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## ARTICLE REVIEW

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### **Disease and Economic Burden of Prostate Cancer in Malaysia: A Review**

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#### **ABSTRACT**

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<b>Introduction</b>	In Malaysia prostate cancer is ranked as fifth type of cancer among male. Unlike other cancers, prostate cancer is slow growth type of cancer; hence most patients may be asymptomatic despite having the disease. The burden associated with prostate cancer disease started from the diagnosis, the progress of disease and the varying impact of the available treatment options till the quality of life. The review focused on the disease and economic burden of prostate cancer disease towards country and patient personally.
<b>Methods</b>	A search was conducted to review related published studies on economic burden of the prostate cancer through PubMed/MEDLINE, Google Scholar and Science Direct searching engines databases using keywords: Prostate cancer, economic burden and disease burden, treatment burden and treatment cost. For exploration on the burden itself, the keywords used were economic cost, mortality, morbidity, quality of life, treatment burden, palliative care. A review on the morbidity and mortality comparing global, Asian and Malaysia situation reviewed from previous review paper and online data.
<b>Conclusions</b>	Economic burden of prostate cancer include quality of life, treatment cost and palliative cost and palliative support care system. Development and improvise of the treatment facilities and equipment, strong knowledge and clinical training of staff in the treatment of cancer should be well planned in order to reduce the increasing burden of prostate cancer in Malaysia.
<b>Keywords</b>	Prostate cancer - Burden of disease - Economic - Cost - Quality of life.

## INTRODUCTION

Cancer is indeed a serious health issue. According to data from Globocan 2012 stated 14.1 million new cancer cases reported with 8.2 million cancer deaths. The burden of cancer also included 32.6 million people living with cancer within 5 years of diagnosis and estimated 5.3 million cancer deaths reported in the less developed regions. Men recorded 25% higher incidence rate of cancer than women in overall age standardized with 205 and 165 per 100 000 respectively.<sup>1</sup> According to the report prostate cancer is the fourth most common cancer combining both sexes with estimated 1.1 million men been diagnosed in 2012 worldwide increasing from 513 000 diagnosed in year 2000.<sup>2</sup> By the year 2030 estimated that 1.7 million new cases of prostate cancer will be diagnosed with projection almost 500 000 death worldwide which bring it as the most common cancer in men in the future.<sup>3</sup> Among men, statistic showed that prostate cancer ranked second most common cancer worldwide with age-standardized rate (ASR) of 28.5 cases per 100 000 persons per year (International Agency for Research in Cancer, 2008) and was the fourth most common cause of cancer death among men with ASR of 7.5 deaths per 100 000 person per year.<sup>1</sup>

Malaysian National Cancer report (MNCR) 2007-2011 stated a total number of 103 507 of new cancer cases been diagnosed over the period of 2007 till 2011 of which 46 794 (45.2%) reported in males. It makes the risk of males been diagnosed with cancer was 1 in 10 and for female was 1 in 9. The yearly cancer incidence in Malaysia has been estimated to be 30 000 per year with the prevalence approximately 90 000 to 100 000 at one time. Colorectal cancer (16.3%), Lung cancer (15.8%), Nasopharynx cancer (8.1%), Lymphoma (6.8%) and prostate cancer (6.7%) reported as the five most common cancers in males while females recorded breast (32.1%), colorectal (10.7%), cervix uteri (7.7%), ovary (6.1%) and lung (5.6%) in their top five most common cancer. Chinese has the highest age standardized incidence of cancer followed by Indian and Malay that reported 8.7, 5.8 and 4.9 per 100 000 populations respectively by ethnicity.<sup>5, 6</sup>

In 2014, Malaysian statistics reported prostate cancer was the fourth most common type of cancer that caused 1 186 number of incidence among male populations (WHO 2014). With an increase of life expectancy and aging population, the incidence of prostate cancer is expected to rise proportionately. In Malaysia the proportion population aged more than 60 years was 4.6% in 1957, escalated to 5.7% in 1990 and projected to be 9.8% in 2010.<sup>7</sup> This study aimed to understand the economic burden of prostate cancer in Malaysia and comparing to other countries.

## METHODS

A search conducted to examine published studies on disease and economic burden of the prostate cancer using MEDLINE / PubMed, Google Scholar and Science Direct databases using keyword: "prostate cancer", "economic cost", "disease burden", "treatment burden", "treatment cost". For exploration on the burden itself, the keywords used were "economic cost", "mortality", "quality of life", "treatment burden", "palliative care". Then Boolean operator "OR" and "AND" been applied in combining search keywords for the study population, comparison, and outcomes in the title search from year 1995 onwards. The abstracts identified were screened based on the inclusion criteria. Full articles were reviewed then comparing with study done in other countries.

