Sexual factors and prostate cancer

G.G. GILES, G. SEVERI*, D.R. ENGLISH, M.R.E. MCCREDIE†, R. BORLAND‡, P. BOYLE* and J.L. HOPPER¶

*Cancer Epidemiology Centre, and ‡Centre for Behavioural Research in Cancer, The Cancer Council Victoria, Melbourne, Australia, *Division of Epidemiology & Biostatistics, European Institute of Oncology, Milan, Italy, †Department of Preventive & Social Medicine, Dunedin Medical School, University of Otago, Dunedin, New Zealand, and ¶Centre for Genetic Epidemiology, University of Melbourne, Melbourne, Australia*

Accepted for publication 12 April 2003

OBJECTIVE

To assess whether prostate cancer might be related to hormone levels and, by inference, to differences in sexual activity.

PATIENTS, SUBJECTS AND METHODS

In a case-control study of men with prostate cancer aged <70 years at diagnosis and age-matched control subjects, information was collected on two aspects of sexual activity; the number of sexual partners and the frequency of total ejaculations during the third to fifth decades of life.

RESULTS

There was no association of prostate cancer with the number of sexual partners or with the maximum number of ejaculations in 24 h. There was a negative trend ($P < 0.01$) for the association between risk and number of ejaculations in the third decade, independent of those in the fourth or fifth. Men who averaged five or more ejaculations weekly in their 20s had an odds ratio (95% confidence interval) of 0.66 (0.49–0.87) compared with those who ejaculated less often.

CONCLUSIONS

The null association with the number of sexual partners argues against infection as a cause of prostate cancer in this population. Ejaculatory frequency, especially in early adult life, is negatively associated with the risk of prostate cancer, and thus the molecular biological consequences of suppressed or diminished ejaculation are worthy of further research.

KEYWORDS

prostate cancer, sexual factors, case-control study

INTRODUCTION

Although it is generally accepted that prostate cancer is a hormone-dependent malignancy, its causes remain poorly understood [1]. The idea that prostate cancer risk might be related to men's hormonal milieu, and therefore possibly to differences in sexual activity, has been pursued in several epidemiological investigations; a recent meta-analysis [2] of published studies reported a higher risk associated with a history of sexually transmitted infections, with an odds ratio (OR) of 1.4 (95% CI 1.2–1.7), with frequency of sexual activity (1.2, 1.1–1.3 for an increase of three times a week) and with increasing numbers of sexual partners (1.2, 1.1–1.3 for an increase of 20 partners). Although ever-married men were suggested to be at a slightly increased risk (1.17, 0.98–1.40), the meta-analysis did not support associations with multiple marriages, age at first intercourse or age at first marriage. Those authors concluded that there was support for an association with sexually transmitted infection and with sexual activity. However, an infection theory is inconsistent with other observations, e.g. the lack of correlation between the incidence of prostate cancer and cancer of the cervix [1], and the increased mortality from prostate cancer in presumably celibate Roman Catholic priests [3].

For the association with sexual activity the review noted possible hormonal influences but concluded that; 'the mechanism through which frequency of sexual activity may be related to prostate cancer is unclear' [2]. In the studies reviewed, the measurement of sexual activity was almost always restricted to episodes of sexual intercourse. If the relevant 'exposure' from sexual activity is the amount of prostatic secretion, then this restriction may lead to substantial misclassification, especially in early adulthood and in later life, when sexual intercourse may be less frequent.

We therefore attempted to clarify associations between the risk of prostate cancer before the age of 70 years and several aspects of sexual activity, with a special focus on total ejaculations rather than sexual intercourse alone. We also attempted to investigate whether associations with sexual activity were age-dependent by estimating ejaculatory frequencies in the patients' third, fourth and fifth decades.

