**A multidisciplinary overview of the issues faced by unaffected men with a family history of prostate cancer.**

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Financial support

This study is supported by a Strategic Research Partnership (STREP) Grant (ID SRP 06-X5) from The Cancer Council of New South Wales. Dr. Meiser is supported by a Career Development Award from the National Health and Medical Research Council of Australia (ID 350989).

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Conflict of interest statement

The authors have no conflicts of interest to declare.

Running title: Unaffected men with a family history of prostate cancer.

Keywords: Prostate cancer, family history, risk, psychological aspects.

**Abstract**

**Purpose:** Despite the established importance of the role of family history in prostate cancer, relatively little research encompasses the psychosocial issues relevant to unaffected men with a family history of prostate cancer. To determine the completeness and quality of available literature on the issues faced by men with a high risk of developing prostate cancer, we conducted a multidisciplinary review of the literature in order to provide some guidance on the information that clinicians might provide to men who are concerned about their family history. **Materials and methods:** A structured literature search was conducted by a multidisciplinary team of clinicians and researchers who reviewed the medical and psychosocial literature and identified 21 relevant studies. **Results:** Research suggests that many high-risk men are concerned about their risk of developing prostate cancer, and some may significantly overestimate that risk. Several studies have shown high screening rates among high-risk men and high levels of interest in genetic testing for prostate cancer risk should it become available, yet many men also report a desire for more information about their personal risk and risk management options. **Conclusions:** Given the lack of clear data on the efficacy of prostate cancer screening among high-risk men, clinicians could consider providing men who are concerned about their family history with information on their personal risk, help them to clarify the potential benefits, limitations and harms of prostate cancer screening in their situation, and then support their choice regarding the management of their prostate cancer risk.

## BACKGROUND

After age, the strongest risk factor for prostate cancer is family history, with approximately 10-20% of men with prostate cancer having a significant family history of the disease.[1] Currently, prostate cancers arising from genetic predisposition cannot be distinguished from sporadic disease on the basis of clinical characteristics, with long-term survival rates being similar across patients with and without a strong family history.[1] Possibly the most prominent clinical feature of prostate cancer in men with a family history is its comparatively early onset, with these men typically being diagnosed 6 to 7 years earlier than men with no family history of the disease.[1]

A distinction can be made between 'familial prostate cancer' (FPC), which involves clustering of prostate cancer in families, and a subset of familial prostate cancer, which is 'hereditary prostate cancer' (HPC). HPC is defined by stronger familial clustering in association with earlier-onset disease. As in other hereditary cancer syndromes these are essentially pragmatic criteria to identify high personal and familial risk, with a higher probability of detection of high-risk gene mutations; beyond this fact there is no clear biological distinction between stronger and weaker forms of familial cancer clustering. Families with HPC can be characterized by having: i) three or more affected relatives within the nuclear family; or ii) three or more affected relatives over three generations (on the same side of the family); or iii) two relatives with prostate cancer occurring before age 55.[2] Some genetic segregation studies suggest that HPC is best explained as an autosomal dominant disorder, but there is also evidence of low penetrant, recessive or X-linked effects.[3] Subsequent studies however, have failed to confirm these findings, making genetic testing for prostate cancer risk not possible at this time.[3] Given the varied definitions and use of the two terms (FPC and HPC) in the literature, this review encompasses articles that describe familial or hereditary prostate cancer syndromes.

Three systematic reviews[4-6] have examined the risk of developing prostate cancer among men who have a family history of the condition, the results of which are presented in Table 1. Briefly, prostate cancer risk increases with i) earlier onset of the disease in other family members; ii) larger total numbers of affected relatives in the family; and iii) larger numbers of first-degree relatives (FDRs) affected by prostate cancer. It has been reported that having a brother affected with prostate cancer carries a higher risk than having a father diagnosed with prostate cancer.[5] This phenomenon might be explained by temporal and environmental influences being more strongly shared by brothers than by fathers and sons, by recessive genetic effects, or by ascertainment or measurement biases, such as discounting the genetic contribution of females in the family.[5] Families with multiple cases of prostate cancer do not appear to have an increased risk of other cancers, with the exception of a weak association with brain tumors and gastric and breast cancers in some families.[7] This observation is in keeping with reports that male carriers of breast/ovarian cancer-mutations (i.e. in the BRCA1 and BRCA2 genes) are at increased risk of both prostate cancer and gastric cancer. However, the increased risk of prostate cancer in these families is small (two- to four-fold), and the breast/ovarian cancer-related mutations cannot account for the majority of familial prostate cancer cases.[7]

----------Insert Table 1 about here----------

Screening for prostate cancer may be offered using a quantitative assay for Prostate Specific Antigen (PSA) in the blood, and this can be combined with a digital rectal examination (DRE). While studies have shown that the PSA test can detect cancers at an earlier and possibly more curable stage in the general population, there is disagreement about the value of the test as it has a low positive predictive value, can lead to false positive results and there is a lack of evidence that early detection and treatment leads to better health outcomes.[8, 9] In addition, the PSA test has low sensitivity, but a high false positive rate (contributing to a low positive predictive value).[8, 9]

Moreover, many prostate cancers are slow growing, potentially leading to the over-diagnosis of up to 50% of prostate cancers that would never have been diagnosed in the absence of screening.[10] Several population studies,[11, 12] as well as large-scale randomized controlled trials,[13, 14] are currently underway in order to ascertain more data on PSA screening effectiveness.

