

Primary care

UK legislation on analgesic packs: before and after study of long term effect on poisonings

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Abstract

Objective To evaluate the long term effect of legislation limiting the size of packs of analgesics sold over the counter.

Design Before and after study.

Setting Suicides in England and Wales, data from six liver units in England and Scotland and five general hospitals in England, and UK data on sales of analgesics, between September 1993 and September 2002.

Data sources Office for National Statistics; six liver units in England and Scotland; monitoring systems in general hospitals in Oxford, Manchester, and Derby; and Intercontinental Medical Statistics Health UK.

Main outcome measures Deaths by suicidal overdose with paracetamol, salicylates, or ibuprofen; numbers of patients admitted to liver units, listed for liver transplant, and undergoing transplantations for paracetamol induced hepatotoxicity; non-fatal self poisonings with analgesics and numbers of tablets taken; and sales figures for analgesics.

Results Suicidal deaths from paracetamol and salicylates were reduced by 22% (95% confidence interval 11% to 32%) in the year after the change in legislation on 16 September 1998, and this reduction persisted in the next two years. Liver unit admissions and liver transplants for paracetamol induced hepatotoxicity were reduced by around 30% in the four years after the legislation. Numbers of paracetamol and salicylate tablets in non-fatal overdoses were reduced in the three years after the legislation. Large overdoses were reduced by 20% (9% to 29%) for paracetamol and by 39% (14% to 57%) for salicylates in the second and third years after the legislation. Ibuprofen overdoses increased after the legislation, but with little or no effect on deaths.

Conclusion Legislation restricting pack sizes of analgesics in the United Kingdom has been beneficial. A further reduction in pack sizes could prevent more deaths.

Introduction

Legislation to limit the size of packs of analgesics (paracetamol, salicylates, and their compounds) sold over the counter was introduced in the United Kingdom on 16 September 1998 to try to reduce the mortality and morbidity associated with deliberate overdoses, especially with paracetamol. The increasing problem of paracetamol overdoses had been highlighted for several years in the United Kingdom and elsewhere.¹⁻⁹ The legislation reduced the previously unrestricted sale limit for pharmacies to a maximum of 32 tablets and for other retail outlets from 24 to 16 tablets.¹⁰ The main aim of the legislation was to reduce

household stocks of analgesics and the associated danger of overdoses from these supplies.^{11 12}

We previously showed noticeable declines in numbers of large overdoses, deaths from paracetamol and salicylate overdose, and paracetamol related liver transplants in the year after the legislation was introduced.⁴ Other evidence largely supported these findings.¹³⁻¹⁶ We have now assessed the legislation's longer term effect and investigated possible substitution of overdose method with the non-steroidal anti-inflammatory drug ibuprofen, which was not included in the legislation.¹⁷

Methods

Outcome measures

Mortality from overdoses

Data on drug related deaths (suicides, open verdicts, and accidental poisonings) in England and Wales, 1993 to 2001, were supplied by the Office for National Statistics. We extracted data on deaths of people aged 12 years and over involving paracetamol, salicylates, or ibuprofen either alone or in combination with other drugs (excluding co-proxamol, which is only available on prescription).

Liver transplantation and referrals to liver units

From all but one of the liver units in England and Scotland we obtained data on numbers of patients admitted after paracetamol overdose, those listed for liver transplant, and those undergoing transplantation, between 1996 and 2002.

Non-fatal self poisoning

Data on presentations between 1997 and 2001 for self poisoning with paracetamol, paracetamol compounds (excluding co-proxamol), salicylates, salicylate compounds, ibuprofen, and other drugs were collected from five general hospitals (one in Oxford and two each in Manchester and Derby). We noted the numbers of tablets taken, and we made standard approximations for imprecise amounts.

Sales data

Intercontinental Medical Statistics supplied data on sales of analgesics in the United Kingdom. We compared sales to pharmacies and other outlets after the legislation was introduced with those in the penultimate year before the change in law (pack sizes were changing in the year before legislation).



