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## Insulin dependent diabetes in children under 5: incidence and ascertainment validation for 1992

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### Abstract

**Objective**—To establish the incidence of insulin dependent diabetes diagnosed in children under 5 years of age in the British Isles during 1992, comparing the national and regional results with those of our 1988 national study, and estimating the 1992 study's level of case ascertainment.

**Design**—Active monthly reporting of cases by consultant paediatricians through the framework of the British Paediatric Surveillance Unit, with additional reports from specialist diabetes nurses and regional health authorities.

**Subjects**—All children diagnosed under the age of 5 years with primary insulin dependent diabetes from 1 January to 31 December 1992 (inclusive) and resident in the British Isles at diagnosis.

**Results**—387 children (208 boys and 179 girls) were confirmed to have insulin dependent diabetes, giving a national incidence of 9.3/100 000/year. This is similar to the 9.9/100 000/year found in 1988. Three sample capture-recapture analysis, which could only be applied across the 12 (out of 18) regions supplying regional information to the study, suggested ascertainment rates of 78% for the British Paediatric Surveillance Unit, 67% for specialist nurses, 69% for regional health authorities, and 99% for the aggregated registry.

**Conclusions**—The national incidence of diabetes in the under 5s in the British Isles did not differ between 1988 and 1992. Nearly complete (99%) ascertainment of cases was possible only for regions for which three data sources were available. Capture-recapture analysis highlighted both the need for more than one data source and for each data source to be complete for the whole study area.

### Introduction

The reported incidence of childhood onset insulin dependent diabetes varies widely, both internationally<sup>1,2</sup> and nationally.<sup>3,5</sup> Moreover, there is evidence of change in these incidences over time.<sup>1,3,5</sup> The 1988 national study on the incidence of insulin dependent diabetes in the British Isles suggested an increase in incidence among children under 16 years of age from 7.7 cases per 100 000 children per year (on the basis of data from the British Diabetic Association register for 1973/74<sup>6</sup>) to 13.5/100 000/year.<sup>3</sup> The study also noted

that the contribution from new patients aged under 5 years had increased considerably from 19% (202/1056, incidence 4.2/100 000/year) in 1973-4 to 25% (404/1600, incidence 9.9/100 000/year) in 1988.<sup>3</sup> In the present study we have therefore concentrated on the incidence of insulin dependent diabetes in children under 5 years of age in the British Isles to assess whether this apparent increase among young children was continuing and whether regional differences were replicated.

In concentrating on children under the age of 5 years, in whom diabetes is so striking and memorable, we expected that ascertainment would be almost complete. However, recent epidemiological studies have highlighted the use of statistical techniques (originally developed by ecologists for estimating animal populations<sup>7</sup>) for validating the completeness of survey data.<sup>8-13</sup> It therefore seemed appropriate to take this opportunity to use capture-recapture analysis to estimate our level of ascertainment.

### Methods

New cases of insulin dependent diabetes in children aged under 5 diagnosed from 1 January 1992 to 31 December 1992 (inclusive) were reported by consultant paediatricians to the British Paediatric Surveillance Unit. This is an active reporting system that involves all paediatricians in the surveillance of certain serious childhood diseases.<sup>14</sup> A report card containing a list of conditions is sent monthly to all the consultant paediatrician members of the British Paediatric Association and other categories of members where appropriate. Respondents are asked to report cases of conditions named on the card that they have seen in the preceding month or to tick a "nil return" box. Diabetes mellitus in children under 5 years of age was included on the card for 12 months (February 1992 to January 1993).

When a case was reported to the surveillance unit the information was sent to the study administrator in Bristol. Each reporting paediatrician was then asked to confirm the case and give some additional details.