## RESULTS

### *Morbidity and Mortality*

The 5-year relative survival rate of prostate cancer for all stages combines has increased from 68.3% to 99.9% in the past 25 year duration. The 10 year and 15 year relative survival rate reported as high as 97.8% and 91.4% respectively.<sup>8</sup> These trends in survival rate have been attributed to a combination of multi factorial aspects such as early detection, improvement of effective treatment of localized and advanced disease, longer lead-time bias as early diagnosis falsely appears to prolong survival, and over diagnosis in cancer screening such as due to wide spread use of Prostate Specific Antigen (PSA) screening.<sup>9-11</sup> However these trends in morbidity and mortality and outcomes are continue to differ across socio demographics, socioeconomic, racial and culture, and ethnic boundaries. There were few studies reported prostate cancer survivors in non-white populations with low economic status and education level were likely to have poorer quality of life with lower likelihood of survival rate.<sup>12-14</sup>

Prostate cancer incidence has been in increasing trend during the past few decades in many Asian countries. WHO reported in 2012, the incidence rates were estimated at 10.5% and 4.5% in East and South-Central Asia respectively. Currently prostate cancer ranked the sixth most frequent cancer in Asian men. The highest incidence reported in Western Asia ranking second and the lowest in South-Central Asia ranking eighth in all cancer incidence. Report from China National Cancer Registry showed the incidence was 9.92 per 100 000 in 2009 while incidence in Korea documented escalation incidence from 8.4 in 1999 to 24.4 per 100 000 population in 2011.<sup>15, 16</sup> Although in general the prostate cancer incidence was reported quite low comparing to western countries ; however with aggressive economic and socio-cultural changes, improvement life expectancy with urbanized lifestyles, the incidence

and mortality rates of prostate cancer in some Asian countries have shown a tremendous increasing trend in which was believed to be one of the serious healthcare and socio-economic problem in the future.<sup>17, 18</sup>

In the year 2012, the overall average mortality rate of prostate cancer in Asian countries reported at 3.8 per 100 000 whereby countries with rapid economy development such as Japan, Singapore, and Korea had their prostate cancer mortality rate of 5, 4.5 and 4.6 per 100 000 populations each. There were also variable trends of mortality seen in countries like China (Hong Kong), Kazakhstan and Korea. Countries like Israel, Kyrgyzstan and Uzbekistan had reported of declining trends of mortality while more stable mortality trends reported in Singapore and Tajikistan.<sup>18</sup>

In Malaysia, Lim et al in 2008 had discussed that the annual mortality rate per 100 000 people from prostate cancer has increased in the past decade by 93.7% since 1990, an average of 4.1% a year with age specific incidence rise after age of 50 years old.<sup>5</sup> By the year of 2030, prostate cancer incidence expected to increase to 1.7 million newly diagnosed cases with 499 000 deaths worldwide. By then prostate cancer will be known as the top most type of cancer in men in the future that contribute to 15% of all new cancer cases in men and it is predicted that 70% of all new cases of the prostate cancer occur in developed countries.<sup>15-18</sup>

#### *Screening and Awareness Program*

Early detection and prompt treatment always be the main vision to improve the chances of cure in any type of cancer. Unfortunately delays in presentation for screening, diagnosis and treatment are commonly found among cancer patients especially prostate cancer. One of the initiatives done to overcome the late presentation is by providing prostate cancer screening such as stated in the Malaysian National Cancer Management Blueprint 2008-2010. However due to lack of strong evidence regarding the advantages in benefit and cost especially in asymptomatic men, the mass population based screening for prostate cancer in Malaysia did not recommended.<sup>19, 20</sup> Schersten et al in 1999 has stated that although the sensitivity and specificity of prostate specific antigen (PSA) gave good result towards prostate abnormalities but the test was not ideal enough due to high false positive and false negative rate. Besides that there was no study reported the PSA threshold or level that effectively able to differentiate between the presence and absence of prostate malignancy.<sup>20</sup> As for now, the clinically practice criteria and abnormal digital rectal examination (DRE) were early predictors for prostate cancer before biopsy been done as the agent causes the development of

prostate cancer is still unknown. It was supported by the relative risk of developing prostate cancer in first degree relatives was 2.5 folds, and 3.5 folds with two affected relatives.<sup>21</sup>

