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Immune-related disease before and after vasectomy: an epidemiological database study

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BACKGROUND: Vasectomy can be followed by an autoimmune-antibody response. We aimed to determine whether men with immune-related diseases were more or less likely than others to have a vasectomy and then to determine whether vasectomy is associated with the subsequent development of immune-related diseases. METHODS: A database of linked records of hospital statistics was analysed. By comparing a population of men who underwent vasectomy with a reference population, we calculated the rate ratios for selected immune-related diseases before and after vasectomy. RESULTS: Some diseases studied (e.g. asthma and diabetes mellitus) were a little less common, prior to operation, in the vasectomy group than in the reference group. Others were not different. The mean period of follow-up was 13 years. We found no long-term elevation of risk following vasectomy of asthma, diabetes mellitus, ankylosing spondylitis, thyrotoxicosis, multiple sclerosis, myasthenia gravis, inflammatory bowel disease, rheumatoid arthritis or testicular atrophy. There was a short-term elevation of risk of orchitis/epididymitis. CONCLUSIONS: In this large study, with many years of follow-up, we found no evidence that vasectomy increases the subsequent long-term risk of immune-related diseases.

Key words: epidemiology/immune-related disease/record linkage/vasectomy

Introduction

Vasectomy is a very common form of permanent birth control. The operation is generally considered to have no long-term side effects, but occasionally doubts are raised about its safety. At various times, concerns have been expressed that vasectomy may elevate the risk of cancer, cardiovascular disease and immune-related diseases. Early interests in the long-term safety of vasectomy were concerned with possible immune-related sequelae (Lepow and Crozier, 1979; Sotolongo, 1982). Sperm antigen develop at puberty, long after the immune system has distinguished 'self' from 'not self', and sperm antigen tend to be sequestered from the immune system behind a functional blood–testis barrier. At vasectomy, sperm antigens are released into the bloodstream and can provoke an intense antisperm autoantibody response (Lepow and Crozier, 1979; Sotolongo, 1982). Although it is probably of no pathological significance, this was a postulated biological basis for the concern about immune-related sequelae of vasectomy (Lepow and Crozier, 1979). Autoimmune orchitis is known to occur after vasectomy in experimental animals (Lepow and Crozier, 1979). It is uncertain whether autoimmune orchitis occurs in man, although granulomatous epididymitis is a well-recognized complication of vasectomy. There are very few studies of immune-related disease after vasectomy in man (Massey *et al.*, 1984).

In a recent study on the long-term safety of vasectomy, we found no evidence for a long-term alteration of risk of cancer, myocardial infarction, other ischaemic heart disease or stroke in men who had undergone a vasectomy (Goldacre *et al.*, 2005). Our method was to use a database of linked records of hospital admission and death after vasectomy. We decided to use the same method to study the occurrence, after vasectomy, of diseases, such as asthma, diabetes, rheumatoid arthritis, myxoedema and inflammatory bowel disease, in which immune-mediated mechanisms play an aetiological role. However, a much smaller percentage of men with these diseases than those with cancer or myocardial infarction (for example) are treated in hospital, and if they have any of the immune-related diseases before vasectomy, they may be admitted with it in the years after vasectomy (or may be not at all). For these reasons, we decided to use the database to study hospitalization for these diseases both before and after vasectomy in men who had undergone the procedure. Our aims were: firstly, to determine whether men with immune-related diseases, as measured by hospitalization, were more or less likely than others to have a vasectomy; secondly,

with the evidence from this combined with information about follow-up after vasectomy, to determine whether there is any evidence of an increase in risk of immune-related disease after vasectomy.

Materials and methods

Population and data

We used data from the Oxford record linkage study, which include brief statistical abstracts of records of all hospital admissions, including day cases, in National Health Service (NHS) hospitals, and all deaths regardless of where they occurred, in defined populations within the former Oxford NHS Region from 1 January 1963 to 31 March 1999 (Goldacre *et al.*, 2000). The hospital data were collected routinely from all NHS hospitals as the region's hospital admission statistics. The death data were compiled from death certificates. Data were collected from part of one health district and its associated hospitals since 1963 (population 350 000), from two districts since 1966 (population 850 000), from six districts since 1974 (population 1.9 million) and from all districts and hospitals in the region since 1983 (population 2.5 million). The data for each individual were linked together routinely as they accrued, with the agreement of the Oxford Region's Data Protection Steering Group, as part of the region's health information system. They are then anonymized and archived. The English NHS Central Office for Research Ethics Committees approved the current programme of analysis using the database (reference number 04/Q2006/176).