PATIENTS, SUBJECTS AND METHODS

We carried out a population-based, case-control study of prostate cancer in Australia, details of which were published previously [4]. Its principal purpose was to examine associations between lifestyle factors and the diagnosis of 'clinically important' prostate cancer. To this end we excluded tumours that were well-differentiated (i.e. low-grade or Gleason score < 5). We also focused on early-onset disease, as we were interested in finding factors relevant to the prevention of prostate cancer that would cause premature mortality. Eligible cases comprised all male residents of Melbourne, Sydney and Perth diagnosed from 1994 to 1997 who were aged <70 years at diagnosis and who were registered to vote on the State Electoral Rolls (adult registration to vote is compulsory in Australia). All cases diagnosed before the age of 60 years and random samples of half of cases diagnosed aged 60–64 and 25% of cases diagnosed aged 65–69 years were selected. Controls were randomly selected from the current State Electoral Rolls, and were frequency-matched to the age distribution of the cases in a ratio of one control per case. The response rate was 65% in cases and 50% in controls [4]. In cases

the response rates declined with age (40–49, 74%; 50–59, 68%; 60–69, 62%) and this was also true in controls (56%, 53% and 49%, respectively). Prior approval of the study protocol was obtained from all relevant Human Research Ethics Committees [4].

Direct interviews were conducted, usually at the man's home, at the end of which a sexual history questionnaire was given to each subject to complete by himself while the interviewer checked through the dietary questionnaires for completeness and obvious errors. The interviewer was available to respond only to the man's questions of definition (each interviewer was provided with plain-language explanations of terms used in the questions). The questionnaire was developed using focus groups to ensure that the language was appropriate and that the questions were acceptable, comprehensible and likely to be answered. On this basis, we chose not to ask questions about sexually transmitted diseases, but included questions about the number of sexual partners before and after the age of 30 years (male and female partners were asked about this separately). The questionnaire focused on ejaculation irrespective of the context in which it occurred (intercourse with another, masturbation, nocturnal emissions, etc.). Men were asked their age at first ejaculation, the maximum number of ejaculations ever experienced in 24 h, and to estimate the average number of times that they had ejaculated per week in their most sexually active year in each of three decades of age (i.e. third, fourth and fifth). To preserve privacy, the subject sealed the questionnaire in an unmarked envelope before returning it to the interviewer.

Unconditional multiple logistic regression was used, adjusting for reference age, study centre, calendar year, family history and country of birth. Polytomous logistic regression was used to assess differences in ORs by tumour grade [5]. All continuous variables were divided into quantiles of the distribution in the controls, except for the number of male partners, which was dichotomized because of the few exposed subjects. For a direct comparison, the number of female partners was presented in the categories used by Rosenblatt *et al.* [6] (1, 2–4, 5–14, 15–29, >29).

Lastly, to examine the effect of the number of ejaculations in the third decade, considering the number of ejaculations in the fifth (as these two were the least correlated decades) a variable was fitted with 16 categories, each representing a combination of the quartiles for the two decades.

Characteristic	Cases (1079) Number (%):	Controls (1259) Number (%):
Reference age group, years		
< 55	169 (15.7)	236 (18.7)
55–59	306 (28.4)	275 (21.8)
60–64	264 (24.5)	358 (28.4)
65–69	340 (31.5)	390 (31.0)
Country of birth		
Not Australia	322 (29.8)	488 (38.8)
Australia	757 (70.2)	771 (61.2)
Educational level		
Primary only	74 (6.9)	118 (9.4)
Secondary only	349 (32.3)	414 (32.9)
Post secondary training	472 (43.7)	541 (43.0)
Tertiary	184 (17.1)	184 (14.6)
Family history		
No 1° relative affected	900 (83.4)	1180 (93.7)
Any 1° relative affected	179 (16.6)	79 (6.3)
Marital status		
Married/living as married	919 (85.2)	1061 (84.3)
Formerly married/widowed	126 (11.7)	132 (10.5)
Never married	33 (3.1)	62 (4.9)
Smoking		
Never	386 (35.8)	438 (34.8)
Current	147 (13.6)	241 (19.1)
Former	546 (50.6)	579 (46.0)

TABLE 1
*The demographic characteristics of cases and controls**

**Some values are missing for educational level, marital status and smoking.*

RESULTS

After excluding men with missing data on the variables to be controlled for in the analysis, there remained 1079 cases and 1259 controls. Table 1 shows that cases were more likely than controls to be born in Australia, and to have at least one first-degree relative affected with prostate cancer. There were no major differences in age, education, smoking habit or marital status distributions between cases and controls.

Table 2 shows that those 'never married' had almost half the risk of the 'ever married' ($P = 0.05$), but there was no evidence that the total number of female sexual partners was associated with risk ($P = 0.8$). Men with a history of male sex partners had about two-thirds the risk ($P = 0.2$) but this was based on few men (≈ 2.5% of controls). Nor was there any evidence that the number of children was associated with risk; the OR (95% CI) for one, two, three and more than three children compared with no children were 0.97 (0.73–1.29), 1.09 (0.81–1.46) and 0.95 (0.70–1.28), respectively (P trend = 0.61).

