Complementary medicine use by men with prostate cancer: A systematic review of prevalence studies

Running title: Complementary medicine use in prostate cancer

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Abstract

Background: Men with prostate cancer are reported as commonly using Complementary and Alternative Medicine (CAM) but surveys have not recently been subjected to a rigorous systematic review incorporating quality assessment.

Materials and Methods: Six electronic databases were searched using pre-defined terms. Detailed information was extracted systematically from each relevant article. Study reporting quality was assessed using a Quality Assessment Tool which demonstrated acceptable inter-rater reliability and produces a % score.

Results: 42 studies are reviewed. All were published in English between 1999 and 2009; 60% were conducted in the USA. The reporting quality was mixed (median score = 66%, range 23% - 94%). Significant heterogeneity precluded formal meta-analysis. 39 studies covering 11,736 men reported overall prevalence of CAM use; this ranged from 8% to 90% (median = 30%). 10 studies reported prevalence of CAM use specifically for cancer care; this ranged from 8% to 50% (median = 30%). Some evidence suggested CAM use is more common in men with higher education/incomes and more severe disease.

Conclusions: The prevalence of CAM use among men with prostate cancer varies greatly across studies. Future studies should use standardised and validated data collection techniques to reduce bias and enhance comparability.

Keywords: alternative therapies, complementary therapies, prostatic neoplasms, review, surveys.

Introduction

Prostate cancer is the most prevalent cancer among men in the Western hemisphere. Since the advent of Prostate Specific Antigen (PSA) testing, detection and hence incidence of prostate cancer have increased, and earlier (and improved) treatments have led to decreased mortality (1-3). Initial treatment options for men with localised prostate cancer in the UK are: watchful waiting, active surveillance, radical prostatectomy, external beam radiotherapy, brachytherapy, high intensity focused ultrasound, cryotherapy(4). However, there is a paucity of high quality evidence comparing these treatments to guide patients and clinicians in their treatment choices (5) and adverse effects including impotence are common, persistent and associated with reduced quality of life (6, 7). Men with prostate cancer may choose to supplement their conventional treatment with one or more forms of complementary or alternative medicine (CAM).

The National Center for Complementary and Alternative Medicine (NCCAM) defines CAM as "a group of diverse medical and health care systems, practices, and products that are not generally considered part of conventional medicine"(8) and identifies five groups of such interventions: whole medical systems (e.g. Ayurveda), mind-body medicine (e.g. meditation), biologically based practices (e.g. dietary supplements), manipulative and body-based practices (e.g. chiropractic), and energy medicine (e.g. Reiki). Of the biologically based practices, saw palmetto is particularly well known for prostate health and its popularity has generated both safety and efficacy research (9, 10). The patented dietary supplement PC-SPES was promoted for and became particularly popular among men with prostate cancer; this induced trials that reported both beneficial and adverse effects (11-13). Safety concerns were then raised that led to the eventual withdrawal of PC-SPES in the USA due to contamination (see the National Cancer Institute for summary (14)). Since the withdrawal of PC-SPES, large-scale studies have been carried out on other biologically based practices for prostate health, notably the SELECT trial of vitamin E and selenium for cancer prevention (15).

Surveys on CAM use in prostate cancer have not recently been subjected to a rigorous systematic review incorporating quality assessment. Previous reviews on the

subject need up-dating and do not provide detailed information focused on CAM use in prostate cancer (16-18). Currently, this makes it difficult to have confidence in assertions about the prevalence of CAM use in prostate cancer. Furthermore, a comprehensive up-to-date review would provide useful information for oncologists that could aide their communication with patients about CAM, inform the research community as to gaps and inconsistencies in this literature and possibly identify new research areas. We therefore carried out a systematic review of surveys on CAM use by men with prostate cancer. Our primary aims were to evaluate the prevalence of use of CAM overall and of specific CAM modalities. Our secondary aims were: to assess the methodological quality of the surveys; to explore the consistency of findings regarding factors associated with CAM use (clinical and demographic characteristics and study characteristics such as date, geographical location, quality); and to explore common reasons for CAM use.

Methods

Literature Search

Our search strategy was designed to identify primary research studies investigating the prevalence of CAM use (i.e. surveys). Studies examining the outcomes of specific therapies (e.g. clinical trials, cohort studies) were excluded, as were qualitative studies. We included full publications published in journals and excluded the 'gray' literature (e.g. conference proceedings or letters). Six electronic databases were searched for articles meeting the above criteria: Medline (1950 – 06/09), AMED (1985 – 06/09), CINAHL (1982 – 06/09), EMBASE (1980 – 06/09), PsychINFO (1985 – 06/09), Web of Science (1970 – 06/09). We have described our pre-specified search strategies elsewhere (19). In brief, we used the following MeSH terms plus free-text equivalents as required for each database: "complementary therapies [exploded]" AND "neoplasms [exploded]" AND "data collection [exploded]". We used End Note Web 2.2 to organise the identified references. Titles and abstracts were reviewed for eligibility. If these contained insufficient information, the complete article was obtained. We did not restrict our searches by language, but did not identify any eligible non-English language papers.

Data Extraction and Quality Assessment

Detailed information related to data collection and results was extracted systematically from each paper and entered into a pre-designed Excel spreadsheet.

