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ORIGINAL REPORT

Increased availability of paracetamol in Sweden and incidence of paracetamol poisoning: using laboratory data to increase validity of a population-based registry study

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ABSTRACT

Purpose To estimate the incidence trend and outcome of paracetamol poisoning, in relation to increased availability of paracetamol from non-pharmacy outlets in 2009.

Method Patients' serum paracetamol results over 14 years (2000–2013) from 20 (out of 21) regions in Sweden were linked to national registers of hospital care, cause of death, and prescriptions. Paracetamol poisonings were defined by serum paracetamol levels, hospital diagnoses, or cause of death. The change in incidence of poisonings following increased availability of paracetamol was analysed by using segmental regression of time series.

Results Of the 12 068 paracetamol poisonings, 85% were classified as intentional self-harm. Following increased availability from non-pharmacy outlets, there was a 40.5% increase in the incidence of paracetamol poisoning, from 11.5/100 000 in 2009 to 16.2/100 000 in 2013. Regression analyses indicated a change in the trend ($p < 0.0001$) but not an immediate jump in the incidence ($p = 0.5991$) following the increased availability. Adjusting for trends in hospital episodes for self-harm, suicides, and the sales volume of paracetamol did not influence the result. All-cause mortality at 30 days (3.2%) did not change over time.

Conclusions The incidence of paracetamol poisoning in Sweden has increased since 2009, contrasting the decreased incidence in the period of 2007–2009. The change in trend was temporally associated with the introduction of availability of paracetamol from non-pharmacy outlets but did not appear to be related to sales volume of paracetamol or general trends in self-harm or suicides. © 2017 Commonwealth of Australia. Pharmacoepidemiology and Drug Safety © 2017 John Wiley & Sons, Ltd.

KEY WORDS—paracetamol; acetaminophen; poisoning; interrupted time series analysis; pharmacoepidaemiology

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INTRODUCTION

Overdoses of paracetamol can cause life-threatening hepatic injury. For intentional poisonings, impulsivity[1,2] and ease of access are considered risk factors.[3–6] The decision in Sweden to allow over-the-counter (OTC) sales of paracetamol also in non-pharmacy outlets (hereafter also referred to as the intervention) in November 2009 was part of a policy change that introduced availability of OTC medicines from non-pharmacy outlets. This was preceded, in May 2009, by a restriction of the maximum OTC pack size for paracetamol to 20 tablets (500 mg). There is no restriction on the number of packs in a single purchase. The Swedish Poisons Information Centre (PC) has described a steady and rapid increase in the number of paracetamol exposure calls following this increased availability of paracetamol.[7] Reliable

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Prior postings and presentations: Preliminary data have been presented by the Medical Products Agency as a government agency at national level to support regulatory action regarding availability of paracetamol.

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estimates of change in incidence over time, related to changes in availability of paracetamol, could support regulatory action aiming to limit the problem with impulse-driven intentional poisonings.

The aim of this study was to identify cases of paracetamol poisoning by using blood levels of paracetamol in combination with hospital discharge diagnoses and cause of death data. The incidence trend and outcome of paracetamol poisoning were studied, focusing on the association between increased availability of paracetamol and incidence of poisoning.

METHODS

Study design and study population

The study design aimed to define a population-based cohort of patients admitted to hospital for paracetamol poisoning. Potential cohort members were identified from hospital discharge diagnoses and cause of death in national health-care databases, as well as laboratory results on serum paracetamol. All 21 regions in Sweden were asked to provide serum paracetamol results from 1 January 2000 to 31 December 2013. Each individual region contributed to the source population from the first year it could deliver laboratory data covering the whole year. The resulting source population covered >94% of the Swedish population from 2007 onwards (Figure S1).

Case definition

All data were linked by using unique person identification number.[8] No international consensus definition of paracetamol poisoning is available. The predefined main case definition was a serum paracetamol level >700 μmol/L, a specific hospital discharge or cause of death diagnosis (as defined in the succeeding texts), or paracetamol >350 μmol/L in combination with alcohol abuse, liver disease, or enzyme-inducing drugs (as defined in the succeeding texts). Additional prespecified case definitions, based exclusively on serum paracetamol level (>350, >700, or >1000 μmol/L), were used in sensitivity analyses. An additional analysis to identify severe poisonings presenting late with low serum paracetamol levels was made by using serum paracetamol >350 μmol/L combined with a somatic length of stay >2 days.

The PC covers the entire Swedish population and provided monthly counts of exposure-related calls concerning paracetamol, including combination products, from health-care professionals.[9] Calling the PC is voluntary.

