SEP-2008 to 31-AUG-2009 according to the 30-days risk periods of seasonal vaccination, the time since transplantation and all covariates (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	33	100.0	46	11613
Data after censoring according to transplantations	33	100.0	45	10094
Data after censoring according to second rejection	33	100.0	33	8892
Subjects with at least one exposure of interest (Acute bacterial infection, Cancer, Chronic viral infection, Opportunistic infection, Respiratory infection, Seasonal vaccination, chemo, transplantation)	23	69.7	23	5642
Seasonal vaccination - Control period before first dose	23	69.7	12	2451
Seasonal vaccination - Risk period after any dose	14	42.4	3	404
Seasonal vaccination - Control period after any dose	12	36.4	8	2787
Seasonal vaccination - Pooled risk periods	14	42.4	3	404
Seasonal vaccination - Pooled control periods	23	69.7	20	5238
Day0 to Day30 after transplantation	8	24.2	3	221
Day31 to Day90 after transplantation	7	21.2	4	383
> 90 days after transplantation	20	60.6	16	5038
Day0 to Day30 after Respiratory infection	1	3.0	0	31
> 30 days after Respiratory infection	23	69.7	23	5611
Day0 to Day30 after Opportunistic infection	2	6.1	1	62
> 30 days after Opportunistic infection	23	69.7	22	5580
> 30 days after Acute bacterial infection	23	69.7	23	5642
> 365 days after Chronic viral infection	23	69.7	23	5642
Day0 to Day365 after Cancer	1	3.0	0	42
> 365 days after Cancer	23	69.7	23	5600
Day0 to Day365 after chemo	1	3.0	1	60

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	Subjects		Rejections	Person*days
	N	%		
> 365 days after chemo	22	66.7	22	5582

Table 180 Kidney transplant rejections from 01-SEP-2008 to 31-AUG-2009 according to the 30-days risk periods of seasonal vaccination and the time since transplantation – with subsequent rejections (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	33	100.0	46	11613
Data after censoring according to transplantations	33	100.0	45	10094
Subjects with at least one exposure of interest (seasonal vaccination, transplantation)	22	66.7	31	6222
seasonal vaccination - Control period before first dose	22	66.7	13	2355
seasonal vaccination - Risk period after any dose	14	42.4	4	428
seasonal vaccination - Control period after any dose	13	39.4	14	3439
seasonal vaccination - Pooled risk periods	14	42.4	4	428
seasonal vaccination - Pooled control periods	22	66.7	27	5794
Day0 to Day30 after transplantation	8	24.2	3	221
Day31 to Day90 after transplantation	7	21.2	5	397
> 90 days after transplantation	20	60.6	23	5604

Table 181 Relative incidence of kidney transplant rejection within 30 days after seasonal vaccination in season 2008-2009 adjusted for the time since transplantation - not accounting for perturbed post-event exposure (Subset 2b)

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	30 days after any dose vs. other periods	2.10	0.68	6.45
Time since transplantation	0-30 vs. >90 days	3.90	0.51	29.53
	31-90 vs. >90 days	5.42	1.00	29.43

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

**Table 182 Liver transplant rejection from 01-SEP-2008 to 31-AUG-2009
according to the 30-days risk periods of seasonal vaccination and
the time since transplantation (Subset 2b)**

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	4	100.0	4	1109
Data after censoring according to transplantations	4	100.0	4	944
Data after censoring according to second rejection	4	100.0	4	944
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	2	50.0	2	643
Seasonal vaccination - Control period before first dose	2	50.0	1	325
Seasonal vaccination - Risk period after any dose	1	25.0	0	31
Seasonal vaccination - Control period after any dose	1	25.0	1	287
Seasonal vaccination - Pooled risk periods	1	25.0	0	31
Seasonal vaccination - Pooled control periods	2	50.0	2	612
Day0 to Day30 after transplantation	1	25.0	1	31
Day31 to Day90 after transplantation	1	25.0	0	60
> 90 days after transplantation	2	50.0	1	552

Table 183 Lung transplant rejection from 01-SEP-2008 to 31-AUG-2009 according to the 30-days risk periods of seasonal vaccination and the time since transplantation (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	1	100.0	1	365
Data after censoring according to transplantations	1	100.0	1	365
Data after censoring according to second rejection	1	100.0	1	365
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	0	0.0		

Table 184 Pancreas transplant rejection from 01-SEP-2008 to 31-AUG-2009 according to the 30-days risk periods of seasonal vaccination and the time since transplantation (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	2	100.0	2	730
Data after censoring according to transplantations	2	100.0	2	303
Data after censoring according to second rejection	2	100.0	2	303
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	2	100.0	2	303
Seasonal vaccination - Control period before first dose	2	100.0	2	279
Seasonal vaccination - Risk period after any dose	1	50.0	0	24
Seasonal vaccination - Pooled risk periods	1	50.0	0	24
Seasonal vaccination - Pooled control periods	2	100.0	2	279
Day0 to Day30 after transplantation	1	50.0	0	31
Day31 to Day90 after transplantation	1	50.0	0	60
> 90 days after transplantation	2	100.0	2	212

12.3. TIV risk period of 60 days**12.3.1. Subset 2A****12.3.1.1. Season 2006-2007****Table 185 SOT rejections from 01-SEP-2006 to 31-AUG-2007 according to the 60-days risk periods of seasonal vaccination and the time since transplantation (Subset 2a)**

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	131	100.0	159	45581
Data after censoring according to transplantations	131	100.0	153	40721
Data after censoring according to second rejection	131	100.0	131	37815
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	74	56.5	74	20560
Seasonal vaccination - Control period before first dose	72	55.0	37	7264
Seasonal vaccination - Risk period after any dose	55	42.0	9	3222
Seasonal vaccination - Control period after any dose	50	38.2	28	10074
Seasonal vaccination - Pooled risk periods	55	42.0	9	3222
Seasonal vaccination - Pooled control periods	74	56.5	65	17338
Day0 to Day30 after transplantation	22	16.8	16	630
Day31 to Day90 after transplantation	22	16.8	6	1127
> 90 days after transplantation	68	51.9	52	18803

Table 186 **Relative incidence of SOT rejection within 60 days after seasonal vaccination in season 2006-2007 adjusted for the time since transplantation (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	0.58	0.24	1.38
Time since transplantation	0-30 vs. >90 days	26.64	4.96	143.16
	31-90 vs. >90 days	4.73	0.98	22.87

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

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Table 187 SOT rejections from 01-SEP-2006 to 31-AUG-2007 according to the 60-days risk periods of seasonal vaccination, the time since transplantation and all covariates (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	128	100.0	156	44486
Data after censoring according to transplantations	128	100.0	150	39787
Data after censoring according to second rejection	128	100.0	128	36881
Subjects with at least one exposure of interest (Acute bacterial infection, Cancer, Chronic viral infection, Opportunistic infection, Respiratory infection, Seasonal vaccination, transplantation)	75	58.6	75	21086
Seasonal vaccination - Control period before first dose	73	57.0	39	8009
Seasonal vaccination - Risk period after any dose	54	42.2	9	3161
Seasonal vaccination - Control period after any dose	49	38.3	27	9916
Seasonal vaccination - Pooled risk periods	54	42.2	9	3161
Seasonal vaccination - Pooled control periods	75	58.6	66	17925
Day0 to Day30 after transplantation	21	16.4	15	599
Day31 to Day90 after transplantation	20	15.6	5	1026
> 90 days after transplantation	69	53.9	55	19461
> 30 days after Respiratory infection	75	58.6	75	21086
Day0 to Day30 after Opportunistic infection	2	1.6	0	60
> 30 days after Opportunistic infection	75	58.6	75	21026
> 30 days after Acute bacterial infection	75	58.6	75	21086
> 365 days after Chronic viral infection	75	58.6	75	21086
Day0 to Day365 after Cancer	9	7.0	8	2252
> 365 days after Cancer	73	57.0	67	18834

Table 188 **Relative incidence of SOT rejection within 60 days after seasonal vaccination in season 2006-2007 adjusted for all covariates (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	0.63	0.26	1.51
Time since transplantation	0-30 vs. >90 days	20.18	4.18	97.39
	31-90 vs. >90 days	3.54	0.77	16.42
Malignancies/ cancers	365 days after any record vs. other periods	4.74	0.35	63.58

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

Note: only subjects with one year of follow-up before the beginning of the season were considered

Table 189 SOT rejections from 01-SEP-2006 to 31-AUG-2007 according to the 60-days risk periods of seasonal vaccination, the time since transplantation and malignancies/cancers (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	128	100.0	156	44486
Data after censoring according to transplantations	128	100.0	150	39787
Data after censoring according to second rejection	128	100.0	128	36881
Subjects with at least one exposure of interest (Cancer, Seasonal vaccination, transplantation)	75	58.6	75	21086
Seasonal vaccination - Control period before first dose	73	57.0	39	8009
Seasonal vaccination - Risk period after any dose	54	42.2	9	3161
Seasonal vaccination - Control period after any dose	49	38.3	27	9916
Seasonal vaccination - Pooled risk periods	54	42.2	9	3161
Seasonal vaccination - Pooled control periods	75	58.6	66	17925
Day0 to Day30 after transplantation	21	16.4	15	599
Day31 to Day90 after transplantation	20	15.6	5	1026
> 90 days after transplantation	69	53.9	55	19461
Day0 to Day365 after Cancer	9	7.0	8	2252
> 365 days after Cancer	73	57.0	67	18834

Table 190 Relative incidence of SOT rejection within 60 days after seasonal vaccination in season 2006-2007 adjusted for the time since transplantation and malignancies/cancers (Subset 2a)

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	0.63	0.26	1.51
Time since transplantation	0-30 vs. >90 days	20.18	4.18	97.39
	31-90 vs. >90 days	3.54	0.77	16.42
Malignancies/ cancers	365 days after any record vs. other periods	4.74	0.35	63.58

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

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Table 191 SOT rejections from 01-SEP-2006 to 31-AUG-2007 according to the 60-days risk periods of seasonal vaccination and the time since transplantation – with subsequent rejections (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	131	100.0	159	45581
Data after censoring according to transplantations	131	100.0	153	40721
Subjects with at least one exposure of interest (seasonal vaccination, transplantation)	74	56.5	83	21781
seasonal vaccination - Control period before first dose	72	55.0	39	7453
seasonal vaccination - Risk period after any dose	55	42.0	11	3302
seasonal vaccination - Control period after any dose	52	39.7	33	11026
seasonal vaccination - Pooled risk periods	55	42.0	11	3302
seasonal vaccination - Pooled control periods	74	56.5	72	18479
Day0 to Day30 after transplantation	22	16.8	16	630
Day31 to Day90 after transplantation	22	16.8	6	1127
> 90 days after transplantation	68	51.9	61	20024

Table 192 **Relative incidence of SOT rejection within 60 days after seasonal vaccination in season 2006-2007 adjusted for the time since transplantation - not accounting for perturbed post-event exposure (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	0.80	0.41	1.59
Time since transplantation	0-30 vs. >90 days	18.50	5.65	60.59
	31-90 vs. >90 days	4.24	1.26	14.26

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Table 193 **Relative incidence of SOT rejection within 60 days after seasonal vaccination in season 2006-2007 adjusted for the time since transplantation and conditioned to previous rejections (Subset 2a)**

No records exist in this table

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Table 194 SOT rejections from 01-SEP-2006 to 31-AUG-2007 according to the 60-days risk periods of seasonal vaccination and the time since transplantation - Subjects without previous rejections (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	65	100.0	74	22811
Data after censoring according to transplantations	65	100.0	71	18802
Data after censoring according to second rejection	65	100.0	65	18290
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	65	100.0	65	18290
Seasonal vaccination - Control period before first dose	63	96.9	33	6496
Seasonal vaccination - Risk period after any dose	47	72.3	7	2814
Seasonal vaccination - Control period after any dose	44	67.7	25	8980
Seasonal vaccination - Pooled risk periods	47	72.3	7	2814
Seasonal vaccination - Pooled control periods	65	100.0	58	15476
Day0 to Day30 after transplantation	22	33.8	16	630
Day31 to Day90 after transplantation	20	30.8	4	1072
> 90 days after transplantation	59	90.8	45	16588

Table 195 Relative incidence of SOT rejection within 60 days after seasonal vaccination in season 2006-2007 adjusted for the time since transplantation - Subjects without previous rejections (Subset 2a)

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	0.48	0.17	1.31
Time since transplantation	0-30 vs. >90 days	20.28	4.66	88.29
	31-90 vs. >90 days	2.76	0.57	13.26

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

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Table 196 SOT rejections from 01-SEP-2006 to 31-AUG-2007 according to the 60-days risk periods of seasonal vaccination, the time since transplantation and previous rejection (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	13	100.0	19	4242
Data after censoring according to transplantations	13	100.0	18	4120
Data after censoring according to second rejection	13	100.0	13	3180
Subjects with at least one exposure of interest (Previous rejection, Seasonal vaccination, transplantation)	13	100.0	13	3180
Seasonal vaccination - Control period before first dose	13	100.0	8	1678
Seasonal vaccination - Risk period after any dose	8	61.5	2	408
Seasonal vaccination - Control period after any dose	6	46.2	3	1094
Seasonal vaccination - Pooled risk periods	8	61.5	2	408
Seasonal vaccination - Pooled control periods	13	100.0	11	2772
Day31 to Day90 after transplantation	2	15.4	2	55
> 90 days after transplantation	13	100.0	11	3125
Day0 to Day180 after Previous rejection	13	100.0	6	898
> 180 days after Previous rejection	11	84.6	7	2282

Table 197 Relative incidence of SOT rejection within 60 days after seasonal vaccination in season 2006-2007 adjusted for the time since transplantation and previous rejection - Subjects with previous rejections (Subset 2a)

No records exist in this table

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Table 198 Heart transplant rejection from 01-SEP-2006 to 31-AUG-2007 according to the 60-days risk periods of seasonal vaccination and the time since transplantation (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	7	100.0	10	2013
Data after censoring according to transplantations	7	100.0	10	1701
Data after censoring according to second rejection	7	100.0	7	1408
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	5	71.4	5	933
Seasonal vaccination - Control period before first dose	5	71.4	3	183
Seasonal vaccination - Risk period after any dose	3	42.9	0	183
Seasonal vaccination - Control period after any dose	3	42.9	2	567
Seasonal vaccination - Pooled risk periods	3	42.9	0	183
Seasonal vaccination - Pooled control periods	5	71.4	5	750
Day0 to Day30 after transplantation	2	28.6	2	17
> 90 days after transplantation	3	42.9	3	916

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Table 199 Kidney transplant rejection from 01-SEP-2006 to 31-AUG-2007 according to the 60-days risk periods of seasonal vaccination and the time since transplantation (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	67	100.0	83	23398
Data after censoring according to transplantations	67	100.0	79	20320
Data after censoring according to second rejection	67	100.0	67	18761
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	49	73.1	49	13686
Seasonal vaccination - Control period before first dose	47	70.1	26	5048
Seasonal vaccination - Risk period after any dose	36	53.7	6	2097
Seasonal vaccination - Control period after any dose	32	47.8	17	6541
Seasonal vaccination - Pooled risk periods	36	53.7	6	2097
Seasonal vaccination - Pooled control periods	49	73.1	43	11589
Day0 to Day30 after transplantation	16	23.9	11	489
Day31 to Day90 after transplantation	15	22.4	3	835
> 90 days after transplantation	46	68.7	35	12362

Table 200 **Relative incidence of kidney transplant rejection within 60 days after seasonal vaccination in season 2006-2007 adjusted for the time since transplantation (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	0.50	0.16	1.60
Time since transplantation	0-30 vs. >90 days	17.79	3.84	82.46
	31-90 vs. >90 days	2.31	0.42	12.86