There was no association with either age at first ejaculation or with maximum ejaculatory frequency in 24 h ($P = 0.8$ and 0.2, respectively). Greater ejaculatory frequency in the most sexually active year in each of the three decades was associated with a significantly lower risk, with men in the upper quartile of ejaculatory frequency having about two-thirds the risk of those in the lower quartile for the third and fourth decade, and four-fifths the risk for the fifth. Ejaculatory frequencies in each of the decades were correlated with one another ($r = 0.5$–0.7). A similar finding related to the total number of ejaculations over the three decades. Those who reported an average of four to five or more ejaculations per week had two-thirds the risk compared with those who, on average, ejaculated less than three times per week.

Adjusting for ejaculatory frequency had little influence on any associations with the other

TABLE 2 The association between marital status and indicators of sexual activity, with prostate cancer in Australian men aged < 70 years

Variable	Controls	Cases	OR (95% CI)	P trend
Marital status				0.05*
Married/living as married	1061	919	1.00	
Formerly married	132	126	1.00 (0.81–1.48)	
Never married	62	33	0.56 (0.34–0.92)	
Total female partners				0.5
1	317	318	1.00	
2–4	326	267	0.86 (0.66–1.11)	
5–14	312	259	0.91 (0.70–1.19)	
15–29	84	75	1.03 (0.69–1.55)	
> 29	89	73	0.88 (0.59–1.32)	
Total male partners				0.7
nil	1153	1011	1.00	
≥ 1	29	24	0.66 (0.35–1.24)	
Age at first ejaculation, years				0.5
< 14	426	379	1.00	
14	302	280	1.11 (0.87–1.42)	
15	169	145	1.10 (0.81–1.49)	
> 15	212	173	0.98 (0.74–1.30)	
Maximum ejaculation frequency/24 h				0.4
< 3	560	468	1.00	
3	309	285	1.14 (0.90–1.44)	
4	168	126	0.87 (0.64–1.18)	
> 4	174	174	1.22 (0.92–1.62)	
Frequency of ejaculations/week:				
in 20s				< 0.01
≤ 3	438	431	1.00	
3–5	258	265	1.09 (0.84–1.40)	
5–7	294	208	0.67 (0.52–0.87)	
> 7	227	148	0.66 (0.49–0.87)	
in 30s				< 0.01
< 3	532	548	1.00	
3–4	194	146	0.77 (0.58–1.03)	
4–7	342	269	0.82 (0.65–1.04)	
> 7	147	94	0.65 (0.47–0.90)	
in 40s				< 0.01
≤ 2	495	485	1.00	
2–3	271	224	0.82 (0.64–1.06)	
3–4	160	134	0.92 (0.68–1.24)	
> 4	282	207	0.79 (0.62–1.02)	
All decades				< 0.01
< 2.33	247	272	1.00	
2.34–3.33	235	219	0.86 (0.64–1.14)	
3.34–4.66	245	222	0.88 (0.66–1.17)	
4.67–7	263	189	0.64 (0.47–0.85)	
> 7	207	142	0.65 (0.47–0.89)	

*Estimates from the logistic model adjusted for age, centre, year of diagnosis/selection, family history of prostate cancer and country of birth. *P from likelihood ratio test that all ORs are equal to unity.*

variables reported in Table 2. Furthermore, analyses restricted to the married/living as married cases, and analyses in which educational status or marital status was also controlled for, gave estimates that differed negligibly from those presented. OR estimates did not differ between moderate and high-grade disease.

When the log OR was estimated as a linear function of the quartile of the number of ejaculations, each quartile increase changed the OR by −15% for the third ($P < 0.001$), −12% for the fourth ($P = 0.007$) and −7% for the fifth decade ($P = 0.1$). When fitted in the same model, the estimates for the second decade remained at −15% ($P = 0.007$), while the estimates for the other two became negligible at −3% ($P = 0.7$) and +2% ($P = 0.8$), respectively. This observation was confirmed by using combinations of the quartiles in the third and fifth decades in the logistic model (Table 3). The decrease in risk with increasing ejaculatory frequency in the third remained irrespective of the ejaculatory frequency in the fifth decade.