Special arrangements were made for children with diabetes diagnosed in the Oxford Regional Health Authority area so as not to interfere with the ongoing Barts-Oxford family study.<sup>4</sup> Information from the Oxford region about each child's age, sex, and date of

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TABLE I—Incidence of insulin dependent diabetes in children under 5 years in the British Isles, 1988 and 1992

Region	1992			1988		
	No of cases	Population under 5*	Incidence per 100 000	No of cases	Population under 5†	Incidence per 100 000
Scotland	51	326 341	15.63	45	322 989	13.93
Northern	29	202 658	14.31	21	198 095	10.60
Mersey	22	165 267	13.31	17	160 342	10.60
Oxford	23	181 619	12.66	19	172 804	11.00
East Anglia	14	134 471	10.41	20	131 456	15.21
West Midlands	38	364 312	10.43	28	346 605	8.08
Northern Ireland	13	129 318	10.05	10	136 862	7.31
Wessex	19	190 630	9.97	21	181 849	11.55
North West Thames	21	245 240	8.56	14	231 952	6.04
Wales	16	191 905	8.34	19	185 956	10.22
Yorkshire	21	252 271	8.32	26	240 037	10.83
South East Thames	20	252 720	7.91	18	234 325	7.68
South Western	15	206 083	7.28	24	195 508	12.28
South West Thames	14	195 962	7.14	16	182 932	8.75
North East Thames	18	272 037	6.62	29	256 705	11.30
Trent	18	313 616	5.74	27	297 275	9.08
North Western	16	285 790	5.60	34	271 679	12.51
Republic of Ireland	19	273 730	6.94	16	324 078	4.94
Total	387	4 183 970	9.25	404	4 071 449	9.92

\*Data from General Register Office for Scotland, mid-1992 estimates based on 1991 census; Office of Population Censuses and Surveys, estimated resident population for 1992 based on the 1991 census; General Register Office for Northern Ireland, mid-1992 estimates based on 1991 census; Central Statistics Office for the Republic of Ireland, population figures issued in the 1991 census.

†Data from General Register Office for Scotland, mid-1988 estimates based on 1981 census; Office of Population Censuses and Surveys, estimated resident population at mid-1988 based on 1981 census; General Register Office for Northern Ireland, mid-1988 estimates based on 1981; Central Statistics Office for the Republic of Ireland, population figures issued in the 1986 census.

TABLE II—Number of cases of insulin dependent diabetes mellitus in children under 5 (total 378) notified by two sources in the British Isles

	British Paediatric Surveillance Unit	
	Yes	No
Nurses:		
Yes	180	77
No	121	?

diagnosis was provided by the study's administrators at intervals of six months.

At the end of the 12 month reporting period several validation exercises were undertaken. These were aimed at both improving and assessing the ascertainment level of the study. Firstly, all paediatricians who had made contact with the study were sent a list of the children they had reported and asked to check that no eligible children were missing from the list. Secondly, all specialist diabetic nurses and health visitors were contacted (through the mailing system of the British Diabetic Association) and asked to list all the children under 5 they had seen with diabetes newly diagnosed in 1992. Lastly, all regional health authorities were approached for a list of the inpatient admissions during 1992 of children under 5 years of age with a diagnosis of diabetes.

Data were analysed by using SPSS and the epidemiological package EGRET.<sup>15</sup> A  $\chi^2$  test was used initially to compare incidence between the two study years, and subsequently Poisson regression models were used to compare incidences between the sexes and between regions in the 1992 data. Student's *t* test was used to compare mean ages at diagnosis, and the Kolmogorov-Smirnov one sample test was used to look for seasonal trend.<sup>16</sup> To estimate the level of underascertainment of the incidence data, capture-recapture modelling techniques were applied.<sup>17,18</sup> Nationally, we used data from the British Paediatric Surveillance Unit and specialist nurses, and we used two sample methodology.<sup>17</sup> To address the problem of possible source dependencies we used three sample methodology<sup>17</sup> for the 12 (out of 18) regions from which regional health authority data were available.