Many studies have shown the mixed reviews though most researchers found a parallel association whereas higher level of education leads to recognition or awareness of the any disease. The good knowledge regarding prostate cancer screening also showed the rate of doing prostate screening is twice amount of respondents compared to group with low level of knowledge. Those with high formal education responded higher in the awareness and had undergone prostate cancer screening practice. Friends, media and workplace played important role in spreading the awareness. It is documented that media that reported on mortality and morbidity of prostate cancer to public will actually raising the awareness on disease to community. Thus, good knowledge of prostate cancer screening plays very important role to raise the awareness either by formal or informal education system.<sup>22</sup>

While in Malaysia there was increment of prevalence prostate cancer with massive promotion where the age-standardized incidence of prostate cancer was 12 per 100 000 populations in 2005 which higher than the incidence of 10.3 per 100 000 population in 2003 however the prevalence seem decreasing to 6.2 in 2006 when there was less screening promotion undergone.<sup>5</sup>

#### *Economic Burden*

In general, prostate cancer management and treatment are depending to the stage of cancer itself. For prostate cancer with early stage, the treatment decision depended to the individualized approach such as hormonal therapy, prostatectomy, radical radiation or active surveillance based on age, comorbidities and side effect of treatment to the patients. As for more advanced stage of prostate cancer, the choice of palliative care, with androgen deprivation therapy with medical or surgical castration been always recommended treatment option according to National Comprehensive Cancer Network, NCCN 2012.<sup>23</sup> Studies in United States had showed that the treatment of prostate cancer had brought a high economic and financial burden; total cost of prostate cancer care was reported at about US\$12 billion in 2010, increasing from US\$10 billion in 2006, US\$1.3 billion in 1994 and projected rise to US\$16 billion in 2020.<sup>24</sup> Another economic burden study by Stokes in 2011 had also predicted a lifetime cost of US\$110 520 per person required for treatment based from the Surveillance Epidemiology and End Results (SEER) model analysis.<sup>25</sup> It was supported by another study by Wilson et al that stated financial commitment in the prostate cancer management were US\$7 740 which range from US\$ 5 843 for

active surveillance to US\$12 590 for hormonal therapy or androgen deprivation therapy while mean cumulative cost was US\$ 42 570 over 5 years that range the least cost on active surveillance (US\$ 32 135) to the highest costs were associated with androgen deprivation therapy (US\$ 69 244) for all risk groups.<sup>26</sup>

In Malaysia, there was a study by Hooi in 1996 stated that duration of admission of cancer patients in hospitals considered as burden of cancer to the country. In 1995, a study conducted in Penang Hospital reported significant inpatient burden or workload from the cancer patient admission. The hospital based study had showed that the average duration of admission of cancer patient in the hospital was 12.7 days (range 1-130 days) that directly projected the need of many manpower from different discipline.<sup>27</sup> This study almost similar to the annual statistics report of Department of Radiotherapy and Oncology of Hospital Kuala Lumpur in 1997 with average stay in hospital of 11.4 days for the cancer patients comparing to the ward stay of whole Hospital Kuala Lumpur of 5.2 days in the same year.<sup>5</sup>

In 2013, Sharifah Ezat et al had discussed burden of cost on skeletal-related event (SRE) such as bone metastases at spine for advanced prostate cancer patient. As Ministry of Health Malaysia had reported that neoplasm contributed about 11.12% out of the ten principal causes in 2011, bone metastases in prostate cancer could bring significant financial effect to the healthcare system or country in providing extensive health facilities and resources.<sup>28</sup> The study also supported by Bernad et al in 2011 that reported cancer patients also have a risk for high economic and financial burden compared with other patients with chronic comorbid as they may have higher out-of-pocket costs or medical expenses. The financial burden were significantly worse with metastases disease who are treated with palliative support care that depended on many factors such as patient's underlying comorbid, daily activities, location of metastases, treating paramedic and physician, and also equipment available.<sup>29, 30</sup> Based on study of health insurance claimed between year 2002 and 2008 by Hagiwara et al in 2011 stated that bone metastases contributed to a 55% increase in average total monthly healthcare expenses or US\$ 12 780 per person year. Another issue of increment of cost burden is late diagnosis of bone metastases that implicate to more invasive and frequent investigations, which can result in increasing resource, equipment and manpower utilization due to complication and prolonged hospitalization.<sup>31</sup> It was proven by model analysis of patients with metastatic breast cancers and prostate cancers study in Portugal that showed the diagnosis of bone metastases had brought a significant 19% to 106% increase in treatment financial costs while Penson

stated that prostate specific antigen (PSA) progression would also contribute to a significant economic burden with disregard of baseline stage, Gleason grade and type of treatment.<sup>32, 33</sup> Another study by George Institute for Global Health in 2015 had stated that 45% of cancer patients may face financial catastrophe after a year of diagnosis. This situation worsen after one year of treatment started when reported 39% were not able to pay for medication, 35 % were not able to pay for medical consultation fees or tests, 22% were not able to pay for rent or mortgage and sadly 19% may actually stop treatment.