Sales data for paracetamol, salicylates, and ibuprofen are on bmj.com

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Table 1 Deaths related to paracetamol and salicylates among people aged 12 years and over in England and Wales, trends in deaths from poisoning 1993-2001, and change associated with legislation

Variable	Mortality before legislation*		Mortality after legislation*		% (95% CI) change for year after legislation v 2 years before		% (95% CI) change for years 2 and 3 after legislation v 2 years before		Annual % trend (95% CI)†		% step change in 1998 (95% CI)†	
	1993-6	1996-8	1998-9	1999-2001	P value	P value	P value	P value	P value	P value		
Paracetamol alone	161	192	137	127	-29 (-41 to -13)	0.001	-34 (-44 to -22)	<0.001	3.6 (-0.8 to 8.3)	0.11	-35 (-43 to -20)	<0.001
Any paracetamol‡	284	327	265	260	-19 (-30 to -6)	0.004	-20 (-29 to -11)	<0.001	2.0 (-1.3 to 5.4)	0.24	-20 (-31 to -6)	0.006
Salicylates alone	34	32	17	10	-46 (-68 to -8)	0.02	-70 (-82 to -50)	<0.001	-6.6 (-15.8 to 3.7)	0.2	-52 (-73 to -16)	0.01
Any salicylates‡	57	46	27	25	-41 (-61 to -9)	0.02	-45 (-61 to -22)	0.001	-7.2 (-14.6 to 0.7)	0.07	-33 (-56 to 2)	0.06
Any paracetamol or salicylates‡	330	364	284	274	-22 (-32 to -11)	<0.001	-25 (-33 to -16)	<0.001	0.9 (-2.2 to 4.1)	0.57	-22 (-33 to -10)	<0.001
All deaths due to poisoning	2092	2242	2186	2086	-2 (-7 to 3)	0.33	-7 (-11 to -3)	0.001	1.8 (0.5 to 3.0)	0.005	-8 (-13 to -3)	0.004

*Suicides, open verdicts, and accidental poisonings.

†Analysis across five years before and three years after legislation.

‡Includes multiple drugs and compounds.

Statistical analyses

We used Poisson regression models to analyse event counts. Models were stratified by hospital and allowed for overdispersion. Using inverse variance weighted averages across hospitals, dosages were analysed with geometric means.

The effects of the legislation were summarised as relative rates and ratios of geometric means, with 95% confidence intervals. From sales data we extracted the numbers of packets and tablets sold in each year for each product type, and we computed mean pack sizes.

Data for different outcomes were available for different years. We grouped these to provide adequate power for analysis. We also analysed the data on mortality by estimating the underlying trend across eight years and by testing for a step change when the legislation was introduced.

Results

Deaths due to paracetamol and salicylate overdoses

Compared with the two years before the legislation, significant decreases in deaths in the year after the legislation involving either paracetamol alone (-29%, 95% confidence interval -13% to -41%) or salicylates alone (-46%, -8% to -68%) were sustained in the subsequent two years (table 1). Findings were similar for paracetamol or salicylates taken with other drugs (including in compounds).

Between September 1993 and September 2001 there were underlying non-significant upward trends in deaths due to paracetamol overdose and downward trends in deaths due to salicylate overdose. Allowing for these trends, we found clear evidence of downward step changes in deaths from overdoses of both paracetamol and salicylates, either taken alone or with other drugs, which corresponded to the timing of the legislation (see table 1).

Analysis of all deaths due to poisoning also showed a downward step change corresponding to the timing of the legislation (see table 1). The change was much smaller, however, than those for the drugs covered by the legislation. All findings were similar when restricted to suicides and open verdicts (data not shown).

On the basis of mortality during 1993-8, 199 deaths were avoided in the three years after the legislation—118 involving paracetamol and 81 involving salicylates.

Deaths due to ibuprofen overdose

Few deaths involved ibuprofen: four accidental deaths and seven open verdict or suicide deaths occurred in the five years before

the legislation and four and nine deaths occurred, respectively, in the subsequent three years. All these deaths also involved other drugs. The increased annual incidence of all deaths represented a 2.2-fold rise (95% confidence interval 0.95 to 4.94) and of open verdicts and suicides a 2.1-fold rise (0.80 to 5.75).

Admissions to liver units and numbers of liver transplants

We found reductions of around 30% in numbers of people admitted to liver units because of paracetamol induced hepatotoxicity, those listed for liver transplant, and actual transplantations in both the first (1998-2000) and second (2000-2) periods after the introduction of the legislation (table 2). A different pattern for one unit produced significant heterogeneity in number of admissions for paracetamol poisoning during 2000-2.

Mean annual admissions for paracetamol poisoning decreased from 349 in the two years before the legislation to 230 in the four years afterwards, listings for liver transplantation decreased from 43 to 30, and transplants decreased from 32 to 21.5.

Non-fatal self poisonings

Overall, there was a 15% (9% to 21%) reduction in presentations to hospital for paracetamol overdoses in the year after the legislation, but no reduction in subsequent years. Numbers of salicylate overdoses did not significantly change, whereas the numbers of ibuprofen overdoses increased by 27% (11% to 44%) in the second and third years (table 3).