## Results

In all, 387 cases were confirmed by paediatricians as eligible for the study (that is, diagnosed as having insulin dependent diabetes during 1992 before their fifth birthday). This figure represents an aggregate total from three sources: 301 children (78%) were reported to the study office through the British Paediatric Surveillance Unit (or by a paediatrician direct to the office); an additional 77 children (20%) were learned of from nurses; and information on a further eight (2%) came from the 12 (out of 18) regional

health authorities that supplied information. One (<1%) extra child was reported by the parents themselves and has, for statistical purposes, been included in the British Paediatric Surveillance Unit category. Excluded from the analysis were six children whose diabetes was a secondary condition and 164 reports (36 through the British Paediatric Surveillance Unit, 20 through nurses, and 108 through regional health authorities) that were not subsequently confirmed by paediatricians.

## NATIONAL INCIDENCE IN 1992

The total number of confirmed cases for the British Isles of children with insulin dependent diabetes aged under 5 years at diagnosis in 1992 was 387, giving a national incidence of 9.3/100 000/year (with population figures based on the 1991 census). This was not significantly different from the 1988 rate of 9.9/100 000/year for under 5s (with population figures based on the 1986 census in Eire and the 1981 census elsewhere). The cases occurred in 208 boys (incidence 9.7/100 000/year) and 179 girls (incidence 8.8/100 000/year); these incidences did not differ significantly (relative risk 1.10, 95% confidence interval 0.90 to 1.35).

## REGIONAL INCIDENCES IN 1992

The regional rates showed significant differences ( $P < 0.001$ ). The Scottish rate (15.6/100 000/year) was almost three times that of the North Western region (5.6/100 000/year) (table I).

## AGE AT DIAGNOSIS; MONTH OF DIAGNOSIS

Age at diagnosis between the sexes did not differ significantly in either 1988 or 1992. Overall, though, the mean age at diagnosis had increased in 1992, being 3.07 years (SD 1.180) in 1992 and 2.89 years (1.235) in 1988,  $t = 2.2$ ,  $P < 0.05$ .

Testing for seasonal trend<sup>16</sup> showed no significant deviation from a uniform seasonal incidence pattern.

## ASCERTAINMENT BY CAPTURE-RECAPTURE METHOD

For the whole of the British Isles, 301 cases were reported through the British Paediatric Surveillance Unit and 257 by nurses. These included 180 cases common to both sources (table II). Assuming that the sources are independent, the maximum likelihood estimate of the total number of cases, reported plus unreported, was 430.<sup>17</sup> The standard error was approximately 11, leading to a 95% confidence interval of 408 to 452. Assuming that the total number of cases was 430, the ascertainment rates for the British Paediatric Surveillance Unit, nurses, and the aggregated registry would be 70%, 60%, and 88% respectively.

A third source, required to investigate source dependency, was data from the regional health authorities, which were available for 12 (out of 18) regional health authorities. The regional health authorities had identified eight new cases, leading to a total of 285 cases within these 12 regions (table III).

The nature of source dependencies was determined by fitting a series of log linear models to the data in table III with SPSS, first with none, then one pair, and finally two pairs of source dependencies. The  $\chi^2$  statistics were calculated to assess goodness of fit. A

TABLE III—No of cases of insulin dependent diabetes mellitus in children under 5 (total 285) notified by three sources over 12 regional health authorities in the British Isles

Regions	Yes		No	
	Yes	No	Yes	No
Nurses				
British Paediatric Surveillance Unit				
Yes	90	65	50	19
No	36	8	17	?

TABLE IV—Goodness of fit for log-linear models fitted to determine source dependencies

Type of model	$\chi^2$	df	P
Three sources independent	11.03	3	<0.025
One pair dependent sources:			
British Paediatric Surveillance Unit and nurse	4.24	2	>0.20
British Paediatric Surveillance Unit and region	10.48	2	<0.01
Nurse and region	8.41	2	<0.025

non-significant  $\chi^2$  value was found after allowance for only one dependency, that between nurses and the British Paediatric Surveillance Unit (table IV). The proportion of cases reported by the nurses was found to be reduced if the cases had been reported through the British Paediatric Surveillance Unit. In this model, the regional health authority source was considered to be independent of the other two sources and the unreported number of cases ("?" in table III) was estimated<sup>17</sup> to be four. The total population was thus estimated to be 285+4=289 (95% confidence interval 284 to 293).