We used a quality assessment tool (QAT) for surveys initially developed in the context of a systematic review of CAM use in pediatric cancer (19), which demonstrated good inter-rater reliability. This tool was based on the specific checklist for cross-sectional studies of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement (20). For the present review we removed two unnecessary items concerning patient gender and cancer diagnosis. In the resulting 15-item QAT the original weighting of items was retained giving a maximum total score of 15.5 points. A percentage score was used as an indicator of overall reporting quality, as not all criteria apply to each paper. Scoring the papers (rather than merely describing their strengths and limitations) allowed us to explore more easily the relationship between reporting quality and outcomes. All papers were scored by two investigators, and according to Cohen's Kappa the inter-rater reliability of all but one item was substantial (kappa above 0.6 (21)) or almost perfect (kappa above 0.8 (21); Table 1); the overall scale had excellent inter-rater reliability (kappa = 0.88).

A number of papers in our review reported on the prevalence of CAM use in prostate cancer and in other types of cancer or the general population. For these papers, data extraction focused exclusively on data specific to the subgroup of patients with prostate cancer. However, quality assessment was carried out considering the entire paper.

Statistical Analyses

We used standard descriptive statistics and Forest plots to depict prevalence rates of overall CAM use and of specific CAM modalities. If studies reported multiple prevalence rates, the rate for CAM use since cancer diagnosis was selected. The relationships between prevalence rates and study-level factors (time, geographical location, quality) were explored graphically. The relationships between CAM use and patient-level factors (socio-demographic and clinical characteristics) were explored by

examining findings across studies. Too few studies reported sufficient information consistently to allow more formal statistical analyses. Furthermore, due to the heterogeneity of the included data we were unable to pool prevalence data in a meta-analysis.

Results

Study Selection and Characteristics

We identified 2311 unique references (after removing 753 duplicates), of which 297 reported on the prevalence of CAM use by patients with any type of cancer. We excluded 255 studies as they reported CAM use either in other specific cancer populations (e.g. breast cancer, colorectal cancer) or in un-differentiated cancer populations (i.e. a study may have surveyed men with prostate cancer but not reported the prevalence of CAM use in this group alone). Forty-two studies reported on the prevalence of CAM use among men with prostate cancer, and are included in this review (22-63). However, only seventeen of these studies focused exclusively on men with prostate cancer (22, 24, 28, 29, 34, 36, 37, 39, 40, 50, 51, 54, 56, 58-60, 62). The remaining studies collected data from broader study populations and reported the prevalence of CAM use for subgroups including men with prostate cancer (23, 25-27, 30-33, 35, 38, 41-49, 52, 53, 55, 57, 61, 63). The characteristics of all 42 included studies are summarised in Table 2. They were all published in English between 1999 and 2009. Most (25, 60%) were conducted in the USA.

Twenty one studies reported some information about time since diagnosis with prostate cancer (22, 24, 25, 27, 29-31, 33, 35, 39, 43, 45, 48-50, 53, 54, 56, 59, 60, 63) using a range of formats (e.g. minimum, maximum, range, mean). Some studies surveyed men who were recently diagnosed (e.g. Steginga et al.'s participants were, on average, 4.25 weeks post-diagnosis at the baseline survey point (56)) while others included men who had been diagnosed many years previously (e.g. 16% of Wilkinson et al.'s participants had been diagnosed at least 5 years before the survey (59)). Thirteen studies reported some information about the stage of cancer at diagnosis, including clinical stage, Gleason score, presence of metastases, and/or PSA levels (22, 28, 34, 36, 40, 45, 50, 51, 53, 58-60, 62). The variety of indicators used, and statistics

reported (e.g. percentages, means), precludes any meaningful summary of this data, but Table 2 describes the disease characteristics of participants as reported in each study. Sixteen studies reported the conventional medical treatments used by their participants for prostate cancer (22, 23, 25, 28, 29, 34, 35, 37, 40, 50, 54, 56, 58-60, 62). These findings are summarised in Table 3. Sixteen studies reported the participants' age (22, 28, 29, 34, 35, 37, 40, 50, 51, 53, 54, 56, 58-60, 62). Mean age ranged from 61.5 years (56) to 70 years (59) in 15 studies. Thirteen studies reported some information about the educational level of their participants (22, 28, 29, 35, 39, 51, 53, 54, 56, 58-60, 62). High school was completed by 73% (60) to 96% (51) of participants in 12 studies

Reporting Quality

Reporting quality was mixed, and total QAT scores ranged from 23% to 94% (median = 66%) (Table 1) In summary, the included literature was adequate for assessing and reporting prevalence of specific CAM modalities; clearly defining CAM both in the paper and for the survey respondents; reporting participants' characteristics, in particular age and SES indicators; reporting response rates. The weaknesses we identified were: common use of data collection strategies that are subject to recall bias (i.e. that ask participants to recall their CAM use over a period of more than 12 months or that do not specify a recall period); lack of reporting of pilot-testing of measures of CAM use; collecting data from samples that are unlikely to be representative of the general population of men with prostate cancer.

Prevalence of CAM use

Prevalence rates for overall use of CAM (as defined by individual studies) were reported in 39 studies including data on 11,736 men with prostate cancer (22-29, 31, 33, 34, 36-63). Across these studies, the prevalence of CAM use ranged from 8% to 90%, while the inter-quartile range was 25% to 43% (median = 30%). Sollner et al (55) report the lowest prevalence rate (8%) but this is based on a very small sample size (n=12). Three of the four studies reporting prevalence rates above 60% focused on the use of dietary or nutritional supplements (45, 54, 60), which are a broad class of therapies some of which (e.g. multivitamins) might now be considered conventional self-care

rather than CAM. The other study reporting over 60% CAM use focused on the use of self-prayer for health (52) – the status of this practice as a form of CAM has also been questioned (64).