DISCUSSION

In this large case-control study of aspects of male sexual life and prostate cancer risk, there was no association with the number of female sexual partners or children, but a positive association with being married. There was also no association with the maximum number of ejaculations ever made in 24 h but a negative association with men's frequency of ejaculations, especially in their most sexually active year during their 20s.

We considered the extent to which our findings might be caused by bias or confounding. Although the response in controls was low, their sociodemographic profile was similar to that of men in the National Health Survey in 1995 [8] and similar to those found in some other case-control studies in recent years [9–11]. Because of the widespread PSA testing that occurred during recruitment [12], we compared moderate- with high-grade tumours; the associations were at least as strong for high-grade prostate cancer. Having controlled for the strongest established risk factors (age and family history) and, given the lack of other known risk factors, we consider that confounding is unlikely to have influenced our findings. We have no information on the sexual histories of the cases and controls not

responding, or whether they differ between cases and controls, and therefore cannot exclude the possibility of response bias influencing our findings.

COMPARISONS WITH OTHER STUDIES

The present positive association with marital status was reported by several studies [2] but its meaningfulness today, given the contemporary heterogeneity of marital status, is difficult to define. Lack of association with the number of female sexual partners is consistent with about half of the published case-control studies covered in the meta-analysis [2] but contrasts strongly with a recent case-control study in Seattle [6] to which we matched our analysis. There are several reports of positive associations with venereal disease and with high-risk behaviour, e.g. intercourse with prostitutes, having sex without condoms and having many sex partners [2]. However, an infection hypothesis is not the only possible explanation for these observations, as the activities they describe could be markers for having a strong sex drive that may hypothetically be associated with increased prostate cancer risk via hormone levels, but this hypothesis is not consistent with the present decreased risk associated with increased number of ejaculations.

There might be three major reasons why our findings for sexual activity are opposite to those from some other studies; (i) the scope of sexual activity included; (ii) the temporal frame covered; and (iii) how the questionnaire was administered. Most other studies have measured sexual activity by reference solely to sexual intercourse [2]. Few have asked about all forms of ejaculation [13,14]. As prostatic secretion is not limited solely to episodes of sexual intercourse, studies that focus only on sexual intercourse do not fully ascertain the exposure, i.e. prostatic secretion by ejaculation. However, should there be a causal sexually transmitted infectious agent, our exposure measure of 'total ejaculations' would dilute any such exposure by including ejaculations experienced without having sexual intercourse. If this is the case, had we been able to remove 'ejaculations associated with sexual intercourse', there should have been an even stronger protective effect of other ejaculations.

The few studies that measured total ejaculations are more consistent in their findings. Banerjee [13] described a significantly lower frequency of ejaculations in cases than in controls during the sexually active parts of their lives. Although statistically insignificant, Hsieh *et al.* [14] also found suggestive evidence that increased ejaculatory frequency early in life might reduce the risk. Our finding is also consistent with that of Steele *et al.* [15], of an increased risk of prostate cancer after some period of reduced sexual activity. It is also consistent with the hypothesis of Isaac [16], that infrequent ejaculation could increase the risk of prostate cancer because of the possible stagnation of carcinogenic secretions in the prostatic acini.

Apart from age at first marriage, few studies [13,14] have measured sexual activity at different times of life. We found that ejaculatory frequencies in the third to fifth decades were highly correlated, but when they were modelled together the strongest effect was for the number of ejaculations in the second, while the effects of the number of ejaculations at other ages became inconsequential. This observation once more indicates earlier life experiences as predictors of much later outcomes.

In attempting to compare studies from different societies, defined both geographically and historically, the probability must be considered that sexual mores and behaviour are socio-culturally determined and have changed over time. In many communities the method of measuring sexual activity might influence not only the scope of questions that might be asked but also the response. Other studies have used both direct (face-to-face) [13,17] and telephone interviews [6,18], compared with the present, in which we used a self-administered questionnaire [4]. It is difficult to believe that men's responses to questions of sexual activity, use of prostitutes, sexual orientation and sexually transmitted disease would not be influenced by the age and gender of the interviewer in a direct or telephone setting, as there would be a strong inclination to give more socially acceptable answers, particularly by participants in the older studies and by older respondents.

