

Is there a champion or will there be a draw?

It's Fight Night!

Is breast cancer giving prostate cancer the knockout in the biggest arena or do they both impact society (and the insurance industry) in a similar way?

It is often said "Prostate cancer is to men what breast cancer is to women." Is the one 'worse' than the other? When one thinks of cancer in South Africa, a fair amount of attention is given to the most common cancer types found in men and women respectively. October marks the month in pink, whereby tremendous awareness campaigning and research efforts are made in support of breast cancer sufferers. November (more famously known as 'Movember') follows closely on the pink ribbons with men growing moustaches in an attempt to raise funds and awareness for prostate cancer

(as well as testicular cancer). But are we covering any ground in our efforts against these cancers? How do they fare against each other in the largest cancer arena? Do we as an insurance industry assess these two cancers wearing similar underwriting hats? In this edition we take a look at breast and prostate cancer side by side and consider some of the overlaps as well as recent advances made and discover that the similarities are more apparent than we may truly appreciate.

According to the South African Cancer Registry, breast cancer is ranked as the most common cancer in women of all races in South Africa, with a lifetime risk of 1 in 33.

Interestingly enough, when we look at the most prevalent non-skin cancer in men, namely prostate cancer, the lifetime risk is very similar to that of breast cancer (1 in 26)¹.

1 2009 National Cancer Registry



A steady increase in overall incidence rates for both cancers is most likely due to effective screening programmes.

The risk of developing either cancer increases with age, however while breast cancer has a peak in both the 45-49 and 70+ age groups in women, prostate cancer is most frequently diagnosed in men between 65 and 69 years of age.

These two cancers have highly similar annual incidence rates (26.94 versus 30.19 per 100,000 persons for breast and prostate cancer respectively) in various countries around the world and their annual age-adjusted death rates are almost identical at 25 per 100,000 cases. A steady increase in the overall incidence rate has been noticed for both cancer types in South Africa and is most likely a result of effective breast and prostate cancer screening programmes, resulting in more diagnoses being made. It is said that all men, if they live long enough, will eventually get prostate cancer. Most of the tumours diagnosed in these much older men will, however, be clinically insignificant and will not even attribute any morbidity or mortality influence on the affected individual. Where an increase in mortality rate is seen in men with prostate cancer, it is mostly due to more men living to an older age, and inevitably being diagnosed with prostate cancer².

2 Babb C et al. Prostate Cancer in South Africa: Pathology Based National Cancer Registry Data (1986-2006) and Mortality Rates (1997-2009). *Prostate Cancer*, vol 2014, Article ID 419801

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- Lifetime risk: The probability that at some stage in life a person will develop a specific type of cancer.
 - Incidence rate: The number of new cancer cases diagnosed per 100,000 people per year.
 - Prevalence: The number of people in a population that have the specific cancer at a point in time.
 - Age-adjusted death rate: The rate that would have existed if the population under study had the same age distribution as the "standard" population. It's a way to make fairer comparisons between two groups with different age distributions, as seen in the age of death in breast cancer versus prostate cancer.
 - 5 year survival rate: The proportion of affected people that will survive five years after being diagnosed with the specific cancer.
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One would not normally think of the breast and prostate gland as being similar tissue types, however when we consider these two more closely, we can appreciate that both are made up of glandular tissue that behave in very similar ways physiologically. Recent emerging evidence suggests that both cancers are influenced and possibly even caused by the same dietary factors (e.g. a western diet high in fat consumption)³. This is based on the notion that obesity (or a fat-rich diet) potentially alters hormonal status. Testosterone is a precursor of oestrogen, and the biosynthesis of oestrogen from testosterone is significantly augmented by the increased presence of fat cells⁴. The increased oestrogen then accelerates the growth of both breast and prostate tissues. This enhanced growth drive results in an increase in cell division error rates, histological atypia (abnormal-looking cells under the microscope), and ultimately formation of cancerous cells. Prostate cancer, not surprisingly, shares many behavioural aspects and qualities with breast cancer, with some of these characteristics outlined in Table 1.

3 Lopez-Otin et al. Breast and Prostate Cancer: An Analysis of Common Epidemiological, Genetic, and Biochemical features. *Endocrine Reviews*. July 01, 2013 <http://dx.doi.org/10.1210/edrv.19.4.0337>

4 Coffey, DS. Similarities of prostate and breast cancer: Evolution, diet, and estrogens. *Urology*, Vol 57(4)-Apr 1, 2001

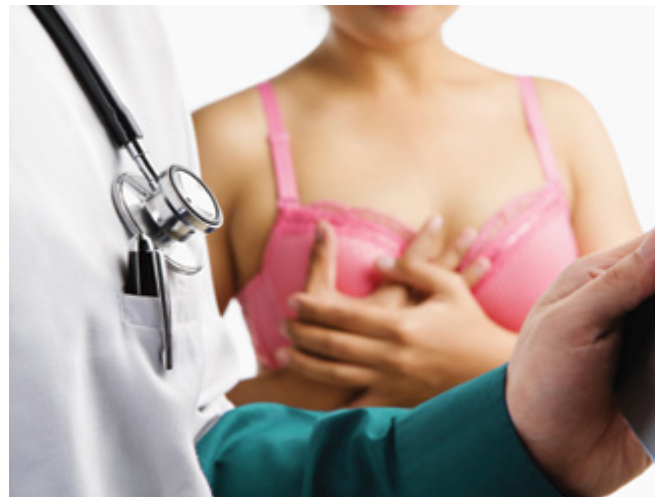
Table 1
Characteristics shared by both breast cancer and prostate cancer ⁵