As shown in Figure 1, 24 of the 39 studies reported how many men used CAM since their cancer diagnosis (22, 24, 27-29, 31, 34, 39, 40, 42-45, 48, 51, 53-61), and 10 of these reported how many men used CAM specifically for their cancer care (22, 29, 31, 34, 39, 40, 42, 51, 55, 56). When considering the 24 studies reporting CAM use since diagnosis, prevalence of CAM use still ranged from 8% (55) to 90% (54) (median = 31%). However, when selecting only the 10 studies reporting CAM use for cancer care, the reported prevalence rates ranged from 8% (55) to 50% (51) (median = 30%). This suggests that CAM use specifically for cancer care appears to be less variable than CAM use in general, amongst men with prostate cancer.

Prevalence rates for use of specific CAM modalities were also reported by a number of studies. Here we focus on the 5 CAM modalities reported most frequently across studies (see Figure 2). Eleven studies reported prevalence of saw palmetto use among 6525 men (22, 24, 28, 34, 36, 51, 54, 56, 58-60); this ranged from 1.9% (60) to 24.5% (54). Eleven studies reported prevalence of selenium use among 7109 men (22, 24, 28, 36, 50, 51, 54, 56, 58-60); this ranged from 4.1% (28) to 26.6% (54). Eleven studies reported the prevalence of herbal medicine and supplement use among 5274 men (24, 29, 34-37, 39, 40, 45, 60, 62); this ranged from 1.2% (35) to 21.7% (37). Nine studies reported on use of vitamins among 1734 men (29, 34, 35, 37, 40, 54, 56, 59, 62); this ranged from 3.6% (62) to 79.3% (54). These studies reported on use of vitamins as an overarching category that was not defined consistently by the authors and could include vitamin E and/or multivitamins. Eight studies reported on use of Vitamin E among 3261 men (22, 28, 34, 36, 50, 51, 54, 60); this ranged from 5.0% (28) to 53.3% (54).

Factors related to CAM use

Visual inspection of scatterplots (not shown) suggested no simple relationship between prevalence of CAM use and study-level variables including sample size, study quality, geographical location. Figures 1 and 2 suggest that the prevalence of CAM use might

have increased slightly over the past 10 years, although this trend was not statistically significant (Pearson's r (n=39) = 0.25, p=.12). The evidence concerning individual patient-level correlates of CAM use was also limited (see Table 4). From these studies it seems unlikely that CAM use among men with prostate cancer is strongly related to marital status or age. There was more consistent evidence to suggest that CAM use might be more likely among men with higher education or higher income, although again a number of studies fail to find significant associations. Similarly, there was some evidence that men with more severe or advanced cancer, assessed both at diagnosis and subsequently, might be more likely to use CAM. There was no clear relationship between overall study quality as assessed by the QAT and whether or not significant relationships were reported between CAM use and patient-level factors.

Common reasons for CAM use

Nine studies (22, 29, 34, 35, 37, 53, 57-59) reported on men's reasons for CAM use (Table 5). A variety of reasons were either specifically asked about by investigators or offered by participants. Commonly reported reasons concerned physical health status (e.g. to treat cancer or side-effects) and psychological wellbeing (e.g. to gain a sense of control or hope). Less commonly endorsed reasons related to the respondent's social networks (e.g. recommendations from friends or health care staff).

Discussion

The primary studies that we have located and reviewed do not allow us to offer any definitive statements concerning the prevalence of CAM use among men with prostate cancer. Indeed, the prevalence of CAM use reported by individual studies ranged from 8% to 90%, and the high degree of heterogeneity in this literature precluded any formal meta-analysis. Previous reviews of the wider literature on CAM use across multiple cancer diagnoses have also found considerable variation across studies (17, 18). The variation in prevalence rates may be a consequence of the varied definitions of CAM use utilised in the original studies. For example, in our primary studies the reported time period over which CAM use is assessed ranged from 'current' CAM use (presumably more akin to incidence than prevalence) through CAM use since diagnosis (a varied time for different participants)/ over the past 4 weeks -12 months, to any

CAM use ever. If we focus exclusively on the use of CAM as part of cancer care, then the prevalence of CAM use ranged from 8% to 50%. It is likely that men with prostate cancer not only use CAM for cancer care but also for other reasons (e.g. general health, other conditions), and many of the studies included in this review did not clearly distinguish these two different types of CAM use. Lack of specificity regarding CAM use for cancer care was also encountered in our analysis of the prevalence of use of specific CAM modalities. The five CAM modalities examined most often in the original studies were saw palmetto, selenium, herbal medicine/supplements in general, vitamins, and vitamin E. It would seem that vitamins in general and vitamin E in particular are used more frequently than saw palmetto, selenium, or herbal medicine/supplements in general. Perhaps vitamin E is more widely available or cheaper than saw palmetto or selenium (income does appear to be associated with CAM use in this population), or perhaps the negative publicity surrounding PC-SPES has encouraged men to use vitamins instead of less well-known supplements. Some supplements have been investigated for prostate cancer prevention (15, 65, 66), but clinical studies on their therapeutic use in prostate cancer are rare (67). It will be interesting to see whether supplement use declines in this population, or if new supplements are sought out, as a result of major trials, such as SELECT (15). At present, further research on the efficacy and safety of such approaches seems warranted given that patients are initiating and/or continuing to use supplements after cancer diagnosis and possibly alongside conventional treatments. Indeed, some of these CAMs have the potential to interact with conventional medical treatments in both beneficial and detrimental ways (68); consequently oncologists need to encourage open dialogue about these interventions to understand whether and what kinds of CAM their individual patients are using.