Frequency (/week) of ejaculation	In most sexually active year during 40s			
	< 2	2–3	3–4	> 4
In the most sexually active year during 20s				
< 3†	1.00 (310/278)	0.50* (67/103)	1.08 (23/19)	1.00 (27/29)
3–5	0.84 (96/93)	1.03 (80/77)	1.06 (61/56)	0.84 (27/30)
5–7	0.48* (47/76)	0.63* (56/63)	0.53* (34/60)	0.68 (69/91)
> 7	0.60 (29/44)	0.77 (21/26)	0.55 (16/25)	0.53* (81/129)

TABLE 3
The combined effect of ejaculations in the third and fifth decade on the risk of prostate cancer in Australian men aged < 70 years

†Reference category;
**P < 0.05 compared with the reference category.*

POSSIBLE BIOLOGICAL MECHANISMS

If men who develop prostate cancer report fewer ejaculations throughout their sexually active life, especially in their most sexually active year of their 20s, why should this be? In the present study, both age at commencing ejaculation and the maximum number of ejaculations achieved in 24 h did not differ between cases and controls, so the two groups of men would appear to have similar powers of ejaculation. What could explain the difference?

The first possible explanation is that any difference in ejaculatory frequency is a result of some form of bias, e.g. cases may have been more truthful in estimating their ejaculatory frequencies, while controls may have embellished their performance, or vice versa. We do not consider such a bias to be very probable, as the questions were self-administered, respondents were not cognisant of any *a priori* hypothesis, and the interviewer was not privy to the responses. Also, if controls had been more disposed than cases to exaggerate their performance, we would have expected the estimates for maximum ejaculatory frequency in 24 h and for the numbers of sexual partners also to have been exaggerated, but they were not.

A second possibility is that men who ejaculate less frequently, especially in early adulthood,

have lower levels of whatever hormones drive sexual desire. The extent to which libido is determined by androgens is poorly understood, as testosterone levels in the normal range do not seem to have an important influence on libido in eugonadal men [19,20]. However, one small study reported a positive association between testosterone levels and orgasm frequency in 33 young men [21]. Another study of Greek army recruits, found that serum dihydrotestosterone (DHT) was the only independent hormonal predictor of frequency of orgasms; an increase of 1.36 nmol/L corresponding to an average increase of one orgasm per week [22]. In the prostate, testosterone is converted to DHT by 5α-reductase type 2. It has been proposed that polymorphisms in the 5α-reductase type 2 gene might affect the levels of circulating DHT (and therefore libido and orgasms) regardless of the abundance of circulating testosterone [23]. Oestrogen (oestradiol) might also be important in stimulating male sexual behaviour [24], but this is not a consistent finding [20], and it has been shown that DHT does not require aromatization to maintain sexual function in men with already established sex lives [25]. On the other hand, levels of bioavailable testosterone decline with age while levels of luteinizing hormone increase and the diminishing ratio of levels of testosterone to luteinizing hormone has been shown to be associated with decreased sexual activity [26]. As well as luteinizing hormone, levels of prolactin also increase with age and are positively associated with loss of libido and diminished frequency of sexual intercourse [27].

Could any of the hormones that influence sexual desire also influence the risk of prostate cancer? Although prostate cancer is known to be hormone-dependent, direct evidence of an influence of hormones on prostate cancer risk has been difficult to establish [1]. A review of eight prospective studies concluded that, with the possible exception of androstanediol glucuronide, there were no large differences in average levels of circulating hormones between men who go on to develop prostate cancer and those who remain free of disease [28]. A more recent review by Bosland [29] commented that associations might have been missed because of inappropriate measurements or failure to adjust levels for those of other hormones. Bosland identified high testosterone to DHT ratios (an indicator of reduced 5α-reductase activity) as one of the more consistent findings, and elevated testosterone or androstenedione, and decreased sex-hormone binding globulin (SHBG) or oestradiol. Only in one of the better prospective cohort studies of serum hormone levels and prostate cancer were appropriate adjustments made for the concentration of other hormones [30]. That study found positive associations with circulating levels of testosterone within the normal range (stronger in older men and men with advanced disease), and negative associations with levels of SHBG and oestradiol and, in older men, DHT [30]. Thus there is emerging evidence that circulating levels of testosterone (and other hormones) are associated with the risk of (some subgroups of) prostate cancer, but their individual actions, time of action, and possible interaction with prostate tissue levels [29], and with other molecular pathways, is far from clear [23].