Laboratory data on serum paracetamol

Serum paracetamol levels above the local reporting level, unique personal identification numbers, and time and date for each test were extracted from laboratory databases. Screening for paracetamol is routinely performed on patients presenting with suspected poisoning without any specific clinical suspicion of paracetamol overdose. Test results <200 μmol/L were not reported from all participating laboratories and were therefore not considered in any of the case definitions. When repeated serum levels were available, the maximum value was used in the analysis.

Hospital care and specialist out-patient visits

Data from the national patient registry (PAR)[10] on in-patient care and specialist out-patient visits were extracted for (i) all individuals with laboratory data, (ii) all individuals with a specific diagnosis of paracetamol poisoning (International Classification of Diseases 10th Edition (ICD-10) code T39.1 or T50.9 with Anatomical Therapeutic Chemical (ATC) code M03BC51, N02AA59, N02BE01, or N02BE51), and (iii) all deaths with a specific underlying or contributing cause of death that indicated paracetamol poisoning (ICD-10 code T39.1). Intentionality was defined from ICD-10 cause of injury codes.[11,12]

Outcomes

Follow-up mortality data were available from the national cause of death register.[13] All-cause mortality was estimated at 30 days but also as time to death with follow-up until 30 September 2014. Cause-specific mortality was defined by ICD-10 code T39.1 as an underlying or contributing cause of death. Adverse effects on the liver were captured by hospital discharge diagnoses (ICD-10 diagnoses K71.1, K71.2, K71.6, K71.9, K72.0, K72.9, K76.7, R17, D68.4, D68.9, or J8024) or liver transplantation (procedure codes JJC00, JJC10, JJC20, JJC30, or JJC40) during the first 30 days. The total number of days alive out of hospital during the first 30 days after the poisoning was calculated, excluding stays with ICD-10 main diagnoses F00-F99 indicating mental and behavioural disorders.

Covariates

Risk factors for increased sensitivity to a paracetamol overdose are mentioned in the PC treatment guidelines. A history of alcohol abuse (ICD-9 codes 291, 303, or 980 or ICD-10 codes F10, T51, or X65) or pre-existing liver disease (ICD-9 codes 570–573 or 456A–456C or ICD-10 codes K70–K76 or I850,

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I859, I864, or I982) was captured from PAR during the preceding 5-year period. Prescriptions of phenytoin (ATC-code N03AB), rifampicin (J04AB02, J04AM02, J04AM05, and J04AM06), barbiturates (N05CA and N05CB), benzodiazepines (N05BA, N05CD, and N05CF), and carbamazepine (N03AF01) during the preceding 6-month period were extracted from the national prescription register. Prescriptions of any paracetamol (M03BC51, N02AA59, N02BE01, or N02BE51) were recorded from the preceding 7-day, 30-day, and 1-year periods. Data on prescribed medications are limited to cases from 2007 to 2013.

The monthly counts of hospital episodes for any self-harm and suicides (defined from ICD-10 cause of injury codes X60-X84) were used to indicate the overall trends of such events.[14] Average monthly total sales volumes of paracetamol were calculated from annual sales data from the Swedish eHealth Agency.

Statistical methods

Incidence estimates are presented per 100 000 population. Regional population counts were provided by Statistics Sweden.[15] Approximate 95% confidence intervals were calculated for main incidence proportions. Person-time accumulated from the index date until the date of death or censoring on 30 September 2014.

Time series analyses were performed based on monthly or quarterly number of cases per 100 000 population. Locally weighted polynomial regression (Locally Weighted Scatterplot Smoothing) generated smoothed trends of time series.[16] Cross-correlation between different time series was calculated.[17] The impact of an intervention was assessed with segmental regression analysis.[18,19] Linear trends before and after intervention were adjusted for seasonal variation and trends of covariate time series.

$$y_{\mathrm{t}} = \beta_1 t + \beta_2 I_t + \beta_3 t_I + \sum_{i=4}^{15} \beta_{\mathrm{i}} Month_{(\mathrm{i}-3)\mathrm{t}} + \sum_{j=16}^{15+N} \beta_{\mathrm{j}} Covariate_{\mathrm{nt}} + \varepsilon_{\mathrm{t.}}$$