We examined possible reasons for and correlates of CAM use by exploring men's reasons for CAM use as reported across studies, by assessing the consistency of evidence concerning clinical and demographic correlates of CAM use, and by exploring possible study-level correlates of CAM use. We were unable to determine with any specificity the most common reasons for CAM use across studies, or to examine how men's reasons for using CAM may differ over time and place. The use of standardised measures would make this possible in future. Only 9 out of the 42 studies reviewed reported men's reasons for using CAM; commonly reported reasons included wanting

to improve or maintain physical health (related to prostate cancer and/or its conventional treatment) and psychological wellbeing and outlook. The variety in prevalence rates reported across our studies may be, at least in part, due to differences in participants' perceived un-met needs concerning their health and wellbeing. It may also be partly due to differences in the demographic or clinical characteristics across participants in the different studies: there was some evidence that men with higher educational achievements or higher incomes are more likely to use CAM, and that men with more severe or advanced cancer are more likely to use CAM. CAM use in the general population is also associated with higher education, but is less commonly associated with income and the evidence concerning clinical characteristics is mixed (69). We found a weak trend for CAM use to have increased over the past 10 years; there was no clear pattern across other study-level factors (quality, location).

Overall, the quality of the studies was reasonable, and was on average higher than the quality of studies in our recent review of CAM use in paediatric cancer (median QAT score 66% versus 50% (19)). We identified common limitations that can be overcome in future studies by, firstly, asking participants to report their current CAM use that is associated with their cancer care (or by limiting recall periods to less than 12 months); secondly, using pilot-tested, validated, and standardised questionnaires or interview protocols to measure CAM use (e.g. (70, 71)); and thirdly, collecting data from large, representative samples of men with prostate cancer identified from population-based registers or, at least, multiple treatment centres.

The conclusions that can be drawn from this review are limited, primary because of the heterogeneity and quality of the original studies but also by our review procedures. While we searched six electronic databases using pre-defined search terms, it is possible that we may have missed relevant publications from other sources in particular if published in languages other than English. Similarly, studies from the USA in particular and the wider English-speaking world dominated our review, and so our conclusions should not be generalised beyond these settings. We considered subgroup and sensitivity analyses to explore the heterogeneity of included data. However, we did not find convincing criteria for homogeneous subsets of studies suitable for pooled analyses such as meta-analysis.

Published surveys on the prevalence of CAM use in men with prostate cancer are generally of reasonable quality but future studies should use standardised data collection tools to decrease methodological heterogeneity and facilitate data pooling in future reviews. Men with prostate cancer do commonly use CAM as part of their cancer care, but the prevalence of use varies substantially across studies from 8% to 50%. This variation is still greater when taking into account studies that do not focus exclusively on CAM use for cancer care. Oncologists, CAM practitioners, and their patients should work towards facilitating open communication about using CAM contemporaneously with conventional prostate cancer care.

Conflict of interest

The authors declare no conflict of interest.

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Table 1.
Summary of Quality Assessment Tool Scores and Reliability

Quality Assessment Tool Item	Cohen's Kappa	Points awarded (a)	Frequency of studies	References
Study Methods:				
Recall bias	.758**			
Low risk (prospective data collection or current use)		2	7 (17%)	(24, 36, 44, 56, 58, 59, 61)
Some risk (retrospective data collection within past 12 months)		1	16 (38%)	(23, 27, 28, 31, 32, 34, 35, 38, 40-42, 45, 48, 49, 51, 54)
Piloted questionnaire (or equivalent)	.761**	1	20 (48%)	(22, 24, 27, 29, 31, 42, 43, 45, 46, 51-55, 57, 59-63)
Describe efforts to address potential sources of bias	.619**	1	21 (50%)	(22, 24, 27, 29-33, 37-39, 42, 43, 45, 48, 51, 52, 55, 59-61)
Adjust for potential confounders in statistical analysis (b)	.847***	1	27 (68%)	(22-24, 27, 28, 30-33, 38-43, 45, 46, 48, 49, 52, 54-59, 61)
Sampling:				
Response rate reported (c)	.858***	1	32 (78%)	(22, 23, 25-33, 35, 37, 39, 41-43, 45, 48, 49, 51-56, 58-63)
Representative sampling strategy	.478*	1	18 (43%)	(22-24, 27, 29, 30, 32, 38, 39, 41-43, 49, 50, 52, 53, 58, 61)
Reporting of participants' characteristics:				
Time since diagnosis	.905***	0.5	23 (55%)	(22, 24, 27, 29-33, 35, 39, 41, 42, 45, 47-50, 53, 54, 56, 59, 60, 63)
Stage of cancer	.854***	0.5	26 (62%)	(22-24, 27, 28, 30, 31, 33, 34, 36, 40, 42, 43, 45, 48-51, 53, 55, 58-63)
Indicator of socio-economic status (e.g. income, education)	.869***	0.5	32 (76%)	(22, 24-30, 32, 33, 35, 37, 39, 41, 42, 45, 46, 48, 49, 51-63)
Age	.844***	0.5	39 (93%)	(22, 23, 25-43, 45-56, 58-63)
Ethnicity	.901***	0.5	26 (62%)	(22, 24, 26, 28-30, 32, 33, 35, 36, 39, 41-46, 48, 49, 51, 52, 54, 57, 59-61)

CAM Use

CAM clearly defined to participants	.779**	2	34 (81%)	(22–24, 28, 30–32, 34–47, 49–53, 55, 57–63)
Assessed CAM use for cancer care or since cancer diagnosis	.674**	2	26 (62%)	(22, 24, 27–32, 34, 35, 39, 40, 42–45, 48, 51, 53–60)
Definition of CAM reported in paper	.837***	1	30 (71%)	(22, 23, 25, 28–30, 33, 35–37, 40, 42, 44–50, 52, 53, 55–63)
Use of CAM modalities assessed	1.00***	1	42 (100%)	(22–63)

* Moderate agreement (0.41–0.60). ** Substantial agreement (0.61–0.80). *** Almost perfect agreement (0.81–1.00). (21).