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

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Table 201 Kidney transplant rejection from 01-SEP-2006 to 31-AUG-2007 according to the 60-days risk periods of seasonal vaccination, the time since transplantation and all covariates (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	65	100.0	81	22668
Data after censoring according to transplantations	65	100.0	77	19751
Data after censoring according to second rejection	65	100.0	65	18192
Subjects with at least one exposure of interest (Acute bacterial infection, Cancer, Chronic viral infection, Opportunistic infection, Respiratory infection, Seasonal vaccination, transplantation)	47	72.3	47	13117
Seasonal vaccination - Control period before first dose	45	69.2	25	4698
Seasonal vaccination - Risk period after any dose	35	53.8	6	2036
Seasonal vaccination - Control period after any dose	31	47.7	16	6383
Seasonal vaccination - Pooled risk periods	35	53.8	6	2036
Seasonal vaccination - Pooled control periods	47	72.3	41	11081
Day0 to Day30 after transplantation	15	23.1	10	458
Day31 to Day90 after transplantation	14	21.5	3	775
> 90 days after transplantation	44	67.7	34	11884
> 30 days after Respiratory infection	47	72.3	47	13117
Day0 to Day30 after Opportunistic infection	1	1.5	0	29
> 30 days after Opportunistic infection	47	72.3	47	13088
> 30 days after Acute bacterial infection	47	72.3	47	13117
> 365 days after Chronic viral infection	47	72.3	47	13117
Day0 to Day365 after Cancer	1	1.5	1	221
> 365 days after Cancer	46	70.8	46	12896

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Table 202 Kidney transplant rejections from 01-SEP-2006 to 31-AUG-2007 according to the 60-days risk periods of seasonal vaccination and the time since transplantation – with subsequent rejections (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	67	100.0	83	23398
Data after censoring according to transplantations	67	100.0	79	20320
Subjects with at least one exposure of interest (seasonal vaccination, transplantation)	49	73.1	55	14426
seasonal vaccination - Control period before first dose	47	70.1	28	5237
seasonal vaccination - Risk period after any dose	36	53.7	7	2143
seasonal vaccination - Control period after any dose	33	49.3	20	7046
seasonal vaccination - Pooled risk periods	36	53.7	7	2143
seasonal vaccination - Pooled control periods	49	73.1	48	12283
Day0 to Day30 after transplantation	16	23.9	11	489
Day31 to Day90 after transplantation	15	22.4	3	835
> 90 days after transplantation	46	68.7	41	13102

Table 203 **Relative incidence of kidney transplant rejection within 60 days after seasonal vaccination in season 2006-2007 adjusted for the time since transplantation - not accounting for perturbed post-event exposure (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	0.71	0.30	1.67
Time since transplantation	0-30 vs. >90 days	11.43	3.53	36.96
	31-90 vs. >90 days	1.99	0.47	8.46

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Table 204 **Relative incidence of kidney transplant rejection within 60 days after seasonal vaccination in season 2006-2007 adjusted for the time since transplantation and conditioned to previous rejections (Subset 2a)**

No records exist in this table

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Table 205 Kidney transplant rejection from 01-SEP-2006 to 31-AUG-2007 according to the 60-days risk periods of seasonal vaccination and the time since transplantation - Subjects without previous rejections (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	43	100.0	50	15498
Data after censoring according to transplantations	43	100.0	47	12542
Data after censoring according to second rejection	43	100.0	43	12209
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	43	100.0	43	12209
Seasonal vaccination - Control period before first dose	41	95.3	24	4724
Seasonal vaccination - Risk period after any dose	30	69.8	4	1777
Seasonal vaccination - Control period after any dose	27	62.8	15	5708
Seasonal vaccination - Pooled risk periods	30	69.8	4	1777
Seasonal vaccination - Pooled control periods	43	100.0	39	10432
Day0 to Day30 after transplantation	16	37.2	11	489
Day31 to Day90 after transplantation	15	34.9	3	835
> 90 days after transplantation	40	93.0	29	10885

Table 206 **Relative incidence of kidney transplant rejection within 60 days after seasonal vaccination in season 2006-2007 adjusted for the time since transplantation - Subjects without previous rejections (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	0.27	0.05	1.45
Time since transplantation	0-30 vs. >90 days	22.58	4.70	108.46
	31-90 vs. >90 days	2.37	0.44	12.89

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

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Table 207 Kidney transplant rejection from 01-SEP-2006 to 31-AUG-2007 according to the 60-days risk periods of seasonal vaccination, the time since transplantation and previous rejection - Subjects with previous rejections (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	9	100.0	14	3101
Data after censoring according to transplantations	9	100.0	13	2979
Data after censoring according to second rejection	9	100.0	9	2341
Subjects with at least one exposure of interest (Previous rejection, Seasonal vaccination, transplantation)	9	100.0	9	2341
Seasonal vaccination - Control period before first dose	9	100.0	5	1188
Seasonal vaccination - Risk period after any dose	6	66.7	2	320
Seasonal vaccination - Control period after any dose	5	55.6	2	833
Seasonal vaccination - Pooled risk periods	6	66.7	2	320
Seasonal vaccination - Pooled control periods	9	100.0	7	2021
> 90 days after transplantation	9	100.0	9	2341
Day0 to Day180 after Previous rejection	9	100.0	3	600
> 180 days after Previous rejection	9	100.0	6	1741

Table 208 **Relative incidence of kidney transplant rejection within 60 days after seasonal vaccination in season 2006-2007 adjusted for the time since transplantation and previous rejection - Subjects with previous rejections (Subset 2a)**

No records exist in this table

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Table 209 **Liver transplant rejection from 01-SEP-2006 to 31-AUG-2007 according to the 60-days risk periods of seasonal vaccination and the time since transplantation (Subset 2a)**

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	12	100.0	14	4061
Data after censoring according to transplantations	12	100.0	13	3473
Data after censoring according to second rejection	12	100.0	12	3337
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	5	41.7	5	1604
Seasonal vaccination - Control period before first dose	5	41.7	4	867
Seasonal vaccination - Risk period after any dose	3	25.0	0	183
Seasonal vaccination - Control period after any dose	3	25.0	1	554
Seasonal vaccination - Pooled risk periods	3	25.0	0	183
Seasonal vaccination - Pooled control periods	5	41.7	5	1421
Day0 to Day30 after transplantation	2	16.7	2	62
Day31 to Day90 after transplantation	4	33.3	1	164
> 90 days after transplantation	5	41.7	2	1378

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Table 210 Lung transplant rejection from 01-SEP-2006 to 31-AUG-2007 according to the 60-days risk periods of seasonal vaccination and the time since transplantation (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	6	100.0	8	2190
Data after censoring according to transplantations	6	100.0	7	1308
Data after censoring according to second rejection	6	100.0	6	1006
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	5	83.3	5	1003
Seasonal vaccination - Control period before first dose	5	83.3	3	346
Seasonal vaccination - Risk period after any dose	3	50.0	0	149
Seasonal vaccination - Control period after any dose	2	33.3	2	508
Seasonal vaccination - Pooled risk periods	3	50.0	0	149
Seasonal vaccination - Pooled control periods	5	83.3	5	854
Day0 to Day30 after transplantation	2	33.3	1	62
Day31 to Day90 after transplantation	3	50.0	2	128
> 90 days after transplantation	4	66.7	2	813

Table 211 Pancreas transplant rejection from 01-SEP-2006 to 31-AUG-2007 according to the 60-days risk periods of seasonal vaccination and the time since transplantation (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	0			
Data after censoring according to transplantations	0			
Data after censoring according to second rejection	0			
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	0			

12.3.1.2. Season 2007-2008**Table 212 SOT rejections from 01-SEP-2007 to 31-AUG-2008 according to the 60-days risk periods of seasonal vaccination and the time since transplantation (Subset 2a)**

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	136	100.0	169	48185
Data after censoring according to transplantations	136	100.0	167	43886
Data after censoring according to second rejection	136	100.0	136	40848
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	81	59.6	81	23406
Seasonal vaccination - Control period before first dose	81	59.6	32	7730
Seasonal vaccination - Risk period after any dose	58	42.6	14	3483
Seasonal vaccination - Control period after any dose	56	41.2	35	12193
Seasonal vaccination - Pooled risk periods	58	42.6	14	3483
Seasonal vaccination - Pooled control periods	81	59.6	67	19923
Day0 to Day30 after transplantation	22	16.2	11	588
Day31 to Day90 after transplantation	23	16.9	7	1266
Day91 to Day180 after transplantation	24	17.6	6	2009
> 180 days after transplantation	71	52.2	57	19543

Table 213 **Relative incidence of SOT rejection within 60 days after seasonal vaccination in season 2007-2008 adjusted for the time since transplantation (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	1.31	0.69	2.48
Time since transplantation	0-30 vs. >180 days	5.41	1.11	26.41
	31-90 vs. >180 days	2.31	0.61	8.66
	91-180 vs. >180 days	1.16	0.29	4.58

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

Table 214 SOT rejections from 01-SEP-2007 to 31-AUG-2008 according to the 60-days risk periods of seasonal vaccination, the time since transplantation and all covariates (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	130	100.0	161	45994
Data after censoring according to transplantations	130	100.0	160	41839
Data after censoring according to second rejection	130	100.0	130	38826
Subjects with at least one exposure of interest (Acute bacterial infection, Cancer, Chronic viral infection, Opportunistic infection, Respiratory infection, Seasonal vaccination, transplantation)	82	63.1	82	23814
Seasonal vaccination - Control period before first dose	82	63.1	36	9093
Seasonal vaccination - Risk period after any dose	55	42.3	14	3300
Seasonal vaccination - Control period after any dose	53	40.8	32	11421
Seasonal vaccination - Pooled risk periods	55	42.3	14	3300
Seasonal vaccination - Pooled control periods	82	63.1	68	20514
Day0 to Day30 after transplantation	21	16.2	11	557
Day31 to Day90 after transplantation	22	16.9	7	1206
Day91 to Day180 after transplantation	23	17.7	5	1919
> 180 days after transplantation	72	55.4	59	20132
> 30 days after Respiratory infection	82	63.1	82	23814
Day0 to Day30 after Opportunistic infection	3	2.3	0	93
> 30 days after Opportunistic infection	82	63.1	82	23721
> 30 days after Acute bacterial infection	82	63.1	82	23814
> 365 days after Chronic viral infection	82	63.1	82	23814
Day0 to Day365 after Cancer	10	7.7	7	2506
> 365 days after Cancer	81	62.3	75	21308

Table 215 **Relative incidence of SOT rejection within 60 days after seasonal vaccination in season 2007-2008 adjusted for all covariates (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	1.43	0.75	2.72
Time since transplantation	0-30 vs. >180 days	6.11	1.22	30.48
	31-90 vs. >180 days	2.52	0.67	9.42
	91-180 vs. >180 days	1.02	0.24	4.41
Malignancies/ cancers	365 days after any record vs. other periods	0.84	0.13	5.53

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

Note: only subjects with one year of follow-up before the beginning of the season were considered

Table 216 SOT rejections from 01-SEP-2007 to 31-AUG-2008 according to the 60-days risk periods of seasonal vaccination, the time since transplantation and malignancies/cancers (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	130	100.0	161	45994
Data after censoring according to transplantations	130	100.0	160	41839
Data after censoring according to second rejection	130	100.0	130	38826
Subjects with at least one exposure of interest (Cancer, Seasonal vaccination, transplantation)	81	62.3	81	23479
Seasonal vaccination - Control period before first dose	81	62.3	35	8758
Seasonal vaccination - Risk period after any dose	55	42.3	14	3300
Seasonal vaccination - Control period after any dose	53	40.8	32	11421
Seasonal vaccination - Pooled risk periods	55	42.3	14	3300
Seasonal vaccination - Pooled control periods	81	62.3	67	20179
Day0 to Day30 after transplantation	21	16.2	11	557
Day31 to Day90 after transplantation	22	16.9	7	1206
Day91 to Day180 after transplantation	23	17.7	5	1919
> 180 days after transplantation	71	54.6	58	19797
Day0 to Day365 after Cancer	10	7.7	7	2506
> 365 days after Cancer	80	61.5	74	20973

Table 217 **Relative incidence of SOT rejection within 60 days after seasonal vaccination in season 2007-2008 adjusted for the time since transplantation and malignancies/cancers (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	1.43	0.75	2.72
Time since transplantation	0-30 vs. >180 days	6.11	1.22	30.48
	31-90 vs. >180 days	2.52	0.67	9.42
	91-180 vs. >180 days	1.02	0.24	4.41
Malignancies/ cancers	365 days after any record vs. other periods	0.84	0.13	5.53

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

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Table 218 SOT rejections from 01-SEP-2007 to 31-AUG-2008 according to the 60-days risk periods of seasonal vaccination and the time since transplantation – with subsequent rejections (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	136	100.0	169	48185
Data after censoring according to transplantations	136	100.0	167	43886
Subjects with at least one exposure of interest (seasonal vaccination, transplantation)	83	61.0	104	25581
seasonal vaccination - Control period before first dose	83	61.0	39	8172
seasonal vaccination - Risk period after any dose	60	44.1	16	3660
seasonal vaccination - Control period after any dose	60	44.1	49	13749
seasonal vaccination - Pooled risk periods	60	44.1	16	3660
seasonal vaccination - Pooled control periods	83	61.0	88	21921
Day0 to Day30 after transplantation	22	16.2	11	588
Day31 to Day90 after transplantation	23	16.9	8	1303
Day91 to Day180 after transplantation	25	18.4	6	2099
> 180 days after transplantation	74	54.4	79	21591

Table 219 **Relative incidence of SOT rejection within 60 days after seasonal vaccination in season 2007-2008 adjusted for the time since transplantation - not accounting for perturbed post-event exposure (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	1.13	0.64	1.98
Time since transplantation	0-30 vs. >180 days	3.54	1.09	11.44
	31-90 vs. >180 days	1.73	0.60	5.02
	91-180 vs. >180 days	0.83	0.28	2.45

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Table 220 **Relative incidence of SOT rejection within 60 days after seasonal vaccination in season 2007-2008 adjusted for the time since transplantation and conditioned to previous rejections (Subset 2a)**

No records exist in this table

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Table 221 SOT rejections from 01-SEP-2007 to 31-AUG-2008 according to the 60-days risk periods of seasonal vaccination and the time since transplantation - Subjects without previous rejections (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	75	100.0	86	26654
Data after censoring according to transplantations	75	100.0	85	22803
Data after censoring according to second rejection	75	100.0	75	21910
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	75	100.0	75	21910
Seasonal vaccination - Control period before first dose	75	100.0	29	7273
Seasonal vaccination - Risk period after any dose	52	69.3	13	3172
Seasonal vaccination - Control period after any dose	52	69.3	33	11465
Seasonal vaccination - Pooled risk periods	52	69.3	13	3172
Seasonal vaccination - Pooled control periods	75	100.0	62	18738
Day0 to Day30 after transplantation	22	29.3	11	588
Day31 to Day90 after transplantation	23	30.7	7	1266
Day91 to Day180 after transplantation	24	32.0	6	2009
> 180 days after transplantation	65	86.7	51	18047

Table 222 **Relative incidence of SOT rejection within 60 days after seasonal vaccination in season 2007-2008 adjusted for the time since transplantation - Subjects without previous rejections (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	1.31	0.67	2.55
Time since transplantation	0-30 vs. >180 days	5.41	1.11	26.40
	31-90 vs. >180 days	2.31	0.61	8.65
	91-180 vs. >180 days	1.16	0.29	4.58

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

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Table 223 SOT rejections from 01-SEP-2007 to 31-AUG-2008 according to the 60-days risk periods of seasonal vaccination, the time since transplantation and previous rejection (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	14	100.0	24	4901
Data after censoring according to transplantations	14	100.0	24	4901
Data after censoring according to second rejection	14	100.0	14	3987
Subjects with at least one exposure of interest (Previous rejection, Seasonal vaccination, transplantation)	14	100.0	14	3987
Seasonal vaccination - Control period before first dose	14	100.0	11	2948
Seasonal vaccination - Risk period after any dose	6	42.9	1	311
Seasonal vaccination - Control period after any dose	4	28.6	2	728
Seasonal vaccination - Pooled risk periods	6	42.9	1	311
Seasonal vaccination - Pooled control periods	14	100.0	13	3676
> 180 days after transplantation	14	100.0	14	3987
Day0 to Day180 after Previous rejection	14	100.0	10	1545
> 180 days after Previous rejection	11	78.6	4	2442

Table 224 **Relative incidence of SOT rejection within 60 days after seasonal vaccination in season 2007-2008 adjusted for the time since transplantation and previous rejection - Subjects with previous rejections (Subset 2a)**