where y_t = monthly count of poisonings per 100 000 population, t = time (months) after start of first segment, I = intervention indicator (0 before intervention and 1 after intervention), t_I = time (months) after intervention (0 before intervention), $Month_{(i-3)t}$ = indicator variable, one for each month ($Month_{1t}$ for January, … $Month_{12t}$ for December), $Covariate_{nt}$ = trend for covariate n in month t, N = total number of covariates, and ε_t = error term. The p-value for β_2 evaluates an immediate change (jump) in incidence level after the intervention, while the p-value for β_3 evaluates a change in the trend (slope). The start of a linear segment before the intervention was set based on visual inspection of the trend and varied in sensitivity analyses. The covariate trends were modelled as linear effects. The trend in suicide rate was distinctly nonlinear and therefore represented by three parameters. The model was primarily fitted by using ordinary least squares, assuming independent error terms. Linear, not Poisson regression, was chosen in order to model incidence rates instead of simple counts.[18] This takes account of the increasing population at risk over time. From the Durbin Watsons test,[20,21] there was no evidence of first-order auto-correlation, and visual inspection of residual plots of the auto-correlation function did not suggest any substantial higher-order auto-correlation.

In a complementary analysis, an optimal autoregressive integrated moving average (ARIMA) model was adapted to the period before the intervention. An automated procedure (auto.arima, R package forecast) was used to select the best fitting model by optimising Akaike's information criterion with a correction for finite sample sizes (AIC_c). This model was used to predict the trend (with 80% and 95% prediction intervals) after intervention.

Data management was done in SAS version 9.4, and all statistical analyses were performed by using R version 3.1.2.

RESULTS

Patient and poisoning event characteristics

In 13 320 individuals, there were 16 859 potential paracetamol poisoning events, and 12 068 of these fulfilled the primary case definition (Figure 1). A paracetamol serum level >1000 μmol/L was seen in 24.6% (2966/12 068), and >700 μmol/L was seen in 41.4% (5001/12 068). Of cases hospitalised not only for psychiatric reasons (i.e. cases not discharged on the admission date), 59.7% had a serum paracetamol level >700 μmol/L.

The median age was 28 years, and 77% (9096/11 857) were female (Table 1). Eighty-five per cent (8841/10 455) were intentional self-harm. Sixteen per cent of these were prescribed paracetamol in the 30-day period preceding the event, compared with 28% of unintentional self-harm. Forty-six per cent of unintentional and 36% of intentional self-harm poisonings had been prescribed paracetamol the preceding year. A previous alcohol-related diagnosis was present in approximately 20% of cases (Table S1). A previous

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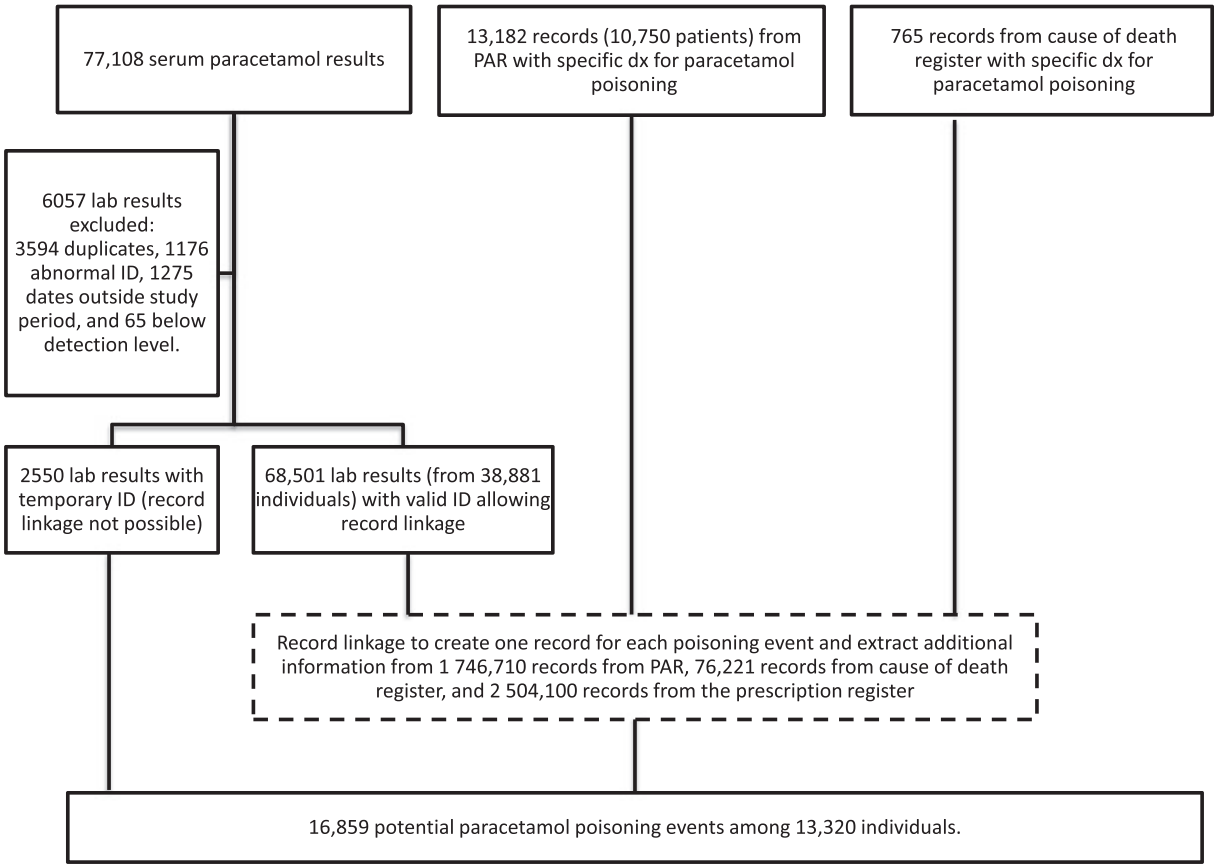