Another explanation is that men who ejaculate less often than the average do so from deliberate choice. The frequency of ejaculation is the product of libido and opportunity, the latter being influenced strongly by social mores. For example, it is conceivable that certain men with normal levels of sexual desire might also have strong inhibitions about masturbation, and for a variety of reasons (the absence of a sexual partner, a partner's loss of interest, or celibacy for religious or other reasons [3]) may have reduced access to sexual intercourse.

If high levels of circulating androgens are associated with both increased libido and increased risk of prostate cancer, our observation of a protective effect of increased ejaculations is difficult to reconcile with this hypothesis. However, it appears likely that hormones other than androgens are involved in male sexual desire, and their importance may be established early in postpubertal life, when the prostate gland is approaching its adult size. The relative abundance in ageing males of luteinizing hormone and prolactin compared with androgens, and its effect on sexual desire and hence prostatic function, might also be worthy of further investigation. Our observation that the protective effect of ejaculation was strongest in the third decade also deserves further consideration. Did the men who ejaculated less than average in their 20s choose to do so, or was this determined by their hormonal milieu? Whatever the reason might be for reduced ejaculatory frequency, it is important to understand its biological consequences and their relevance to prostatic carcinogenesis.

In conclusion, we consider that the present results are consistent with the original observations of Steele *et al.* [15], that a reduced ejaculatory output in otherwise normal males is associated with an increased risk of prostate cancer, especially if this commences early in adulthood. The role of circulating hormones in this phenomenon remains an open question, as does the possible molecular biological consequences to the prostate not only of inhibiting ejaculation around the time when the gland grows to maturity and undergoes terminal differentiation, but also decreased ejaculatory frequency in later life. The concept of prostatic carcinogenesis involving the chronic modulation/interaction of prostatic glandular cells with their luminal fluid [16] provides a framework for further research on these questions.

ACKNOWLEDGEMENTS

This study was funded by a grant from the National Health and Medical Research Council (940394) and was further supported by funding from Tattersall's and The Whitten Foundation, as well as infrastructure provided by The Cancer Council Victoria. The contribution of Dr Severi and Prof Boyle was within the framework of support from the Italian Association of Cancer Research (Associazione Italiana per la Ricerca sul Cancro). We acknowledge the work of our consultant urologist Mr Warren Johnson, the study coordinator Margaret Staples and the research team, Bernadette McCudden, John Connal, Richard Thorowgood, Chris Costa, Melodie Kevan and Sue Palmer. We thank the many urologists who kindly assisted us by providing information and access to their patients. We also express our gratitude to the many men who participated.

REFERENCES

1 Ross RK, Schottenfeld D. Prostate cancer. In Schottenfeld D, Fraumeni JF Jr eds, *Cancer Epidemiology and Prevention*, 2nd edn. New York: Oxford University Press, 1996: 1180–206

