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Author(s)	Choi, EPH; Wong, CKH; Tsu, JHL; Chin, WY; Kung, K; Wong, CKW; Yiu, MK
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Title Page

Health-related Quality of Life of Chinese Patients with Prostate Cancer in Comparison to **General Population and Other Cancer Populations**

Order of Authors: Edmond P.H. Choi^{1*}, Carlos K.H. Wong², James H.L. Tsu³, W.Y. Chin²,

Kenny Kung², Charles K.W. Wong³, M.K. Yiu³

Running Title: HRQOL of Chinese prostate cancer patients

¹ School of Nursing, The University of Hong Kong, Pokfulam, Hong Kong

² Department of Family Medicine and Primary Care, The University of Hong Kong, Ap Lei Chau,

Hong Kong

³ Division of Urology, Department of Surgery, The University of Hong Kong, Pokfulam, Hong

Kong

* Corresponding author

Corresponding Author Information:

Edmond P.H. Choi

School of Nursing, The University of Hong Kong, Pokfulam, Hong Kong

Address: 3/F, 4/F, William M.W. Mong Block 21 Sassoon Road, Pokfulam, Hong Kong

Tel: (+852) 3917-6600 Fax: (+852) 2872-6079

Email: h0714919@connect.hku.hk

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Abstract

Purpose: To compare the health-related quality of life (HRQOL) of Chinese patients with prostate cancer against the general population and patients with colorectal cancer, breast cancer, nasopharyngeal cancer and leukaemia.

Methods: Chinese male patients (n=291) with a confirmed diagnosis of prostate cancer were recruited from a urological specialist outpatient clinic in Hong Kong. HRQOL was measured by a condition-specific Functional Assessment of Cancer Therapy-Prostate (FACT-P) and a generic Chinese (HK) SF-12 Health Survey Version 2 (SF-12v2) questionnaire. Mean HRQOL scores of condition-specific and generic questionnaires were compared to available scores derived from other cancers and age-matched male general population, respectively.

Results: Chinese patients with prostate cancer had lower General Health and Vitality domains and lower Mental Component Summary scores than the age-matched Hong Kong normative population. Patients with prostate cancer reported better condition-specific HRQOL (physical well-being, emotional well-being and function well-being) when compared to general cancer population, patients with breast cancer, colorectal cancer, nasopharyngeal cancer and leukaemia in Hong Kong.

Conclusions: Patients with prostate cancer substantially perceived their HRQOL to be better, compared to patients with other cancers, with overall health, energy and mental health below of Hong Kong general population. Interventions should target at these domains in order to improve the HRQOL of patients with prostate cancer. It is reassuring to find that prostate cancer had less negative impact on HRQOL than other cancer types did.

Manuscript Text

Introduction

According to the worldwide burden of cancer study in 2008, prostate cancer is the second most frequently diagnosed cancer in men [1]. 93% have a prognosis for prolonged survival for at least 5 years and 72.1% for at least 10 years [2]. Due to the effectiveness of prostate specific antigen screening, nowadays, early detection of prostate cancer and curative treatments can decrease prostate cancer-specific mortality [3]. Since many patients with prostate cancer survive for prolonged periods, the impact of illness and its treatments on patients' daily life are an important outcome of interest for clinicians. Quantitative and qualitative studies suggested that the impact of prostate cancer are multifaceted including, but not limited to, sexuality, urinary and bowl functions, physical functioning and mental health, to the detriment of health-related quality of life (HRQOL) [2,4-7].