Figure 1. Flow chart describing the compilation of the study population from laboratory data, the national patient register, and national cause of death register. The lab results with abnormal IDs removed represent IDs repeatedly used for routine calibration analyses. A large proportion of the lab results collected had levels <200 μmol/L and were consequently not used to define the study population

hepatic diagnosis or prescription of other enzyme-inducing drugs that could increase sensitivity to paracetamol was uncommon.

Incidence of paracetamol poisoning

The incidence of paracetamol poisoning increased by 103% from the year 2000 to 16.2 cases per 100 000 population in 2013 (Figure 2). Cases with serum paracetamol >700 μmol/L increased slightly over the study period (Figure S2). Using lower threshold levels of serum paracetamol to identify cases, the trend more closely resembles the trend of the primary case definition. There was no appreciable increase in the number of cases with serum paracetamol >1000 μmol/L. The incidence of cases with serum paracetamol >350 μmol/L and a hospital stay of >2 days with a non-psychiatric main diagnosis remained stable over the study period (data not shown).

Major fluctuations in the trend of incidence over time were predominantly observed in intentional self-harm cases (Figure S3). The trend in children younger than 15 years remained stable over time (data not shown).

The incidence trend based on hospital discharge diagnoses and deaths was highly correlated with the primary case definition (r = 0.94; Figure 2). The trend for PC exposure calls correlated less well with the primary case definition during earlier time periods (r = 0.76). Both PC exposure calls and hospital discharge diagnoses underestimated incidence. The number of hospital encounters or deaths with a paracetamol poisoning diagnosis was 44% lower than the primary case definition in 2009. This discrepancy decreased to 23% in 2013. The number of PC exposure calls was 32% lower than the primary case definition in 2009 and 14% lower in 2013.

Incidence trend in relation to increased availability of paracetamol

After the intervention in November 2009, there was a 40.5% increase in the incidence of paracetamol poisonings (Figure 2). This was mainly driven by hospital

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Table 1. Baseline characteristics of the study population based on whether poisoning was intentional

				Unintentional		Intentional self-harm		Undetermined intent		Missing information	
				(*n* = 830)		(*n* = 8841)		(*n* = 784)		(*n* = 1613)	
			n	%	*n*	%	*n*	%	*n*	%	*n*
Age			11 979								
0–14 years				13	108	5	401	5	36	4	64
15–24 years				26	218	41	3634	31	246	30	463
25–39 years				21	178	26	2256	26	204	24	363
40–64 years				24	202	24	2143	29	227	29	442
65 years				15	124	5	407	9	71	13	192
Sex			11 857								
Female				66	541	79	6922	73	574	72	1059
Any paracetamol prescription (7 days prior)[‡]			8548								
Yes				18	115	7	449	9	50	10	108
Any paracetamol prescription (30 days prior)[‡]			8548								
Yes				28	185	16	1007	22	116	23	239
Any paracetamol prescription (1 year prior)[‡]			8548								
Yes				46	302	36	2287	42	226	40	427
Study rational for categorising a case as paracetamol poisoning			12 068								
Hospital admission	Specific diagnosis	S-paracetamol available									
Yes	No	Yes		13	105	27	2391	15	121	50	802
Yes	Yes	No		33	273	17	1512	21	161	18	297
Yes	Yes	Yes		49	410	54	4796	54	427	15	236
No	No	Yes (7-day cut-off)		0	0	0	0	0	0	17	276
No	No	Yes (1-day cut-off)		0	0	0	0	0	0	0	0
No	Yes (from cause of death only)	No		5	42	2	142	10	75	0	2
Peak serum paracetamol[†]			12 068								
0–200 μmol/L or missing				59	488	30	2612	43	338	23	368
201–350 μmol/L				8	66	8	685	9	72	2	40
351–700 μmol/L				16	131	20	1726	18	140	25	401
701–1000 μmol/L				8	66	17	1480	13	102	24	387
>1000 μmol/L				10	79	26	2338	17	132	26	417

[†]Paracetamol level unit conversion: μmol/L × 0.151 = mg/L.
[‡]Data on prescribed medications are limited to cases from 2007 to 2013.

discharge diagnoses, as there was only a 12.6% increase in the number of cases with serum paracetamol >700 μmol/L (Figure S2). The number of cases with serum paracetamol levels >1000 μmol/L remained stable.