No records exist in this table

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Table 225 Heart transplant rejection from 01-SEP-2007 to 31-AUG-2008 according to the 60-days risk periods of seasonal vaccination and the time since transplantation (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	8	100.0	9	2859
Data after censoring according to transplantations	8	100.0	9	2225
Data after censoring according to second rejection	8	100.0	8	2206
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	7	87.5	7	1840
Seasonal vaccination - Control period before first dose	7	87.5	3	651
Seasonal vaccination - Risk period after any dose	4	50.0	0	244
Seasonal vaccination - Control period after any dose	4	50.0	4	945
Seasonal vaccination - Pooled risk periods	4	50.0	0	244
Seasonal vaccination - Pooled control periods	7	87.5	7	1596
Day0 to Day30 after transplantation	2	25.0	2	29
Day31 to Day90 after transplantation	2	25.0	0	96
Day91 to Day180 after transplantation	2	25.0	1	180
> 180 days after transplantation	5	62.5	4	1535

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Table 226 Kidney transplant rejection from 01-SEP-2007 to 31-AUG-2008 according to the 60-days risk periods of seasonal vaccination and the time since transplantation (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	84	100.0	110	29421
Data after censoring according to transplantations	84	100.0	109	26177
Data after censoring according to second rejection	84	100.0	84	23853
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	57	67.9	57	15815
Seasonal vaccination - Control period before first dose	57	67.9	26	5825
Seasonal vaccination - Risk period after any dose	40	47.6	7	2385
Seasonal vaccination - Control period after any dose	38	45.2	24	7605
Seasonal vaccination - Pooled risk periods	40	47.6	7	2385
Seasonal vaccination - Pooled control periods	57	67.9	50	13430
Day0 to Day30 after transplantation	17	20.2	8	466
Day31 to Day90 after transplantation	18	21.4	7	990
Day91 to Day180 after transplantation	18	21.4	3	1495
> 180 days after transplantation	50	59.5	39	12864

Table 227 **Relative incidence of kidney transplant rejection within 60 days after seasonal vaccination in season 2007-2008 adjusted for the time since transplantation (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	0.82	0.36	1.86
Time since transplantation	0-30 vs. >180 days	5.95	1.03	34.30
	31-90 vs. >180 days	3.05	0.71	13.08
	91-180 vs. >180 days	0.65	0.12	3.59

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

Table 228 Kidney transplant rejection from 01-SEP-2007 to 31-AUG-2008 according to the 60-days risk periods of seasonal vaccination, the time since transplantation and all covariates (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	81	100.0	107	28323
Data after censoring according to transplantations	81	100.0	106	25079
Data after censoring according to second rejection	81	100.0	81	22755
Subjects with at least one exposure of interest (Acute bacterial infection, Cancer, Chronic viral infection, Opportunistic infection, Respiratory infection, Seasonal vaccination, transplantation)	54	66.7	54	14717
Seasonal vaccination - Control period before first dose	54	66.7	26	5688
Seasonal vaccination - Risk period after any dose	37	45.7	7	2202
Seasonal vaccination - Control period after any dose	35	43.2	21	6827
Seasonal vaccination - Pooled risk periods	37	45.7	7	2202
Seasonal vaccination - Pooled control periods	54	66.7	47	12515
Day0 to Day30 after transplantation	17	21.0	8	466
Day31 to Day90 after transplantation	18	22.2	7	990
Day91 to Day180 after transplantation	18	22.2	3	1495
> 180 days after transplantation	47	58.0	36	11766
> 30 days after Respiratory infection	54	66.7	54	14717
Day0 to Day30 after Opportunistic infection	2	2.5	0	62
> 30 days after Opportunistic infection	54	66.7	54	14655
> 30 days after Acute bacterial infection	54	66.7	54	14717
> 365 days after Chronic viral infection	54	66.7	54	14717
Day0 to Day365 after Cancer	3	3.7	2	525
> 365 days after Cancer	53	65.4	52	14192

Table 229 **Relative incidence of kidney transplant rejection within 60 days after seasonal vaccination in season 2007-2008 adjusted for all covariates (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	0.92	0.40	2.10
Time since transplantation	0-30 vs. >180 days	5.89	1.02	33.95
	31-90 vs. >180 days	3.01	0.70	12.93
	91-180 vs. >180 days	0.64	0.12	3.58

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

Note: only subjects with one year of follow-up before the beginning of the season were considered

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Table 230 Kidney transplant rejections from 01-SEP-2007 to 31-AUG-2008 according to the 60-days risk periods of seasonal vaccination and the time since transplantation – with subsequent rejections (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	84	100.0	110	29421
Data after censoring according to transplantations	84	100.0	109	26177
Subjects with at least one exposure of interest (seasonal vaccination, transplantation)	58	69.0	76	17580
seasonal vaccination - Control period before first dose	58	69.0	30	6149
seasonal vaccination - Risk period after any dose	41	48.8	9	2501
seasonal vaccination - Control period after any dose	41	48.8	37	8930
seasonal vaccination - Pooled risk periods	41	48.8	9	2501
seasonal vaccination - Pooled control periods	58	69.0	67	15079
Day0 to Day30 after transplantation	17	20.2	8	466
Day31 to Day90 after transplantation	18	21.4	8	1027
Day91 to Day180 after transplantation	19	22.6	3	1585
> 180 days after transplantation	52	61.9	57	14502

Table 231 **Relative incidence of kidney transplant rejection within 60 days after seasonal vaccination in season 2007-2008 adjusted for the time since transplantation - not accounting for perturbed post-event exposure (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	0.78	0.37	1.62
Time since transplantation	0-30 vs. >180 days	4.62	1.22	17.44
	31-90 vs. >180 days	2.65	0.82	8.59
	91-180 vs. >180 days	0.67	0.16	2.79

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Table 232 **Relative incidence of kidney transplant rejection within 60 days after seasonal vaccination in season 2007-2008 adjusted for the time since transplantation and conditioned to previous rejections (Subset 2a)**

No records exist in this table

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Table 233 Kidney transplant rejection from 01-SEP-2007 to 31-AUG-2008 according to the 60-days risk periods of seasonal vaccination and the time since transplantation - Subjects without previous rejections (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	52	100.0	61	18330
Data after censoring according to transplantations	52	100.0	61	15534
Data after censoring according to second rejection	52	100.0	52	14666
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	52	100.0	52	14666
Seasonal vaccination - Control period before first dose	52	100.0	23	5437
Seasonal vaccination - Risk period after any dose	35	67.3	6	2135
Seasonal vaccination - Control period after any dose	35	67.3	23	7094
Seasonal vaccination - Pooled risk periods	35	67.3	6	2135
Seasonal vaccination - Pooled control periods	52	100.0	46	12531
Day0 to Day30 after transplantation	17	32.7	8	466
Day31 to Day90 after transplantation	18	34.6	7	990
Day91 to Day180 after transplantation	18	34.6	3	1495
> 180 days after transplantation	45	86.5	34	11715

Table 234 **Relative incidence of kidney transplant rejection within 60 days after seasonal vaccination in season 2007-2008 adjusted for the time since transplantation - Subjects without previous rejections (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	0.74	0.30	1.79
Time since transplantation	0-30 vs. >180 days	6.02	1.05	34.62
	31-90 vs. >180 days	3.08	0.72	13.21
	91-180 vs. >180 days	0.66	0.12	3.60

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

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Table 235 Kidney transplant rejection from 01-SEP-2007 to 31-AUG-2008 according to the 60-days risk periods of seasonal vaccination, the time since transplantation and previous rejection - Subjects with previous rejections (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	11	100.0	19	3876
Data after censoring according to transplantations	11	100.0	19	3876
Data after censoring according to second rejection	11	100.0	11	3046
Subjects with at least one exposure of interest (Previous rejection, Seasonal vaccination, transplantation)	11	100.0	11	3046
Seasonal vaccination - Control period before first dose	11	100.0	9	2285
Seasonal vaccination - Risk period after any dose	5	45.5	1	250
Seasonal vaccination - Control period after any dose	3	27.3	1	511
Seasonal vaccination - Pooled risk periods	5	45.5	1	250
Seasonal vaccination - Pooled control periods	11	100.0	10	2796
> 180 days after transplantation	11	100.0	11	3046
Day0 to Day180 after Previous rejection	11	100.0	8	1203
> 180 days after Previous rejection	8	72.7	3	1843

Table 236 **Relative incidence of kidney transplant rejection within 60 days after seasonal vaccination in season 2007-2008 adjusted for the time since transplantation and previous rejection - Subjects with previous rejections (Subset 2a)**

No records exist in this table

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Table 237 Liver transplant rejection from 01-SEP-2007 to 31-AUG-2008 according to the 60-days risk periods of seasonal vaccination and the time since transplantation (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	6	100.0	7	2191
Data after censoring according to transplantations	6	100.0	7	1983
Data after censoring according to second rejection	6	100.0	6	1958
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	3	50.0	3	860
Seasonal vaccination - Control period before first dose	3	50.0	2	536
Seasonal vaccination - Risk period after any dose	1	16.7	0	61
Seasonal vaccination - Control period after any dose	1	16.7	1	263
Seasonal vaccination - Pooled risk periods	1	16.7	0	61
Seasonal vaccination - Pooled control periods	3	50.0	3	799
Day0 to Day30 after transplantation	2	33.3	1	62
Day31 to Day90 after transplantation	2	33.3	0	120
Day91 to Day180 after transplantation	2	33.3	1	180
> 180 days after transplantation	3	50.0	1	498

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Table 238 Lung transplant rejection from 01-SEP-2007 to 31-AUG-2008 according to the 60-days risk periods of seasonal vaccination and the time since transplantation (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	1	100.0	1	366
Data after censoring according to transplantations	1	100.0	1	366
Data after censoring according to second rejection	1	100.0	1	366
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	1	100.0	1	366
Seasonal vaccination - Control period before first dose	1	100.0	0	45
Seasonal vaccination - Risk period after any dose	1	100.0	0	61
Seasonal vaccination - Control period after any dose	1	100.0	1	260
Seasonal vaccination - Pooled risk periods	1	100.0	0	61
Seasonal vaccination - Pooled control periods	1	100.0	1	305
Day91 to Day180 after transplantation	1	100.0	0	86
> 180 days after transplantation	1	100.0	1	280

Table 239 Pancreas transplant rejection from 01-SEP-2007 to 31-AUG-2008 according to the 60-days risk periods of seasonal vaccination and the time since transplantation (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	1	100.0	1	366
Data after censoring according to transplantations	1	100.0	1	6
Data after censoring according to second rejection	1	100.0	1	6
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	1	100.0	1	6
Seasonal vaccination - Control period before first dose	1	100.0	1	6
Seasonal vaccination - Pooled control periods	1	100.0	1	6
Day0 to Day30 after transplantation	1	100.0	1	6

12.3.1.3. Season 2008-2009**Table 240 SOT rejections from 01-SEP-2008 to 31-AUG-2009 according to the 60-days risk periods of seasonal vaccination and the time since transplantation (Subset 2a)**

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	168	100.0	216	58205
Data after censoring according to transplantations	168	100.0	211	52640
Data after censoring according to second rejection	168	100.0	168	48524
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	92	54.8	92	25217
Seasonal vaccination - Control period before first dose	92	54.8	34	7135
Seasonal vaccination - Risk period after any dose	72	42.9	12	4213
Seasonal vaccination - Control period after any dose	68	40.5	46	13869
Seasonal vaccination - Pooled risk periods	72	42.9	12	4213
Seasonal vaccination - Pooled control periods	92	54.8	80	21004
Day0 to Day30 after transplantation	20	11.9	11	593
Day31 to Day90 after transplantation	19	11.3	8	954
Day91 to Day180 after transplantation	19	11.3	3	1174
> 180 days after transplantation	77	45.8	70	22496

Table 241 **Relative incidence of SOT rejection within 60 days after seasonal vaccination in season 2008-2009 adjusted for the time since transplantation (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	0.64	0.31	1.33
Time since transplantation	0-30 vs. >180 days	25.86	3.22	207.75
	31-90 vs. >180 days	13.88	1.65	117.01
	91-180 vs. >180 days	1.49	0.39	5.70

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

Table 242 SOT rejections from 01-SEP-2008 to 31-AUG-2009 according to the 60-days risk periods of seasonal vaccination, the time since transplantation and all covariates (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	160	100.0	208	55571
Data after censoring according to transplantations	160	100.0	203	50278
Data after censoring according to second rejection	160	100.0	160	46162
Subjects with at least one exposure of interest (Acute bacterial infection, Cancer, Chronic viral infection, Opportunistic infection, Respiratory infection, Seasonal vaccination, transplantation)	94	58.8	94	25969
Seasonal vaccination - Control period before first dose	94	58.8	36	7887
Seasonal vaccination - Risk period after any dose	72	45.0	12	4213
Seasonal vaccination - Control period after any dose	68	42.5	46	13869
Seasonal vaccination - Pooled risk periods	72	45.0	12	4213
Seasonal vaccination - Pooled control periods	94	58.8	82	21756
Day0 to Day30 after transplantation	19	11.9	10	562
Day31 to Day90 after transplantation	18	11.3	8	894
Day91 to Day180 after transplantation	18	11.3	3	1138
> 180 days after transplantation	80	50.0	73	23375
Day0 to Day30 after Respiratory infection	1	0.6	0	31
> 30 days after Respiratory infection	94	58.8	94	25938
Day0 to Day30 after Opportunistic infection	3	1.9	2	93
> 30 days after Opportunistic infection	94	58.8	92	25876
> 30 days after Acute bacterial infection	94	58.8	94	25969
> 365 days after Chronic viral infection	94	58.8	94	25969
Day0 to Day365 after Cancer	8	5.0	5	1565
> 365 days after Cancer	93	58.1	89	24404

Table 243 **Relative incidence of SOT rejection within 60 days after seasonal vaccination in season 2008-2009 adjusted for all covariates (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	0.64	0.31	1.32
Time since transplantation	0-30 vs. >180 days	23.45	2.89	190.50
	31-90 vs. >180 days	14.32	1.71	120.10
	91-180 vs. >180 days	1.50	0.39	5.73
Malignancies/ cancers	365 days after any record vs. other periods	1.11	0.29	4.19

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

Note: only subjects with one year of follow-up before the beginning of the season were considered

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Table 244 SOT rejections from 01-SEP-2008 to 31-AUG-2009 according to the 60-days risk periods of seasonal vaccination, the time since transplantation and malignancies/cancers (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	160	100.0	208	55571
Data after censoring according to transplantations	160	100.0	203	50278
Data after censoring according to second rejection	160	100.0	160	46162
Subjects with at least one exposure of interest (Cancer, Seasonal vaccination, transplantation)	93	58.1	93	25604
Seasonal vaccination - Control period before first dose	93	58.1	35	7522
Seasonal vaccination - Risk period after any dose	72	45.0	12	4213
Seasonal vaccination - Control period after any dose	68	42.5	46	13869
Seasonal vaccination - Pooled risk periods	72	45.0	12	4213
Seasonal vaccination - Pooled control periods	93	58.1	81	21391
Day0 to Day30 after transplantation	19	11.9	10	562
Day31 to Day90 after transplantation	18	11.3	8	894
Day91 to Day180 after transplantation	18	11.3	3	1138
> 180 days after transplantation	79	49.4	72	23010
Day0 to Day365 after Cancer	8	5.0	5	1565
> 365 days after Cancer	92	57.5	88	24039

Table 245 Relative incidence of SOT rejection within 60 days after seasonal vaccination in season 2008-2009 adjusted for the time since transplantation and malignancies/cancers (Subset 2a)

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	0.64	0.31	1.32
Time since transplantation	0-30 vs. >180 days	23.45	2.89	190.50
	31-90 vs. >180 days	14.32	1.71	120.10
	91-180 vs. >180 days	1.50	0.39	5.73
Malignancies/ cancers	365 days after any record vs. other periods	1.11	0.29	4.19

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

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Table 246 SOT rejections from 01-SEP-2008 to 31-AUG-2009 according to the 60-days risk periods of seasonal vaccination and the time since transplantation – with subsequent rejections (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	168	100.0	216	58205
Data after censoring according to transplantations	168	100.0	211	52640
Subjects with at least one exposure of interest (seasonal vaccination, transplantation)	92	54.8	114	27710
seasonal vaccination - Control period before first dose	92	54.8	37	7618
seasonal vaccination - Risk period after any dose	72	42.9	14	4314
seasonal vaccination - Control period after any dose	70	41.7	63	15778
seasonal vaccination - Pooled risk periods	72	42.9	14	4314
seasonal vaccination - Pooled control periods	92	54.8	100	23396
Day0 to Day30 after transplantation	20	11.9	11	593
Day31 to Day90 after transplantation	19	11.3	9	968
Day91 to Day180 after transplantation	20	11.9	6	1313
> 180 days after transplantation	80	47.6	88	24836

Table 247 **Relative incidence of SOT rejection within 60 days after seasonal vaccination in season 2008-2009 adjusted for the time since transplantation - not accounting for perturbed post-event exposure (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	0.80	0.45	1.43
Time since transplantation	0-30 vs. >180 days	22.62	4.10	124.88
	31-90 vs. >180 days	13.35	2.46	72.49
	91-180 vs. >180 days	3.42	0.96	12.22

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

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Table 248 Relative incidence of SOT rejection within 60 days after seasonal vaccination in season 2008-2009 adjusted for the time since transplantation and conditioned to previous rejections (Subset 2a)

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
seasonal vaccination in cases without previous rejection	60 days after any dose vs. other periods	0.69	.	.
seasonal vaccination in cases without previous rejection in cases with previous rejection	60 days after any dose vs. other periods	0.39	.	.
Time since transplantation	0-30 vs. >180 days	25.86	.	.
	31-90 vs. >180 days	13.88	.	.
	91-180 vs. >180 days	1.49	.	.