Analysis

Our methods have been described in detail elsewhere (Goldacre *et al.*, 2000; Goldacre *et al.*, 2005). In brief, we compared rates of occurrence of immune-related diseases in men who underwent vasectomy with those in a reference group of men who had been admitted to hospital with other, mainly minor, medical or surgical conditions. This is our standard reference group that we have used in a range of other studies (Goldacre *et al.*, 2000; 2005). In the first analysis, we did a case–control study, comparing men who had undergone vasectomy with the reference group, identifying those in each group who had been admitted to hospital with each immune-related condition before admission for vasectomy or reference condition. In the second analysis, we did a cohort study, comparing the vasectomy group with the reference group, identifying those in each group who had been admitted to hospital for the immune-related conditions after the vasectomy or reference condition. Men who had the immune-related disease recorded only in the admission for vasectomy (or reference condition) were excluded.

In comparing the vasectomy group with the reference group, in both the case–control and the cohort study, the rates of occurrence of immune-related disease were standardized for age group (in 5-year bands), for the year of first admission for vasectomy or reference condition and for district of residence to ensure that the results of group comparisons were equivalent in these respects. In the reference cohort, we included all the people in the database with the comparison conditions in each age group. We did this to maximize the numbers in each stratum in the reference cohort and thereby to maximize the statistical power of the study.

We then used standard methods to calculate the ratio of the immune-related disease in the vasectomy group to that in the reference group with 95% confidence intervals (CIs) on the rate ratio (Breslow and Day, 1987). We confined the analysis to men who underwent vasectomy between the ages of 20 and 59. The immune-related conditions sought were ankylosing spondylitis, asthma in people aged <55 years, coeliac disease, Crohn's disease, ulcerative colitis, diabetes mellitus subdivided by age into people admitted aged <30 and 30–49, Hashimoto's thyroiditis, idiopathic thrombocytopenic purpura, multiple sclerosis, myasthenia gravis, myxoedema, pernicious anaemia, primary biliary cirrhosis, psoriasis, and thyrotoxicosis. We subdivided the analysis of diabetes mellitus by age as a proxy for type 1 and type 2 diabetes. The type of diabetes is often unrecorded on hospital statistical abstracts, and only type 1 has been demonstrated to have an autoimmune component. Most, if not all, men with diabetes under 30 would have had type 1, those aged 30–49 will include a mix and the great majority >50 would have had type 2. We restricted the analysis of asthma by age because asthma is less reliably differentiated from non-asthmatic chronic obstructive pulmonary disease in older than in younger men. In the cohort study, we included subsequent admissions for testicular atrophy, and for orchitis and epididymitis, because it has been suggested that these may be the possible immune-mediated or granuloma-associated adverse effects of vasectomy (McDonald *et al.*, 1996). The International Classification of Diseases, the coding system used in the database, does not distinguish between orchitis and epididymitis. Accordingly, we refer to the two conditions together.

Results

There were 23 988 men in the vasectomy group and 146 040 in the reference group (Table I). In the matching by age, as Table I shows, there were at least two men in each stratum in the reference group for every one in the vasectomy group, and, in most age groups, there were many more. The mean period of follow-up after vasectomy was 12.8 years and that after hospital care for the reference conditions was 13.2 years.

Case–control study: disease prior to vasectomy

Admission rates for some but not all of the immune-related diseases were low in the vasectomy group, compared with the reference group, in the case–control study (Table II). For example, asthma was significantly less common prior to vasectomy than in the reference group of patients (rate ratio 0.53, comparing the vasectomy and reference group, 95% CI

Table I. Number of men admitted to hospital for vasectomy in each age-group stratum, number of men in the reference group in each age group and the matching ratio of number of men in the reference group matched with those in the vasectomy group

Age groups (years)	Vasectomy group		Reference group	
	n	%	*n*	Matching ratio
20–24	175	0.7	24 825	142
25–29	2757	11.5	22 452	8
30–34	7767	32.4	19 099	2
35–39	7428	31.0	16 723	2
40–44	3825	15.9	15 821	4
45–49	1443	6.0	15 647	11
50–54	432	1.8	15 906	37
55–59	161	0.7	15 567	97
Total	23 988	100.0	146 040	6