(a) Points were awarded for each item on the quality assessment tool and a total score was then calculated for each study (as a %, see text for details). This enabled the reporting quality of individual studies to be summarised numerically for comparison and further analysis. Individual studies' total scores are reported in Table 2.

(b) 2 studies did not examine correlates of CAM use and so were not judged on this criterion

(c) 1 study could not report a response rate (data were obtained from insurance records) and so was not judged on this criterion.

Table 2
Characteristics of Included Studies

Citation	Year	Place	N	CAM use (%)	QAT score (%)	Respondents' disease characteristics	Operational definition of CAM use
Studies that focus exclusively on men with prostate cancer							
Boon et al (22)	**2003**	Canada	534	30	87	2-3 years since diagnosis; 80% diagnosed at stage A or B.	CAM used for cancer care, where CAM is "the broad domain of healing resources that encompass all health systems, modalities, and practices and their accompanying theories and beliefs, other than those intrinsic to the politically dominant health system of a particular society or culture in a given historical period." (p.850)
Chan et al (24)	**2005**	USA	2582	33	84	6 months – 4 years post diagnosis;	Current CAM use (assessed at multiple time points), defined through a check-list of 52 specific modalities and space for additional modalities (named modalities included "19 herbals, 12 vitamins, minerals, and nutritional supplements, 3 diet-modification items, 5 items on meditation, massage and bodywork, acupuncture and acupressure, and Asian medicine, 3 homeopathic items, and 7 miscellaneous CAM." (p1224)
Diefenbach et al (28)	**2003**	USA	417	19	71	Mean PSA at diagnosis = 8.9 (SD =12.8); Mean Gleason score at diagnosis = 6.3 (SD=1.0)	CAM use initiated after cancer diagnosis, where CAM is defined through a checklist of 42 therapies based on literature and internet searches and which were " grouped into categories suggested by the National Institutes of Health Office of Alternative Medicine" (p.167)
Eng et al (29)	**2003**	Canada	451	12 (a)	65	Mean time since diagnosis = 13 months (SD=3.9)	CAM used for cancer care, where CAM is " an approach to diagnosis, treatment, and care that falls outside of conventional therapies widely used in North America" (p.212)
Hall et al (34)	**2003**	USA	238	37	48	All at clinical stage T1c - T3	CAM used for cancer care in the past month, where CAM is defined for participants as vitamins, herbal medicines, dietary therapy, or 'other complementary or alternative forms of healthcare ' (p606)
Jones et al (36)	**2002**	USA	84	37	48	T1 38%; T2 23%; T3 13%; T4 0%; unknown T 13%; M1 11%	Current CAM use where CAM "included any unproved therapy used by patients with cancer for (a) treatment of their cancer or other medical diagnosis [our emphasis]; (b) management of symptoms related to cancer; (c) management of side effects of a conventional cancer

Study	Year	Country					CAM definition
Kao et al (37)	2000	USA	46	37	45		CAM use, where CAM "encompass a wide range of therapies the efficacy of which has not been proven, as determined by the National Institute of Health Office of Alternative Medicine" (p615) and was defined on the patient questionnaire as herbal remedies (e.g. saw palmetto, coenzyme Q, garlic), old time remedies (e.g. hot toddies), vitamin therapy (high dose vitamins), and special diets (e.g. macrobiotic).
Lee et al (39)	2002	USA	543	30	71	1-3 years post diagnosis	CAM used for cancer care, where CAM is "macrobiotic diet, megavitamin therapy, and other dietary methods (i.e., low-fat or vegetarian diets, homeopathy, herbal remedies, and psychologic methods, such as meditation or imagery; faith and spiritual healing; and physical methods, including massage, relaxation, acupressure, and acupuncture)" (72 p.42)
Lippert et al (40)	1999	USA	190	43	58	T1 40%; T2 46%; T3 2%	CAM used for cancer care in the past month, where CAM is "therapies that are unproven" (p2643) and a checklist of 18 items (plus 'other') is given to participants.
Ponholzer et al (50)	2003	Austria	822	30	42	Mean time since diagnosis = 3.9 years (SD 3.1); 11.5% metastases at diagnosis.	Previous or current CAM use, where CAM is " any kind of supportive measures used to complement evidence based treatment"(p604) and participants were given a list of CAM therapies.
Porter et al (51)	2008	USA	177	50	76	Mean pre-treatment Gleason Score = 6.2 (SD 0.81). Mean current PSA level 1.3ng/ml (SD 2.3)	Current CAM use for prostate health, assessed with a list of 17 modalities ("10 biologically based therapies, of which there were 6 dietary supplements, 1 dietary system and 3 nutritional foods, and 7 non-biologically based therapies of which there were 5 mind-body therapies and 2 spiritually based therapies" (p320)
Sheriff et al (54)	2005	USA	184	90	58	1 year or less post diagnosis	Any vitamin/supplement use since cancer diagnosis (excluding multi-vitamins).
Steginga et al (56)	2004	Australia	111	25 (b)	61	At baseline, mean time since diagnosis = 4 weeks (SD 4.6)	Current CAM use (at baseline = average 4 weeks post cancer diagnosis), where CAM is "Treatments that are used specifically to alter the course of the cancer and that are not used as standard medical treatments because of their non-medical nature or lack of proven efficacy" (p72)