To date, evidence about the HRQOL of patients with prostate cancer has been inconclusive or lacked generalizability. A study in Japan found that cancer stage was not a factor associated with HRQOL [8] while a study in the US found that patients with advanced cancer stage had poorer HRQOL [9]. The Chinese are a major population of interest representing 20% of the global population. However, to date, information about the impact of prostate cancer on HRQOL is lacking. Several comparative studies [10,5] assessed the differences in HRQOL between prostate cancer and general population but findings in western populations might not be transferrable to Chinese populations because (i) HRQOL is culturally specific [11] and (ii) the health belief of Chinese, which is strongly influenced by traditional Chinese medicine, is distinct from that of western populations [12]. The lack of knowledge about the impact of prostate cancer on the HRQOL of Chinese patients necessitates the present study. Knowledge and understanding of the

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impacts of prostate cancer on HRQOL can assist clinicians and policymakers to formulate interventions that target at specific HRQOL domains.

The aim of this study was to evaluate the HRQOL of Chinese patients with prostate cancer. The specific objectives were (i) to compare the HRQOL of prostate cancer patients with that of the Hong Kong population norm by using a generic HRQOL measure; and (ii) to compare HRQOL between prostate cancer patients and other cancer patient populations by using a disease-specific HRQOL measure.

Methods

Study design and subjects

This study was part of a prospective longitudinal study which evaluated the health status and HRQOL of Chinese patients with prostate cancer in Hong Kong. The baseline data of the study was used to evaluate the HRQOL of Chinese patients with prostate cancer. The inclusion criterion was Chinese patients with confirmed diagnosis of prostate cancer. Subject who went to a urological specialist outpatient clinic of Queen Mary Hospital in Hong Kong between May 2013 and January 2014 for medical follow-up appointment were recruited by convenience sampling. Patients were excluded if they could not understand Cantonese, refused to participate or were too ill to give consent. Subjects who consented were asked to provide their contact details and were subsequently contacted by a trained interviewer who administered the study questionnaire by face-to-face interview. The interviewer was required to read the study questionnaire verbatim in a standardized face-to-face interview approach. Details of patient recruitment data collection have been reported elsewhere [13].

Study Instrument

The Chinese (HK) SF-12 Health Survey Version 2 (SF-12 v2) is a 12-item generic HRQOL instrument, which measures eight domains including physical functioning (PF), role limitation due to physical problems (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role limitation due to emotional problems (RE) and mental health (MH) [14]. Moreover, the SF-12 v2 can be summarized into physical and mental component summary (MCS) scores. The higher the SF-12 v2 scores, the better the HRQOL. The SF-12 v2 has been validated in Hong Kong general population and the population norm of the SF-12 v2 has been established for Chinese adults in Hong Kong [15,16]. Using the generic HRQOL instrument allows us to compare the HRQOL of our subjects to the age adjusted male population norm.

The Functional Assessment of Cancer Therapy-Prostate (version 4) (FACT-P) is a 39-item prostate cancer-specific HRQOL instrument, which contains five subscales namely physical well-being (PWB), social/family well-being (SWB), emotional well-being (EWB), functional well-being (FWB) and prostate cancer subscale [17]. The PWB, SWB, EWB and FWB subscales are the core module of the Functional Assessment of Chronic Illness Therapy (FACIT), which is applicable to all cancer patients. The prostate cancer subscale is only applicable to patients with prostate cancer. The higher the FACT-P scores, the better the HRQOL. The instrument was administered to supplement the generic instrument because the condition-specific instrument is more sensitive in capturing the specific impact of prostate cancer on HRQOL [18]. Traditional Chinese version of FACT-P has shown to be valid and reliable for use in Hong Kong Chinese patients with prostate cancer [13].

Previous studies in Hong Kong also administered FACIT instrument to assess the condition-specific HRQOL of cancer patients such as (i) general cancer patients [19], (ii) patients with nasopharyngeal carcinoma (NPC) who underwent radiotherapy [20], (iii) patients with breast

cancer [21], (iv) patients with colorectal cancer (CRC) [22] and (v) patients with acute leukaemia, chronic leukaemia, lymphoma and others [23]. Notably, three studies[19-21] conducted in early 2000s administered an earlier version (Version 3) of the FACIT instrument which subsequently underwent changes in item wording and scale structure to become the latest version (Version 4) of FACIT instrument. When comparing subscale scores between the two versions, EWB subscale was re-scored in Version 4 and not available for fair comparison.