Table II. Occurrence of disease prior to vasectomy or reference group[a]: observed number of men with each disease prior to vasectomy, expected number of men with each disease, ratio of observed to expected and 95% confidence intervals (CIs) for the ratio

Disease (ICD code)[b]	Observed number of men in vasectomy group	Expected number of men in vasectomy group[c]	Rate ratio (observed/expected)[c]	95% CIs
Ankylosing spondylitis (720)	4	10.52	0.38	0.10–0.97
Asthma <55 (493)	56	106	0.53	0.40–0.68
Coeliac disease (579.0)	1	1.71	0.59	0.01–3.26
Crohn's disease (555)	31	29.89	1.04	0.70–1.47
Diabetes <30 years (250)	8	10.79	0.74	0.32–1.46
Diabetes 30–49 years	46	71.66	0.64	0.47–0.86
Hashimoto's thyroiditis (245)	0	0.12	0	0–30.7
Idiopathic thrombocytopenia purpura (287.3)	0	0.66	0	0–5.59
Multiple sclerosis (340)	17	14.45	1.18	0.69–1.88
Myasthenia gravis (358)	10	11.5	0.87	0.41–1.59
Myxoedema (244)	2	2.77	0.72	0.09–2.61
Pernicious anaemia (281)	2	2.62	0.76	0.09–2.76
Primary biliary cirrhosis (571.6)	0	0.02	0	0–184
Psoriasis (696.0, 696.1, 696.8, 696.9)	15	14.78	1.01	0.57–1.67
Rheumatoid arthritis (714)	16	13.54	1.18	0.68–1.92
Thyrotoxicosis (242)	4	12.32	0.32	0.09–0.83
Ulcerative colitis (556)	18	26.23	0.69	0.41–1.08

[a]Conditions used in the reference group, with ICD9 code for diagnosis (with equivalent codes used for other coding editions) and Office of Population, Censuses and Surveys (OPCS) code edition 3 for operations: otitis externa, otitis media (ICD9 380–382), upper respiratory tract infections (ICD9 460–466), deflected nasal septum, nasal polyp (ICD9 470–471), impacted tooth and other disorders of teeth (ICD9 520–521), inguinal hernia (ICD9 550), ingrowing toenail and other diseases of nail (ICD9 703), sebaceous cyst (ICD9 706.2), internal derangement of knee (ICD9 717), bunion (ICD9 727.1), strabismus (ICD9 378), selected fractures (ICD9 810–816, 823–826), dislocations, sprains and strains (ICD9 830–839, 840–848), superficial injury and contusion (ICD9 910–919, 920–924), tonsillectomy/adenoidectomy (OPCS 230–236), knee arthroplasty (OPCS 812; excluded from the reference cohort for rheumatoid arthritis) and hip arthroplasty (OPCS 810, 811; excluded from the reference cohort for rheumatoid arthritis).
[b]ICD 9 codes for each immune–related condition (equivalent codes were used for cases coded in ICD Revisions 7, 8 and 10).
[c]On the basis of the occurrence rate in the reference group, applied to the number of people in the vasectomy group, adjusted for age in 5-year bands, district of residence and for time period in single calendar years.

0.40–0.68), as was diabetes mellitus (0.72, 0.55–0.92), ankylosing spondylitis (0.38, 0.10–0.97) and thyrotoxicosis (0.32, 0.09–0.83). This suggests that men who underwent vasectomy were selectively 'healthy' in respect of these diseases compared with the reference cohort. For other conditions, admission rates were similar, prior to vasectomy, to those in the reference cohort; for example, the rate ratios were 1.04 (0.70–1.47) for Crohn's disease, 1.18 (0.69–1.88) for multiple sclerosis and 1.18 (0.68–1.92) for rheumatoid arthritis (Table II).