Without the regional health authority data, the dependency between the British Paediatric Surveillance Unit and nurses would have been ignored, and the estimated number found by using two sample methodology would have been 309 (292 to 325)—that is, seriously overestimated. Using the estimated population of 289, the estimated ascertainment rates were 78% for the British Paediatric Surveillance Unit, 67% for nurses (63% if cases were also picked up through the British Paediatric Surveillance Unit, 82% otherwise), 69% for the regional health authorities, and 99% for the aggregated registry.

### Discussion

This study was designed as a sequel to the 1988 National Survey of Childhood Onset Diabetes. Both studies were carried out through the British Paediatric Surveillance Unit framework and through reports obtained from specialist nurses; in addition, the 1992 study approached all regional health authorities for information. No significant difference was found between the incidence in under 5s for 1988 and 1992. An assumption that annual incidence was similar in the intervening years suggests either that the incidence increased between 1973-4 and 1988 but remained steady thereafter, or that the British Diabetic Association register of 1973-4 was incomplete and the true incidence has not changed over the subsequent 15 years. Data from other non-national studies for 1985-6<sup>4</sup> and 1968-76<sup>19</sup> support a true increase in incidence. Moreover, as we argued in a previous paper,<sup>3</sup> even if ascertainment by the 1973-4 British Diabetic Association register had been as low as 60% the 1988 data would still suggest a real change in the national incidence. Nevertheless, the 1992 study may suggest that the apparent increase in incidence over those 15 years simply reflects improved ascertainment in more recent studies, with the British Diabetic Association's earlier register (which required voluntary active reporting by clinicians) having an ascertainment rate well below 60%.

Regionally, as in the 1988 survey, incidence rates varied greatly across the British Isles. However, regional rates did not vary significantly between the two studies, and, as in 1988, there was no obvious geographical pattern in incidence.

The 1988 and 1992 studies showed two other differences relating to diabetes diagnosed in children under the age of 5 years. Firstly, the mean age of the children at diagnosis was slightly (but significantly) higher in the 1992 survey. Secondly, the seasonal trend in incidence seen in 1988, which was most notable in older children,<sup>3</sup> was not repeated for children under 5

in 1992. This absence of seasonal variation for under 5s is consistent with other studies.<sup>6, 20</sup>

### COMPLETENESS OF ASCERTAINMENT

An attempt was made to estimate the completeness of ascertainment of cases in this survey. Confirmed cases were divided into groups according to reporting source (that is, those reported either through the British Paediatric Surveillance Unit, specialist nurses, or regional health authorities). Three sample capture-recapture analysis suggested an ascertainment rate of 99% for the aggregated registry when all three sources of data were used to identify cases. This was possible in only the 12 (out of 18) regional health authorities from which we received information. The analysis suggested that data collected solely through the British Paediatric Surveillance Unit underestimated the number of children under 5 who developed diabetes in 1992 and that a reliable ascertainment estimate was possible only by using all three data sources because of dependencies between the data collected through the British Paediatric Surveillance Unit and the specialist nurses. We suspect that this dependency arose because in some cases nurses, when contacted by us for a list of all the under 5s they had seen, consulted the paediatricians and forwarded details only of children they thought had not previously been reported to the study, rather than a complete list. Nevertheless, ascertainment over the regional health authorities from which we received information is virtually complete. Unfortunately, six regions did not supply information to the study. Consequently, ascertainment across the whole of the British Isles cannot be estimated reliably, nor the accuracy of the national incidence truly assessed.