As genetic testing for prostate cancer risk is not currently available, men at increased risk must make decisions about their risk management and screening on the basis of their family history alone. Despite the controversy regarding PSA screening in the general population, the positive predictive value (and hence the benefit to harm ratio) of PSA screening will be higher in men with a strong family history of prostate cancer because their of prior risk status. Moreover, the earlier age of onset of prostate cancer in these families has the potential to increase the gain in terms of years of life saved and reduce the potential over-diagnosis of non-significant tumours, thereby theoretically increasing its value in this population. Hence, several studies and professional groups recommend more frequent, or earlier, screening in this population. Table 2 presents the current positions of key professional groups with regard to PSA screening in the general population *versus* in men at higher risk of developing prostate cancer.

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**AIMS**

Despite the high incidence of prostate cancer in most populations worldwide, and the established importance of the role of family history in the development of the disease, surprisingly little literature is available that describes the psychological and social issues relevant to unaffected men with a strong family history of prostate cancer. Thus, the aim of this paper is to bring together previous research in many speciality areas to provide a comprehensive, multidisciplinary review of the available data on psychological morbidity amongst this group of men, their perceived risk of

developing prostate cancer, attitudes toward and participation in screening, and interest in genetic testing for prostate cancer risk (should it become available). This review will help clinicians and researchers to be aware of the broad range of psychosocial issues to consider when counseling unaffected men presenting to their clinic concerned about their family history of prostate cancer.

## METHODS

Three strategies were employed to conduct the literature search. First, the electronic databases from MEDLINE, Medline In-Process or other non-indexed citations, PsychInfo and EMBASE were searched from 1980 onwards using the keywords "prostate cancer" and "family history" or "hereditary" or "familial" in combination. Second, the reference lists of all publications identified were examined. Studies were considered eligible for inclusion in the review if they were: published in a peer-reviewed journal; involved human subjects; were published in the English language; and covered the population and topics of interest (ie. psychological morbidity, perceived risk, attitudes and participation in screening and interest in genetic testing in men with a family history of prostate cancer). Articles were excluded from the literature review if they were reviews, single case reports, letters, commentaries or conference abstracts. We grouped together multiple articles that appeared to describe the same study samples and, where necessary, we incorporated only the data from the largest dataset, or the most recent article in these groups.

## RESULTS

A total of 943 articles were identified using the above search terms and 21 articles met all inclusion criteria. Table 3 describes the search criteria and provides a list of the main reasons each excluded article was not included in the analysis. The great majority of articles originated from the United States (n=16), with the remainder from Sweden (n=3), France (n=1) and Australia (n=1). Most studies have ascertained study participants through FDRs who have previously been diagnosed with prostate cancer; however, one population-based study is also available.[15]

----------Insert Table 3 about here----------

Psychological morbidity and perceived risk

Several articles have reported that psychological morbidity among FDRs of prostate cancer patients is within the normal population range.[16, 17] However, most unaffected men with a family history of prostate cancer are concerned about their risk of developing cancer, and men who are younger, have a son, or have more than one affected relative have been shown to experience higher levels of psychological morbidity and cancer-specific worry.[17-21]

A small number of studies have shown that men with a family history of prostate cancer overestimate their risk of developing prostate cancer,[22, 23] and that high levels of perceived risk are associated with depression and cancer worry which affects daily living.[18] Moreover, a recent study reported that 75% of men with a family history of prostate cancer indicated a need for help to deal with their fears of developing cancer, suggesting that these men may benefit from appropriate counseling to manage cancer-specific worry and anxiety.[24]

Attitudes toward, and participation in screening

Most studies have demonstrated a positive relationship between the presence of family history and screening behaviors (see Table 4).[21, 22, 25-28] Self-reported screening uptake rates however vary significantly between studies, with data ranging from one US-based study which reported that 50% of the sample had had a PSA test prior to entry into the study,[21] through to recent Australian data which showed that over 75% of the 280 men with a family history of prostate cancer in the study had undergone PSA testing and a DRE.[29] The highest screening rates in unaffected men with a family history were reported by Bock *et al* in 2003, in which approximately 95% of their sample of

