Voluntary surveillance systems are subject to under-reporting. Figures may underestimate true numbers. Miscategorisation of probable country of infection by presuming the country with the highest prevalence as the likely country of infection will underestimate the number of infections acquired in the United Kingdom, particularly among people originating from countries with high prevalence. New HIV diagnoses do not represent new HIV infections, as diagnosis can occur at any point between infection and death, which in the natural course of infection is typically 10-12 years. Furthermore, surveillance reports do not distinguish between partners infected in high prevalence countries while visiting and partners infected before migrating from those countries.

The number of people becoming infected with HIV through heterosexual intercourse in the United Kingdom is rising steadily. As the number of heterosexuals living with HIV (diagnosed and undiagnosed) in the United Kingdom grows, the likelihood of heterosexual transmission within the country will increase, particularly among ethnic minorities.

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Competing interests: None declared.

Ethical approval: No patients' names are collected; instead surname Soundex codes are used and strict confidentiality of the data is maintained. The voluntary reporting system has approval under the section 60 regulations of the Health and Social Care Act (Statutory Instrument 1438—June 2002).

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RESEARCH POINTERS

Metformin and reduced risk of cancer in diabetic patients

Josie M M Evans, Louise A Donnelly, Alistair M Emslie-Smith, Dario R Alessi, Andrew D Morris

Division of Community Health Sciences, Section of Public Health, University of Dundee, Dundee DD2 4BF
Josie M M Evans *lecturer in epidemiology*
Louise A Donnelly *statistician*

Mill Practice, Dundee
Alistair M Emslie-Smith *principal in general practice*

School of Life Sciences, University of Dundee
Dario R Alessi *principal investigator*

Division of Medicine, University of Dundee
Andrew D Morris *professor of diabetic medicine*

Correspondence to: J M M Evans j.m.m.stansfield@dundee.ac.uk

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Metformin, widely given to patients with type 2 diabetes, works by targeting the enzyme AMPK (AMP activated protein kinase), which induces muscles to take up glucose from the blood. A recent breakthrough has found the upstream regulator of AMPK to be a protein kinase known as LKB1.[1 2] LKB1 is a well recognised tumour suppressor. Activation of AMPK by metformin and exercise requires LKB1, and this would also explain why exercise is beneficial in the primary and secondary prevention of certain cancers.[3] We hypothesise that metformin use in patients with type 2 diabetes may reduce their risk of cancer.

Participants, methods, and results

We tested this hypothesis using record linkage databases developed in Tayside, Scotland: a diabetes clinical information system (DARTS) and a database of dispensed prescriptions (MEMO).[4] We did a pilot case-control study using previously validated methods.[5]

From 314 127 people who were resident (or died) in Tayside in 1993-2001, 11 876 had been newly diagnosed with type 2 diabetes. Of these, 923 were subsequently admitted to hospital with an ICD-9 or ICD-10 (international classification of diseases, 9th or 10th revision) diagnostic code for malignant cancer in study period (for which first admission occurred at least one year after diagnosis of diabetes). The index date of these cases was the date of first admission. We generated random controls from the diabetic population (two for each case); patients without cancer matched for age, year of diagnosis, and sex, and we gave them matching index dates.

What this paper suggests

Metformin may reduce the risk of cancer in patients with type 2 diabetes

What research is needed now

A more rigorous cohort study, before experimental work is initiated

We collated information about use of metformin for all cases and controls and calculated unadjusted odds ratios using conditional logistic regression (taking matching into account). The proportions of cases and controls for whom confounding data were available were smoking 73%, body mass index 62%, blood pressure 67%, and postcode rank for material deprivation 99%. We categorised continuous variables into quartile groups, with missing values forming a separate category. We adjusted odds ratios for these possible confounders.