Cohort study: disease after vasectomy

Immune-related diseases that were low before vasectomy were similarly low in the cohort study of admission rates for disease after vasectomy. For example, the rate ratio for asthma after vasectomy was similar (0.54, 0.43–0.67; Table III) to that before it (Table II), as was that for diabetes (0.68, 0.57–0.82), ankylosing spondylitis (0.57, 0.27–1.08) and thyrotoxicosis (0.45, 0.16–0.99). Considering other diseases with reasonably large numbers, the rate ratios for Crohn's disease were 1.04 and 0.96, respectively, before and after vasectomy; for ulcerative colitis, they were 0.69 and 0.70, respectively, before and after; for multiple sclerosis, they were, respectively, 1.18 and 0.99, before and after (see the tables for CIs, and for other less common diseases). This suggests that vasectomy did not influence the risk of these diseases. There was also no association with testicular atrophy (0.83, 0.27–1.99; Table III), but there was an elevated risk of orchitis/epididymitis after vasectomy (1.45, 1.18–1.78; Table III).

Time intervals after vasectomy

We analysed the data by time intervals after vasectomy to determine whether there was any evidence of an increasing risk of disease with increasing time intervals after operation. Table IV shows the long-term rate ratios after vasectomy for diseases with at least 10 newly recorded cases at ≥10 after operation. There was no evidence for any increase in risk, with increasing time intervals from vasectomy, for asthma, diabetes or multiple sclerosis, considering time intervals of 1–4, 5–9, 10–14 and ≥15 years after vasectomy (Table IV). The rate ratio for orchitis/epididymitis was highest within a year of vasectomy (2.67, 1.80–3.87; Table IV). The rate ratio was still elevated 1–4 years after vasectomy, but was of borderline significance (1.48, 1.00–2.13; Table IV) and it dropped to 0.92 (0.44–1.71) at 10–14 years after vasectomy. There was no evidence of an increase in risk with increasing time intervals after operation for the other diseases with smaller numbers (data available from the authors).

Discussion

The strengths of the study include the facts that it is large in scale and it covers a long mean period of follow-up. The original recording of vasectomy and the original recording of subsequent disease were independent of one another. The records were only linked subsequently. This study design precludes any biases, such as response bias, that might occur in interview-based studies.

Table III. Occurrence of disease after vasectomy: observed number of people in the reference group[a] with each disease, observed and expected number of people with disease in the vasectomy group, ratio of rate in the vasectomy group to that in the reference group and 95% CIS for the rate ratio

Disease(ICD code)[b]	Observed number in reference group[b]	Observed number in vasectomy group	Expected number in vasectomy group[c]	Adjusted rate ratio[c]	95% CIs
Ankylosing spondylitis (720)	190	10	16.8	0.57	0.27–1.08
Asthma <55 (493)	2148	89	160	0.54	0.43–0.67
Coeliac disease (579.0)	130	4	5.4	0.73	0.20–1.92
Crohn's disease (555)	344	20	20.8	0.96	0.58–1.50
Diabetes <30 years (250)	160	1	1.70	0.58	0.02–3.27
Diabetes 30–49 years	700	53	87.9	0.57	0.43–0.76
Hashimoto's thyroiditis (245)	60	3	1.30	2.37	0.47–7.25
Idiopathic thrombocytopenia purpura (287.3)	48	2	3.10	0.62	0.07–2.37
Multiple sclerosis (340)	396	30	30.2	0.99	0.66–1.44
Myasthenia gravis (358)	140	3	4.50	0.66	0.13–1.96
Myxoedema (244)	513	6	9.60	0.62	0.23–1.37
Pernicious anaemia (281)	134	6	5.10	1.19	0.43–2.67
Primary biliary cirrhosis (571.6)	43	3	1.40	2.15	0.43–6.72
Psoriasis (696.0, 696.1, 696.8, 696.9)	337	15	22.0	0.67	0.37–1.12
Rheumatoid arthritis (714)	1393	49	52.0	0.94	0.69–1.25
Thyrotoxicosis (242)	422	6	13.1	0.45	0.16–0.99
Ulcerative colitis (556)	531	28	38.9	0.70	0.46–1.03
Testicular atrophy (608.3)	159	5	6.0	0.83	0.27–1.99
Orchitis/epididymitis (604.9)	907	106	75.5	1.45	1.18–1.78