64 unaffected sons of prostate cancer patients reported having had a PSA test and 97% reported having undergone a previous DRE.[25]

While high screening rates have been reported in many populations of men with a family history of prostate cancer, it seems that not all groups have similar screening rates, with one recent study showing significantly lower screening rates in African-American men with a strong family history of prostate cancer compared to Caucasians with a similar family history profile.[30] In this study, only 45% of African-American men with a strong family history of prostate cancer (having more than four affected relatives) reported having ever had a PSA test, and only 35% reported ever having had a DRE.[30] As well, another US-based study reported that a sample of 56 men with an affected FDR were no more likely to have undergone PSA testing or DRE when compared to a sample of 100 men with no FDRs previously affected by prostate cancer.[23]

Several studies have assessed the sociodemographic, medical and psychological characteristics associated with prostate cancer screening amongst men with a family history of prostate cancer. It has been reported that men with a family history of prostate cancer who are older,[17, 23, 29, 31] married,[15] and have higher incomes[15, 19, 21, 29] are more likely to undergo PSA screening. As well, having a larger number of affected relatives[18, 19, 29] and having discussed screening with a clinician[17] have been reported as predictors of increased frequency of screening. By contrast, men appear less likely to screen regularly if they have high levels of cancer-specific distress. Specifically, one Swedish study showed that men with a strong family history of prostate cancer (three or more affected relatives) were less likely to engage in screening if they had high levels of avoidant thoughts related to their chance of developing prostate cancer.[18]

Two studies have investigated the psychological impact of screening on men in this population,[17, 32] and have showed little effect on anxiety,[17, 32] depression,[32] cancer worry,[32] and health-related

quality of life[17] when undergoing screening. However both these studies were small (N= 220 and N=57 respectively) for the purpose of assessing the impact of screening, and included no or few men who experienced an abnormal screening test result.

Interestingly, a recent Australian study found that female partners of men with a family history of prostate cancer did not significantly influence men's interest in attending multidisciplinary familial prostate cancer services.[24] However, the partner's level of involvement in men's screening was associated with increased PSA screening. Little information is currently available about the role, needs, and concerns of women whose unaffected partners have a strong family history of prostate cancer. They may, however, play a critical role in patients' ability to cope with their family history of cancer as well as in their medical decision-making. More research in this area could help to further distinguish predictors of screening in this population.

----------Insert Table 4 about here----------

Attitudes toward genetic testing for prostate cancer risk

Should it become available in clinics, the introduction of genetic testing for prostate cancer risk would be likely to impact the demand for genetic counseling and testing for men with a strong family history of prostate cancer. Indeed, research suggests that these men show a strong interest in learning about the inheritance of cancer predisposition and genetic testing, as well as in actually undergoing genetic testing. Specifically, the studies listed in Table 5 indicate that up to 90% of men at risk of familial prostate cancer are interested in having genetic testing if it were to be available.[16, 18, 33, 34] These figures are relatively consistent across countries and cultural backgrounds, with data from France, for example, reporting that 98% of men with at least one FDR with prostate cancer were interested in genetic testing, while a similar proportion (94%) of unaffected men with a strong family history in Sweden reported that they would undergo genetic testing if it became available.[18]

Figures for the US are comparable, ranging from 74% to 89% in two separate studies.[34, 35] In both of these studies, levels of interest in genetic testing were similar in all participants, irrespective of their family history status, however in Diefenbach *et al* (2000) men with a family history of the disease reported being willing to pay more for genetic testing than men with no family history.[35] Interestingly, despite a reported lack of uptake of prostate cancer screening in African American men with a strong family history of prostate cancer,[30] Weinrich *et al* (2002) reported that 87% of African American men with a strong family history of prostate cancer were interested in genetic testing for prostate cancer risk should it become available.[33]

It must be noted, however, that previous surveys of attitudes toward genetic testing for other hereditary cancer syndromes have shown that the anticipated uptake of genetic testing to predict the development of a condition is likely to be higher than the observed rate of uptake once such testing becomes available.[36] Also, actual uptake rate appears to be dependent on the perceived treatability of the condition, with the actual uptake of genetic testing being higher for hereditary colorectal cancer than for hereditary breast-ovarian cancer.[36]

Previous studies demonstrate that intention to undergo genetic testing is determined by a complex set of family history, sociodemographic and psychological variables. The following predictors of interest in genetic testing for prostate cancer risk have been identified amongst men at increased risk: having a greater number of relatives with prostate cancer;[17, 35] having children[16, 18]; educational level, with men with lower levels of education showing greater interest in undergoing genetic testing in the future[16]; marital status, with married men being more likely to report interest in genetic testing[33]; emotional distress and worry;[35] and concerns about treatment side effects and efficacy.[35] Men may also feel concerned about the prostate cancer risks imparted to their sons by their family history, with one study reporting that 93% of men who had sons wanted their sons to know their risk, and 89% wanted their sons to have a genetic test.[18]