Data Analysis

Independent t-test was used to assess the difference in mean SF-12 v2 domain and summary scores between subjects and age-matched males from Hong Kong general population [16]. For such normative comparison in our study, we identified the same of matching subjects from the Hong Kong population norm study dataset [16] which has been utilized for normative comparisons in other disease[12,24] conditions. In other words, a match was defined as male subjects of the same exact age in year. The SF-12 v2 data were in-house data Besides, independent t-test was used to assess the difference in PWB, SWB, EWB and FWB scores between our patients and (i) general cancer patients (n=1108) [19], (ii) patients with NPC who underwent radiotherapy (n=211) [20], (iii) patients with breast cancer (n=259) [21], (iv) patients with CRC (n=286) [22], and patients with acute leukaemia, chronic leukaemia, lymphoma and others (n=134) [23] reported in other studies sampling in Queen Mary Hospital, Hong Kong. These data about the HRQOL of cancer patients were all obtained from published manuscripts. In order to further understand the impact of prostate cancer treatment on HRQOL, we compared the SF-12 v2 scores between Hong Kong general population and different types of treatment, and

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the FACT-P scores between different types of treatment by one-way ANOVA with Tukey's HSD test.

Cohen's d effect size was calculated to estimate the clinical significance of HRQOL differences. According to the suggestion by Sloan et al, the 1/2 standard deviation is a conservative estimate of an effect size that is likely to be clinically meaningful [25]. Cohen's d effect size 0.5 means that the two means are 1/2 standard deviation apart [26].

Ethics approval

The study protocol was approved by the institutional review boards: HKWC (Ref No.: UW13-239).

Results

A total of 339 patients with prostate cancer were invited to join the study. Of the 339 patients, 29 patients refused to participate. A further 19 patients were excluded because of hearing problems, inability to communicate in Chinese/Cantonese, cognitive impairments or being too ill to complete the questionnaire. Among them, 291 eligible subjects (response rate: 85.9 %) were included in HRQOL assessment. Table 1 shows the socio-demographics and clinical characteristics of prostate cancer patients. 35.05 % of subjects completed radical prostatectomy, 40.21 % of subjects completed androgen deprivation/ combined androgen blockade, 15.46 % of subjects completed radical curative radiation, 2.75 % of subjects completed adjuvant radiation and 1.37 % of subjects completed chemotherapy at the time of subject recruitment. Concerning HRQOL data complete rate, all subjects (100%) completed FACT-P whilst 289 subjects (99.3%) completed SF-12 v2.

Table 2 shows the means and the standard deviations (SD) of the SF-12 v2 scores and their comparison with normative population in Hong Kong. The SF-12 v2 GH, VT, and MCS scores of our subject lower than the adjusted population norms (p-value <0.01), with effect size ≥ 0.5 . Although the MH scores of out subjects were lower than the adjusted population norms (p-value <0.01), the effect size was smaller than 0.5, which was probably not clinically significant. Furthermore, the SF-12 v2 PF score of our subjects was significantly higher than the adjusted norm (p-value <0.01) but the effect size was only 0.40, which was probably not clinically significant.

Table 3 shows the FACT-P scores of prostate cancer patients and their comparison with patients with other cancer types. Overall, prostate cancer patients had better physical well-being (p-value <0.05, effect size =0.61) and functional well-being (p-value <0.05, effect size =1.07) than general cancer patient populations in Hong Kong. Moreover, prostate cancer patients perceived better physical well-being than patients with leukaemia (p-value<0.05, effect size =0.59). Prostate cancer patients perceived better emotional well-being than patients with leukaemia patients (p-value<0.05), with effect size 0.71. Prostate cancer patients perceived better functional well-being than patients with NPC who underwent radiotherapy or breast cancer patients (p-value<0.05), with effect size >0.5.