Wilkinson et al (58)	**2002** USA	1099	18	81	-	Current CAM use, defined as "supportive methods used to complement evidence based treatment" (p2505) with an exclusive focus on "nutritional interventions including herbs, vitamins and minerals" (p2506)
Wilkinson et al (59)	**2008** UK	294	25	93	At least 5yrs post diagnosis 16%; 4yrs post diagnosis 12%; 3yrs post diagnosis 19%; 2 yrs post diagnosis 24%; <=1yr post diagnosis 25%. Currently no evidence of cancer 45%; Currently cancer present 32%.	Current CAM use, assessed through list of 30 modalities and open questions, where CAM is "'a broad domain of healing resources that encompasses all health systems, modalities, and practices and their accompanying theories and beliefs, other than those intrinsic to the politically dominant health systems of a particular society or culture in a given historical period" (Ernst & White 2000" (p492)
Wiygul et al (60)	**2005** USA	805	73 (c)	74	Median time post diagnosis = 40 months. Loco-regional disease 95%, Distant disease 2%.	Current and ever use of CAM, where the focus is on supplements defined as vitamins, minerals, and herbals.
Yoshimura et al (62)	**2003** Japan	138	20	48	T1 53%; T2 12%; T3 36%	Ever used CAM, defined as "therapies the efficacy of which has not been proven" (p26) and assessed with a 17 item checklist (plus 'other').

Studies in which men with prostate cancer are a sub-sample of a larger sample including other cancer diagnoses

Bruns et al (23)	**2006** Germany	81	47	58	-	CAM use within the past 4 weeks, where CAM is "diverse medical and health care systems, practices, and products that are presently not considered to be part of conventional medicine, as practiced by holders of M.D. (medical doctor) degrees and by their allied health professionals" (p318) and assessed by a list of 10 modalities (special diets, psychotherapy, movement and physical therapy, mind/body

therapies, spiritual practices, nutrition co-factors and supplements, traditional Chinese medicine, immuno-augmentative treatment, other approaches, other unconventional approaches).

Study	Year	Country				Timeframe	Definition
Cheung et al (25)	**2004**	Hong Kong	18	28	26	2 – 24 months since completing radiation therapy	CAM use, where CAM is "used as an adjunct to mainstream cancer medicine for symptom management and to enhance cancer medicine for symptom management and to enhance quality of life. Ernst and Cassileth gave a more detailed definition: "diagnosis, treatment and/or prevention which complements mainstream medicine by contributing to a common whole, by satisfying a demand not met by orthodox methods or by diversifying the conceptual framework of medicine"." (p7)
Chrystal et al (26)	**2003**	New Zealand	18	50	23	-	CAM use where CAM is not clearly defined in the paper.
Corner et al (27)	**2009**	England	42	14	71	6months or less post diagnosis	CAM used since cancer diagnosis, where CAM is defined on the basis of "both the House of Lords Science and Technology Select Committee (2000) definition of CAM and Thomas et al.'s (2001) questionnaire-based survey." (p.272)
Gansler et al (30)	**2008**	USA	814	(d)	81	10-24 months post diagnosis	CAM used for cancer care, where CAM is "the broad range of scientifically unproven treatments and practices that are not presently considered part of conventional medicine" (p1048) and CAM use is assessed with a 19-item checklist.
Girgis et al (31)	**2005**	Australia	64	13	74	At least 3 months post diagnosis	CAM used for cancer care or related symptoms over the past 6 months, where CAM is not clearly defined/operationalised in the paper.
Goldstein et al (32)	**2008**	USA	241	(e)	77	-	CAM use in general and for cancer care, where CAM is defined through a list of 11 CAM providers, special diets, 32 dietary supplements, self-directed prayer, support groups, 8 unconventional cancer therapies(e.g. chelation).
Gotay (33)	**1999**	USA	99	28	48	4-6 months post diagnosis	CAM use, where CAM " is a broad domain of healing resources that encompasses all health systems, modalities, and practices and their accompanying theories and beliefs…CAM includes all such practices and ideas self-defined by their users as preventing or treating illness or promoting health and well-being." (p49)
Hann et al (35)	**2005**	USA	82	(f)	65	1-12 months post diagnosis (Mean = 5 months)	Current CAM use, where CAM was defined following "the American Cancer Society as 'those [methods] that patients use along with conventional medicine'." (p284) and assessed with a 44-item checklist.
Lafferty et al (38)	**2004**	USA	782	12	52	-	CAM use during year 2000, where CAM use is a visit to one of four types of practitioner: Chiropractor, Naturopath, Acupuncturist,