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## DISCUSSION

In this review of original studies on psycho-social issues affecting men with a family history of prostate cancer published between 1980 and July 2007, we found 21 relevant articles from four countries. The review demonstrated that while unaffected men with a strong family history of prostate cancer are concerned about their prostate cancer risk, the majority do not experience clinically-relevant levels of psychological morbidity as a result of their family history. In most groups, men with a family history of prostate cancer have a positive attitude toward screening, are more likely to participate in screening programs and are interested in genetic testing for prostate cancer should it become available in the future. However, the review revealed a lack of relevant studies, particularly those that focus primarily on men at significantly high risk of developing prostate cancer (i.e. those from families with 3 or more affected relatives) and more detailed studies of these men's perceptions of prostate cancer (eg. perceived severity, treatability and causes of prostate cancer, which could be additional predictors of psychological distress and/or screening). The majority of studies originated in the United States, and this may limit broader significance of these findings when considering different health systems and cultural contexts.

Men at increased risk for prostate cancer on the basis of family history are confronted with difficult decisions regarding the management of their prostate cancer risk, and the absence of evidence exacerbates the difficulty of these decisions. Due to the lack of clear data on the performance of prostate cancer screening among high-risk men, many professional bodies promote an informed choice model of prostate cancer screening for this group, whereby individual clinicians may recommend screening to interested men, as well as providing information on the benefits, limitations and harms of screening.[9, 37] It can also be argued that, in the absence of clear guidelines

and evidence of benefit, clinicians should not be raising issues of prostate cancer screening or recommending a particular course of action to this population. In such circumstances, the decision regarding screening should certainly lie with the at-risk person but, given the concern expressed by this population and their high uptake of PSA, it seems preferable that this decision is informed with accurate information being provided by a clinician or other reputable source.

Research suggests that some men who are, or perceive themselves to be, at increased risk of prostate cancer on the basis of their family history have significant unmet information needs and desire more information about personal risk and management options.[16, 24] The risk assessment of men at high risk of prostate cancer would necessarily involve the recording of both age and family history (the two strongest determinants of prostate cancer risk). In addition, the PSA level in relation to age (especially in young men) and the trend in PSA level over time may also be useful parameters in risk assessment. Figure 1 presents a flowchart of information exchange that concerned unaffected men at high risk of developing prostate cancer may find helpful to ascertain their risk and make decisions about their screening options.

----------Insert Figure 1 about here----------

There are a number of routes by which information about prostate cancer risk could be delivered. Health professionals, particularly urologists and GPs, were named as the preferred source of information in a recent Australian study of unaffected men with a family history of prostate cancer, [24] and these clinicians are well placed to respond to men's concerns. Men concerned about their risk may well present to their GPs requesting information, but there may also be value in identifying men at risk through routine collection of cancer family history and, if the family history is suggestive of a high risk of developing prostate cancer, referring the patient to a familial cancer clinic for genetic counseling. A recent systematic review suggests that discussing risk information

in a genetics context can result in improvement of risk perception without causing adverse outcomes such as anxiety, cancer-related worry and depression.[38] Genetic counseling for cancer risk encompasses issues such as perceived risk, experiences of cancer, loss and anxiety, and it is the supportive or emotional elements of the consultation, rather than the communication of risk alone, that have been found to provide the greatest benefit.[38]

Written information, another preference of at-risk men,[24] can be provided by clinicians to complement a consultation or may be accessed via cancer or men's health information services. Written information has the advantage of allowing men to consider the available options in their own time, to discuss issues with their partner, and also to pass information on to other at-risk relatives. Online delivery of patient information is becoming increasingly popular because of its increased accessibility for patients and decreased production and distribution costs, although the design and usability of Internet-based education are crucial factors which need to be carefully considered when developing online resources for patients.

## FUTURE DIRECTIONS

This article has reviewed and summarized the available literature on the psychosocial issues relevant to unaffected men with a family history of prostate cancer. The review revealed a dearth of psycho-social studies in unaffected men with a strong family history of prostate cancer (as opposed to having only one affected relative). Future studies focussing on this population, and from different international perspectives, are critical in order to develop a more comprehensive view of the issues to consider when counseling this group. Another interesting topic for review would be the prostate cancer treatment choices of men with a family history of prostate cancer, in order to investigate whether or not their treatment choices are different to men with no family history of the disease.