2 Dennis LK, Dawson DV. Meta-analysis of measures of sexual activity and prostate cancer. *Epidemiology* 2002; **13**: 72–9
3 Ross RK, Deapen DM, Casagrande JT, Paganini-Hill A, Henderson BE. A cohort study of mortality in Catholic priests. *Br J Cancer* 1981; **43**: 233–5
4 Giles GG, Severi G, Sinclair R *et al.* Androgenetic alopecia and prostate cancer: findings from an Australian case-control study. *Cancer Epidemiol Biomarkers Prev* 2002; **11**: 549–53
5 Hosmer DW, Lemeshow S. *Applied Logistic Regression*. New York: Wiley, 1989
6 Rosenblatt KA, Wicklund KG, Stanford JL. Sexual factors and the risk of prostate cancer. *Am J Epidemiol* 2001; **153**: 1152–8
7 Easton DF, Peto J, Babicker AG. Floating absolute risk. An alternative to relative risk in survival and case-control analysis avoiding an arbitrary reference group. *Statistics Med* 1991; **10**: 1025–35
8 McCredie MRE, Staples M, Johnson W, English D, Giles GG. Prevalence of urinary symptoms in a population-based sample of Australian men. *J Epidemiol Biostats* 2001; **6**: 211–8
9 Jain MG, Hislop GT, Howe GR, Ghadirian P. Plant foods, antioxidants, and prostate cancer risk: findings from case-control studies in Canada. *Nutr Cancer* 1999; **34**: 173–84
10 Rohan TE, Howe GR, Burch JD, Jain M. Dietary factors and risk of prostate cancer: a case-control study in Ontario. *Can Cancer Causes Control* 1995; **6**: 145–54
11 Kolonel LN, Hankin JH, Whittemore AS *et al.* Vegetables, fruits, legumes and prostate cancer: a multiethnic case-control study. *Cancer Epidemiol Biomarkers Prev* 2000; **9**: 795–804
12 Smith DP, Armstrong BK. Prostate-specific antigen testing in Australia and association with prostate cancer incidence in New South Wales. *Med J Aust* 1998; **169**: 17–20
13 Banerjee AK. Carcinoma of the prostate and sexual activity. *Urology* 1986; **28**: 159
14 Hsieh CC, Thanos A, Mitropoulos D, Deliveliotis C, Mantzoros CS, Trichopoulos D. Risk factors for prostate cancer: a case-control study in Greece. *Int J Cancer* 1999; **80**: 699–703
15 Steele R, Lees RE, Kraus AS, Rao C. Sexual factors in the epidemiology of cancer of the prostate. *J Chronic Dis* 1971; **24**: 29–37
16 Isaacs JT. Prostatic structure and function in relation to the etiology of prostatic cancer. *The Prostate* 1983; **4**: 351–66
17 Mandel JS, Schuman LM. Sexual factors and prostatic cancer: results from a case-control study. *J Gerontol* 1987; **42**: 259–64
18 Honda GD, Bernstein L, Ross RK, Greenland S, Gerkins V, Henderson BE. Vasectomy, cigarette smoking and age at first sexual intercourse as risk factors for prostate cancer in middle aged men. *Br J Cancer* 1998; **57**: 326–31
19 Anderson RA, Bancroft J, Wu FC. The effects of endogenous testosterone on sexuality and mood of normal men. *J Clin Endocrinol Metab* 1992; **75**: 1503–7
20 Buena F, Swerdloff RS, Steiner BS *et al.* Sexual function does not change when serum testosterone levels are pharmacologically varied within the normal male range. *Fertil Steril* 1993; **59**: 1118–23
21 Knussman R, Chrisiansen K, Couwenbergs C. Relations between sex hormone levels and sexual behaviour in men. *Arch Sex Behav* 1986; **15**: 429–45
22 Mantzoros CS, Georgiadis EI, Trichopouos D. Contribution of dihydrotestosterone to male sexual behaviour. *Br Med J* 1995; **310**: 1289–91
23 Ross RK, Coetzee GA, Pearce CL *et al.* Androgen metabolism and prostate cancer: establishing a model of genetic susceptibility. *Eur Urol* 1999; **35**: 355–61
24 Carani C, Rochira V, Faustini-Fustini M, Balestrieri A, Granata AR. Role of oestrogens in male sexual behaviour: insights from the natural model of aromatase deficiency. *Clin Endocrinol (Oxf)* 1999; **51**: 517–24
25 Gooren LJ. Human male sexual functions do not require aromatization of testosterone: a study using tamoxifen, testolactone and dihydrotestosterone. *Arch Sex Behav* 1985; **14**: 539–48
26 Schiavi RC, Schreiner-Engel P, White D, Mandell J. The relationship between pituitary-gonadal function and sexual behaviour. *Psychsom Med* 1991; **53**: 363–74
27 Weizman A, Weizman R, Hart J, Maoz B, Wijsenbeek H, Ben David M. The correlation of increased prolactin levels with decreased sexual desire in elderly men. *J Am Geriatr Soc* 1983; **31**: 485–8
28 Eaton NE, Reeves GK, Appleby PN, Key TJ. Endogenous sex hormones and prostate cancer: a quantitative review of prospective studies. *Br J Cancer* 1999; **80**: 930–4
29 Bosland MC. The role of steroid hormones in prostate carcinogenesis. *J Natl Cancer Inst Monogr* 2000; **27**: 39–66
30 Gann PH, Hennekens CH, Ma J, Longcope C, Stampfer MJ. Prospective study of sex hormone levels and risk of prostate cancer. *J Natl Cancer Inst* 1996; **88**: 1118–26

Correspondence: Prof. G.G. Giles, Cancer Epidemiology Centre, The Cancer Council Victoria, 1 Rathdowne Street, Carlton South, 3053, Australia.
e-mail: Graham.Giles@cancervic.org.au

Abbreviations: **DHT**, dihydrotestosterone; **SHBG**, sex hormone-binding globulin; **OR**, odds ratio.