95% CI = 95% percentile bootstrap confidence interval

LL =lower limit

UL =upper limit

Number of bootstrap steps: NA

Table 249 SOT rejections from 01-SEP-2008 to 31-AUG-2009 according to the 60-days risk periods of seasonal vaccination and the time since transplantation - Subjects without previous rejections (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	78	100.0	95	27316
Data after censoring according to transplantations	78	100.0	95	23124
Data after censoring according to second rejection	78	100.0	78	21091
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	78	100.0	78	21091
Seasonal vaccination - Control period before first dose	78	100.0	30	6251
Seasonal vaccination - Risk period after any dose	58	74.4	10	3442
Seasonal vaccination - Control period after any dose	56	71.8	38	11398
Seasonal vaccination - Pooled risk periods	58	74.4	10	3442
Seasonal vaccination - Pooled control periods	78	100.0	68	17649
Day0 to Day30 after transplantation	20	25.6	11	593
Day31 to Day90 after transplantation	19	24.4	8	954
Day91 to Day180 after transplantation	18	23.1	3	1152
> 180 days after transplantation	63	80.8	56	18392

Table 250 **Relative incidence of SOT rejection within 60 days after seasonal vaccination in season 2008-2009 adjusted for the time since transplantation - Subjects without previous rejections (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	0.69	0.32	1.51
Time since transplantation	0-30 vs. >180 days	28.89	3.45	242.10
	31-90 vs. >180 days	15.50	1.76	136.34
	91-180 vs. >180 days	1.72	0.40	7.33

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

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Table 251 SOT rejections from 01-SEP-2008 to 31-AUG-2009 according to the 60-days risk periods of seasonal vaccination, the time since transplantation and previous rejection (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	22	100.0	37	7359
Data after censoring according to transplantations	22	100.0	36	7140
Data after censoring according to second rejection	22	100.0	22	5776
Subjects with at least one exposure of interest (Previous rejection, Seasonal vaccination, transplantation)	22	100.0	22	5776
Seasonal vaccination - Control period before first dose	22	100.0	12	2534
Seasonal vaccination - Risk period after any dose	14	63.6	2	771
Seasonal vaccination - Control period after any dose	12	54.5	8	2471
Seasonal vaccination - Pooled risk periods	14	63.6	2	771
Seasonal vaccination - Pooled control periods	22	100.0	20	5005
Day91 to Day180 after transplantation	1	4.5	0	22
> 180 days after transplantation	22	100.0	22	5754
Day0 to Day180 after Previous rejection	22	100.0	14	2410
> 180 days after Previous rejection	19	86.4	8	3366

Table 252 **Relative incidence of SOT rejection within 60 days after seasonal vaccination in season 2008-2009 adjusted for the time since transplantation and previous rejection - Subjects with previous rejections (Subset 2a)**

No records exist in this table

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Table 253 Heart transplant rejection from 01-SEP-2008 to 31-AUG-2009 according to the 60-days risk periods of seasonal vaccination and the time since transplantation (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	7	100.0	7	2555
Data after censoring according to transplantations	7	100.0	7	2555
Data after censoring according to second rejection	7	100.0	7	2555
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	4	57.1	4	1460
Seasonal vaccination - Control period before first dose	4	57.1	0	219
Seasonal vaccination - Risk period after any dose	4	57.1	1	244
Seasonal vaccination - Control period after any dose	4	57.1	3	997
Seasonal vaccination - Pooled risk periods	4	57.1	1	244
Seasonal vaccination - Pooled control periods	4	57.1	3	1216
> 180 days after transplantation	4	57.1	4	1460

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Table 254 Kidney transplant rejection from 01-SEP-2008 to 31-AUG-2009 according to the 60-days risk periods of seasonal vaccination and the time since transplantation (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	98	100.0	142	34626
Data after censoring according to transplantations	98	100.0	138	30365
Data after censoring according to second rejection	98	100.0	98	26600
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	63	64.3	63	16396
Seasonal vaccination - Control period before first dose	63	64.3	28	5219
Seasonal vaccination - Risk period after any dose	47	48.0	6	2688
Seasonal vaccination - Control period after any dose	43	43.9	29	8489
Seasonal vaccination - Pooled risk periods	47	48.0	6	2688
Seasonal vaccination - Pooled control periods	63	64.3	57	13708
Day0 to Day30 after transplantation	16	16.3	7	469
Day31 to Day90 after transplantation	15	15.3	8	805
Day91 to Day180 after transplantation	15	15.3	3	988
> 180 days after transplantation	51	52.0	45	14134

Table 255 **Relative incidence of kidney transplant rejection within 60 days after seasonal vaccination in season 2008-2009 adjusted for the time since transplantation (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	0.42	0.15	1.21
Time since transplantation	0-30 vs. >180 days	22.83	2.26	230.30
	31-90 vs. >180 days	18.33	1.76	191.03
	91-180 vs. >180 days	2.12	0.39	11.57

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

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Table 256 Kidney transplant rejection from 01-SEP-2008 to 31-AUG-2009 according to the 60-days risk periods of seasonal vaccination, the time since transplantation and all covariates (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	97	100.0	141	34261
Data after censoring according to transplantations	97	100.0	137	30000
Data after censoring according to second rejection	97	100.0	97	26235
Subjects with at least one exposure of interest (Acute bacterial infection, Cancer, Chronic viral infection, Opportunistic infection, Respiratory infection, Seasonal vaccination, transplantation)	64	66.0	64	16761
Seasonal vaccination - Control period before first dose	64	66.0	29	5584
Seasonal vaccination - Risk period after any dose	47	48.5	6	2688
Seasonal vaccination - Control period after any dose	43	44.3	29	8489
Seasonal vaccination - Pooled risk periods	47	48.5	6	2688
Seasonal vaccination - Pooled control periods	64	66.0	58	14073
Day0 to Day30 after transplantation	16	16.5	7	469
Day31 to Day90 after transplantation	15	15.5	8	805
Day91 to Day180 after transplantation	15	15.5	3	988
> 180 days after transplantation	52	53.6	46	14499
Day0 to Day30 after Respiratory infection	1	1.0	0	31
> 30 days after Respiratory infection	64	66.0	64	16730
Day0 to Day30 after Opportunistic infection	2	2.1	1	62
> 30 days after Opportunistic infection	64	66.0	63	16699
> 30 days after Acute bacterial infection	64	66.0	64	16761
> 365 days after Chronic viral infection	64	66.0	64	16761
Day0 to Day365 after Cancer	3	3.1	0	245
> 365 days after Cancer	64	66.0	64	16516

Table 257 **Relative incidence of kidney transplant rejection within 60 days after seasonal vaccination in season 2008-2009 adjusted for all covariates (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	0.42	0.15	1.21
Time since transplantation	0-30 vs. >180 days	22.83	2.26	230.30
	31-90 vs. >180 days	18.33	1.76	191.03
	91-180 vs. >180 days	2.12	0.39	11.57

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

Note: only subjects with one year of follow-up before the beginning of the season were considered

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Table 258 Kidney transplant rejections from 01-SEP-2008 to 31-AUG-2009 according to the 60-days risk periods of seasonal vaccination and the time since transplantation – with subsequent rejections (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	98	100.0	142	34626
Data after censoring according to transplantations	98	100.0	138	30365
Subjects with at least one exposure of interest (seasonal vaccination, transplantation)	63	64.3	83	18551
seasonal vaccination - Control period before first dose	63	64.3	31	5702
seasonal vaccination - Risk period after any dose	47	48.0	8	2789
seasonal vaccination - Control period after any dose	45	45.9	44	10060
seasonal vaccination - Pooled risk periods	47	48.0	8	2789
seasonal vaccination - Pooled control periods	63	64.3	75	15762
Day0 to Day30 after transplantation	16	16.3	7	469
Day31 to Day90 after transplantation	15	15.3	9	819
Day91 to Day180 after transplantation	16	16.3	6	1127
> 180 days after transplantation	54	55.1	61	16136

Table 259 **Relative incidence of kidney transplant rejection within 60 days after seasonal vaccination in season 2008-2009 adjusted for the time since transplantation - not accounting for perturbed post-event exposure (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	0.64	0.30	1.35
Time since transplantation	0-30 vs. >180 days	19.56	3.01	127.08
	31-90 vs. >180 days	17.21	2.86	103.53
	91-180 vs. >180 days	4.43	1.08	18.13

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

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Table 260 Relative incidence of kidney transplant rejection within 60 days after seasonal vaccination in season 2008-2009 adjusted for the time since transplantation and conditioned to previous rejections (Subset 2a)

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
seasonal vaccination in cases without previous rejection	60 days after any dose vs. other periods	0.42	.	.
seasonal vaccination in cases without previous rejection in cases with previous rejection	60 days after any dose vs. other periods	0.44	.	.
Time since transplantation	0-30 vs. >180 days	22.83	.	.
	31-90 vs. >180 days	18.33	.	.
	91-180 vs. >180 days	2.12	.	.

95% CI = 95% percentile bootstrap confidence interval

LL =lower limit

UL =upper limit

Number of bootstrap steps: NA

Table 261 Kidney transplant rejection from 01-SEP-2008 to 31-AUG-2009 according to the 60-days risk periods of seasonal vaccination and the time since transplantation - Subjects without previous rejections (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	50	100.0	65	17558
Data after censoring according to transplantations	50	100.0	65	14330
Data after censoring according to second rejection	50	100.0	50	12635
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	50	100.0	50	12635
Seasonal vaccination - Control period before first dose	50	100.0	24	4398
Seasonal vaccination - Risk period after any dose	34	68.0	4	1978
Seasonal vaccination - Control period after any dose	32	64.0	22	6259
Seasonal vaccination - Pooled risk periods	34	68.0	4	1978
Seasonal vaccination - Pooled control periods	50	100.0	46	10657
Day0 to Day30 after transplantation	16	32.0	7	469
Day31 to Day90 after transplantation	15	30.0	8	805
Day91 to Day180 after transplantation	15	30.0	3	988
> 180 days after transplantation	38	76.0	32	10373

Table 262 **Relative incidence of kidney transplant rejection within 60 days after seasonal vaccination in season 2008-2009 adjusted for the time since transplantation - Subjects without previous rejections (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	0.42	0.12	1.38
Time since transplantation	0-30 vs. >180 days	22.83	2.26	230.30
	31-90 vs. >180 days	18.33	1.76	191.03
	91-180 vs. >180 days	2.12	0.39	11.57

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

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Table 263 Kidney transplant rejection from 01-SEP-2008 to 31-AUG-2009 according to the 60-days risk periods of seasonal vaccination, the time since transplantation and previous rejection - Subjects with previous rejections (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	20	100.0	35	6975
Data after censoring according to transplantations	20	100.0	34	6756
Data after censoring according to second rejection	20	100.0	20	5392
Subjects with at least one exposure of interest (Previous rejection, Seasonal vaccination, transplantation)	20	100.0	20	5392
Seasonal vaccination - Control period before first dose	20	100.0	11	2452
Seasonal vaccination - Risk period after any dose	13	65.0	2	710
Seasonal vaccination - Control period after any dose	11	55.0	7	2230
Seasonal vaccination - Pooled risk periods	13	65.0	2	710
Seasonal vaccination - Pooled control periods	20	100.0	18	4682
> 180 days after transplantation	20	100.0	20	5392
Day0 to Day180 after Previous rejection	20	100.0	13	2301
> 180 days after Previous rejection	18	90.0	7	3091

Table 264 **Relative incidence of kidney transplant rejection within 60 days after seasonal vaccination in season 2008-2009 adjusted for the time since transplantation and previous rejection - Subjects with previous rejections (Subset 2a)**

No records exist in this table

Table 265 Liver transplant rejection from 01-SEP-2008 to 31-AUG-2009 according to the 60-days risk periods of seasonal vaccination and the time since transplantation (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	16	100.0	17	4857
Data after censoring according to transplantations	16	100.0	17	4428
Data after censoring according to second rejection	16	100.0	16	4322
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	9	56.3	9	2854
Seasonal vaccination - Control period before first dose	9	56.3	4	889
Seasonal vaccination - Risk period after any dose	7	43.8	1	427
Seasonal vaccination - Control period after any dose	7	43.8	4	1538
Seasonal vaccination - Pooled risk periods	7	43.8	1	427
Seasonal vaccination - Pooled control periods	9	56.3	8	2427
Day0 to Day30 after transplantation	2	12.5	2	62
Day31 to Day90 after transplantation	2	12.5	0	120
Day91 to Day180 after transplantation	2	12.5	0	126
> 180 days after transplantation	8	50.0	7	2546

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Table 266 Lung transplant rejection from 01-SEP-2008 to 31-AUG-2009 according to the 60-days risk periods of seasonal vaccination and the time since transplantation (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	5	100.0	5	1611
Data after censoring according to transplantations	5	100.0	5	972
Data after censoring according to second rejection	5	100.0	5	972
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	4	80.0	4	607
Seasonal vaccination - Control period before first dose	4	80.0	2	169
Seasonal vaccination - Risk period after any dose	2	40.0	0	122
Seasonal vaccination - Control period after any dose	2	40.0	2	316
Seasonal vaccination - Pooled risk periods	2	40.0	0	122
Seasonal vaccination - Pooled control periods	4	80.0	4	485
Day0 to Day30 after transplantation	2	40.0	2	62
Day31 to Day90 after transplantation	2	40.0	0	29
Day91 to Day180 after transplantation	1	20.0	0	38
> 180 days after transplantation	2	40.0	2	478

Table 267 Pancreas transplant rejection from 01-SEP-2008 to 31-AUG-2009 according to the 60-days risk periods of seasonal vaccination and the time since transplantation (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subset 2a	0			
Data after censoring according to transplantations	0			
Data after censoring according to second rejection	0			
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	0			

12.3.1.4. Pooled seasons**Table 268 SOT rejections according to the 60-days risk periods of seasonal vaccination and the time since transplantation - pooled seasons (Subset 2a)**

	Subjects		Rejections	Person*days
	N	%		
Subjects with at least one exposure of interest (seasonal vaccination, transplantation) in any of the seasons*	218	100.0	218	61162
Subjects with data from season 06-07	74	33.9	74	20560
Subjects with data from season 07-08	74	33.9	74	21441
Subjects with data from season 08-09	70	32.1	70	19161
seasonal vaccination - Control period before first dose	216	99.1	93	20299
seasonal vaccination - Risk period after any dose	156	71.6	31	9287
seasonal vaccination - Control period after any dose	149	68.3	94	31576
seasonal vaccination - Pooled risk periods	156	71.6	31	9287
seasonal vaccination - Pooled control periods	218	100.0	187	51875
Day0 to Day30 after transplantation	64	29.4	38	1811
Day31 to Day90 after transplantation	64	29.4	21	3347
Day91 to Day180 after transplantation	62	28.4	13	4831
> 180 days after transplantation	182	83.5	146	51173

*Only the first season with data on exposures of interest is considered for each patient

Table 269 **Relative incidence of SOT rejection within 60 days after seasonal vaccination in seasons 2006-2009 adjusted for the time since transplantation (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	0.88	0.56	1.38
Time since transplantation	0-30 vs. >180 days	16.84	6.03	47.04
	31-90 vs. >180 days	5.69	2.17	14.89
	91-180 vs. >180 days	1.98	0.73	5.35