In the primary regression analysis, the start of the segment before the intervention was set to January 2008 and the intervention to December 2009. This suggested a trend change following the intervention unlikely to be a chance finding (β_3 = 0.0234; $p < 0.0001$), but there was no substantial immediate change (jump) in the incidence level (β_2 = 0.0368; $p = 0.5991$) (Figure 3 and Table S2).

Adjustment for the trend in hospital episodes for any self-harm or the average monthly sales volume of paracetamol (Figure 4) indicated that neither of these trends were associated with the incidence of poisonings ($p = 0.787$ and $p = 0.484$ respectively). The suicide rate was also not associated with the incidence of poisonings ($p = 0.799$, 0.827, and 0.865 respectively). After adjustment for the trend in sales, self-harm, or suicides, there was still a notable change in the incidence trend of paracetamol poisoning ($p = 0.0002$, $p < 0.0001$, and $p = 0.0034$ respectively); however, there was no immediate change in incidence level after the intervention ($p = 0.407$, 0.584, and 0.636 respectively). In sensitivity analyses, the result remained essentially unchanged (see online only supplementary material).

Finally, we used an ARIMA regression model (fitting the entire time series before the intervention in December 2009) to predict the trend after the intervention (Figure S4). The observed number of poisonings after the intervention tended to exceed the expected number based on this ARIMA model.

Outcome of paracetamol poisoning

A total of 5.8% (695/11 923) of the patients either required more than 2 days of hospital care with a non-

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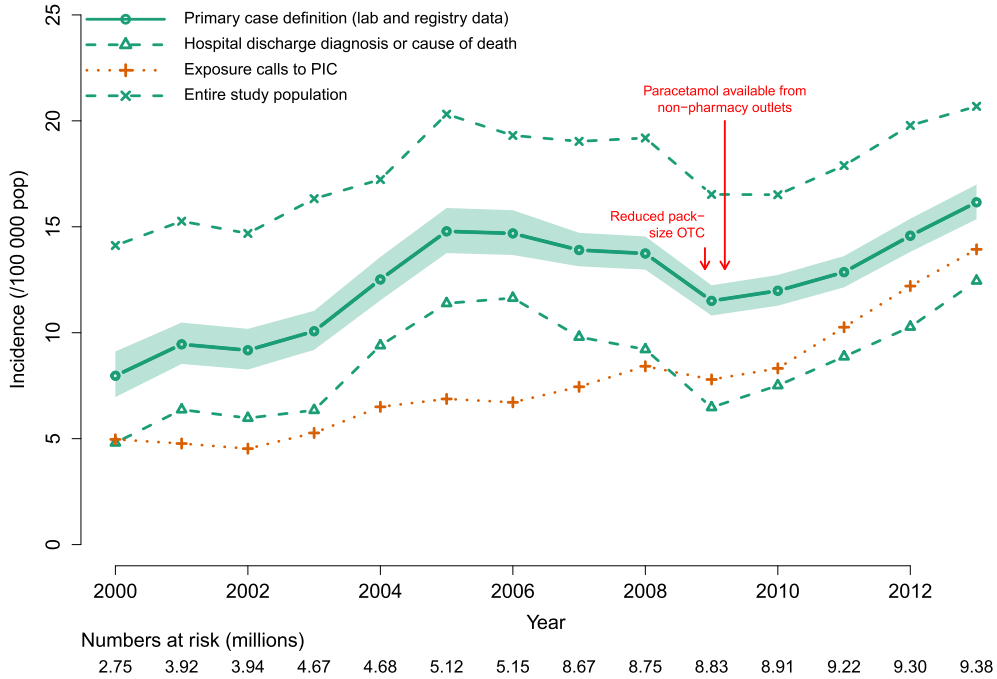