Given the complexity of the issues described above, educational materials (or specific decision support materials) to assist unaffected men with a family history of prostate cancer decide whether to undergo prostate cancer screening would be valuable. For men who do decide to undergo screening, it would also be essential to help them to decide at what age to start, how often to undergo screening and at what age to stop screening. Several screening decision aids for men at average risk of prostate cancer have been developed and have been shown to reduce men's uncertainty and increase knowledge about prostate cancer screening (see Evans *et al*[39] for a review). We are not aware, however, of any screening decision aids designed specifically for unaffected men with a strong family history of prostate cancer.

**Acknowledgements**

We gratefully acknowledge the valuable input to this paper provided by Dr. Melina Gattelari, who previously developed a prostate cancer decision aid for men at average risk of developing prostate cancer, Dr. Carole Pinnock at the Australian Prostate Cancer Collaboration (APCC), and Dr. Nadine Kasparian at the Psychosocial Research Group, Department of Oncology, Prince of Wales Hospital, Australia.

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**Legends**

Table 1: Summary of results of the three published systematic reviews of prostate cancer risk by family history type.

Table 2. Summary of current positions of key professional groups with regards to prostate cancer screening.

Table 2: Systematic review of prostate cancer and family history studies from January 1980 to July 2007.

Table 4: Studies of psychosocial aspects of prostate cancer screening in unaffected men with a family history of prostate cancer.

Table 5: Studies of interest in genetic testing for prostate cancer risk in unaffected men with a family history of prostate cancer.

Figure 1: Suggested flowchart of information exchange for concerned unaffected men at high risk of developing prostate cancer.

**Table 1: Summary of results of the three published systematic reviews of prostate cancer risk by family history type.**

| Authors | Sample size and study type | Family history type* | Risk figure (95% Confidence interval)** |
|---|---|---|---|
| Zeegers et al (2003)[4] | Meta-analysis: 33 studies published up to December 2002 | 1 FDR | 2.57 (2.32-2.84) |
| | | Brother only | 3.37 (2.97-3.83) |
| | | Father only | 2.17 (1.90-2.49) |
| | | 2 or more FDRs | 5.08 (3.31-7.79) |
| | | 1 FDR diagnosed under 65 yrs | 2.47 (1.71-3.55) |
| | | 1 FDR diagnosed over 65 yrs | 1.72 (1.41-2.10) |
| Watkins Bruner et al (2003)[5] | Meta-analysis: 24 studies published up to November 2000 | Any affected family member | 1.93 (1.65-2.26) |
| | | One or more affected FDRs | 2.22 (2.06-2.40) |
| | | One or more affected SDRs | 1.88 (1.54-2.30) |
| | | Father only | 2.12 (1.82-2.51) |
| | | Brother only | 2.87 (2.21-3.73) |
| Johns & Houlston (2003)[6] | Meta-analysis: 13 studies published up to August 2002 | Any affected FDR | 2.5 (2.2-2.8) |
| | | 2 or more FDRs | 3.5 (2.6-4.8) |
| | | Father only | 2.5 (2.1-3.1) |
| | | Brother only | 3.4 (2.9-4.1) |
| | | 1 affected family member diagnosed under 60 years | 4.3 (2.9-6.3) |

* FDR: First-degree relative, SDR: Second-degree relative.

** Zeegers *et al* presented summary recurrence risk ratio statistics, while Bruner *et al.*, and Johns & Houlston presented pooled relative risks.

**Table 2: Summary of current positions of key professional groups with regards to prostate cancer screening.**

| Professional group | Recommended community screening* | Definition of 'higher risk' groups | Recommended screening in higher risk groups |
|---|---|---|---|
| American Urological Association.[40] | Annual PSA and DRE from age 50, for men with a life expectancy of more than 10 years. | One affected FDR or African American heritage. | Annual PSA and DRE from age 40 years. |
| American Cancer Society.[41] | Annual PSA and DRE from age 50, for men with a life expectancy of more than 10 years. | 1) One affected FDR diagnosed under 65 or African American heritage. 2) Several affected FDRs diagnosed at an early age. | 1) Annual PSA and DRE at or before age 45.<br>2) PSA and DRE at age 40. Depending on test results, either annual screening, or next screen at age 45. |
| US Preventive Services Task Force.[42] | Evidence is insufficient to recommend for or against routine screening using PSA testing or DRE. | Not applicable. | No screening. |
| NHS National Screening Committee, UK.[43] | No screening, but concerned men can be offered annual PSA and DRE after education about benefits and harms. | Not applicable. | No definitive guidelines for screening in high risk families in the UK. |
| Urological Society of Australia and New Zealand.[44] | No screening, but concerned men aged 50-70 years with at least a 10 year life-expectancy, should be offered annual PSA and DRE. | Men with a strong family history. | PSA and DRE after age 40 for concerned men. |
| The Cancer Council Australia.[45] | No screening. | Not applicable. | Screening decisions should take into account individual risk factors such as family history, but no recommended surveillance. |
| Cancer Society of New Zealand.[46] | No screening. | Not applicable. | No screening. |

Abbreviations: PSA: Prostate-Specific Antigen screening, DRE: Digital Rectal Examination, FDR: First degree relative.