Besides, we found that prostate cancer patients perceived better physical well-being than patients with breast cancer (p-value<0.05) but poor physical well-being than CRC patients (p-value<0.05), but the effect size statistics were both smaller than 0.5, which was probably not clinically significant. There was no statistically significant difference in social well-being among different cancer patients, except for breast cancer patients who had better social well-being than

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prostate cancer patients (p-value<0.05). However, the small effect size (0.17) was probably not clinically significant.

Sub-group analysis by one-way ANOVA found no statistical difference (p-value >0.05) in any SF-12 scores between Hong Kong population and subjects in different treatment groups. Furthermore, there was no statistical difference in PWB, SWB, EWB and FWB scores among subjects in different treatment group. The post hoc analysis found that subjects who underwent radical curative radiation (mean: 33.1, SD: 9.0) had poorer HRQOL as measured by prostate cancer subscale of the FACT-P than those who underwent radical prostatectomy (mean 37.0, SD: 5.1) with effect size 0.53 (p-value=0.015).

Discussions

To the best of our knowledge, it was the first study to examine the generic and disease-specific HRQOL of general prostate cancer patients in the Chinese population. We recruited patients with a wide range of clinical characteristics, instead of patients undergoing a specific treatment, in order to strengthen the external validity of our study findings.

The impact of prostate cancer on HRQOL measured by the SF-12 v2

Our prostate cancer subjects had poorer HRQOL in MCS with moderate effect sizes (Cohen's d effect size >0.5) than the adjusted population norms. It appears the prostate cancer had more negative impacts on the mental components than on the physical components of HRQOL. A previous study in the US found that people with prostate cancer had poorer HRQOL in all domains as measured by the SF-12 [5]. The study also found the MCS was much lower than the norm (9.2 out of 100-point), compared with the PCS (2.3 out of 100-point) [5], implying that prostate cancer substantially jeopardized mental well-being over that of physical well-being.

Psychological distress is evident throughout the course of prostate cancer [2,27,28]. A recent systematic review and meta-analysis by Watts found that both anxiety and depression were prevalent throughout the course of prostate cancer [29]. Another systematic review by Dale found that 10-36 % of males with prostate cancer had anxiety [30]. A study by Korfage found that 27 % of prostate cancer patients have depression [31]. Patients with prostate cancer might be concerned about metastasis and the side effects of treatments.

In addition to the mental aspects of HRQOL, our subjects had poorer HRQOL in the GH and VT domains with moderate effect sizes (Cohen's d effect size >0.5) than the adjusted population norms. It is probably because treatments for prostate cancer such as androgen deprivation therapy often have side effects causing reduced energy, sexual dysfunction and loss of bone and muscle mass [32,33]. Besides, our findings were consistent with the findings of a previous study on Chinese patients with lower urinary tract symptoms (LUTS) which found that Chinese patients with LUTS had poorer HRQOL in the VT and GH domains with moderate effect sizes than the adjusted population norms [12]. The presenting symptoms of prostate cancer are similar to those of LUTS. Furthermore, according to traditional Chinese medicine, urological and reproductive diseases are always associated with "kidney gi and yang deficiency", which also lead to the deterioration of masculinity, energy and overall health function in males [12,34,35]. People with prostate cancer might perceive that their general health and sexual function declined, which lead to poorer HRQOL in GH and VT domains. We also found that the VT score of prostate cancer patients was 13.73-point lower than the adjusted population. Decrease in vitality is disabling. Previous study found that a 10-point reduction in VT score of the SF-36 would increase the risk of inability to work due to fatigue, job loss at one year, hospitalization at one year and short-term (0-18 months) and long-term (19 months or more) mortality [36].