Earlier study in year 2002 by Max et al stated economic burden of prostate cancer not only involving medical treatment such as cost of admission to the hospital, clinics follow ups, hormonal or chemotherapy drugs, palliative support care but also involving mortality costs in which is the estimate expected patient individual's future salary or wages based on their age diagnosed till retire age. These calculations may also involving patient expected life expectancy and possibility in increment of salary in future age. In total the burden of prostate cancer calculated may reach till US\$ 360 million which involving US\$ 180 million from direct health care cost and another US\$ 180 million came from total loss of productivity due to premature death due to prostate cancer.<sup>34</sup>

### *Quality of Life*

Generally quality of life means the state of wellbeing which consist of two main components that involving patient to undergo their daily activities including physical ability, psychological status, communications and social well-being and patient satisfaction towards functioning and control of the disease. Numbers of quality of life study found that disease and treatment related symptoms gave low level score and poor impact on cancer patients. The treatments itself gave significant impact to the quality of life especially those were diagnosed late in the advanced stage as their main priority treatment that include radical radiotherapy, chemotherapy and pain medications aimed to delay or avoid bone metastases and pain management that believed may able to improve patient daily activities and quality of life.<sup>35, 36</sup>

Measuring patient quality of life provides information that may help prostate cancer patient evaluating their physical, psychological, social and functional abilities during and after treatment. Generally these prostate cancer patients were worried about the side effects of treatment and implications of prostate cancer in their lives. Although most of them may perform normal daily physical activities, some may still worried about their sexual function and ability to satisfy their sexual partner relationship. By measuring the

quality of life these prostate cancer patients are able to understand the complications and consequences of the disease from their treatments and also helping physicians to know patient's acceptance towards treatment.<sup>37</sup>

Study in Malaysia on quality of life among prostate cancer patients by Mohamad Rodi Isa in 2012 been done and reported that they were likely to develop anxiety disorder as they were repeatedly exposed to multiple investigations and treatment that potentially induced anxiety and fear during treatment such as monitoring of prostate specific antigen (PSA). However, anxiety level decreased with ongoing repeated investigations and increasing age. There were study reported that mean anxiety level had declined from 20% to 12% which include in reduction of psychomotor, agitation, weakness, fatigue and pessimism. The study also mentioned that those patients who had tolerated the cancer management and treatment will have low level on anxiety disorder. Mohamad Rodi also discussed that the physical health status and mental health status in Malaysia may be varied due to the ability of improvise and adaptation mechanism to the cancer.<sup>38</sup> A study in Canada on health related quality of life (HRQOL) documented that the level varied among prostate cancer patients with different type of treatment that include radical prostatectomy, radiotherapy and brachytherapy. The study also reported that patients who undergone radiation therapy with early prostate cancer will have good urinary control and sexual function while brachytherapy had gave obstructive irritated implications to patients.<sup>39</sup>

#### *Palliative care*

Palliative care or supportive care may also cause economic burden as it needs a multidiscipline team to improve the quality of life of prostate cancer patients. This palliative care aimed to educate care giver or families with cancer pain management, prevention and relief of suffering due to cancer symptoms. Commonly practice palliative care usually based on three main objectives or goals which are improving morbidities due to prostate cancer disease, morbidities due to the treatment and quality of life after diagnosis.