* No major medical or professional groups, including the American Cancer Society (ACS), American Urological Association (AUA), US Preventive Services Task Force (USPSTF), American College of Physicians (ACP), National Cancer Institute (NCI), American Academy of Family Physicians (AAFP), and American College of Preventive Medicine (ACPM) support population-based screening for prostate cancer at this time, and all groups recommend that interested or concerned patients are told the potential harms and benefits of screening and are able to make an informed decision regarding screening.

**Table 3: Systematic review of 'prostate cancer' and 'family history' studies from January 1980 to July 2007.***

| Inclusion search criteria | No. of studies meeting inclusion criteria |
|---|---|
| 1) "family history" + "prostate cancer"+ limited to 1980-2007 | 943 |
| Duplicate articles | 343 |
| 2) Subtotal, with duplicates removed | 600 |
| Non-English language | 41 |
| Non-human studies | 4 |
| 3) Subtotal | 555 |
| **Exclusion criteria** | **No. of studies meeting exclusion criteria** |
| Epidemiological/risk factor/prevention studies eg. studies of occupational exposure, smoking, physical activity, obesity. | 93 |
| Molecular genetics studies. | 84 |
| Diagnosis/treatment/outcome studies. | 83 |
| Prostate cancer risk studies. | 29 |
| Screening studies (not psycho-social) | 28 |
| Other primary cancer site e.g. breast cancer, melanoma, lymphoma. | 56 |
| Other primary conditions e.g cardiovascular disease, diabetes, asthma, osteoporosis. | 7 |
| Reviews. | 68 |
| Editorial comments/letters. | 30 |
| Case studies. | 7 |
| Clinical guidelines/recommendations. | 6 |
| Psycho-social study, but included only unaffected men with no family history, or only affected men with a family history, or did not specify family history status of participants. | 28 |
| Other e.g. studies of cancer survivors, clinician attitudes surveys, studies of accuracy of family history reporting, general population surveys. | 30 |
| Total studies included in review | 21 |

* Databases searched included: Medline, Medline In-Process or other non-indexed citations, EMBASE and PsychInfo.

**Table 4: Studies of psychosocial aspects of prostate cancer screening in unaffected men with a family history of prostate cancer.**

| References | Outcomes | Sample characteristics[#] | Findings |
|---|---|---|---|
| Meiser et al (2007)[29] Australia | Screening rate (PSA and DRE). | 280 unaffected men with family history of prostate cancer (FPC). | Over 75% reported ever having had PSA and DRE. PSA more common in men with larger numbers of affected relatives and married men. DRE more common in older men, men with high perceived risk and men with sons. |
| Shah et al (2007)[26] USA | Screening rate (PSA). | 3,995 men, of whom 226 had an FDR with prostate cancer (FPC).* | Men with a family history of prostate cancer more likely to undergo PSA. |
| Spencer et al (2006)[15] USA | Screening rate (PSA). | 8,713 men aged 45-79, of whom 492 had an FDR with prostate cancer (FPC). * | Men with family history more likely to have undergone PSA in the 12 months prior to the study. Age was the strongest predictor of screening uptake. |
| Bloom et al (2006)[27] USA | Screening rate (PSA and DRE). | 208 African American men, of whom 88 had at least one self-reported affected FDR (FPC). | Men with a family history more likely to undergo PSA, but not DRE. |
| Sweetman et al (2006)[19] USA | Predictors of PSA screening. | 128 FDRs of young prostate cancer patients diagnosed at 65 years or less (FPC). | Only predictor of screening was past screening. Past screening was associated with higher numbers of affected relatives, perceived risk, perceived benefits of PSA, social class and education. |
| Weinrich (2006)[30] USA | Screening rate (PSA and DRE). | 134 African American men with 4 or more affected relatives (HPC).** | African American men with a strong family history report low screening rates: about 35% had ever had a DRE, and about 45% had ever had a PSA test. |
| Ross et al (2005)[28] USA | Screening rate (PSA). | 736 African-American men, some with family history (FPC).* | Men with a family history more likely to be have PSA test. |
| Jacobsen et al (2004)[22] USA | Screening rate. | 83 men (aged 40-80) with family history (FPC) compared with 83 men with no family history. | Men with family history reported more PSA tests had higher levels of intention to undergo PSA tests in future and were more likely to request information about prostate cancer. |
| Vadaparampil et al (2004)[21] USA | Predictors of screening. | 82 unaffected men aged 40-75 with a FDR with prostate cancer (FPC). | 50% had PSA prior to study, and 50% had PSA during study. No relationship between perceived risk and PSA, however PSA more likely in older men and men with higher incomes and self-efficacy. |
| Bock et al (2003)[25] USA | Screening rate (PSA and DRE). | 60 affected and 64 unaffected sons of prostate cancer patients (FPC). | Approx. 95% of unaffected men reported having had a PSA test and 97% reported previous DRE. |