Paradoxically, the PF domain of the subjects was better with a moderate effect size 0.40 although the effect size was smaller than 0.5, which was probably not clinical significant. This finding was similar to that found in Japan [8]. It was hard to explain why the PF score in patients with prostate cancer were higher than that of the population norm. One possible explanation is the "response shift theory" [37]. Prostate cancer patients might reframe their expectation for their activity of daily living, which in turn leads to changes in the internal standard about physical functioning. As a result, they might have "better" PF scores than the corresponding norm. Further studies are required to confirm this finding and to explore the underlying reason.

Condition-specific HRQOL between prostate cancer and other cancers

We found that patients with prostate cancer had better condition-specific HRQOL than the general cancer population in Hong Kong, especially for the physical and functional aspects.

Moreover, compared with patients with breast cancer, CRC, NPC or leukaemia in Hong Kong, our subjects had better condition-specific HRQOL. The findings are reassuring. It was possible that prostate cancer is relatively "indolent" with a slow progressive course and consequently, when compared with other cancer types, prostate cancer may have a less aggressive impact on patients' HRQOL. Furthermore, compared with the side effects of the treatment for other cancer types such as radiotherapy for NPC patients and mastectomy for breast cancer, those for prostate cancer such as watchful waiting and hormonal therapy are less aggressive. Studies have suggested that HRQOL is greatly impaired by leukaemia because of aggressive treatments [38] and complication of bone marrow transplantation [39]. Data about the comparison of different cancer types are not well documented, which calls for the need of comparison studies to examine HRQOL patterns among different cancer types.

In regard to the Prostate Cancer Subscale, there was no difference (independent t-test p-value >0.05) in the subscale score between our study subject and the FACT-P validation sample (n= 96; mean score= 36.9, standard deviation= 6.6) recruited in the University of Chicago[17]. Actually, it is hard to compare our study findings with others because the study samples of the majority of studies were selective such as patients undergoing surgical intervention or hormonal therapy, and patients with watching waiting. The difference in clinical characteristics hinders comparison.

The HRQOL and prostate cancer treatments

Our subgroup analysis found no difference in the SF-12 v2 scores between age-adjusted Hong Kong population norm and subject in different treatment groups, and the FACT-G scores in subjects in different treatment groups. Our findings were consistent with those of previous studies [40-42]. A study on men with localized prostate cancer in the US found no difference in SF-36 and FACT-G scores between control group, surgery group, radiation group and watchful waiting group [40]. Another study in the US also found no difference in the SF-12 and FACT-G scores between control group, surgery group and radiation group[42]. There were some possible explanations. First, the SF-12 v2 is a generic HRQOL measure. The question items might not be specific and sensitive enough to capture of the impact of diseases or different treatments on HRQOL [43]. Furthermore, the FACT core module is applicable for all cancer patients.

Therefore, it might contain irrelevant domains and may miss specific concerns held by our prostate cancer patients. Besides, the relatively small sample size in subgroup analysis might lead to insignificant results. Further studies with larger sample size are needed to confirm our findings.

On the contrary, our subgroup analysis found that subjects who underwent radical curative radiation had poorer HRQOL as measured by prostate cancer subscale of the FACT-P than those who underwent radical prostatectomy (3.9-point, with effect size 0.53). Based on the suggestion by Sloan et al [25], the 1/2 standard deviation (Cohen's d effect size 0.5 [26]) is likely to have clinically meaningful difference. Furthermore, a previous study estimated that the clinically distinguishable score of the prostate cancer subscale of the FACT-P ranged from 2 to 3-point [44]. Thus, the difference in HRQOL detected between two groups in the present study was very likely to be clinically meaningful.

The study in the US found that subjects who underwent brachytherapy (mean: 33.2) tended to have poorer HRQOL as measured by the FACT-P prostate cancer subscale than those who underwent radical prostatectomy (mean: 37.8) [42]. A literature review suggested that there are more risks of urinary voiding difficulties and difficulties with bowel function for radiation treatment [45]. The study in the US also found that patients who underwent radiotherapy tended to have poorer irrigative urinary symptoms, bowel symptoms, sexual functions and obstructive voiding symptoms than those who underwent radical prostatectomy [42].