Numbers of tablets taken in paracetamol and salicylate overdoses significantly decreased in the three years after the legislation (table 4). Reductions in the second and third years after the legislation were significantly larger than in the first year for overdoses involving paracetamol and salicylates, but not for overdoses with paracetamol alone. We found no major change for overdoses with ibuprofen alone, although the mean number of tablets in overdoses that involved ibuprofen decreased during the second and third years after the legislation.

Only large (more than 32 tablets) paracetamol overdoses decreased significantly in the year after the legislation (table 5). Significant decreases in large overdoses of paracetamol alone and of any paracetamol and salicylates occurred in the second and third years after the legislation. Numbers of large ibuprofen overdoses did not change significantly.

Sales data

Mean pack sizes decreased significantly between 1996-7 and 1998-9 for paracetamol (35 to 24 tablets per packet) and aspirin

Table 2 Annual numbers and relative incidence rates for admissions for liver transplants, listings, and transplantations due to paracetamol poisoning. Values are incidence rate ratios (95% confidence intervals) unless stated otherwise

Variable related to paracetamol poisoning	Period in relation to introduction of legislation						Pooled incidence rate ratio; P value	Years 3 and 4 after v years 1 and 2 before	Pooled incidence rate ratio; P value	P value for years 3 and 4 after v years 1 and 2 after	
	2nd year before	Year before	Year after	2nd year after	3rd year after	4th year after					
Admissions:											
Birmingham	82	53	40	28	35	47	0.50 (0.38 to 0.67)	0.71 (0.60 to 0.84); <0.001	0.61 (0.46 to 0.80)	0.61 (0.48 to 0.77); <0.001	0.25
Edinburgh	59	32	40	32	45	37	0.79 (0.58 to 1.08)		0.90 (0.67 to 1.21)		
London (Royal Free)	19	12	10	9	21	20	0.61 (0.35 to 1.08)		1.32 (0.83 to 2.10)		
London (King's College)	102	127	103	79	49	35	0.79 (0.65 to 0.97)		0.37 (0.29 to 0.47)		
Leeds	73	76	60	47	39	38	0.72 (0.56 to 0.92)		0.52 (0.39 to 0.68)		
Newcastle	34	29	18	28	28	32	0.73 (0.50 to 1.07)		0.95 (0.67 to 1.35)		
Total	369	329	271	223	217	209					
Test for between centre differences							Q=7.55, df=5	0.18	Q=41.7, df=5	<0.001	
Listing for liver transplant:											
Birmingham	5	7	1	3	5	5	0.33 (0.11 to 1.03)	0.69 (0.48 to 0.99); 0.04	0.83 (0.36 to 1.93)	0.71 (0.49 to 1.02); 0.06	0.88
Edinburgh	7	2	3	7	3	2	1.11 (0.45 to 2.73)		0.56 (0.19 to 1.66)		
London (Royal Free)	2	1	0	0	3	0	0*		1.00 (0.20 to 4.95)		
London (King's College)	11	20	12	12	10	5	0.77 (0.45 to 1.32)		0.48 (0.26 to 0.90)		
Leeds	9	8	9	4	6	4	0.76 (0.37 to 1.57)		0.59 (0.27 to 1.28)		
Newcastle	10	4	3	5	8	10	0.57 (0.24 to 1.36)		1.29 (0.64 to 2.59)		
Total	44	42	28	31	35	26					
Test for between centre differences							Q=6.43, df=5	0.27	Q=5.09, df=5	0.41	
Liver transplants:											
Birmingham	4	6	1	2	4	4	0.30 (0.08 to 1.09)	0.64 (0.43 to 0.95); 0.03	0.80 (0.32 to 2.03)	0.70 (0.48 to 1.03); 0.07	0.72
Edinburgh	5	2	1	6	3	2	1.00 (0.35 to 2.85)		0.71 (0.23 to 2.25)		
London (Royal Free)	2	1	0	0	3	0	0*		1.00 (0.20 to 4.95)		
London (King's College)	8	12	9	9	7	3	0.90 (0.48 to 1.70)		0.50 (0.23 to 1.07)		
Leeds	6	7	4	3	3	3	0.54 (0.21 to 1.35)		0.46 (0.18 to 1.21)		
Newcastle	8	3	2	4	4	9	0.55 (0.20 to 1.47)		1.18 (0.53 to 2.64)		
Total	33	31	17	24	24	21					
Test for between centre differences							Q=6.48, df=5	0.26	Q=3.43, df=5	0.63	

*Inestimable.