Figure 2. Incidence of paracetamol poisoning using the primary case definition that combines laboratory results with diagnoses from registry data. The shaded area indicates a 95% confidence interval. For comparison, estimates based on the entire study population, hospital discharge or cause of death diagnoses only, and counts of poison information centre exposure calls from health-care personnel are presented. The numbers at risk in the population are indicated below the plot. The timings of some notable regulatory interventions involving paracetamol are indicated. In May 2009, the maximum pack size for paracetamol sold over the counter was restricted to 10 g (500-mg tablets). In November 2009, marketing of paracetamol in non-pharmacy outlets was allowed [Colour figure can be viewed at wileyonlinelibrary.com]

psychiatric diagnosis or died during the 30-day period following the index date (Table 2). There was a diagnosis indicating hepatic injury in 2.4% (282/11 923), and 10 cases (0.08%) required a liver transplant within a 30-day period (Table 2). Thirty-day mortality remained essentially unchanged at 3.2% (379/11 923) over the study period (Figure S5). The median age of these deaths was 55 years, and 57% were female. Most deaths occurred within the first days following the event, and mortality risk increased with age (Figure S6).

DISCUSSION

This population-based study of paracetamol poisoning describes a 40% increase in incidence that seems temporally associated with the November 2009 decision to make paracetamol available from non-pharmacy outlets. This is in contrast to the decreased incidence seen during the period of 2007–2009. This change in trend is unlikely to be random variation. The change in incidence could be related to other factors than the increased availability through non-pharmacy outlets, but no associations with overall trends in the sales volume of paracetamol, suicide rates, and hospital care for self-harm were detected. The policy for management of paracetamol poisoning in Sweden did not change during the study period. No specific alternative explanation could be identified from the data available.

When using case definitions exclusively based on serum paracetamol levels, the incidence trend varied depending on the threshold level used. Cases defined by low serum paracetamol levels (>200 μmol/L) displayed a trend similar to the main case definition. With higher threshold levels, the change over time was increasingly attenuated. This suggests that variability in the incidence was mainly due to less severe cases. This interpretation is supported by a stable frequency of liver transplantation and a stable mortality rate.

Strengths and limitations of the current study

The main strength of this study is the availability of serum paracetamol levels covering >94% of the Swedish population from 2007. To our knowledge, this is the first large-scale population-based study to use laboratory data to increase the overall reliability of the paracetamol poisoning diagnosis from registry data. Segmented regression analysis allowed adjustment for the total paracetamol sales volume and trends in

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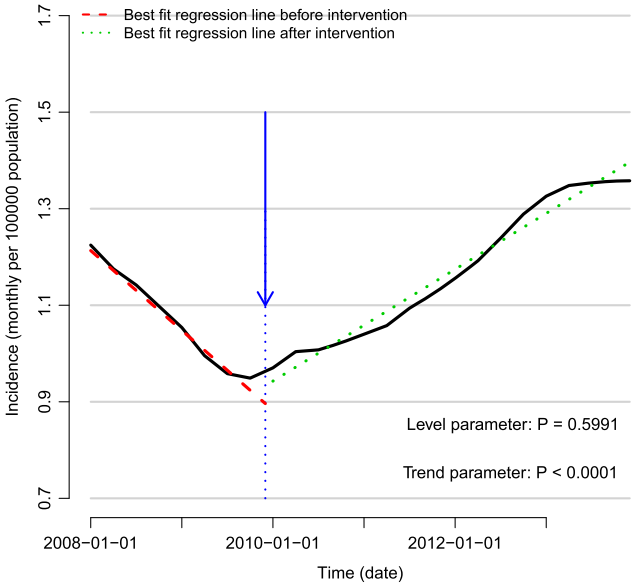

Figure 3. Interrupted time series analysis, using a pre-intervention period starting in January 2008 and intervention assumed to take effect in December 2009. The underlying local regression (Locally Weighted Scatterplot Smoothing) trend was derived from decomposition of the observed time series of monthly count of paracetamol poisonings per 100 000 population. The timing of the intervention is indicated with the vertical arrow. Adapted linear trends before and after intervention are indicated (broken red and dotted green lines). The main analysis results with the *p*-values for the parameters representing the immediate change (jump) in incidence level (level parameter) and change in slope (trend parameter) are provided [Colour figure can be viewed at wileyonlinelibrary.com]

hospitalised self-harm or suicide. Monthly sales are, however, extrapolations from annual sales volumes, and frequency of self-harm is based on health-care utilisation which may limit the covariate analyses. In May 2009, a restriction of the maximum pack size allowed for OTC sales to 20 tablets (500 mg) may have resulted in underestimation of the impact of non-pharmacy sales. Causality behind changes in incidence of paracetamol poisoning are likely multifactorial. Other unidentified factors besides those considered in the analyses may also influence the incidence trend. The ability for causal inference remains limited in this type of study design.