Clinical implications and further studies

Since patients with prostate cancer had poorer mental components of HRQOL, the anxiety and concern of patients with prostate cancer should be assessed and addressed. Counseling and pastoral care should be a part of routine care for patients with prostate care with close attention to the possibility of poorer HRQOL related to general health and energy. First, clinicians should educate Chinese patients about the etiology of prostate cancer and reorient Chinese patients that prostate cancer is not related to problems of the kidney but the reproductive system. Second, in

addition to treatments for prostate cancer, patients might also need some interventions about life style modification in order to improve their general well-being and energy. Furthermore, previous studies found that physical exercise such as resistance exercise can reduced fatigue and improve muscular fitness and HRQOL in men with prostate cancer [46,47].

Strengths and Limitations

There are some strengths in the present study. First, most studies about the HRQOL of patients with prostate cancer were based on clinical trials. The selection criteria for subject recruitment limited the external validity of the study findings. Our study recruited patients with diverse clinical characteristics which makes our study findings more generalizable. Second, we used both generic and condition-specific HRQOL instruments, which provided a more comprehensive HRQOL assessment. Third, to our knowledge, it should be the first study to compare the FACT-G scores among different primary tumor sites. Several limitations should be noted in the present study. First, historical comparison was conducted to compare the prostate cancer and general population groups that were not recruited during the same period of time. Second, due to the paucity of patient-level data of other cancer types, comparison of other cancer types did not match to minimize bias of differences in HRQOL between prostate cancer and other cancer types. Third, some factors such as mental health, health belief, socio-demographics were not collected in the present study [48,49]. Further studies should be explored the impacts of these factors on HRQOL in prostate cancer patients.

Conclusion

This preliminary study suggested that prostate cancer patients have poorer HRQOL, particularly in the GH domain, VT domain and mental component summary of the SF-12 v2 than the normal

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population. It suggested that prostate cancer jeopardizes the overall health perception and mental health in Chinese patients. It is reassuring to find that compared with other cancer types, patients with prostate cancer had better HRQOL as measured by the condition-specific instrument. It might be due to the less aggressive nature of prostate cancer, relative to other cancers.

Conflicts of Interest

The authors have no financial conflicts of interest.

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Table 1. Baseline socio-demographic and clinical characteristics

Demographic	Total (N=291)		Clinical	Total (N=291)	
Characteristics	N % Characteristics		N	%	
Age (years, Mean±SD)	74.92	2 ± 8.61	PSA		
Education			<0.1ng/ml	109	37.46 %
No formal schooling	46	15.81 %	≥0.1 & <10ng/ml	121	41.58 %
Primary	98	33.68 %	$\geq 10 ng/ml$	39	13.40 %
Secondary	90	30.93 %	Unknown	22	7.56 %
Tertiary or above	53	18.21 %	AJCC Cancer Staging		
Unknown	4	1.37 %	I	58	19.93 %
Marital Status			II	75	25.77 %
Married	222	76.29 %	III	31	10.65 %
Not married	65	22.33	IV	112	38.49 %
Unknown	4	1.37 %	Unknown	15	5.15 %
			Distant metastasis	59	20.27 %
Currently Working			KPS		
Yes	25	8.59 %	Mean±SD	91.39 ± 12.50	
No	262	90.03 %	≤70	23	7.90 %
Unknown	4	1.37 %	80	34	11.68 %
Monthly income (HKD\$)			90	64	21.99 %
≤20,000	238	81.79 %	100	138	47.42 %
>20,000	49	16.84 %	Missing	32	11.00 %
Unknown	4	1.37 %	Treatments #		
			Watchful waiting/active	24	8.25
			surveillance	24	
			Radical prostatectomy	102	35.05
			Androgen deprivation/		
			Combined androgen	117	40.21 %
			blockade		
			Radical curative radiation	45	15.46
			Adjuvant radiation	8	2.75
			Chemotherapy	4	1.37
CD -411-11-4'					

SD=standard deviation;

PSA=Prostate-specific antigen;

KPS=Karnofsky performance status; AJCC=American Joint Committee on Cancer

It shows the treatments that patients have undergone. Some patients might have received more than one treatment.