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

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Table 270 SOT rejections according to the 60-days risk periods of seasonal vaccination, the time since transplantation and all covariates - pooled seasons (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subjects with at least one exposure of interest (Acute bacterial infection, Cancer, Chronic viral infection, Opportunistic infection, Respiratory infection, seasonal vaccination, transplantation) in any of the seasons*	210	100.0	210	58815
Subjects with data from season 06-07	71	33.8	71	19626
Subjects with data from season 07-08	70	33.3	70	20155
Subjects with data from season 08-09	69	32.9	69	19034
seasonal vaccination - Control period before first dose	208	99.0	89	19123
seasonal vaccination - Risk period after any dose	152	72.4	31	9043
seasonal vaccination - Control period after any dose	145	69.0	90	30649
seasonal vaccination - Pooled risk periods	152	72.4	31	9043
seasonal vaccination - Pooled control periods	210	100.0	179	49772
Day0 to Day30 after transplantation	61	29.0	36	1718
Day31 to Day90 after transplantation	60	28.6	20	3126
Day91 to Day180 after transplantation	58	27.6	12	4525
> 180 days after transplantation	175	83.3	142	49446
> 30 days after Respiratory infection	210	100.0	210	58815
Day0 to Day30 after Opportunistic infection	7	3.3	2	215
> 30 days after Opportunistic infection	210	100.0	208	58600
> 30 days after Acute bacterial infection	210	100.0	210	58815
> 365 days after Chronic viral infection	210	100.0	210	58815
Day0 to Day365 after Cancer	14	6.7	12	3366
> 365 days after Cancer	207	98.6	198	55449

*Only the first season with data on exposures of interest is considered for each patient

Table 271 **Relative incidence of SOT rejection within 60 days after seasonal vaccination in seasons 2006-2009 adjusted for all covariates (Subset 2a)**

No records exist in this table

Table 272 SOT rejections according to the 60-days risk periods of seasonal vaccination, the time since transplantation and opportunistic infections - pooled seasons (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subjects with at least one exposure of interest (Opportunistic infection, seasonal vaccination, transplantation) in any of the seasons*	218	100.0	218	61162
Subjects with data from season 06-07	74	33.9	74	20560
Subjects with data from season 07-08	74	33.9	74	21441
Subjects with data from season 08-09	70	32.1	70	19161
seasonal vaccination - Control period before first dose	216	99.1	93	20299
seasonal vaccination - Risk period after any dose	156	71.6	31	9287
seasonal vaccination - Control period after any dose	149	68.3	94	31576
seasonal vaccination - Pooled risk periods	156	71.6	31	9287
seasonal vaccination - Pooled control periods	218	100.0	187	51875
Day0 to Day30 after transplantation	64	29.4	38	1811
Day31 to Day90 after transplantation	64	29.4	21	3347
Day91 to Day180 after transplantation	62	28.4	13	4831
> 180 days after transplantation	182	83.5	146	51173
Day0 to Day30 after Opportunistic infection	7	3.2	2	215
> 30 days after Opportunistic infection	218	100.0	216	60947

*Only the first season with data on exposures of interest is considered for each patient

Table 273 **Relative incidence of SOT rejection within 60 days after seasonal vaccination in seasons 2006-2009 adjusted for the time since transplantation and opportunistic infections (Subset 2a)**

No records exist in this table

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Table 274 SOT rejections according to the 60-days risk periods of seasonal vaccination, the time since transplantation and malignancies/cancers - pooled seasons (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subjects with at least one exposure of interest (Cancer, seasonal vaccination, transplantation) in any of the seasons*	210	100.0	210	58815
Subjects with data from season 06-07	71	33.8	71	19626
Subjects with data from season 07-08	70	33.3	70	20155
Subjects with data from season 08-09	69	32.9	69	19034
seasonal vaccination - Control period before first dose	208	99.0	89	19123
seasonal vaccination - Risk period after any dose	152	72.4	31	9043
seasonal vaccination - Control period after any dose	145	69.0	90	30649
seasonal vaccination - Pooled risk periods	152	72.4	31	9043
seasonal vaccination - Pooled control periods	210	100.0	179	49772
Day0 to Day30 after transplantation	61	29.0	36	1718
Day31 to Day90 after transplantation	60	28.6	20	3126
Day91 to Day180 after transplantation	58	27.6	12	4525
> 180 days after transplantation	175	83.3	142	49446
Day0 to Day365 after Cancer	14	6.7	12	3366
> 365 days after Cancer	207	98.6	198	55449

*Only the first season with data on exposures of interest is considered for each patient

Table 275 **Relative incidence of SOT rejection within 60 days after seasonal vaccination in seasons 2006-2009 adjusted for the time since transplantation and malignancies/cancers (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	0.92	0.59	1.45
Time since transplantation	0-30 vs. >180 days	15.36	5.45	43.31
	31-90 vs. >180 days	5.43	2.07	14.22
	91-180 vs. >180 days	1.83	0.66	5.09
Malignancies/ cancers	365 days after any record vs. other periods	3.34	0.42	26.93

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

Table 276 SOT rejections according to the 60-days risk periods of seasonal vaccination and the time since transplantation – with subsequent rejections - pooled seasons (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subjects with at least one exposure of interest (seasonal vaccination, transplantation) in any of the seasons*	218	100.0	250	64659
Subjects with data from season 06-07	74	33.9	83	21781
Subjects with data from season 07-08	74	33.9	85	22374
Subjects with data from season 08-09	70	32.1	82	20504
seasonal vaccination - Control period before first dose	216	99.1	101	21240
seasonal vaccination - Risk period after any dose	156	71.6	34	9421
seasonal vaccination - Control period after any dose	152	69.7	115	33998
seasonal vaccination - Pooled risk periods	156	71.6	34	9421
seasonal vaccination - Pooled control periods	218	100.0	216	55238
Day0 to Day30 after transplantation	64	29.4	38	1811
Day31 to Day90 after transplantation	64	29.4	23	3398
Day91 to Day180 after transplantation	64	29.4	19	5124
> 180 days after transplantation	189	86.7	170	54326

*Only the first season with data on exposures of interest is considered for each patient

Table 277 **Relative incidence of SOT rejection within 60 days after seasonal vaccination in seasons 2006-2009 adjusted for the time since transplantation - not accounting for perturbed post-event exposure (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	0.95	0.65	1.39
Time since transplantation	0-30 vs. >180 days	13.92	6.13	31.62
	31-90 vs. >180 days	5.47	2.47	12.12
	91-180 vs. >180 days	2.54	1.22	5.27

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

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Table 278 **Relative incidence of SOT rejection within 60 days after seasonal vaccination in seasons 2006-2009 adjusted for the time since transplantation and conditioned to previous rejections (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
seasonal vaccination	60 days after any dose vs. other periods	0.90	.	.
seasonal vaccination in cases with previous rejection	60 days after any dose vs. other periods	0.69	.	.
Time since transplantation	0-30 vs. >180 days	16.78	.	.
	31-90 vs. >180 days	5.68	.	.
	91-180 vs. >180 days	1.97	.	.

95% CI = 95% percentile bootstrap confidence interval

LL =lower limit

UL =upper limit

Number of bootstrap steps: NA

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Table 279 SOT rejections according to the 60-days risk periods of seasonal vaccination and the time since transplantation - Subjects without previous rejections - pooled seasons (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subjects with at least one exposure of interest (seasonal vaccination, transplantation) in any of the seasons*	204	100.0	204	57109
Subjects with data from season 06-07	65	31.9	65	18290
Subjects with data from season 07-08	73	35.8	73	21118
Subjects with data from season 08-09	66	32.4	66	17701
seasonal vaccination - Control period before first dose	202	99.0	88	19162
seasonal vaccination - Risk period after any dose	143	70.1	29	8574
seasonal vaccination - Control period after any dose	138	67.6	87	29373
seasonal vaccination - Pooled risk periods	143	70.1	29	8574
seasonal vaccination - Pooled control periods	204	100.0	175	48535
Day0 to Day30 after transplantation	64	31.4	38	1811
Day31 to Day90 after transplantation	62	30.4	19	3292
Day91 to Day180 after transplantation	60	29.4	13	4692
> 180 days after transplantation	169	82.8	134	47314

*Only the first season with data on exposures of interest is considered for each patient

Table 280 Relative incidence of SOT rejection within 60 days after seasonal vaccination in seasons 2006-2009 adjusted for the time since transplantation - Subjects without previous rejections (Subset 2a)

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	0.90	0.57	1.44
Time since transplantation	0-30 vs. >180 days	15.16	5.52	41.65
	31-90 vs. >180 days	4.86	1.87	12.67
	91-180 vs. >180 days	1.98	0.74	5.29

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

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Table 281 SOT rejections according to the 60-days risk periods of seasonal vaccination, the time since transplantation and previous rejection - pooled seasons (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subjects with at least one exposure of interest (Previous rejection, seasonal vaccination, transplantation) in any of the seasons*	14	100.0	14	4053
Subjects with data from season 06-07	9	64.3	9	2270
Subjects with data from season 07-08	1	7.1	1	323
Subjects with data from season 08-09	4	28.6	4	1460
seasonal vaccination - Control period before first dose	14	100.0	5	1137
seasonal vaccination - Risk period after any dose	13	92.9	2	713
seasonal vaccination - Control period after any dose	11	78.6	7	2203
seasonal vaccination - Pooled risk periods	13	92.9	2	713
seasonal vaccination - Pooled control periods	14	100.0	12	3340
Day31 to Day90 after transplantation	2	14.3	2	55
Day91 to Day180 after transplantation	2	14.3	0	139
> 180 days after transplantation	13	92.9	12	3859
Day0 to Day180 after Previous rejection	14	100.0	6	1187
> 180 days after Previous rejection	13	92.9	8	2866

*Only the first season with data on exposures of interest is considered for each patient

Table 282 **Relative incidence of SOT rejection within 60 days after seasonal vaccination in seasons 2006-2009 adjusted for the time since transplantation and previous rejection - Subjects with previous rejections (Subset 2a)**

No records exist in this table

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Table 283 Heart transplant rejection according to the 60-days risk periods of seasonal vaccination and the time since transplantation - pooled seasons (Subset 2a)

	Subjects			
	N	%	Rejections	Person*days
Subjects with at least one exposure of interest (seasonal vaccination, transplantation) in any of the seasons*	15	100.0	15	3882
Subjects with data from season 06-07	5	33.3	5	933
Subjects with data from season 07-08	6	40.0	6	1489
Subjects with data from season 08-09	4	26.7	4	1460
seasonal vaccination - Control period before first dose	15	100.0	6	983
seasonal vaccination - Risk period after any dose	10	66.7	1	610
seasonal vaccination - Control period after any dose	10	66.7	8	2289
seasonal vaccination - Pooled risk periods	10	66.7	1	610
seasonal vaccination - Pooled control periods	15	100.0	14	3272
Day0 to Day30 after transplantation	4	26.7	4	46
Day31 to Day90 after transplantation	2	13.3	0	96
Day91 to Day180 after transplantation	2	13.3	1	180
> 180 days after transplantation	11	73.3	10	3560

*Only the first season with data on exposures of interest is considered for each patient

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Table 284 Kidney transplant rejection according to the 60-days risk periods of seasonal vaccination and the time since transplantation - pooled seasons (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subjects with at least one exposure of interest (seasonal vaccination, transplantation) in any of the seasons*	144	100.0	144	38892
Subjects with data from season 06-07	49	34.0	49	13686
Subjects with data from season 07-08	51	35.4	51	14217
Subjects with data from season 08-09	44	30.6	44	10989
seasonal vaccination - Control period before first dose	142	98.6	70	14495
seasonal vaccination - Risk period after any dose	98	68.1	16	5783
seasonal vaccination - Control period after any dose	92	63.9	58	18614
seasonal vaccination - Pooled risk periods	98	68.1	16	5783
seasonal vaccination - Pooled control periods	144	100.0	128	33109
Day0 to Day30 after transplantation	49	34.0	26	1424
Day31 to Day90 after transplantation	48	33.3	18	2630
Day91 to Day180 after transplantation	47	32.6	9	3720
> 180 days after transplantation	120	83.3	91	31118

*Only the first season with data on exposures of interest is considered for each patient

Table 285 **Relative incidence of kidney transplant rejection within 60 days after seasonal vaccination in seasons 2006-2009 adjusted for the time since transplantation (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	0.59	0.32	1.08
Time since transplantation	0-30 vs. >180 days	14.32	4.59	44.71
	31-90 vs. >180 days	5.67	1.97	16.33
	91-180 vs. >180 days	1.58	0.50	4.97

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

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Table 286 Kidney transplant rejection according to the 60-days risk periods of seasonal vaccination, the time since transplantation and all covariates - pooled seasons (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subjects with at least one exposure of interest (Acute bacterial infection, Cancer, Chronic viral infection, Opportunistic infection, Respiratory infection, seasonal vaccination, transplantation) in any of the seasons*	139	100.0	139	37228
Subjects with data from season 06-07	47	33.8	47	13117
Subjects with data from season 07-08	48	34.5	48	13122
Subjects with data from season 08-09	44	31.7	44	10989
seasonal vaccination - Control period before first dose	137	98.6	69	14008
seasonal vaccination - Risk period after any dose	94	67.6	16	5539
seasonal vaccination - Control period after any dose	88	63.3	54	17681
seasonal vaccination - Pooled risk periods	94	67.6	16	5539
seasonal vaccination - Pooled control periods	139	100.0	123	31689
Day0 to Day30 after transplantation	48	34.5	25	1393
Day31 to Day90 after transplantation	47	33.8	18	2570
Day91 to Day180 after transplantation	46	33.1	9	3630
> 180 days after transplantation	115	82.7	87	29635
> 30 days after Respiratory infection	139	100.0	139	37228
Day0 to Day30 after Opportunistic infection	5	3.6	1	153
> 30 days after Opportunistic infection	139	100.0	138	37075
> 30 days after Acute bacterial infection	139	100.0	139	37228
> 365 days after Chronic viral infection	139	100.0	139	37228
Day0 to Day365 after Cancer	4	2.9	3	745
> 365 days after Cancer	137	98.6	136	36483

*Only the first season with data on exposures of interest is considered for each patient

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Table 287 Kidney transplant rejections from 01-SEP-2006 to 31-AUG-2007 according to the 60-days risk periods of seasonal vaccination and the time since transplantation – with subsequent rejections - pooled seasons (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subjects with at least one exposure of interest (seasonal vaccination, transplantation) in any of the seasons*	144	100.0	171	41777
Subjects with data from season 06-07	49	34.0	55	14426
Subjects with data from season 07-08	51	35.4	61	15125
Subjects with data from season 08-09	44	30.6	55	12226
seasonal vaccination - Control period before first dose	142	98.6	77	15411
seasonal vaccination - Risk period after any dose	98	68.1	18	5883
seasonal vaccination - Control period after any dose	94	65.3	76	20483
seasonal vaccination - Pooled risk periods	98	68.1	18	5883
seasonal vaccination - Pooled control periods	144	100.0	153	35894
Day0 to Day30 after transplantation	49	34.0	26	1424
Day31 to Day90 after transplantation	48	33.3	20	2681
Day91 to Day180 after transplantation	49	34.0	14	3972
> 180 days after transplantation	126	87.5	111	33700

*Only the first season with data on exposures of interest is considered for each patient

Table 288 **Relative incidence of kidney transplant rejection within 60 days after seasonal vaccination in seasons 2006-2009 adjusted for the time since transplantation - not accounting for perturbed post-event exposure (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	0.68	0.41	1.14
Time since transplantation	0-30 vs. >180 days	12.52	4.94	31.77
	31-90 vs. >180 days	6.00	2.44	14.73
	91-180 vs. >180 days	2.43	1.03	5.72

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

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Table 289 **Relative incidence of kidney transplant rejection within 60 days after seasonal vaccination in seasons 2006-2009 adjusted for the time since transplantation and conditioned to previous rejections (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
seasonal vaccination	60 days after any dose vs. other periods	0.56	.	.
seasonal vaccination in cases with previous rejection	60 days after any dose vs. other periods	0.87	.	.
Time since transplantation	0-30 vs. >180 days	14.49	.	.
	31-90 vs. >180 days	5.70	.	.
	91-180 vs. >180 days	1.59	.	.