Massage Practitioner

Mao et al (41)	**2007**	USA	195	26	58	-	CAM use over the past 12 months, where CAM is 27 named therapies (10 provider-based and 17 not necessarily provider-based).
Mao et al (42)	**2008**	USA	93	44	94	3.5-4 years post diagnosis	CAM use for cancer care in the past year, where CAM "represents a group of health practices that are not routinely taught in medical schools or provided in hospitals"(p117) and is assessed through questions about 11 specific CAM modalities.
Maskarinec et al (43)	**2000**	USA	242	19	74	Diagnosis of invasive cancer during 1996	CAM use since diagnosis where CAM is defined for participants with a list of 21 therapies (plus 'other alternative therapy').
Metz et al (44)	**2001**	USA	51	37	55	-	Current CAM use, where CAM is "any unproven therapy utilized by a cancer patient for treatment of their cancer or other medical diagnosis, management of symptoms related to cancer, management of side effects of a conventional cancer treatment, or prevention of an additional cancer" and specific questions to participants name vitamins, herbal supplements, guided imagery, biofeedback, meditation, shark cartilage or "any other natural supplement" (p150).
Miller et al (45)	**2009**	USA	115	77	87	4-8 years post diagnosis (Mean = 6 years)	Use of one (or more) dietary supplements at least once a week for the past month, where dietary supplements " include products containing vitamins and minerals as well as herbs or other botanicals, amino acids, glandular extracts or other non-nutrient ingredients" (p61) and are measured with a 34-item checklist and open-ended questions.
Molassiotis et al (46)	**2005**	Europe	30	30	48	-	CAM use, where CAM is " 'any diagnosis, treatment or prevention that complements mainstream medicine by contributing to a common whole, by satisfying a demand not met by orthodoxy or by diversifying the conceptual framework of medicine'"(p1 of 9) and is assessed with a checklist of 26 therapies (plus 'other').
Newsom-Davis et al (47)	**2009**	UK	33	24	32	Included newly diagnosed and long-term follow-up patients	CAM use, where CAM is "any medicine, vitamin supplement or food supplement not prescribed by an allopathic doctor" (p312).
Paltiel et al (48)	**2001**	Israel	38	37 (g)	68	At least 2 months post diagnosis	CAM use since cancer diagnosis, where CAM is "any therapy not included in the orthodox biomedical framework of care for patients with cancer (including homeopathy, special diets such as macrobiotic or homeopathic diet, fasting, therapeutic enemas, megavitamins, metabolic therapy, naturopathy, reflexology, massage, acupuncture,

and healing" (p 2440)

Patterson et al (49)	2002	USA	114	59	68	24 months or less since diagnosis	CAM use over the past 12 months, where CAM is "health care and medical practices not currently an integral part of conventional medicine" (p478) and participants were specifically asked about alternative providers (acupuncturists, naturopaths, spiritual advisors), mental or other therapies (e.g. biofeedback, hypnotism, guided imagery), and vitamin mineral herbal or other supplements.
Ross et al (52)	2008	USA	350	62	68	-	Use of prayer for own health, ever.
Salmenpera (53)	2002	Finland	190	27	71	52% more than 2 years post diagnosis. 16% had metastases at time of study.	CAM use since cancer diagnosis, where CAM is "treatments whose effectiveness has not been scientifically established and are therefore not covered by legislation governing official medicine" (p44)
Sollner et al (55)	2000	Austria	12	8	74	-	CAM use ever, assessed by a list of 16 therapies and defined as: "alternative therapies are treatments that are used specifically to influence the course of cancer and that are not used as standard medical treatments because of their nonmedical character or the lack of proven efficacy; complementary therapies are treatments aimed at symptom control or enhancing the quality of patients lives" (p.874)
Vapiwala et al (57)	2006	USA	77	39	58	-	CAM use since cancer diagnosis, where CAM forms listed for participants were: "herbal supplements, soy or other phytoestrogen-containing products, omega-3 fatty acid supplements, medicinal skin balms and salves, acupuncture, massage therapy and guided imagery" (p468).
Wyatt et al (61)	1999	USA	206	32	84	-	Current use of CAM assessed with a checklist of 17 items where CAM is defined as: " ' a broad domain of healing resources that encompasses all health systems, modalities, practices and their accompanying theories and beliefs, other than those intrinsic to the politically dominant health system of a particular society or culture in a given historical period'" and "therapies used along with conventional medicine that are non-invasive, pleasant, stress-reducing, and can be used in states of sickness or health"" (p136)
Yoshimura et al (63)	2005	Japan	171	47	52	1 year post diagnosis	Ever used CAM, defined as "the set of treatments whose efficacy has not been proven by the National Institutes of Health Office of Alternative

a. This figure is prevalence of CAM use specifically for cancer. The paper also reports prevalence of CAM use in general (= 39%)
b. This figure is prevalence of CAM use at baseline. The paper also reports prevalence of CAM use 12 months post-baseline (14%) and 2 months post-baseline (16%), where baseline is, on average, 4 weeks post-diagnosis.
c. Overall prevalence of CAM use in relation to cancer is not reported (although use of specific modalities in relation to cancer care is reported).
d. Overall prevalence of CAM use is not reported for prostate cancer only (paper reports a breakdown into NCCAM categories, which are not mutually exclusive).
e. Overall prevalence of CAM use is not reported for prostate cancer only (paper reports a breakdown into three non-mutually exclusive categories – use of CAM provider, use of dietary/nutritional supplement/use of other CAM therapy, some of which are further separated into use to treat cancer or prevent cancer recurrence).
f. Overall prevalence of CAM use is not reported for prostate cancer only (paper reports a breakdown into specific individual CAM modalities which are not mutually exclusive).
g. This figure is prevalence of CAM use since diagnosis. The paper also reports prevalence of CAM use in the past 3 months (2.6%).