The potential benefit of using capture-recapture techniques in diabetes monitoring has been discussed elsewhere,<sup>9</sup> but our experience, while emphasising the value of collecting data from more than one source wherever possible, also highlights the need for that information to be complete for the whole study area. We expected near complete ascertainment from paediatricians, since very young children developing diabetes are almost always admitted to hospital (although this is not policy everywhere<sup>21</sup>). However, of all the confirmed cases in the study, 22% were not reported by paediatricians

### CONCLUSIONS

The incidence of diabetes in children under 5 years in the British Isles was not different in 1992 from the rate found in 1988. This contrasts with the apparent increase between 1973-4 and 1988. Although we expected near complete ascertainment of cases from paediatricians alone, this was more nearly achieved by using data from two other sources, yielding an ascertainment rate of 99%. Capture-recapture analysis using at least three sources would seem to be an excellent statistical tool for validating epidemiological incidence studies when complete data for the whole study area is available from each source. While this study provides no evidence that the incidence of insulin dependent diabetes in children under 5 has

### Key messages

- There is no evidence that the incidence of diabetes in children under 5 years has increased since 1988
- Capture-recapture methodology is a useful tool for epidemiological surveys, but sources of data must be complete for the whole study area

increased since 1988, every year nine in 100 000 children under 5 develop diabetes, each with the daily burden of diabetes management and a risk of early death and subsequent morbidity in adult life.

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## Abnormal liver growth in utero and death from coronary heart disease

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Evidence is growing that the metabolic abnormalities which lead to coronary heart disease are programmed by undernutrition in utero. Undernutrition of the fetus leads to small size and disproportionate body form at birth, which are now known to be linked to metabolic abnormalities in later life.<sup>1</sup> Abdominal circumference may be measured routinely at birth and indicates liver growth in utero as well as the fatness of the abdominal wall. A recent study showed that men who had a small abdominal circumference at birth had raised serum concentrations of total and low density lipoprotein cholesterol.<sup>2</sup> They also had raised plasma concentrations of fibrinogen, another major risk factor for coronary heart disease that is regulated by the liver.<sup>3</sup> These associations were independent of social class, current body weight, cigarette smoking, and alcohol consumption. They suggest that impaired liver growth in utero may be an early stage in the pathogenesis of coronary heart disease.

### Methods and results

A standardised record form was kept for each woman admitted to the Jessop Maternity Hospital in Sheffield. From 1922 onwards, abdominal circumference was included among the measurements made on the baby at birth. We have traced 1973 (79%) of 2513 singleton boys born alive during 1922-30. The method of follow up has been described.<sup>2,3</sup> The abdominal circumference of 1819 of the 1973 boys had been recorded. A total of 174 of them had died from coronary heart disease (*International Classification of Diseases* (9th revision) codes 4100-4149).

The men's mean birth weight was 7.5 pounds (3400 g) and their mean abdominal circumference was 12.3 inches (31.2 cm). The table shows their death rates from coronary heart disease, expressed as standardised mortality ratios with the average for England and Wales as 100. Men with below average birth weight had higher death rates, as would be expected from previous findings.<sup>1</sup> Mortality ratios showed a U shaped relation with abdominal circumference. Further examination showed that this was the result of opposing trends at birth weights below and above the average. Below the mean birth weight standardised mortality ratios fell with increasing abdominal circumference whereas above it they rose. The difference in these two trends was significant ( $\chi^2=8.2$ ,  $P=0.004$  interaction term in log-linear model). P values for the individual trends were 0.11 and 0.02, respectively.

Standardised mortality ratios for coronary heart disease according to abdominal circumference at birth among 1819 men born during 1922-30. Values in parentheses are numbers of deaths unless stated otherwise

Abdominal circumference at birth (inches (cm))	All men			Men born at >37 weeks' gestation		
	Average birth weight or less	Above average birth weight	All	Average birth weight or less	Above average birth weight	All
≤11.5 (29.2)	123 (39)	48 (2)	114 (41)	102 (17)	35 (1)	92 (18)
-12.0 (30.5)	113 (36)	58 (11)	93 (47)	110 (23)	43 (6)	83 (29)
-12.5 (31.8)	79 (12)	102 (14)	90 (26)	73 (7)	95 (9)	84 (16)
-13.0 (33.0)	68 (7)	110 (26)	97 (33)	74 (5)	112 (18)	101 (23)
>13.0 (33.0)	101 (3)	125 (24)	122 (27)	49 (1)	126 (16)	115 (17)
All	106 (97)	97 (77)	101 (174)	95 (53)	91 (50)	93 (103)

Average birth weight = 7.5 lb (3400 g).