[a]Conditions used in the reference group, with ICD9 code for diagnosis (with equivalent codes used for other coding editions) and Office of Population, Censuses and Surveys (OPCS) code edition 3 for operations: otitis externa, otitis media (ICD9 380–382), upper respiratory tract infections (ICD9 460–466), deflected nasal septum, nasal polyp (ICD9 470–471), impacted tooth and other disorders of teeth (ICD9 520–521), inguinal hernia (ICD9 550), ingrowing toenail and other diseases of nail (ICD9 703), sebaceous cyst (ICD9 706.2), internal derangement of knee (ICD9 717), bunion (ICD9 727.1), strabismus (ICD9 378), selected fractures (ICD9 810–816, 823–826), dislocations, sprains and strains (ICD9 830–839, 840–848), superficial injury and contusion (ICD9 910–919, 920–924), tonsillectomy/adenoidectomy (OPCS 230–236), knee arthroplasty (OPCS 812; excluded from the reference cohort for rheumatoid arthritis) and hip arthroplasty (OPCS 810, 811; excluded from the reference cohort for rheumatoid arthritis).
[b]ICD 9 codes for each immune–related condition (equivalent codes were used for cases coded in ICD Revisions 7, 8 and 10).
[c]On the basis of the occurrence rate in the reference group, applied to the number of people in the vasectomy group, adjusted for age in 5-year bands, district of residence and for time period in single calendar years.

Men who undergo vasectomy might be more healthy (or less healthy) than men in the general population in respect of particular diseases. However, we took account of this possibility by using a study design that allowed us to study and compare the rate ratios for each individual disease before and after vasectomy. Our stratification, in analysis, meant that the comparisons between rates in the vasectomy and reference groups compare 'like with like' with respect to age, year of event and district of treatment.

The study design also has some inherent weaknesses. We were unable to take account of other potential but unrecorded sources of bias. The study was confined to men who underwent vasectomy in a hospital setting, as day-case patients or inpatients, and omits operations at ambulatory care settings. We think that, in this population, selection for vasectomy in a hospital rather than an ambulatory care clinic was more a function of service provision and surgeons' preference than of patients' clinical characteristics. However, selection biases relevant to our study are possible. If patients' clinical characteristics influenced the decision to admit, men with chronic diseases, such as those studied by us, would have been more likely than others to have been admitted. In other words, if biases related to the decision to admit patients were present, disease rates would have been relatively high rather than low at the time of operation in the vasectomy population, but they were not. The simplest explanation for our findings about admission for disease before vasectomy is that, in this English population, men with some chronic diseases, such as asthma, diabetes or thyrotoxicosis, were a little less likely than others to choose vasectomy as a method of contraception. We were unable to identify any literature on the contraceptive methods preferred in England by partners of men with chronic diseases. It seems reasonable to speculate, however, that they may differ from the general population; for example, fertility may be reduced in some men with thyrotoxicosis and some clinicians may prefer not to operate on people with diabetes because of the risk of wound-associated infection.

Our data on disease, before or after vasectomy, are confined to patients who received hospital care either as day cases or as inpatients. It would be useful to be able to express the hospitalized population with each disease as a percentage of the total population with the disease. However, there are no data available, for the time and population covered by this study, on which to base such a calculation. Over a mean period of 13 years, that is, the mean period of follow-up in this study, the percentage of all people with the disease who receive specialist hospital care is likely to be fairly high for some diseases (e.g. multiple sclerosis, Crohn's disease, ulcerative colitis) and low for others (e.g. asthma and perhaps diabetes). Thus, our findings on each disease are confined to people whose disease is severe enough to warrant day-case or inpatient care. This is the case for both the vasectomy cohort and the reference cohort with which the vasectomized men were compared. We cannot discount the possibility that vasectomy results in an elevation of risk that is confined to milder disease only and that this would be missed by our methods,

Table IV. Rate ratios for selected diseases and time intervals after vasectomy.

Disease (years after vasectomy)	Observed number in vasectomy cohort	Expected number in vasectomy cohort[a]	Adjusted rate ratio[a]	95% CIs
Asthma <55				
<1 year	6	13.7	0.42	0.16–0.92
1–4 years	27	44.6	0.59	0.39–0.85
5–9 years	26	42.2	0.60	0.39–0.88
10–14 years	18	30.8	0.57	0.34–0.90
≥ 15 years	12	28.7	0.41	0.21–0.71
Diabetes <50				
<1 year	6	9.2	0.65	0.24–1.42
1–4 years	13	30.8	0.42	0.22–0.72
5–9 years	19	26.5	0.68	0.41–1.08
10–14 years	9	15.4	0.56	0.25–1.06
≥ 15 years	7	9.9	0.67	0.27–1.39
Multiple sclerosis				
<1 year	4	5.4	0.72	0.19–1.93
1–4 years	10	9.9	1.01	0.47–1.92
5–9 years	5	4.5	1.12	0.35–2.72
10–14 years	5	5.2	0.96	0.31–2.25
≥ 15 years	6	6.0	1.00	0.36–2.19
Rheumatoid arthritis				
<1 year	0	3.6	0	0–1.01
1–4 years	11	12.1	0.90	0.45–1.62
5–9 years	12	13.5	0.88	0.46–1.55
10–14 years	6	10.3	0.58	0.21–1.27
≥ 15 years	20	18.1	1.10	0.67–1.70
Orchitis/epididymitis				
<1 year	37	16.2	2.67	1.80–3.87
1–4 years	34	23.9	1.48	1.00–2.13
5–9 years	19	18.2	1.11	0.66–1.76
10–14 years	10	11.6	0.92	0.44–1.71
≥ 15 years	6	14.0	0.46	0.17–1.00