Table 3. Percentage of participants using different types of conventional treatments for prostate cancer

Study	Radical prostatectomy/ 'surgery'	Hormone therapy	(External beam) radiation therapy	Brachy-therapy	Watchful waiting/ surveillance	Combined and other treatments
Boon (22)	37 (RP)	35	35	7	10	1 (Other)
Bruns (23)	-	-	-	-	-	100 (unspecified radiation therapy)-
Cheung (25)	-	-	-	-	-	100 (unspecified radiation therapy)-
Diefenbach (28)	15 (S)	-	54	25	5	-
Eng (29)	29 (a) (RP)	16	42 (a)	8	10	3 (Orchiectomy) 2 (not started treatment) 1 (declined conventional treatment)
Hall (34)	44 (RP)	-	-	22	-	34 (brachytherapy & external beam radiation)
Hann (35)	42 (S)	27	-	-	-	46 (unspecified radiation therapy) 4 (Chemotherapy) 1 (Bone marrow transplant) 1 (Immuno-therapy)
Kao (37)	-	-	-	-	-	100 (unspecified radiation therapy)
Lippert (40)	21 (RP)	-	-	48	-	31 (brachytherapy & external beam radiation)
Ponholzer (50)	54 (RP)	23	12	-	-	7 (radiotherapy & endocrine therapy) 4 (unspecified)
Sheriff (54)	57 (RP)	-	-	-	-	32 (unspecified) 10 (no conventional treatment)
Steginga (56)	56 (RP)	-	-	-	26	18 (unspecified radiation therapy)
Wilkinson (58)	45 (RP)	12	12	3	13	1 (cryotherapy) 4 (prostatectomy & hormonal therapy) 4 (prostatectomy & external beam radiation)
Wilkinson (59)	39 (S)	38	40	9	6	-
Wiygul (60)	76 (S)	-	6 (a)	-	-	18 (unspecified)
Yoshimura (62)	68 (RP)	-	32 (a)	-	-	-

Note: Categories not always mutually exclusive.

(a) with or without hormone therapy

Table 4
Summary of Evidence of Patient-Level Correlates of CAM Use

Demographic or Clinical Factor	Number of studies testing association with CAM use	Number (and %) of studies finding significant association with increased CAM use	Number (and %) of studies finding no significant association
Younger age	14	2 studies (14%) (22, 59) All score >50% on QAT	12 studies (86%) (28, 29, 35-37, 39, 40, 50, 56, 58, 60, 62) 8 score >50% on QAT
Marital Status	8	0 (0%)	8 studies (100%) (22, 24, 28, 29, 35, 39, 58, 59) All score >50% on QAT
Higher (i.e. more) education	13	7 studies (54%) (24, 28, 35, 37, 39, 58, 60) 6 score >50% on QAT	6 studies (46%) (22, 29, 54, 56, 59, 62) 4 score >50% on QAT
Higher income	7	3 studies (43%) (24, 37, 58) 2 score >50% on QAT	4 studies (57%) (22, 39, 59, 62) 3 score >50% on QAT
Increased cancer severity or stage at diagnosis	8	4 studies (50%) (22, 24, 40, 62) 3 score >50% on QAT	4 studies (50%) (28, 36, 50, 59) 2 score >50% on QAT
Worse current cancer status	6	3 studies (50%) (22, 53, 58) All score >50% on QAT	3 studies (50%) (50, 59, 60) 2 score >50% on QAT
Ethnicity	7	2 studies (29%) report white men more likely to use CAM than non-white men (36, 60) 1 scores >50% on QAT 1 study (14%) reports ethnic minority men more likely to use CAM than white men (28) Scores >50% on QAT	4 studies (57%) (24, 35, 54, 59) 3 score >50% on QAT
Conventional treatment	7	3 studies (43%) find CAM use varies with conventional treatment (conventional treatments differ across individual studies) (50, 58, 59) 2 score >50% on QAT	4 studies (57%) (40, 54, 60, 62) 2 score >50% on QAT

Table 5.
Summary of Reasons for CAM use

Extent of Endorsement by Participants	Reasons for CAM use
Very common(by >50% of respondents in any one study)	To cure cancer, to prevent recurrence or spread of cancer, to increase life expectancy, to improve quality of life, to relieve symptoms in general, to have more control over recovery, to give hope, to play a more active role in recovery, to boost immune system, to help manage stress, to manage or treat side-effects of conventional treatment.
Common (by 25-50% of respondents in any one study)	To 'feel better', to improve general overall health, to slow disease progression, to have a greater sense of control over cancer, for psychological support, because it is completely safe.
Less common (by <25% of respondents in any one study)	Because of medical or scientific information, because friends had good experiences of CAM, wanted to experiment, recommended by health care professional, because of current poor health status, disappointed by or not satisfied with conventional treatment, healthcare staff disinterested, because it is giving good results, to manage specific cancer symptoms (e.g. pain, fatigue), to experience a more holistic approach, to have a more involved relationship with a practitioner, felt pressured by family or friends

Figure Legends

Figure 1. Prevalence of CAM use in prostate cancer.

Figure 2. Prevalence of use of specific CAM modalities in prostate cancer.

VITAMIN E:
Jones (2002)
Ponholzer (2003)
Hall (2003)
Diefenbach (2003)
Boon (2003)
Wiygul (2005)
Sheriff (2005)
Porter (2008)

HERBALS:
Lippert (1999)
Kao (2000)
Lee (2002)
Jones (2002)
Yoshimura (2003)
Hall (2003)
Eng (2003)
Wiygul (2005)
Hann (2005)
Chan (2005)
Miller (2009)

VITAMINS:
Lippert (1999)
Yoshimura (2003)
Hall (2003)
Eng (2003)
Steginga (2004)
Sheriff (2005)
Hann (2005)
Wilkinson (2008)

SELENIUM:
Wilkinson (2002)
Jones (2002)
Ponholzer (2003)
Diefenbach (2003)
Boon (2003)
Steginga (2004)
Wiygul (2005)
Sheriff (2005)
Chan (2005)
Wilkinson (2008)
Porter (2008)

SAW PALMETTO:
Porter (2008)
Chan (2005)
Wiygul (2005)
Sheriff (2005)
Steginga (2004)
Boon (2003)
Diefenbach (2003)
Hall (2003)
Wilkinson (2002)
Jones (2002)
Wilkinson (2008)

Prevalence of CAM Use (with 95% CI)