(61 to 25 tablets per packet), although they subsequently increased slightly (see figure on [bmj.com](http://www.bmj.com)). The sales of paracetamol rose after the legislation, so overall there was little effect on total numbers of tablets sold (520 million in 1996-7, 580 million in 2001-2). Sales data for paracetamol compounds followed a similar pattern. The sales of aspirin remained almost constant (11 million packs in 1996-7, 12 million packs in 2001-2) whereas the number of tablets sold was approximately halved.

Discussion

Legislation introduced in the United Kingdom in September 1998 to reduce the size of packs of paracetamol and salicylates

sold over the counter has significantly reduced the size of overdoses, with consequent reductions in morbidity and mortality. Although some substitution of self poisoning with ibuprofen may have occurred, few deaths due to poisoning involved ibuprofen, and in all cases other drugs were involved. Ibuprofen is known to be relatively safe in overdose¹⁸ and is therefore unlikely to have been the cause of death. The numbers of tablets used in ibuprofen overdoses did not change significantly after the legislation was introduced, suggesting that the legislation's effect on overdose size was restricted to the targeted drugs.

An unavoidable limitation of our study is its naturalistic design; thus other factors might have influenced our findings. Allowing for underlying trends, however, our analysis showed a

Table 3 Annual numbers of non-fatal self poisonings (Oxford, Manchester, and Derby combined) due to specific drug categories, and percentage change in number of overdoses. Values are percentage change in numbers (95% confidence intervals) unless stated otherwise

Drug	Annual No of non-fatal self poisonings in relation to introduction of legislation				Year after legislation v year before	P value	Years 2 and 3 after legislation v year before	P value	P value for difference between years 2 and 3 after legislation v year after
	Year before	Year after	2nd year after	3rd year after					
Paracetamol alone	825	624	757	781	-24 (-32 to -16)	<0.001	-7 (-14 to 1)	0.1	<0.001
Any paracetamol	1733	1472	1681	1686	-15 (-21 to -9)	<0.001	-3 (-8 to 3)	0.33	<0.001
Salicylates alone	79	64	77	64	-19 (-42 to 13)	0.21	-11 (-32 to 18)	0.42	0.52
Any salicylates	329	307	312	295	-7 (-20 to 9)	0.38	-8 (-19 to 5)	0.24	0.87
Ibuprofen alone	96	113	156	133	18 (-10 to 55)	0.24	51 (19 to 90)	0.001	0.03
Any ibuprofen	316	332	399	402	5 (-10 to 23)	0.53	27 (11 to 44)	<0.001	0.004

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Table 4 Numbers of tablets taken during overdose in non-fatal self poisonings (Oxford, Manchester, and Derby combined). Values are percentage change in geometric mean numbers (95% confidence intervals) unless stated otherwise

Drug	Mean No (95% CI) of tablets in relation to introduction of legislation				Year after legislation v year before	P value	Years 2 and 3 after legislation v year before	P value	P value for difference between years 2 and 3 after v year 1 after
	Year before	Year after	2nd year after	3rd year after					
Paracetamol alone	24.3 (23.1 to 25.5)	23.3 (22.1 to 24.6)	22.4 (20.7 to 24.3)	23.3 (21.1 to 25.8)	-4 (-7 to -1)	0.01	-5 (-8 to -3)	<0.001	0.24
Any paracetamol	21.1 (20.2 to 22.0)	19.8 (19.0 to 20.7)	19.2 (17.7 to 20.8)	19.0 (17.9 to 20.3)	-6 (-8 to -4)	<0.001	-10 (-12 to -8)	<0.001	<0.001
Salicylates alone	30.7 (24.7 to 38.1)	26.6 (21.1 to 33.6)	20.7 (17.3 to 24.7)	21.9 (18.4 to 26.2)	-14 (-25 to -3)	0.02	-31 (-39 to -23)	<0.001	<0.001
Any salicylates	18.8 (16.9 to 20.9)	16.5 (15.0 to 18.2)	15.9 (14.0 to 18.0)	14.0 (12.6 to 15.5)	-12 (-18 to -7)	<0.001	-21 (-25 to -16)	<0.001	<0.001
Ibuprofen alone	20.0 (16.6 to 24.1)	20.0 (17.2 to 23.3)	17.4 (15.3 to 19.8)	20.1 (17.6 to 22.9)	1 (-9 to 12)	0.86	-7 (-15 to 2)	0.14	0.07
Any ibuprofen	14.9 (13.2 to 16.9)	14.8 (13.4 to 16.4)	13.6 (11.8 to 15.8)	14.5 (12.8 to 16.3)	0 (-6 to 6)	1.00	-6 (-10 to -1)	0.03	0.05