95% CI = 95% percentile bootstrap confidence interval

LL =lower limit

UL =upper limit

Number of bootstrap steps: NA

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Table 290 Kidney transplant rejection according to the 60-days risk periods of seasonal vaccination and the time since transplantation - Subjects without previous rejections - pooled seasons (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subjects with at least one exposure of interest (seasonal vaccination, transplantation) in any of the seasons*	134	100.0	134	35997
Subjects with data from season 06-07	43	32.1	43	12209
Subjects with data from season 07-08	50	37.3	50	13894
Subjects with data from season 08-09	41	30.6	41	9894
seasonal vaccination - Control period before first dose	132	98.5	67	13865
seasonal vaccination - Risk period after any dose	88	65.7	14	5219
seasonal vaccination - Control period after any dose	83	61.9	53	16913
seasonal vaccination - Pooled risk periods	88	65.7	14	5219
seasonal vaccination - Pooled control periods	134	100.0	120	30778
Day0 to Day30 after transplantation	49	36.6	26	1424
Day31 to Day90 after transplantation	48	35.8	18	2630
Day91 to Day180 after transplantation	47	35.1	9	3720
> 180 days after transplantation	110	82.1	81	28223

*Only the first season with data on exposures of interest is considered for each patient

Table 291 **Relative incidence of kidney transplant rejection within 60 days after seasonal vaccination in seasons 2006-2009 adjusted for the time since transplantation - Subjects without previous rejections (Subset 2a)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	0.56	0.29	1.08
Time since transplantation	0-30 vs. >180 days	14.49	4.64	45.21
	31-90 vs. >180 days	5.70	1.99	16.38
	91-180 vs. >180 days	1.59	0.51	4.98

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

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Table 292 Kidney transplant rejection according to the 60-days risk periods of seasonal vaccination, the time since transplantation and previous rejection - Subjects with previous rejections - pooled seasons (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subjects with at least one exposure of interest (Previous rejection, seasonal vaccination, transplantation) in any of the seasons*	10	100.0	10	2895
Subjects with data from season 06-07	6	60.0	6	1477
Subjects with data from season 07-08	1	10.0	1	323
Subjects with data from season 08-09	3	30.0	3	1095
seasonal vaccination - Control period before first dose	10	100.0	3	630
seasonal vaccination - Risk period after any dose	10	100.0	2	564
seasonal vaccination - Control period after any dose	9	90.0	5	1701
seasonal vaccination - Pooled risk periods	10	100.0	2	564
seasonal vaccination - Pooled control periods	10	100.0	8	2331
> 180 days after transplantation	10	100.0	10	2895
Day0 to Day180 after Previous rejection	10	100.0	4	845
> 180 days after Previous rejection	10	100.0	6	2050

*Only the first season with data on exposures of interest is considered for each patient

Table 293 **Relative incidence of kidney transplant rejection within 60 days after seasonal vaccination in seasons 2006-2009 adjusted for the time since transplantation and previous rejection - Subjects with previous rejections (Subset 2a)**

No records exist in this table

Table 294 **Liver transplant rejection according to the 60-days risk periods of seasonal vaccination and the time since transplantation - pooled seasons (Subset 2a)**

	Subjects		Rejections	Person*days
	N	%		
Subjects with at least one exposure of interest (seasonal vaccination, transplantation) in any of the seasons*	16	100.0	16	4950
Subjects with data from season 06-07	5	31.3	5	1604
Subjects with data from season 07-08	3	18.8	3	857
Subjects with data from season 08-09	8	50.0	8	2489
seasonal vaccination - Control period before first dose	16	100.0	10	2211
seasonal vaccination - Risk period after any dose	10	62.5	1	610
seasonal vaccination - Control period after any dose	10	62.5	5	2129
seasonal vaccination - Pooled risk periods	10	62.5	1	610
seasonal vaccination - Pooled control periods	16	100.0	15	4340
Day0 to Day30 after transplantation	6	37.5	5	186
Day31 to Day90 after transplantation	8	50.0	1	404
Day91 to Day180 after transplantation	8	50.0	2	656
> 180 days after transplantation	14	87.5	8	3704

*Only the first season with data on exposures of interest is considered for each patient

Table 295 Lung transplant rejection according to the 60-days risk periods of seasonal vaccination and the time since transplantation - pooled seasons (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subjects with at least one exposure of interest (seasonal vaccination, transplantation) in any of the seasons*	9	100.0	9	1824
Subjects with data from season 06-07	5	55.6	5	1003
Subjects with data from season 07-08	1	11.1	1	365
Subjects with data from season 08-09	3	33.3	3	456
seasonal vaccination - Control period before first dose	9	100.0	5	527
seasonal vaccination - Risk period after any dose	5	55.6	0	271
seasonal vaccination - Control period after any dose	4	44.4	4	1026
seasonal vaccination - Pooled risk periods	5	55.6	0	271
seasonal vaccination - Pooled control periods	9	100.0	9	1553
Day0 to Day30 after transplantation	4	44.4	3	124
Day31 to Day90 after transplantation	5	55.6	2	157
Day91 to Day180 after transplantation	4	44.4	0	207
> 180 days after transplantation	4	44.4	4	1336

*Only the first season with data on exposures of interest is considered for each patient

Table 296 Pancreas transplant rejection according to the 60-days risk periods of seasonal vaccination and the time since transplantation - pooled seasons (Subset 2a)

	Subjects		Rejections	Person*days
	N	%		
Subjects with at least one exposure of interest (seasonal vaccination, transplantation) in any of the seasons*	1	100.0	1	6
Subjects with data from season 07-08	1	100.0	1	6
seasonal vaccination - Control period before first dose	1	100.0	1	6
seasonal vaccination - Pooled control periods	1	100.0	1	6
Day0 to Day30 after transplantation	1	100.0	1	6

*Only the first season with data on exposures of interest is considered for each patient

12.3.2. Subset 2B**12.3.2.1. Season 2006-2007****Table 297 SOT rejections from 01-SEP-2006 to 31-AUG-2007 according to the 60-days risk periods of seasonal vaccination and the time since transplantation (Subset 2b)**

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	46	100.0	53	15771
Data after censoring according to transplantations	46	100.0	53	14272
Data after censoring according to second rejection	46	100.0	46	13834
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	26	56.5	26	7227
Seasonal vaccination - Control period before first dose	25	54.3	11	2192
Seasonal vaccination - Risk period after any dose	20	43.5	7	1197
Seasonal vaccination - Control period after any dose	19	41.3	8	3838
Seasonal vaccination - Pooled risk periods	20	43.5	7	1197
Seasonal vaccination - Pooled control periods	26	56.5	19	6030
Day0 to Day30 after transplantation	9	19.6	8	234
> 30 days after transplantation	24	52.2	18	6993

Table 298 **Relative incidence of SOT rejection within 60 days after seasonal vaccination in season 2006-2007 adjusted for the time since transplantation (Subset 2b)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	2.13	0.72	6.25
Time since transplantation	0-30 vs. >30 days	39.75	4.98	317.48

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

Table 299 SOT rejections from 01-SEP-2006 to 31-AUG-2007 according to the 60-days risk periods of seasonal vaccination, the time since transplantation and all covariates (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	45	100.0	52	15406
Data after censoring according to transplantations	45	100.0	52	13907
Data after censoring according to second rejection	45	100.0	45	13469
Subjects with at least one exposure of interest (Acute bacterial infection, Cancer, Chronic viral infection, Opportunistic infection, Respiratory infection, Seasonal vaccination, chemo, transplantation)	28	62.2	28	7945
Seasonal vaccination - Control period before first dose	27	60.0	13	2910
Seasonal vaccination - Risk period after any dose	20	44.4	7	1197
Seasonal vaccination - Control period after any dose	19	42.2	8	3838
Seasonal vaccination - Pooled risk periods	20	44.4	7	1197
Seasonal vaccination - Pooled control periods	28	62.2	21	6748
Day0 to Day30 after transplantation	9	20.0	8	234
> 30 days after transplantation	26	57.8	20	7711
Day0 to Day30 after Respiratory infection	1	2.2	0	31
> 30 days after Respiratory infection	28	62.2	28	7914
Day0 to Day30 after Opportunistic infection	2	4.4	0	62
> 30 days after Opportunistic infection	28	62.2	28	7883
> 30 days after Acute bacterial infection	28	62.2	28	7945
> 365 days after Chronic viral infection	28	62.2	28	7945
Day0 to Day365 after Cancer	4	8.9	4	1022
> 365 days after Cancer	26	57.8	24	6923
Day0 to Day365 after chemo	1	2.2	1	264
> 365 days after chemo	28	62.2	27	7681

Table 300 SOT rejections from 01-SEP-2006 to 31-AUG-2007 according to the 60-days risk periods of seasonal vaccination and the time since transplantation – with subsequent rejections (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	46	100.0	53	15771
Data after censoring according to transplantations	46	100.0	53	14272
Subjects with at least one exposure of interest (seasonal vaccination, transplantation)	26	56.5	31	7539
seasonal vaccination - Control period before first dose	25	54.3	11	2192
seasonal vaccination - Risk period after any dose	20	43.5	7	1197
seasonal vaccination - Control period after any dose	19	41.3	13	4150
seasonal vaccination - Pooled risk periods	20	43.5	7	1197
seasonal vaccination - Pooled control periods	26	56.5	24	6342
Day0 to Day30 after transplantation	9	19.6	8	234
> 30 days after transplantation	24	52.2	23	7305

Table 301 Relative incidence of SOT rejection within 60 days after seasonal vaccination in season 2006-2007 adjusted for the time since transplantation - not accounting for perturbed post-event exposure (Subset 2b)

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	1.66	0.65	4.21
Time since transplantation	0-30 vs. >30 days	38.96	4.44	341.82

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Table 302 Heart transplant rejection from 01-SEP-2006 to 31-AUG-2007 according to the 60-days risk periods of seasonal vaccination and the time since transplantation (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	4	100.0	5	918
Data after censoring according to transplantations	4	100.0	5	606
Data after censoring according to second rejection	4	100.0	4	492
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	2	50.0	2	17
Seasonal vaccination - Control period before first dose	2	50.0	2	17
Seasonal vaccination - Pooled control periods	2	50.0	2	17
Day0 to Day30 after transplantation	2	50.0	2	17

Table 303 Kidney transplant rejection from 01-SEP-2006 to 31-AUG-2007 according to the 60-days risk periods of seasonal vaccination and the time since transplantation (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	22	100.0	27	7694
Data after censoring according to transplantations	22	100.0	27	6864
Data after censoring according to second rejection	22	100.0	22	6632
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	16	72.7	16	4790
Seasonal vaccination - Control period before first dose	15	68.2	6	1488
Seasonal vaccination - Risk period after any dose	13	59.1	5	770
Seasonal vaccination - Control period after any dose	12	54.5	5	2532
Seasonal vaccination - Pooled risk periods	13	59.1	5	770
Seasonal vaccination - Pooled control periods	16	72.7	11	4020
Day0 to Day30 after transplantation	5	22.7	4	155
> 30 days after transplantation	16	72.7	12	4635

Table 304 **Relative incidence of kidney transplant rejection within 60 days after seasonal vaccination in season 2006-2007 adjusted for the time since transplantation (Subset 2b)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	2.13	0.53	8.53
Time since transplantation	0-30 vs. >30 days	26.75	3.03	236.13

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

Table 305 Kidney transplant rejection from 01-SEP-2006 to 31-AUG-2007 according to the 60-days risk periods of seasonal vaccination, the time since transplantation and all covariates (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	22	100.0	27	7694
Data after censoring according to transplantations	22	100.0	27	6864
Data after censoring according to second rejection	22	100.0	22	6632
Subjects with at least one exposure of interest (Acute bacterial infection, Cancer, Chronic viral infection, Opportunistic infection, Respiratory infection, Seasonal vaccination, chemo, transplantation)	17	77.3	17	5143
Seasonal vaccination - Control period before first dose	16	72.7	7	1841
Seasonal vaccination - Risk period after any dose	13	59.1	2	388
Seasonal vaccination - Control period after any dose	13	59.1	8	2914
Seasonal vaccination - Pooled risk periods	13	59.1	2	388
Seasonal vaccination - Pooled control periods	17	77.3	15	4755
Day0 to Day30 after transplantation	5	22.7	4	155
> 30 days after transplantation	17	77.3	13	4988
Day0 to Day30 after Respiratory infection	1	4.5	0	31
> 30 days after Respiratory infection	17	77.3	17	5112
Day0 to Day30 after Opportunistic infection	1	4.5	0	31
> 30 days after Opportunistic infection	17	77.3	17	5112
> 30 days after Acute bacterial infection	17	77.3	17	5143
> 365 days after Chronic viral infection	17	77.3	17	5143
Day0 to Day365 after Cancer	1	4.5	1	221
> 365 days after Cancer	16	72.7	16	4922
Day0 to Day365 after chemo	1	4.5	1	264
> 365 days after chemo	17	77.3	16	4879

Table 306 Kidney transplant rejections from 01-SEP-2006 to 31-AUG-2007 according to the 60-days risk periods of seasonal vaccination and the time since transplantation – with subsequent rejections (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	22	100.0	27	7694
Data after censoring according to transplantations	22	100.0	27	6864
Subjects with at least one exposure of interest (seasonal vaccination, transplantation)	16	72.7	20	5010
seasonal vaccination - Control period before first dose	15	68.2	6	1488
seasonal vaccination - Risk period after any dose	13	59.1	5	770
seasonal vaccination - Control period after any dose	12	54.5	9	2752
seasonal vaccination - Pooled risk periods	13	59.1	5	770
seasonal vaccination - Pooled control periods	16	72.7	15	4240
Day0 to Day30 after transplantation	5	22.7	4	155
> 30 days after transplantation	16	72.7	16	4855

Table 307 **Relative incidence of kidney transplant rejection within 60 days after seasonal vaccination in season 2006-2007 adjusted for the time since transplantation - not accounting for perturbed post-event exposure (Subset 2b)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	1.63	0.53	5.01
Time since transplantation	0-30 vs. >30 days	24.88	2.54	243.45

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

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Table 308 Liver transplant rejection from 01-SEP-2006 to 31-AUG-2007 according to the 60-days risk periods of seasonal vaccination and the time since transplantation (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	6	100.0	6	2190
Data after censoring according to transplantations	6	100.0	6	2073
Data after censoring according to second rejection	6	100.0	6	2073
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	2	33.3	2	703
Seasonal vaccination - Control period before first dose	2	33.3	1	179
Seasonal vaccination - Risk period after any dose	2	33.3	0	122
Seasonal vaccination - Control period after any dose	2	33.3	1	402
Seasonal vaccination - Pooled risk periods	2	33.3	0	122
Seasonal vaccination - Pooled control periods	2	33.3	2	581
Day0 to Day30 after transplantation	1	16.7	1	31
> 30 days after transplantation	2	33.3	1	672

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Table 309 Lung transplant rejection from 01-SEP-2006 to 31-AUG-2007 according to the 60-days risk periods of seasonal vaccination and the time since transplantation (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	1	100.0	1	365
Data after censoring according to transplantations	1	100.0	1	125
Data after censoring according to second rejection	1	100.0	1	125
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	1	100.0	1	125
Seasonal vaccination - Control period before first dose	1	100.0	1	125
Seasonal vaccination - Pooled control periods	1	100.0	1	125
Day0 to Day30 after transplantation	1	100.0	1	31
> 30 days after transplantation	1	100.0	0	94

Table 310 Pancreas transplant rejection from 01-SEP-2006 to 31-AUG-2007 according to the 60-days risk periods of seasonal vaccination and the time since transplantation (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	1	100.0	1	365
Data after censoring according to transplantations	1	100.0	1	365
Data after censoring according to second rejection	1	100.0	1	365
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	1	100.0	1	365
Seasonal vaccination - Control period before first dose	1	100.0	0	54
Seasonal vaccination - Risk period after any dose	1	100.0	0	61
Seasonal vaccination - Control period after any dose	1	100.0	1	250
Seasonal vaccination - Pooled risk periods	1	100.0	0	61
Seasonal vaccination - Pooled control periods	1	100.0	1	304
> 30 days after transplantation	1	100.0	1	365