| | | | |
|---|---|---|---|
| Bratt et al (2003)[32] Sweden | Impact of screening. | 74 unaffected men with 3 or more affected relatives (HPC). Same sample as in Bratt (2000).[18] | Anxiety and depression no higher than general population. No significant change in anxiety, depression or cancer worry on the day of screening compared to 4-6 weeks later. |
| Cormier et al (2003)[47] USA | Screening rate | 138 FDRs (aged 40-70) of prostate cancer patients (FPC). | 62% had undergone PSA and DRE in the last 2 years. Screening more likely in older men, those who had discussed screening with their doctor and those with good screening knowledge. |
| Cormier et al (2002)[48] USA | Attitudes toward screening. | 139 FDRs (aged 40-70) of prostate cancer patients (FPC). Same sample as Cormier et al 2003. [47] | Most participants held favorable attitudes toward screening. Only 62% believed they were at higher risk than the average American man. |
| Cormier et al (2002)[17] France | Impact of screening. | 334 FDRs (aged 40-70) of men with prostate cancer (FPC). | Approx. 20% had increased anxiety and reduced HRQOL after PSA test (largest impact in men aged 50-60, with more than 2 affected relatives, an anxious personality, higher education and no children). |
| Miller et al (2001)[23] USA | Screening rate Perceived risk | 56 men with an affected FDR (FPC) compared to 100 men with no affected FDR. | FDRs no more likely to have PSA or DRE, however reported higher levels of vulnerability to prostate cancer and overestimated their risk. PSA screening most likely in older men. |
| Bratt et al (2000)[18] Sweden | Screening rate. | 110 unaffected men (aged 40-72) with 3 or more affected relatives (HPC). | 68% of those over 50 were regularly screened. Screening more likely in men with larger numbers of affected relatives and those with less avoidant thoughts. |
| Bratt (1997)[16] Sweden | Attitudes toward screening. | 100 sons of men with prostate cancer (FPC). | 90% reported that they probably or definitely wanted screening. |
| Taylor (1999)[49] USA | Reasons for screening. | 50 men with a family history of prostate cancer (FPC) and 76 with no family history. | Self-referral most common reason for attending screening and men with a family history not more distressed than those without a family history. |

FDR: First-degree relative. *Data from the 2000 National Health Interview Survey (NHIS). The NHIS is an annual, national, cross-sectional household interview. In 2000, the study included interviews with 32,374 adults. **AAHPC: African American Hereditary Prostate Cancer Study. Data from this study was compared with the data collected for the NHIS 2000 study.

[#]FPC: Familial prostate cancer: Incorporated studies that include men with any family history of prostate cancer (i.e. at least one affected reactive). HPC: Hereditary prostate cancer: Incorporated studies that include only men from high risk families, mostly with at least 3 affected relatives in the family.

**Table 5: Studies of interest in genetic testing for prostate cancer risk in unaffected men with a family history of prostate cancer.**

| References | Outcomes | Sample characteristics[#] | Findings |
|---|---|---|---|
| Weinrich (2002)[33] USA | Interest in genetic testing. | 320 African American men (HPC) compared with 249 men with no family history.** | 87% of men interested in genetic testing, irrespective of family history. Married men most likely to report interest. |
| Cormier et al (2002)[50] France | Worry and interest in genetic testing. | 277 men with an FDR with prostate cancer (FPC). | 98% men reported being interested in genetic testing. Men with the largest number of affected relatives most likely to report interest in testing. |
| Diefenbach et al (2000)[35] USA | Interest in genetic testing. | 43 men with an FDR with prostate cancer (FPC), compared with 83 men without a family history. | 74% of men reported they would undergo testing, irrespective of family history. Higher interest in testing in men with high cancer-related distress and concerns about treatment side effects. |
| Miesfeldt et al (2000)[34] USA | Interest in learning about or undergoing testing. | 342 men attending prostate screening, 38 of whom had at least one affected FDR (FPC). | 92% of men were interested in learning about the availability of genetic testing and 89% indicated they would be willing to undergo testing, irrespective of family history. |
| Bratt et al (2000)[18] Sweden | Interest in genetic testing. | 110 unaffected men with 3 or more affected relatives (HPC). | 98% were interested in finding out if prostate cancer in their family was inherited. 94% said they would undergo testing. |
| Bratt (1997)[16] Sweden | Attitudes toward genetic testing. | 100 sons (aged over 18) of men with prostate cancer (FPC). | About 90% reported they would undergo genetic testing if there were multiple affected men in the family. Men who were most concerned about cancer and had less education were most interested in genetic testing. |

FDR: First-degree relative. *Data from the 2000 National Health Interview Survey (NHIS). The NHIS is an annual, national, cross-sectional household interview. In 2000, the study included interviews with 32,374 adults. **Data collected from two studies: AAHPC: African American Hereditary Prostate Cancer Study and SCPCESS: South Carolina Prostate Cancer Education and Screening Study.