In Malaysia, palliative care program is usually initiated and organized either by government of private sector or non-governmental organizations (NGO) such as hospice home that include the training of medical doctors, nurses, medical assistants and public volunteers. Ideally the management cancer care patients after their discharge from hospital should be carried out by certified medical personnel either in the peripheral hospitals or their homes. These personnel must been trained in basic cancer care, ability to recognized and complications due to cancer or treatment and able to communicate with the

oncologist that actually lead to tremendous amount of out of pocket money. Although the palliative care system in Malaysia quite established there is still area to improve including the limitation of palliative personnel to deliver best supportive care due to lack of knowledge such as the underuse of aqueous morphine in the severe cancer pain in advance stage of prostate cancer patients. Besides that it is necessary for the palliative care personnel to manage any morbidity caused by prostate cancer itself such as those patients with bone metastases, spinal cord compression, urinary obstruction and also any related psychological implications including depression, poor coping mechanism including intimacy issues.<sup>40</sup>

Many literatures and randomized trial studies overwhelmingly support the establishment of palliative care in treating cancer especially in advanced stage. The studies believed that these palliative support care centers capable to improve quality of life including relieving symptoms, improved patient expectation and also able to reduce health care expenses.<sup>41, 42</sup> There were trials by Temel and colleague that reported palliative supportive care implementation resulted significant longer median survival of 11.6 months comparing 8.9 months (p-value 0.02) in patient without palliative care. Another study by Rabow also reported that prostate cancer patients who went palliative care intervention had statistically significant improvement in fatigue, anxiety, depression, quality of life and spiritual well-being.<sup>40</sup>

However, one of the main limitation of this palliative care program is late referrals due to lack of knowledge to recognize end life symptoms in cancer patients while Dalal et al stated that the barrier to this care was the name "palliative care" itself. It was proven after he managed to receive many consultations after he replaced the group's name to "supportive care" that actually lead to shorter time of diagnosis to consultation.<sup>44</sup>

One of the initiatives to empower palliative care, World Health Organization (WHO) had recommended that palliative care component to be part of national educational syllabus. In Malaysia, this initiative been applied to local medical universities that offer palliative care in their postgraduate courses of family medicine and nursing teaching programs while in hospital, regular workshops and seminars are being organized to the palliative care units to empower their knowledge and skills towards good quality of palliative support care.<sup>45</sup>

## **DISCUSSION**

As prostate cancer is one of the commonest diagnosed malignancies in men, the burden of this disease is likely to increase. Although prostate cancer mortality rates are declining with the 5-year

survival rate for prostate cancer patients is reaching 99%, 10-year survival is 91% and 15-year survival is 76%, the economic burden of disease treatment is growing fast. This growing economic burden is surely give big impact for Malaysia as developing country where health care expenditures need to compete with other sector such as social welfare, education and infrastructures. The economic burden of any disease can be divided to direct and indirect costs incurred by cancer patients. The direct costs include services for health care such as treatment, procedures, laboratory investigations, screening and health care professionals while indirect costs represent the reduced productivity associated with lost or impaired ability to work because of illness and the loss of economic productivity because of premature death.

There are a lot of studies reported that most of economic burden in prostate cancer associated with direct cost as it occurred in elderly men. Health Canada estimates direct costs for all forms of cancer amounted to \$3.2 billion, Netherlands reported for 5% to 6% of total healthcare budget of direct health care costs for all cancers in 1988 and Sweden estimated at 5.8% of all disease burden and approximately 25% of total costs for medical care were incurred during the first year after diagnosis.<sup>46</sup> However the study reported that indirect cost burden of prostate cancer were relatively lower as most of the patient diagnosed at the age of more than 70 years old.<sup>46</sup> The study analysis from a patient perspective and includes reimbursement payments made to physicians, facilities and other healthcare professionals for the medical services that were provided to cancer patients. Other components of the economic burden including out-of-pocket spending on direct medical care as well as the indirect costs associated with reduced productivity and lost work time for both caregivers and patients were not included in this study. These cost components have been shown to represent an important proportion of the total cost burden.

### *Cost-effectiveness studies*

As for cost effectiveness the introduction of PSA screening seem to be speculative as it gave more economic burden due to increasing number of patients diagnosed with prostate cancer. Hence few strategies were identified such as treating those cancers which will become clinically significant would considerably reduce treatment costs. This is supported by Stokes et al that stated higher costs in the early stage of prostate cancer that comparing his finding with Riley.<sup>25, 46-47</sup>

## CONCLUSION

In conclusion, the burden of prostate cancer in Malaysia is really worrying and be focused holistically. Multi sectoral agencies should work

together in order to reduce the incidence rate, morbidities and mortality of prostate cancer. In order to improve the quality of life of cancer patients, policies that focused on cancer prevention, early screening and diagnosis, effective treatment, best palliative support care and rehabilitation must be revised and improved. More economic and costing studies should be done on economic burden of prostate cancer in order to understand the total burden of the prostate cancer disease in Malaysia.

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