substantial downward step change in numbers of deaths from paracetamol and salicylate poisoning immediately after the legislation was introduced, with only a small change in overall deaths due to poisoning. This, together with decreases in the size of overdoses and statistics from liver units on paracetamol induced hepatotoxicity, suggests that the legislation has had a specific effect. A decrease in overall suicide rates (including open verdicts) occurred in England and Wales between 1998 and 2001 (-11.8% for males and -7.0% for females),¹⁹ but this was much less than the results presented here.

Clearly the legislation does not prevent an individual intent on obtaining large supplies from purchasing through multiple outlets. Self poisoning is, however, often impulsive^{20 21} and involves tablets readily available in households.¹¹ Other countries that have addressed this problem, such as France²² and Ireland, have had greater reductions in pack sizes than the United Kingdom. Physiological investigations suggest that the risk of hepatotoxicity after paracetamol overdose substantially increases with consumption of 250 mg/kg or more tablets—that is, 30 tablets or more for a person weighing 60 kg.²³ A further small reduction in pack sizes of paracetamol and salicylates would be unlikely to inconvenience users and could have further beneficial effects in preventing deaths from self poisoning.

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Contributors: KH, SS, and JD designed the study. KH and SS coordinated the study and wrote the report with JD, with the help of the other investigators. JC, AJ, KW, MA, WB, BG, MH, DS, and KS participated in the planning,

data collection, and writing of the report. JD conducted the data analysis. KH is the guarantor.

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Table 5 Numbers of non-fatal self poisonings with more than 32 tablets (Oxford, Manchester, and Derby combined). Values are percentage change in numbers (95% confidence intervals) unless stated otherwise

Drug	Mean (No) of tablets in relation to period of legislation				Year after legislation v year before	P value	Years 2 and 3 after legislation v year before	P value	P value for differences between years 2 and 3 after v year 1 after
	Year before	Year after	2nd year after	3rd year after					
Paracetamol alone	30.7 (27.3 to 34.0)	26.1 (22.5 to 29.6)	23.0 (19.9 to 26.0)	28.1 (24.6 to 31.6)	-15 (-31 to 4)	0.12	-16 (-29 to -1)	0.04	0.87
Any paracetamol	26.4 (24.2 to 28.7)	22.0 (19.8 to 24.3)	20.7 (17.9 to 23.5)	22.0 (19.9 to 24.1)	-17 (-28 to -3)	0.02	-20 (-29 to -9)	0.001	0.63
Salicylates alone	41.2 (29.9 to 52.4)	31.0 (19.8 to 42.3)	17.7 (8.5 to 26.8)	17.9 (8.2 to 27.6)	-24 (-57 to 35)	0.36	-56 (-74 to -24)	0.004	0.07
Any salicylates	22.2 (17.3 to 27.1)	16.2 (11.8 to 20.5)	14.8 (10.0 to 19.7)	11.6 (7.7 to 15.5)	-28 (-51 to 6)	0.1	-39 (-57 to -14)	0.005	0.35
Ibuprofen alone	27.4 (18.0 to 36.8)	25.4 (16.9 to 33.8)	15.4 (9.4 to 21.3)	22.9 (15.4 to 30.3)	-9 (-38 to 58)	0.74	-33 (-59 to 10)	0.11	0.22
Any ibuprofen	17.5 (12.9 to 22.1)	17.5 (13.0 to 22.1)	11.0 (7.7 to 14.4)	14.6 (10.8 to 18.3)	-2 (-34 to 47)	0.93	-29 (-50 to 2)	0.07	0.09

What is already known on this topic

Self poisoning with paracetamol and salicylates was a major problem in the United Kingdom in the 1980s and 1990s

Outcomes included deaths, non-fatal self poisoning, and liver transplantation due to paracetamol induced hepatotoxicity

Legislation limiting the size of packs of analgesics seemed to have a beneficial initial effect

What this study adds

Legislation limiting pack sizes of analgesics has had sustained beneficial effects

Decreases have occurred in mortality, size of non-fatal overdoses, and in admissions to liver units and liver transplants due to paracetamol poisoning

Although some substitution with ibuprofen may have occurred, there is no evidence that this has affected mortality

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