[#]FPC: Familial prostate cancer: Incorporated studies that include men with any family history of prostate cancer (ie. at least one affected reactive). HPC: Hereditary prostate cancer: Incorporated studies that include only men from high risk families, mostly with at least 3 affected relatives in the family.

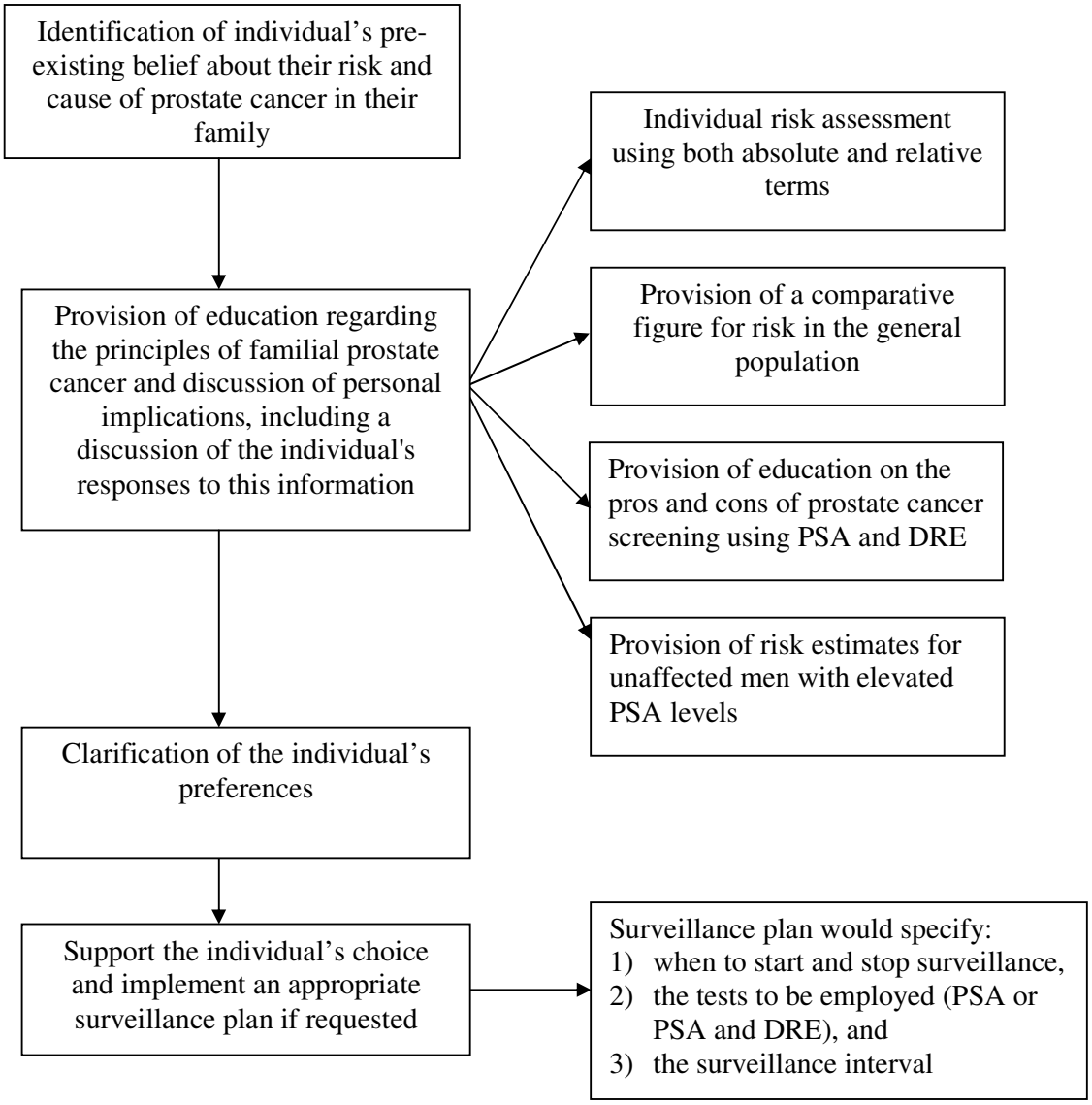


**Figure 1: Suggested flowchart of information exchange for concerned unaffected men at high risk of developing prostate cancer.**