

Maternal ischaemic heart disease events and number of previous spontaneous losses of early pregnancy losses. Figures are hazard ratios (95% confidence interval)*

No (%) of events	No of losses of early pregnancy			
	0†(n=117 538)	1-2(n=11 371)	≥3(n=381)	≥1(n=11 752)
Crude	261 (0.2)	48 (0.4)	4 (1.0)	52 (0.4)
Adjusted for case mix‡	1.0	1.44 (1.06 to 1.97), P=0.02	2.34 (0.87 to 6.32), P=0.09	1.49 (1.10 to 2.01), P=0.009
Adjusted for case mix‡ and obstetric complications§	1.0	1.47 (1.08 to 2.00), P=0.02	2.32 (0.86 to 6.27), P=0.10	1.51 (1.12 to 2.04), P=0.007
Adjusted for case mix‡ and obstetric complications§	1.0	1.48 (1.09 to 2.02), P=0.01	2.35 (0.87 to 6.36), P=0.09	1.52 (1.13 to 2.06), P=0.006

*All covariates in multivariate models were significantly associated with ischaemic heart disease. Proportional hazard assumption tested with Stata "stptest" command with Schoenfeld residuals. There was no evidence for violation of assumption in any model (all P>0.5).

†Reference category.

‡Age, height, deprivation, and essential hypertension in first pregnancy.

§Lowest fifth of birthweight distribution, preterm delivery, pre-eclampsia.

with spontaneous early pregnancy loss (0.93, 0.55 to 1.59), suggesting that there was no bias due to selective migration. We did not have data on the smoking status of women in the 1981-5 cohort. However, we had data on 181 636 women who had a first livebirth from 1992 to 1998, inclusive. The proportion of women who were current smokers at the first attendance for prenatal care was only marginally higher among women with a history of spontaneous loss of early pregnancy (28.4%) than among those with no such history (26.8%).

Comment

To our knowledge, this is the first study to show a specific association between spontaneous abortion and maternal risk of IHD. Our findings may explain the results of previous studies that have found an association between the total number of pregnancies and maternal risk of IHD as women who suffer recurrent losses of early pregnancy must have more pregnancies to achieve their target family size.³ However, it is unlikely that the association between spontaneous abortion and maternal IHD is simply an effect of parity as there was no association with therapeutic abortion.

The strengths of our study are that prospective data collection precluded bias and, in contrast with a case-control study, we were able to include women who subsequently died. However, further studies are required to corroborate our findings and to confirm that the association is independent of smoking and other confounding factors, such as maternal disease (for example, diabetes and polycystic ovarian syndrome).

Several studies have shown associations between acquired and inherited thrombophilias and both spontaneous loss of early pregnancy² and IHD.^{4,5} Implantation of the embryo and development of the placenta involve complex adaptations of the mother's cardiovascular and microvascular systems. We hypothesise that occult cardiovascular, microvascular, or haemostatic dysfunction result in pregnancy complications during reproductive years and in overt cardiovascular disease in later life. A woman's reproductive history may, therefore, inform future cardiovascular risk.

Contributors: GCSS had the original concept, reviewed previous publications, undertook the statistical analyses, and is guarantor. GCSS and JPP wrote the initial draft. DW performed the record linkage. GCSS, JPP, and DW agreed the study design, interpreted the results, revised the original draft, and approved the final version.

Competing interests: None declared.

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Incidence of erectile dysfunction and characteristics of patients before and after the introduction of sildenafil in the United Kingdom: cross sectional study with comparison patients

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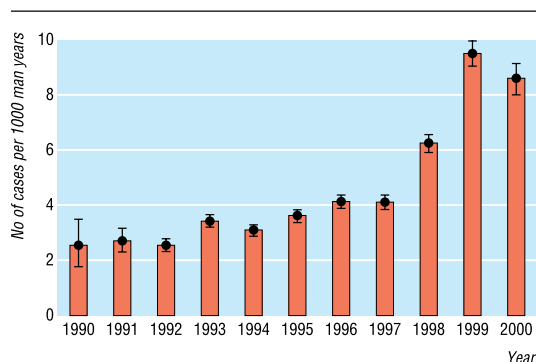
BMJ 2003;326:424-5