Table 2: the SF-12 v2 scores of study subjects

GF 12 2	Subjects with Prostate Cancer +	Age-sex adjusted HK norm [16] +		
SF-12 v2 scores	n=142	n=142		
	Mean (SD)	Mean (SD)		Effect size ^
Physical Functioning	84.33 (25.20)	73.06 (30.95)	*	0.40
Role Physical	79.14 (27.28)	75.97 (25.40)		0.12
Bodily Pain	81.16 (25.30)	79.58 (24.48)		0.06
General Health	48.80 (30.81)	63.49 (26.36)	*	0.51
Vitality	60.92 (31.15)	74.65 (22.87)	*	0.50
Social Functioning	82.75 (25.82)	80.46 (23.65)		0.09
Role Emotional	83.45 (22.41)	86.00 (20.55)		0.12
Mental Health	71.65 (21.00)	81.51 (19.51)	*	0.49
Physical Component Summary score	48.82 (10.63)	46.10 (12.56)		0.23
Mental Component Summary score	52.08 (10.16)	57.45 (9.80)	*	0.54

SD=standard deviation; AJCC=American Joint Committee on Cancer

^{*}Significant difference between subjects with prostate cancer (overall) and HK norm[16] (P< 0.01).

⁺of 2763 respondents in the study of the population norm of the SF-12 v2, only 142 respondents could match our study subjects (by age and sex) [16].

[^] Cohen's d effect size was calculated as the difference between mean scores, divided by pooled SD.

[#] of those who had AJCC staging, one subjects did not complete SF-12 v2

Table 3: the FACT-P scores of study subjects

	Prostate cancer	General Cancers [19]		Nasopharyngeal carcinoma [20] n=211		Breast Cancer [21] n=259		Colorectal cancer [22] n=286		Leukaemia [23] n= 134	
	n=291										
FACT -P scores	Mean (SD)	Mean (SD)	Effect size ^	Mean (SD)	Effect size ^	Mean (SD)	Effect size ^	Mean (SD)	Effect size ^	Mean (SD)	Effect size ^
Physical Well- Being	24.63 (3.64)	21.80 (5.50)*	0.61	24.00 (4.00)	0.16	23.07 (4.87)*	0.36	25.62 (3.09)*	0.29	22.1 (4.8)*	0.59
Social/Family Well-Being	19.62 (5.18)	19.30 (4.60)	0.07	19.60 (4.40)	0.00	20.48 (4.97)*	0.17	20.17 (4.34)	0.12	20.4 (5.3)	0.15
Emotional Well-Being #	21.08 (3.76)	N/A	N/A	N/A	N/A	N/A	N/A	21.40 (2.82)	0.10	18.3 (4.1)*	0.71
Functional Well-Being	19.72 (5.38)	13.70 (5.90)*	1.07	16.00 (5.40)*	0.69	15.42 (6.12)*	0.75	19.03 (4.38)	0.14	19.2 (5.3)	0.10
Prostate Cancer Subscale	35.82 (6.61)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

SD=standard deviation; AJCC=American Joint Committee on Cancer

^{*} independent t-test was used to compare the scores between two groups (p<0.05)

[^] Cohen's d effect size was calculated as the difference between mean scores, divided by pooled SD.

[#] Those studies used FACT-G (version 3). The composition of emotional well-being score is different version 3 and version 4. Thus, the scores cannot be compared.