A further limitation is the lack of information on the time interval from drug intake. Poisonings presenting late may be severe in spite of a low serum paracetamol. There was, however, no obvious trend over time among cases with low serum paracetamol and prolonged hospital stay. The lack of data on the source for the paracetamol products used in each poisoning event makes a detailed mediation analysis of the potential effect of availability in non-pharmacy outlets impossible. Several factors such as proximity to a store, opening hours, ease of access, and pricing could potentially be of importance. Another factor is that non-pharmacy outlets are not allowed to give advice on the choice of medicines.[22]

Mortality estimates must be interpreted with caution given that paracetamol is a common toxicological finding in suicides from other causes[23] and the lack of uniformity of diagnostic criteria used to determine paracetamol-induced death.[24] Prescription data are only available since 2006 and consequently cover only a part of the study population.

Comparisons with other studies

In Sweden, the overall incidence of hospitalisation for poisoning was estimated to 22/100 000 population in 2014.[25] Attempts to estimate the incidence of paracetamol poisoning in Sweden from hospital discharge data are difficult because the use of unspecific codes for poisoning in PAR is substantial and has increased over time (unpublished data). This hampers direct estimations based on PAR only. The incidence estimate of 16.2 per 100 000 in 2013 as provided from the current study is comparable to observations in other countries.[26–31] The results on the association between availability and poisoning incidence remain contradictory. A Canadian study reported no apparent increase in hospitalisations after place-of-sale restrictions on paracetamol pack sizes were lifted.[32] In the UK, pack-size restrictions resulted in fewer deaths and registrations for liver transplants,[33] but this conclusion has been challenged.[24]

While the present study indicates a reduced incidence during 2007–2009, a study from Oxford indicates that paracetamol was increasingly involved in poisonings during this period but then decreased again.[34] International comparisons must, however, be interpreted with caution. Incidence estimates have mostly been based on diagnoses from hospital encounters, sometimes combined with chart review.[27] The use of serum paracetamol levels in this study increases the sensitivity of the case definition.

Reliable and readily available indicators for incidence of paracetamol poisoning are important. Trends based on health-care utilisation may be unreliable.[35] However, both hospital discharge data and PC calls correlated well with, but underestimated, the trend in incidence. Other studies have also reported a good correlation between PC exposure calls and hospital data.[26,36]

As expected, the cases were mainly younger women, with the majority classified as intentional self-harm.[27,37] In other settings, unintentional overdoses have been more common than in our study.[28] A history of alcohol misuse was frequent and is

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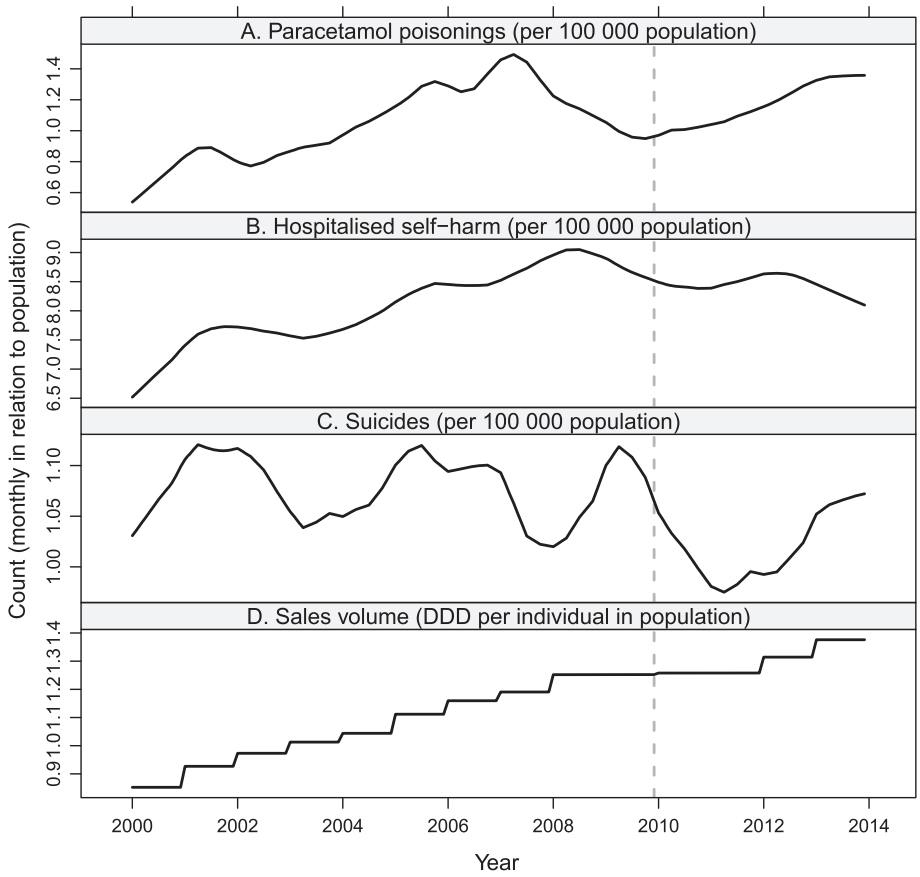