12.3.2.2. Season 2007-2008**Table 311 SOT rejections from 01-SEP-2007 to 31-AUG-2008 according to the 60-days risk periods of seasonal vaccine and the time since transplantation (Subset 2b)**

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	51	100.0	72	18114
Data after censoring according to transplantations	51	100.0	72	16291
Data after censoring according to second rejection	51	100.0	51	14639
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	32	62.7	32	8823
Seasonal vaccination - Control period before first dose	32	62.7	14	3482
Seasonal vaccination - Risk period after any dose	21	41.2	5	1278
Seasonal vaccination - Control period after any dose	20	39.2	13	4063
Seasonal vaccination - Pooled risk periods	21	41.2	5	1278
Seasonal vaccination - Pooled control periods	32	62.7	27	7545
Day0 to Day30 after transplantation	9	17.6	5	271
Day31 to Day90 after transplantation	10	19.6	3	577
Day91 to Day180 after transplantation	10	19.6	2	862
> 180 days after transplantation	28	54.9	22	7113

Table 312 **Relative incidence of SOT rejection within 60 days after seasonal vaccination in season 2007-2008 adjusted for the time since transplantation (Subset 2b)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	1.07	0.38	3.05
Time since transplantation	0-30 vs. >180 days	9.39	1.14	77.04
	31-90 vs. >180 days	2.97	0.46	19.06
	91-180 vs. >180 days	1.24	0.27	5.75

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

Table 313 SOT rejections from 01-SEP-2007 to 31-AUG-2008 according to the 60-days risk periods of seasonal vaccine the time since transplantation and all covariates (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	49	100.0	69	17387
Data after censoring according to transplantations	49	100.0	69	15702
Data after censoring according to second rejection	49	100.0	49	14075
Subjects with at least one exposure of interest (Acute bacterial infection, Cancer, Chronic viral infection, Opportunistic infection, Respiratory infection, Seasonal vaccination, chemo, transplantation)	37	75.5	37	10488
Seasonal vaccination - Control period before first dose	37	75.5	20	5479
Seasonal vaccination - Risk period after any dose	20	40.8	5	1217
Seasonal vaccination - Control period after any dose	19	38.8	12	3792
Seasonal vaccination - Pooled risk periods	20	40.8	5	1217
Seasonal vaccination - Pooled control periods	37	75.5	32	9271
Day0 to Day30 after transplantation	8	16.3	5	240
Day31 to Day90 after transplantation	9	18.4	3	517
Day91 to Day180 after transplantation	9	18.4	1	772
> 180 days after transplantation	33	67.3	28	8959
Day0 to Day30 after Respiratory infection	7	14.3	2	248
> 30 days after Respiratory infection	37	75.5	35	10240
Day0 to Day30 after Opportunistic infection	2	4.1	0	44
> 30 days after Opportunistic infection	37	75.5	37	10444
> 30 days after Acute bacterial infection	37	75.5	37	10488
> 365 days after Chronic viral infection	37	75.5	37	10488
Day0 to Day365 after Cancer	5	10.2	5	1420
> 365 days after Cancer	36	73.5	32	9068

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	Subjects			
	N	%	Rejections	Person*days
Day0 to Day365 after chemo	5	10.2	3	802
> 365 days after chemo	36	73.5	34	9686

Table 314 **Relative incidence of SOT rejection within 60 days after seasonal vaccination in season 2007-2008 adjusted for all covariates (Subset 2b)**

No records exist in this table

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Table 315 SOT rejections from 01-SEP-2007 to 31-AUG-2008 according to the risk periods of seasonal vaccine the time since transplantation and respiratory infections (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	51	100.0	72	18114
Data after censoring according to transplantations	51	100.0	72	16291
Data after censoring according to second rejection	51	100.0	51	14639
Subjects with at least one exposure of interest (Respiratory infection, Seasonal vaccination, transplantation)	35	68.6	35	9901
Seasonal vaccination - Control period before first dose	35	68.6	17	4560
Seasonal vaccination - Risk period after any dose	21	41.2	5	1278
Seasonal vaccination - Control period after any dose	20	39.2	13	4063
Seasonal vaccination - Pooled risk periods	21	41.2	5	1278
Seasonal vaccination - Pooled control periods	35	68.6	30	8623
Day0 to Day30 after transplantation	9	17.6	5	271
Day31 to Day90 after transplantation	10	19.6	3	577
Day91 to Day180 after transplantation	10	19.6	2	862
> 180 days after transplantation	31	60.8	25	8191
Day0 to Day30 after Respiratory infection	8	15.7	3	292
> 30 days after Respiratory infection	35	68.6	32	9609

Table 316 Relative incidence of SOT rejection within 60 days after seasonal vaccination in season 2007-2008 adjusted for the time since transplantation and respiratory infections (Subset 2b)

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	1.03	0.35	3.01
Time since transplantation	0-30 vs. >180 days	10.51	1.13	97.42
	31-90 vs. >180 days	3.39	0.43	26.39
	91-180 vs. >180 days	1.39	0.27	7.19
Respiratory infections	30 days after infection vs. other periods	6.00	1.58	22.77

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

Table 317 SOT rejections from 01-SEP-2007 to 31-AUG-2008 according to the 60-days risk periods of seasonal vaccine the time since transplantation and malignancies/cancers (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	49	100.0	69	17387
Data after censoring according to transplantations	49	100.0	69	15702
Data after censoring according to second rejection	49	100.0	49	14075
Subjects with at least one exposure of interest (Cancer, Seasonal vaccination, transplantation)	32	65.3	32	8991
Seasonal vaccination - Control period before first dose	32	65.3	15	3982
Seasonal vaccination - Risk period after any dose	20	40.8	5	1217
Seasonal vaccination - Control period after any dose	19	38.8	12	3792
Seasonal vaccination - Pooled risk periods	20	40.8	5	1217
Seasonal vaccination - Pooled control periods	32	65.3	27	7774
Day0 to Day30 after transplantation	8	16.3	5	240
Day31 to Day90 after transplantation	9	18.4	3	517
Day91 to Day180 after transplantation	9	18.4	1	772
> 180 days after transplantation	28	57.1	23	7462
Day0 to Day365 after Cancer	5	10.2	5	1420
> 365 days after Cancer	31	63.3	27	7571

Table 318 **Relative incidence of SOT rejection within 60 days after seasonal vaccination in season 2007-2008 adjusted for the time since transplantation and malignancies/cancers (Subset 2b)**

No records exist in this table

Table 319 SOT rejections from 01-SEP-2007 to 31-AUG-2008 according to the risk periods of seasonal vaccine the time since transplantation and chemotherapy (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	49	100.0	69	17387
Data after censoring according to transplantations	49	100.0	69	15702
Data after censoring according to second rejection	49	100.0	49	14075
Subjects with at least one exposure of interest (Chemotherapy, Seasonal vaccination, transplantation)	32	65.3	32	8991
Seasonal vaccination - Control period before first dose	32	65.3	15	3982
Seasonal vaccination - Risk period after any dose	20	40.8	5	1217
Seasonal vaccination - Control period after any dose	19	38.8	12	3792
Seasonal vaccination - Pooled risk periods	20	40.8	5	1217
Seasonal vaccination - Pooled control periods	32	65.3	27	7774
Day0 to Day30 after transplantation	8	16.3	5	240
Day31 to Day90 after transplantation	9	18.4	3	517
Day91 to Day180 after transplantation	9	18.4	1	772
> 180 days after transplantation	28	57.1	23	7462
Day0 to Day365 after Chemotherapy	5	10.2	3	802
> 365 days after Chemotherapy	31	63.3	29	8189

Table 320 **Relative incidence of SOT rejection within 60 days after seasonal vaccination in season 2007-2008 adjusted for the time since transplantation and chemotherapy (Subset 2b)**

No records exist in this table

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Table 321 SOT rejections from 01-SEP-2007 to 31-AUG-2008 according to the 60-days risk periods of seasonal vaccine and the time since transplantation – with subsequent rejections (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	51	100.0	72	18114
Data after censoring according to transplantations	51	100.0	72	16291
Subjects with at least one exposure of interest (seasonal vaccine, transplantation)	33	64.7	48	9853
seasonal vaccine - Control period before first dose	33	64.7	19	3614
seasonal vaccine - Risk period after any dose	22	43.1	7	1342
seasonal vaccine - Control period after any dose	22	43.1	22	4897
seasonal vaccine - Pooled risk periods	22	43.1	7	1342
seasonal vaccine - Pooled control periods	33	64.7	41	8511
Day0 to Day30 after transplantation	9	17.6	5	271
Day31 to Day90 after transplantation	10	19.6	3	577
Day91 to Day180 after transplantation	10	19.6	3	865
> 180 days after transplantation	29	56.9	37	8140

Table 322 **Relative incidence of SOT rejection within 60 days after seasonal vaccination in season 2007-2008 adjusted for the time since transplantation - not accounting for perturbed post-event exposure (Subset 2b)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	1.03	0.43	2.44
Time since transplantation	0-30 vs. >180 days	2.27	0.39	13.13
	31-90 vs. >180 days	0.84	0.14	4.83
	91-180 vs. >180 days	0.61	0.11	3.31

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

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Table 323 Heart transplant rejection from 01-SEP-2007 to 31-AUG-2008 according to the 60-days risk periods of seasonal vaccine and the time since transplantation (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	1	100.0	1	366
Data after censoring according to transplantations	1	100.0	1	366
Data after censoring according to second rejection	1	100.0	1	366
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	1	100.0	1	366
Seasonal vaccination - Control period before first dose	1	100.0	1	366
Seasonal vaccination - Pooled control periods	1	100.0	1	366
Day31 to Day90 after transplantation	1	100.0	0	56
Day91 to Day180 after transplantation	1	100.0	0	90
> 180 days after transplantation	1	100.0	1	220

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Table 324 Kidney transplant rejection from 01-SEP-2007 to 31-AUG-2008 according to the 60-days risk periods of seasonal vaccine and the time since transplantation (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	34	100.0	53	11917
Data after censoring according to transplantations	34	100.0	53	10302
Data after censoring according to second rejection	34	100.0	34	8941
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	23	67.6	23	5787
Seasonal vaccination - Control period before first dose	23	67.6	11	2353
Seasonal vaccination - Risk period after any dose	15	44.1	3	912
Seasonal vaccination - Control period after any dose	14	41.2	9	2522
Seasonal vaccination - Pooled risk periods	15	44.1	3	912
Seasonal vaccination - Pooled control periods	23	67.6	20	4875
Day0 to Day30 after transplantation	7	20.6	4	209
Day31 to Day90 after transplantation	7	20.6	3	401
Day91 to Day180 after transplantation	7	20.6	1	592
> 180 days after transplantation	19	55.9	15	4585

Table 325 **Relative incidence of kidney transplant rejection within 60 days after seasonal vaccination in season 2007-2008 adjusted for the time since transplantation (Subset 2b)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	0.72	0.21	2.50
Time since transplantation	0-30 vs. >180 days	21.23	1.38	326.24
	31-90 vs. >180 days	9.36	0.94	92.69
	91-180 vs. >180 days	1.56	0.24	10.31

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

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Table 326 Kidney transplant rejection from 01-SEP-2007 to 31-AUG-2008 according to the 60-days risk periods of seasonal vaccine the time since transplantation and all covariates (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	33	100.0	52	11551
Data after censoring according to transplantations	33	100.0	52	9936
Data after censoring according to second rejection	33	100.0	33	8575
Subjects with at least one exposure of interest (Acute bacterial infection, Cancer, Chronic viral infection, Opportunistic infection, Respiratory infection, Seasonal vaccination, chemo, transplantation)	27	81.8	27	6918
Seasonal vaccination - Control period before first dose	27	81.8	16	3816
Seasonal vaccination - Risk period after any dose	14	42.4	3	434
Seasonal vaccination - Control period after any dose	14	42.4	8	2668
Seasonal vaccination - Pooled risk periods	14	42.4	3	434
Seasonal vaccination - Pooled control periods	27	81.8	24	6484
Day0 to Day30 after transplantation	7	21.2	4	209
Day31 to Day90 after transplantation	7	21.2	3	401
Day91 to Day180 after transplantation	7	21.2	1	592
> 180 days after transplantation	23	69.7	19	5716
Day0 to Day30 after Respiratory infection	5	15.2	1	186
> 30 days after Respiratory infection	27	81.8	26	6732
Day0 to Day30 after Opportunistic infection	2	6.1	0	44
> 30 days after Opportunistic infection	27	81.8	27	6874
> 30 days after Acute bacterial infection	27	81.8	27	6918
> 365 days after Chronic viral infection	27	81.8	27	6918
Day0 to Day365 after Cancer	2	6.1	2	568
> 365 days after Cancer	26	78.8	25	6350

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	Subjects			
	N	%	Rejections	Person*days
Day0 to Day365 after chemo	3	9.1	2	423
> 365 days after chemo	27	81.8	25	6495

Table 327 Kidney transplant rejection from 01-SEP-2007 to 31-AUG-2008 according to the risk periods of seasonal vaccine the time since transplantation and respiratory infections (Subset 2b)

	Subjects			
	N	%	Rejections	Person*days
Subset 2b	34	100.0	53	11917
Data after censoring according to transplantations	34	100.0	53	10302
Data after censoring according to second rejection	34	100.0	34	8941
Subjects with at least one exposure of interest (Respiratory infection, Seasonal vaccination, transplantation)	25	73.5	25	6499
Seasonal vaccination - Control period before first dose	25	73.5	13	3065
Seasonal vaccination - Risk period after any dose	15	44.1	3	912
Seasonal vaccination - Control period after any dose	14	41.2	9	2522
Seasonal vaccination - Pooled risk periods	15	44.1	3	912
Seasonal vaccination - Pooled control periods	25	73.5	22	5587
Day0 to Day30 after transplantation	7	20.6	4	209
Day31 to Day90 after transplantation	7	20.6	3	401
Day91 to Day180 after transplantation	7	20.6	1	592
> 180 days after transplantation	21	61.8	17	5297
Day0 to Day30 after Respiratory infection	6	17.6	2	230
> 30 days after Respiratory infection	25	73.5	23	6269

Table 328 **Relative incidence of kidney transplant rejection within 60 days after seasonal vaccination in season 2007-2008 adjusted for the time since transplantation and respiratory infections (Subset 2b)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	0.62	0.20	1.97
Time since transplantation	0-30 vs. >180 days	27.63	1.46	523.69
	31-90 vs. >180 days	12.44	0.97	159.95
	91-180 vs. >180 days	1.92	0.25	14.91
Respiratory infections	30 days after infection vs. other periods	7.49	1.63	34.44

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

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Table 329 Kidney transplant rejections from 01-SEP-2007 to 31-AUG-2008 according to the 60-days risk periods of seasonal vaccine and the time since transplantation – with subsequent rejections (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	34	100.0	53	11917
Data after censoring according to transplantations	34	100.0	53	10302
Subjects with at least one exposure of interest (seasonal vaccine, transplantation)	24	70.6	38	6792
seasonal vaccine - Control period before first dose	24	70.6	15	2460
seasonal vaccine - Risk period after any dose	16	47.1	5	976
seasonal vaccine - Control period after any dose	16	47.1	18	3356
seasonal vaccine - Pooled risk periods	16	47.1	5	976
seasonal vaccine - Pooled control periods	24	70.6	33	5816
Day0 to Day30 after transplantation	7	20.6	4	209
Day31 to Day90 after transplantation	7	20.6	3	401
Day91 to Day180 after transplantation	7	20.6	2	595
> 180 days after transplantation	20	58.8	29	5587

Table 330 **Relative incidence of kidney transplant rejection within 60 days after seasonal vaccination in season 2007-2008 adjusted for the time since transplantation - not accounting for perturbed post-event exposure (Subset 2b)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	0.81	0.29	2.21
Time since transplantation	0-30 vs. >180 days	3.80	0.35	41.67
	31-90 vs. >180 days	1.90	0.19	18.81
	91-180 vs. >180 days	0.91	0.09	9.06

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Table 331 Liver transplant rejection from 01-SEP-2007 to 31-AUG-2008 according to the 60-days risk periods of seasonal vaccine and the time since transplantation (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	4	100.0	5	1459
Data after censoring according to transplantations	4	100.0	5	1251
Data after censoring according to second rejection	4	100.0	4	1226
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	2	50.0	2	494
Seasonal vaccination - Control period before first dose	2	50.0	2	494
Seasonal vaccination - Pooled control periods	2	50.0	2	494
Day0 to Day30 after transplantation	2	50.0	1	62
Day31 to Day90 after transplantation	2	50.0	0	120
Day91 to Day180 after transplantation	2	50.0	1	180
> 180 days after transplantation	2	50.0	0	132