Two tables comparing prevalences of medical conditions appear on bmj.com

Erectile dysfunction, the consistent inability to achieve or maintain an erection sufficient for satisfactory sexual performance, is reported to occur in association with cardiovascular disease, diabetes, hypertension,

hypercholesterolaemia, smoking, spinal cord injury, prostate cancer, genitourinary surgery, psychiatric disorders, and the use of many drugs, including alcohol.¹ Sildenafil (Viagra), an oral treatment for erec-



Annual incidence (95% confidence intervals) of erectile dysfunction among men aged 40-79, before and after introduction of sildenafil in 1998 in the United Kingdom

tile dysfunction that was licensed in the United Kingdom in September 1998, selectively inhibits cyclic guanosine monophosphate specific phosphodiesterase type 5, thereby enhancing the vasodilating effect of endogenous nitric oxide. Sildenafil is contraindicated in men being treated with organic nitrates and should be used with caution in men with cardiovascular disease.² Because sildenafil has been promoted extensively, and because no large, population based studies on the incidence of erectile dysfunction had been reported from the United Kingdom, we were interested in the incidence of the disorder and the characteristics of men with a diagnosis and whether these changed after the introduction of sildenafil.

Subjects, methods, and results

We used data up to April 2001 from 272 practices contributing to the UK general practice research database.^{3,4} Cases were men aged 40-79 years with at least two years of recorded medical history who had a first time diagnosis of erectile dysfunction that was recorded between January 1990 and December 2000. We compared cases before (January 1990 to August 1998) and after (September 1998 to December 2000) the introduction of sildenafil. We matched cases with comparison patients who had no recorded diagnosis of erectile dysfunction. Comparison patients were matched to the cases in a ratio of 5:1 by sex, year of birth, general practice, and date of diagnosis. We calculated a prevalence ratio for various conditions by dividing the prevalence of the condition at the time of first diagnosis of erectile dysfunction by the prevalence among the comparison patients.

We identified 10 371 first time recorded cases of erectile dysfunction for an estimated 2.3 million man years of observation. The annual incidence of erectile dysfunction increased gradually during the mid-1990s then rose twofold to threefold during the years 1998 to 2000 (figure). The increase occurred in all age groups (40-49, 50-59, 60-69, and 70-79 years).

The prevalence of ischaemic heart disease among men with erectile dysfunction decreased from 15.7% to 11.3% after sildenafil was introduced, and the prevalence ratio decreased from 1.51 (95% confidence interval 1.42 to 1.61) to 0.89 (0.81 to 0.99) (see table A on bmj.com). Current nitrate use also decreased. Prevalence ratios were even lower for men who were

prescribed sildenafil (table B on bmj.com). The prevalence ratios for diabetes, hypertension, hyperlipidaemia, and smoking changed less or did not change significantly.

Comment

Recorded diagnoses of erectile dysfunction more than doubled after sildenafil was introduced in the United Kingdom. This does not necessarily mean that the number of men with erectile dysfunction increased. The prevalence of ischaemic heart disease among men with erectile dysfunction decreased after the introduction of sildenafil. However, doctors should not be any less concerned about the possibility of undiagnosed ischaemic heart disease in men presenting with erectile dysfunction. The clinical characteristics of men with a diagnosis of erectile dysfunction evidently changed at least in part because of a contraindication or precaution in the use of the new drug.

Studies into the causes of erectile dysfunction should consider the period in which the study population was identified. Moreover, the inverse association we observed between ischaemic heart disease and erectile dysfunction calls into question the value of observational studies that compare the risk of adverse cardiovascular events among sildenafil users with the risk among the general population.⁵

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Contributors: JAK conceived and designed the study, gathered the data for analysis, analysed the data, and drafted the manuscript. HJ contributed to the study design, data analysis, and writing of the manuscript. JAK is guarantor.

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Endpiece

Reality

People would rather be deceived than have the truth cause them anxiety.

Caleb Carr, derived from the Latin, "mundus vult decipi," which means "the world wishes to be deceived."

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