Figure 4. Monthly time trends of covariates smoothed with local regression (Locally Weighted Scatterplot Smoothing). Panel A: Number of paracetamol poisonings using the primary case definition. Panel B: Number of individuals hospitalised for self-harm. Panel C: Number of suicides. Panel D: Average monthly sales volume of paracetamol by prescription and over the counter derived from annual sales volumes. The vertical broken line indicates when paracetamol was made available from non-pharmacy outlets. DDD, defined daily dose

Table 2. Outcomes of paracetamol poisoning cases based on intent linked to mortality data. Days alive after hospital discharge during the 30-day period following the index date, hospital care with a diagnosis indicating hepatic injury or liver transplantation, and all-cause mortality risks are shown

	Unintentional (n = 830)	Intentional self-harm (n = 8841)	Undetermined intent (n = 784)	Missing information on intent (n = 1613)
Days alive out of hospital during first 30 days				
0–2 days	5% (44)	2% (168)	11% (86)	1% (22)
3–27 days	3% (25)	3% (258)	3% (22)	5% (70)
28–30 days	92% (761)	95% (8415)	86% (676)	94% (1376)
Hepatic diagnosis within 30 days	5% (38)	2% (146)	3% (25)	5% (73)
Hepatic diagnosis within 90 days	5% (38)	2% (156)	3% (25)	5% (75)
Liver transplant within 30 days	0% (0)	0% (7)	0% (1)	0% (2)
Death within 30 days	6% (47)	2% (195)	11% (89)	3% (48)
Death within 90 days	6% (51)	3% (236)	12% (95)	4% (59)
Death within 1 year	8% (65)	4% (365)	14% (111)	6% (92)

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commonly seen in association with this type of self-harm.[34] The proportion of patients having been prescribed paracetamol prior to an event was largely comparable to previously reported results.[38]

The outcomes observed are also largely in line with previous studies. While paracetamol poisoning is the most common cause of acute liver failure in Sweden,[39] and in other countries,[40,41] liver transplantation was only seen 1–2 times per year. Mortality rate and incidence of cases with high serum paracetamol levels remained stable over time. This suggests that fluctuations in incidence mainly involve less severe cases and cases related to impulse-driven low-dose intentional poisonings.

KEY POINTS

- The majority of paracetamol poisonings are intentional overdoses for which impulsivity and ease of access are risk factors.
- Studies on the impact of changes in availability through regulatory interventions are scarce and have produced conflicting results.
- This study suggests a temporal association between increased availability to paracetamol in non-pharmacy outlets and a 40% increase in the incidence of paracetamol poisoning.
- This increase in incidence was not related to sales volume of paracetamol or overall trends in hospitalised self-harm or suicide.

CONCLUSIONS

The results suggest a temporal association between the increase in availability of paracetamol and an increased incidence of mainly intentional poisonings. This association could not be explained by trends in sales volume, hospitalised self-harm, or suicide rates. While there may be other explanations, accessibility to means is considered to be a risk factor for self-harm.[42] The balance between ease of access for normal use and trying to limit the problem of impulse-driven intentional paracetamol poisonings remains a challenge for regulators.[5,32,43,44] In the future, regulatory interventions that influence availability of paracetamol should be evaluated for their potential impact on the incidence and outcome of poisonings. The approach with linkage of hospital discharge and causes of death to laboratory data provides a more robust case definition for such evaluations. It is also important to consider the potential for channelling to NSAIDs if restrictions to paracetamol availability are made.[45]

CONFLICT OF INTEREST

All authors declare that there are no support from any organisation for the submitted work, no financial relationships with any organisations that might have an interest in the submitted work in the previous 3 years, and no other relationships or activities that could appear to have influenced the submitted work. The study involves evaluation of a regulatory decision made by the Medical Products Agency, which is a Swedish Government authority. All authors except one (BS) are affiliated to the Medical Products Agency.

ETHICS STATEMENT

The study was approved by the Regional Ethics Review Board in Uppsala. The requirement for individual patient consent was waived.

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