Table 332 Lung transplant rejection from 01-SEP-2007 to 31-AUG-2008 according to the 60-days risk periods of seasonal vaccine and the time since transplantation (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	0			
Data after censoring according to transplantations	0			
Data after censoring according to second rejection	0			
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	0			

Table 333 Pancreas transplant rejection from 01-SEP-2007 to 31-AUG-2008 according to the 60-days risk periods of seasonal vaccine and the time since transplantation (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	1	100.0	1	366
Data after censoring according to transplantations	1	100.0	1	366
Data after censoring according to second rejection	1	100.0	1	366
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	0	0.0		

12.3.2.3. Season 2008-2009**Table 334 SOT rejections from 01-SEP-2008 to 31-AUG-2009 according to the 60-days risk periods of seasonal vaccination and the time since transplantation (Subset 2b)**

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	58	100.0	73	20171
Data after censoring according to transplantations	58	100.0	70	17923
Data after censoring according to second rejection	58	100.0	58	16576
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	32	55.2	32	8280
Seasonal vaccination - Control period before first dose	32	55.2	13	2842
Seasonal vaccination - Risk period after any dose	23	39.7	6	1276
Seasonal vaccination - Control period after any dose	20	34.5	13	4162
Seasonal vaccination - Pooled risk periods	23	39.7	6	1276
Seasonal vaccination - Pooled control periods	32	55.2	26	7004
Day0 to Day30 after transplantation	10	17.2	5	283
Day31 to Day90 after transplantation	9	15.5	4	449
> 90 days after transplantation	28	48.3	23	7548

Table 335 **Relative incidence of SOT rejection within 60 days after seasonal vaccination in season 2008-2009 adjusted for the time since transplantation (Subset 2b)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	1.18	0.40	3.47
Time since transplantation	0-30 vs. >90 days	9.30	0.85	101.53
	31-90 vs. >90 days	6.65	0.55	81.16

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

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Table 336 SOT rejections from 01-SEP-2008 to 31-AUG-2009 according to the 60-days risk periods of seasonal vaccination, the time since transplantation and all covariates (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	57	100.0	72	19806
Data after censoring according to transplantations	57	100.0	69	17558
Data after censoring according to second rejection	57	100.0	57	16211
Subjects with at least one exposure of interest (Acute bacterial infection, Cancer, Chronic viral infection, Opportunistic infection, Respiratory infection, Seasonal vaccination, chemo, transplantation)	34	59.6	34	8794
Seasonal vaccination - Control period before first dose	34	59.6	15	3356
Seasonal vaccination - Risk period after any dose	23	40.4	6	1276
Seasonal vaccination - Control period after any dose	20	35.1	13	4162
Seasonal vaccination - Pooled risk periods	23	40.4	6	1276
Seasonal vaccination - Pooled control periods	34	59.6	28	7518
Day0 to Day30 after transplantation	10	17.5	5	283
Day31 to Day90 after transplantation	9	15.8	4	449
> 90 days after transplantation	30	52.6	25	8062
Day0 to Day30 after Respiratory infection	2	3.5	0	62
> 30 days after Respiratory infection	34	59.6	34	8732
Day0 to Day30 after Opportunistic infection	3	5.3	1	93
> 30 days after Opportunistic infection	34	59.6	33	8701
> 30 days after Acute bacterial infection	34	59.6	34	8794
> 365 days after Chronic viral infection	34	59.6	34	8794
Day0 to Day365 after Cancer	3	5.3	2	460
> 365 days after Cancer	33	57.9	32	8334
Day0 to Day365 after chemo	3	5.3	2	685

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	Subjects			
	N	%	Rejections	Person*days
> 365 days after chemo	32	56.1	32	8109

Table 337 SOT rejections from 01-SEP-2008 to 31-AUG-2009 according to the 60-days risk periods of seasonal vaccination and the time since transplantation – with subsequent rejections (Subset 2b)

	Subjects			
	N	%	Rejections	Person*days
Subset 2b	58	100.0	73	20171
Data after censoring according to transplantations	58	100.0	70	17923
Subjects with at least one exposure of interest (seasonal vaccination, transplantation)	32	55.2	42	9457
seasonal vaccination - Control period before first dose	32	55.2	15	3111
seasonal vaccination - Risk period after any dose	23	39.7	7	1330
seasonal vaccination - Control period after any dose	21	36.2	20	5016
seasonal vaccination - Pooled risk periods	23	39.7	7	1330
seasonal vaccination - Pooled control periods	32	55.2	35	8127
Day0 to Day30 after transplantation	10	17.2	5	283
Day31 to Day90 after transplantation	9	15.5	5	463
> 90 days after transplantation	29	50.0	32	8711

Table 338 **Relative incidence of SOT rejection within 60 days after seasonal vaccination in season 2008-2009 adjusted for the time since transplantation - not accounting for perturbed post-event exposure (Subset 2b)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	1.21	0.51	2.89
Time since transplantation	0-30 vs. >90 days	6.58	1.08	40.24
	31-90 vs. >90 days	5.57	1.04	29.87

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

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Table 339 Heart transplant rejection from 01-SEP-2008 to 31-AUG-2009 according to the 60-days risk periods of seasonal vaccination and the time since transplantation (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	3	100.0	3	1095
Data after censoring according to transplantations	3	100.0	3	1095
Data after censoring according to second rejection	3	100.0	3	1095
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	2	66.7	2	730
Seasonal vaccination - Control period before first dose	2	66.7	0	136
Seasonal vaccination - Risk period after any dose	2	66.7	1	122
Seasonal vaccination - Control period after any dose	2	66.7	1	472
Seasonal vaccination - Pooled risk periods	2	66.7	1	122
Seasonal vaccination - Pooled control periods	2	66.7	1	608
> 90 days after transplantation	2	66.7	2	730

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Table 340 Kidney transplant rejection from 01-SEP-2008 to 31-AUG-2009 according to the 60-days risk periods of seasonal vaccination and the time since transplantation (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	33	100.0	46	11613
Data after censoring according to transplantations	33	100.0	45	10094
Data after censoring according to second rejection	33	100.0	33	8892
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	22	66.7	22	5277
Seasonal vaccination - Control period before first dose	22	66.7	11	2086
Seasonal vaccination - Risk period after any dose	14	42.4	3	764
Seasonal vaccination - Control period after any dose	12	36.4	8	2427
Seasonal vaccination - Pooled risk periods	14	42.4	3	764
Seasonal vaccination - Pooled control periods	22	66.7	19	4513
Day0 to Day30 after transplantation	8	24.2	3	221
Day31 to Day90 after transplantation	7	21.2	4	383
> 90 days after transplantation	19	57.6	15	4673

Table 341 **Relative incidence of kidney transplant rejection within 60 days after seasonal vaccination in season 2008-2009 adjusted for the time since transplantation (Subset 2b)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	0.82	0.16	4.26
Time since transplantation	0-30 vs. >90 days	5.01	0.45	55.63
	31-90 vs. >90 days	5.90	0.44	79.94

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Asymptotic sandwich estimator of covariance matrix

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Table 342 Kidney transplant rejection from 01-SEP-2008 to 31-AUG-2009 according to the 60-days risk periods of seasonal vaccination, the time since transplantation and all covariates (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	33	100.0	46	11613
Data after censoring according to transplantations	33	100.0	45	10094
Data after censoring according to second rejection	33	100.0	33	8892
Subjects with at least one exposure of interest (Acute bacterial infection, Cancer, Chronic viral infection, Opportunistic infection, Respiratory infection, Seasonal vaccination, chemo, transplantation)	23	69.7	23	5642
Seasonal vaccination - Control period before first dose	23	69.7	12	2451
Seasonal vaccination - Risk period after any dose	14	42.4	3	404
Seasonal vaccination - Control period after any dose	12	36.4	8	2787
Seasonal vaccination - Pooled risk periods	14	42.4	3	404
Seasonal vaccination - Pooled control periods	23	69.7	20	5238
Day0 to Day30 after transplantation	8	24.2	3	221
Day31 to Day90 after transplantation	7	21.2	4	383
> 90 days after transplantation	20	60.6	16	5038
Day0 to Day30 after Respiratory infection	1	3.0	0	31
> 30 days after Respiratory infection	23	69.7	23	5611
Day0 to Day30 after Opportunistic infection	2	6.1	1	62
> 30 days after Opportunistic infection	23	69.7	22	5580
> 30 days after Acute bacterial infection	23	69.7	23	5642
> 365 days after Chronic viral infection	23	69.7	23	5642
Day0 to Day365 after Cancer	1	3.0	0	42
> 365 days after Cancer	23	69.7	23	5600
Day0 to Day365 after chemo	1	3.0	1	60

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	Subjects			
	N	%	Rejections	Person*days
> 365 days after chemo	22	66.7	22	5582

Table 343 Kidney transplant rejections from 01-SEP-2008 to 31-AUG-2009 according to the 60-days risk periods of seasonal vaccination and the time since transplantation – with subsequent rejections (Subset 2b)

	Subjects			
	N	%	Rejections	Person*days
Subset 2b	33	100.0	46	11613
Data after censoring according to transplantations	33	100.0	45	10094
Subjects with at least one exposure of interest (seasonal vaccination, transplantation)	22	66.7	31	6222
seasonal vaccination - Control period before first dose	22	66.7	13	2355
seasonal vaccination - Risk period after any dose	14	42.4	4	818
seasonal vaccination - Control period after any dose	13	39.4	14	3049
seasonal vaccination - Pooled risk periods	14	42.4	4	818
seasonal vaccination - Pooled control periods	22	66.7	27	5404
Day0 to Day30 after transplantation	8	24.2	3	221
Day31 to Day90 after transplantation	7	21.2	5	397
> 90 days after transplantation	20	60.6	23	5604

Table 344 **Relative incidence of kidney transplant rejection within 60 days after seasonal vaccination in season 2008-2009 adjusted for the time since transplantation - not accounting for perturbed post-event exposure (Subset 2b)**

Variable	Compared periods	Relative Incidence	95% CI	
			LL	UL
Seasonal influenza vaccination	60 days after any dose vs. other periods	1.03	0.34	3.09
Time since transplantation	0-30 vs. >90 days	3.90	0.51	29.53
	31-90 vs. >90 days	5.42	1.00	29.43

95% CI = 95% Wald confidence interval

LL =lower limit

UL =upper limit

Table 345 **Liver transplant rejection from 01-SEP-2008 to 31-AUG-2009 according to the 60-days risk periods of seasonal vaccination and the time since transplantation (Subset 2b)**

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	4	100.0	4	1109
Data after censoring according to transplantations	4	100.0	4	944
Data after censoring according to second rejection	4	100.0	4	944
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	2	50.0	2	643
Seasonal vaccination - Control period before first dose	2	50.0	1	325
Seasonal vaccination - Risk period after any dose	1	25.0	0	61
Seasonal vaccination - Control period after any dose	1	25.0	1	257
Seasonal vaccination - Pooled risk periods	1	25.0	0	61
Seasonal vaccination - Pooled control periods	2	50.0	2	582
Day0 to Day30 after transplantation	1	25.0	1	31
Day31 to Day90 after transplantation	1	25.0	0	60
> 90 days after transplantation	2	50.0	1	552

Table 346 Lung transplant rejection from 01-SEP-2008 to 31-AUG-2009 according to the 60-days risk periods of seasonal vaccination and the time since transplantation (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	1	100.0	1	365
Data after censoring according to transplantations	1	100.0	1	365
Data after censoring according to second rejection	1	100.0	1	365
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	0	0.0		

Table 347 Pancreas transplant rejection from 01-SEP-2008 to 31-AUG-2009 according to the 60-days risk periods of seasonal vaccination and the time since transplantation (Subset 2b)

	Subjects		Rejections	Person*days
	N	%		
Subset 2b	2	100.0	2	730
Data after censoring according to transplantations	2	100.0	2	303
Data after censoring according to second rejection	2	100.0	2	303
Subjects with at least one exposure of interest (Seasonal vaccination, transplantation)	2	100.0	2	303
Seasonal vaccination - Control period before first dose	2	100.0	2	279
Seasonal vaccination - Risk period after any dose	1	50.0	0	24
Seasonal vaccination - Pooled risk periods	1	50.0	0	24
Seasonal vaccination - Pooled control periods	2	100.0	2	279
Day0 to Day30 after transplantation	1	50.0	0	31
Day31 to Day90 after transplantation	1	50.0	0	60
> 90 days after transplantation	2	100.0	2	212

Annex 1 List of stand-alone documents

Number	Document reference number	Date	Title
1.	116602	17-MAR-2014	Annex 1: List of stand-alone documents
2.	116602	17-MAR-2014	Annex 2: Glossary of Terms
3.	116602	17-MAR-2014	Annex 3: Trademarks
4.	116602	17-MAR-2014	Annex 4: Changes in the conduct of the study
5.	116602	17-MAR-2014	Annex 5: Report sign-off

Annex 2 Glossary of Terms

eTrack:	GSK's tracking tool for clinical/epidemiology trials.
Non-interventional (observational) Human Subject Research:	Studies where medicinal products, should they be administered, are prescribed in normal (routine) medical practice. No medical care or medical/scientific procedures as required in a research protocol are administered to participants except as part of routine medical care.
Post-Authorisation Safety Study (PASS):	<p>A pharmaco-epidemiological study or a clinical trial carried out in accordance with the terms of the marketing authorisation, conducted with the aim of identifying or quantifying a safety hazard relating to an authorised medicinal product. This includes all GSK sponsored non-interventional studies and clinical trials conducted anywhere in the world that are in accordance with the terms of the European marketing authorisation and where the investigation of safety is the specific stated objective.</p> <p>Note: The phrase, 'In accordance with the terms of the European marketing authorisation' means that the product is used according to the European label (e.g. within the recommended dose range, the approved formulation, indication etc.).</p>
Self-controlled case-series	Method developed to investigate associations between acute outcomes and transient exposures such as vaccination, using only data on cases, that is, on individuals who have experienced the outcome of interest. Inference is within individuals, and hence fixed covariates effects are implicitly controlled for within a proportional incidence framework.

Annex 3 Trademarks

Trademarks of the GlaxoSmithKline group of companies	Generic description
Pandemrix®	GSK Biologicals' licensed AS03-adjuvanted H1N1 pandemic influenza vaccine
Arepanrix™	GSK Biologicals' licensed AS03-adjuvanted H1N1 pandemic influenza vaccine
Trademarks not owned by the GlaxoSmithKline group of companies	Generic description
Celvapan® (Baxter)	Baxter's licensed influenza vaccine (H1N1): whole virion, inactivated, prepared in cell culture

Annex 4 Changes in the conduct of the study

Please refer to Section 10.9.5 of the main study report [EPI-FLU H1N1-012, 2013].

Annex 5 Report sign-off

Please refer to the modular appendices to the annex study report.

List of Independent Ethics Committees /Institutional Review Boards

The study protocol, the protocol amendment, and other information that required pre-approval were reviewed and approved by the Independent Scientific Advisory Committee (ISAC) of the Clinical Practice Research Datalink General Practitioner OnLine Database (CPRD GOLD).

CONFIDENTIAL

116602 (EPI-FLU H1N1-012 VS UK DB)
Annex Report Final

**Signatures of principal or coordinating investigator(s) or
sponsor's responsible medical officer**

**GlaxoSmithKline Biologicals
Vaccine Value and Health Science
Sponsor Signatory Approval Page**

Please note that by signing this page, you take responsibility for the content of the
Annex Study Report, including appendices

STUDY TITLE: Risk of solid organ transplant rejection following vaccination with
Pandemrix™ in the United Kingdom

Study: 116602 (EPI-FLU H1N1-012 VS UK DB) Development Phase: N/A

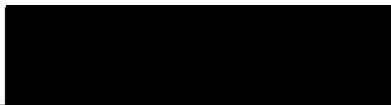
*I have read this report and confirm that to the best of my knowledge it accurately
describes the conduct and results of the study.*

Name of Sponsor Signatory:



Title of Sponsor Signatory:

Director, Lead Epidemiologist,
GSK Biologicals



Signature:

Date:

26 March 2014

For internal use only

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