More than half of the patients with cancer (488; 53%) were men. Mean age was 73 (standard deviation 9.8) years and mean duration of diabetes was 8.5 (6.4) years. More than a third (336; 36.4%) of the cases had been given at least one prescription for metformin in the year before their index date compared with 732 (39.7%) of the controls. The unadjusted odds ratio was 0.86 (95%

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Metformin use in patients with type 2 diabetes and controls in Tayside, Scotland, 1993-2001

	No (%)			
	Cases (n=983)	Controls (n=1846)	Unadjusted odds ratios (95% CI)	Adjusted odds ratios (95% CI)
Exposure during year before index date:				
No	587 (63.6)	1114 (60.4)	1.00	1.00
Yes	336 (36.4)	732 (39.7)	0.86 (0.73 to 1.02)	0.85 (0.71 to 1.01)
Any exposure to metformin since January 1993:				
No	547 (59.3)	996 (54.0)	1.00	1.00
Yes	376 (40.7)	850 (46.0)	0.79 (0.67 to 0.93)	0.77 (0.64 to 0.92)
Duration (days):				
0	547 (59.3)	996 (54.0)	1.00	1.00
1-634	127 (13.8)	282 (15.3)	0.81 (0.64 to 1.02)	0.80 (0.62 to 1.02)
635-1806	143 (15.5)	273 (14.8)	0.93 (0.74 to 1.17)	0.92 (0.72 to 1.17)
>1806	106 (11.5)	295 (16.0)	0.62 (0.47 to 0.80)	0.56 (0.43 to 0.74)
Total prescriptions dispensed:				
0	547 (59.3)	996 (54.0)	1.00	1.00
1-11	127 (13.8)	282 (15.3)	0.82 (0.65 to 1.04)	0.82 (0.64 to 1.04)
12-31	122 (13.2)	281 (15.2)	0.77 (0.61 to 0.99)	0.75 (0.58 to 0.97)
>31	127 (13.8)	291 (15.8)	0.76 (0.60 to 0.98)	0.73 (0.56 to 0.94)
Total amount of metformin dispensed (mg):				
0	547 (59.3)	996 (54.0)	1.00	1.00
14 000-672 000	130 (14.1)	279 (15.1)	0.84 (0.67 to 1.06)	0.83 (0.65 to 1.06)
673 000-964 000	138 (15.0)	279 (15.1)	0.88 (0.69 to 1.10)	0.86 (0.68 to 1.10)
>964 000	108 (11.7)	292 (15.8)	0.63 (0.49 to 0.82)	0.57 (0.43 to 0.75)

confidence interval 0.73 to 1.02). The unadjusted odds ratio for any exposure to metformin since 1993 was 0.79 (0.67 to 0.93).

We also investigated total duration of exposure (time between first and last metformin prescription), total number of prescriptions, and total amount of metformin dispensed since January 1993 (table). Adjustment did not greatly affect the risk estimates, indicating no substantial confounding effects.

Comment

Taking metformin may be associated with reduced risk of cancer in patients with type 2 diabetes, and a biologically plausible mechanism exists. Of particular interest is the suggestion of a dose-response relationship (table).

The strengths of the study were its population based sampling, the objective method used to define metformin exposure, detailed dispensed prescribing histories available for patients, and adjustment for confounders. Because this is a pilot observational study, however, we must consider alternative explanations. We used a crudely defined case series of cancer patients. The index date used for the cases was their date of first admission to hospital for cancer. If cases' actual dates of diagnosis of cancer were much earlier, this could affect clinicians' prescribing.

We are planning a large cohort study linked to a cancer registration database. We will identify a more tightly defined case series of specific cancers, with more precise dates of diagnosis, to explore this further.

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Contributors: JMME designed the study and wrote the paper. LAD did the statistical analysis. DRA formulated the hypothesis. AME-S and ADM contributed to the study design. All the authors wrote up the study. JMME is guarantor.

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Competing interests: AME-S has received fees for lecturing from Merck-Lipha (manufacturer of metformin).

Ethical approval: Tayside Committee for Medical Research Ethics.

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One hundred years ago

The spitting nuisance

THE police authorities of New York appear now to be thoroughly in earnest in carrying out the municipal enactments forbidding expectoration in public places. Quite recently ten well-dressed men were fined two dollars each for spitting in one of the subway stations. Persons who do not happen to have sufficient money about them to pay the fine are sent to gaol, a procedure which of itself is likely to have a wholesome educative influence on the public mind. The wardens of some of the police court prisons say they have more public spitters in their custody than any other class of offender. In some courts the average number of charges of this kind dealt with daily is about half a dozen. When will our own civil authorities follow the excellent example of New York, and instead of leaving it to the discretion of omnibus and railway companies to put up notices mildly deprecating expectoration, set themselves resolutely to put down the disgusting and noxious practice? (*BMJ* 1905;i:205a)