[a]On the basis of the occurrence rate in the reference group, applied to the number of people in the vasectomy group, adjusted for age in 5-year bands, district of residence and for time period in single calendar years.

but a causal relationship between vasectomy and only mild disease seems unlikely.

Is it possible that clinicians' knowledge of patients' vasectomy status could have influenced the decision to admit them for subsequent disease? For each of the diseases studied by us, it seems unlikely that clinicians would be selectively less likely to admit men whom they knew to have been vasectomized than others. It also seems unlikely that they would be selectively more likely to admit men who had been vasectomized than others, with the possible exception of admission for a diagnosis of testicular atrophy or orchitis/epididymitis. This type of selection bias could lead to an apparent elevation of risk of these diseases when identified from hospital records alone. However, we did not find any elevation of risk of testicular atrophy associated with vasectomy, but found an elevation of risk of orchitis/epididymitis, which we discuss further below.

It is possible that our follow-up is too short to detect an elevation of risk if it occurs after a very long latent period. Sotolongo (1982) reported that the highest levels of sperm-related autoantibody titres are typically found about a year after vasectomy. However, he also commented on the evidence that, in some subjects, antibody titres may either remain at the same level or increase over a period of 5–12 years post-operatively. For asthma, diabetes, multiple sclerosis, rheumatoid arthritis and orchitis/epididymitis—conditions with sufficient cases for us to compare time intervals in detail after vasectomy (Table IV)—it is reassuring that there is no evidence of increasing rate ratios with increasing time from vasectomy.

The one significantly raised risk after vasectomy was that for orchitis/epididymitis. Unfortunately, we cannot distinguish the two and have no access to clinical and pathological sample data. The association was strongest in the short term (Table IV), and the most likely explanation is that the elevation of risk is for post-operative granulomatous lesions. Assuming that the excess cases of orchitis/epididymitis in our vasectomy group ($106 - 75.5 = 30.5$; Table III) are all attributable to vasectomy, this gives an attributable risk of 0.1 cases per 100 operations (30.5 in 23 988 men). Schmidt (1995) reported on a series of 6248 vasectomized men in whom there were subsequent spermatic granuloma in 0.9% (56 men) and granuloma that required epididymectomy for pain in 0.1% (6 men). Thus, the rate of complications serious enough to warrant hospital admission for epididymitis in our study, and to warrant epididymectomy in Schmidt's, is broadly similar.

The simplest explanation for our findings about admission for other diseases after vasectomy is that vasectomy does not increase the risk of these diseases. It is possible that the diseases studied, and found to have low rate ratios before and after vasectomy, were systematically low because the vasectomy group and the reference group differ from one another

in respect of unidentified confounders. Thus, for example, if the vasectomy group was systematically healthier in respect of lifestyle or other aspects of socio-economic status, and if these same factors protect against the immune-related conditions, a lower rate ratio in the vasectomy cohort than the reference group would be expected. However, given that we compared the same people before and after vasectomy, the rate ratio would be similarly low both before and after vasectomy if there is no increase in risk associated with vasectomy. This is what we found, and the conclusion that vasectomy does not subsequently increase the risk of the diseases still holds.

The most important evidence in our data, supporting the hypothesis that vasectomy does not increase the long-term risk of the diseases studied, is that on time intervals after operation. None of the diseases studied was more common than expected at long time intervals after operation, and comparing risk ratios at short and long time intervals after operation, there was no evidence of an increase in risk with increasing time from vasectomy.

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