- Have a higher risk of development when the infamous BRCA2⁶ faulty gene is inherited.
- Have very similar physiology and endocrinology.
- May manifest with very slow tumour growth.
- Require gonads for development and typically respond to hormonal treatment manoeuvres.
- Gonadal removal reduces the risk significantly in both sexes.
- May be clinically silent and remain asymptomatic.
- May be unmasked during active screening programmes.
- May present clinically for the first time as metastases.
- Carry an excellent prognosis if detected early.
- Have a high incidence of both benign disease and small incidental cancers as well as early pre-cancerous lesions.
- Have a high tendency towards bone metastases.
- Contain hormone receptors such as oestrogen, androgen and progesterone receptors and are influenced strongly by the associated steroid hormones.
- Anti-oestrogens foods (e.g. compounds found in citrus fruits, broccoli, avocado) are beneficial and possibly preventive for breast cancer while anti-androgen foods (including compounds found in soy proteins) are beneficial and possibly preventive for prostate cancer.

A closer look at the punches and bruises

While many victims of breast or prostate cancer are successfully cured from their cancer, remission is typically accompanied by important complications of varying severities. We know that both these cancers carry an excellent prognosis if the tumours are still localised (i.e. they have not spread to the lymph nodes, distant organs or bone) at the time of diagnosis, with both having a 5 year survival rate greater than 90%⁷.

Breast cancer and prostate cancer can both potentially be surgically cured when the cancer is diagnosed at an early localised stage of the disease. While a mastectomy (total removal of the breast tissue) is the gold standard procedure for breast



Breast cancer carries an excellent prognosis if the tumours are still localised thus early detection is vital.

cancer, prostate cancer is often treated with a radical prostatectomy being done (removal of entire prostate gland along with some of the surrounding tissue).

The morbidity associated with a having a mastectomy or radical prostatectomy is potentially significant, and although some complications are short-lived, others may persist and could be tremendously burdensome for an ongoing period of time. When radiation therapy or chemotherapy are the selected treatment options for either cancer, morbidity tends to be even more severe, with additional side-effects, complications and long-term risks, including secondary cancers (e.g. lymphomas) arising at the irradiated tissue site.

History's first surgical cure for a cancer – a radical mastectomy, was first performed in the 1880s. Although not typically a very painful procedure, the discomfort associated with having had a mastectomy can be managed with acute analgesia. In most cases, this pain is short-lived and regresses as wound healing progresses. Of more distress to the individual, is the potential development of a seroma (collection of fluid that develops around the surgical site) which, along with pain and discomfort, can result in oozing of fluid from the wound site, and may require multiple drainage attempts ⁸.

5 Coffey,DS. Similarities of prostate and breast cancer: Evolution, diet, and estrogens. Urology, Vol 57(4)-Apr 1,2001 <http://www.cancerresearchuk.org/our-research/our-research-by-cancer-type/our-research-on-prostate-cancer>

6 BRCA1 (Breast Cancer 1 gene) and BRCA2 (Breast Cancer 2 gene) are genes that all people have. An abnormality of either gene significantly increases the risk of developing breast cancer as well as other cancers. The risk of prostate cancer is predominantly associated with the BRCA2 genetic abnormality.

7 <http://www.cancerresearchuk.org/about-cancer/type/prostate-cancer/treatment/statistics-and-outlook-for-prostate-cancer>

8 Kanchan et al. Simple Mastectomy. Medscape. Updated Sept 12, 2013

While the physical impact of a mastectomy is undoubtedly profound, the surgical removal of one or both breasts can have an enormous impact on an individual's mental health and psychological well-being. The prominence of having 'loss of self-esteem' and 'post-mastectomy depression' was investigated and it was found that the peak of emotional distress occurred around three months after the mastectomy was performed - a finding which may be influenced by both treatment as well as the return to regular responsibilities. Although the prevalence of long-term psychological impact was not very different from the emotional impact caused by other cancer types, by virtue of breast cancer having a relatively high incidence and prevalence, a substantial number of women may be affected ⁹.

Non-surgical treatment options (including radiation therapy as well as chemotherapy) are also burdensome, both during treatment, immediately afterwards, and even several months later, in some cases. Complications most commonly experienced are the skin changes seen with radiation therapy. This includes pain, skin discolouration, burning sensations and also redness and swelling of the skin tissue. Most of these skin changes resolve with time.

More troublesome, is the development of a condition called "lymphoedema", which can persist even after a cancer has been successfully treated. Lymphoedema occurs when irradiated lymph nodes in the armpits are damaged and block lymphatic drainage from the associated arm. This results in a person's arm swelling excessively which not only results in pain, but also distress to the individual. Lymphoedema is difficult to treat and often requires elevation of the arm above the level of the head to allow for passive lymph drainage down the arm. Radiation and chemotherapy can also result in conditions that carry a poor prognosis or extreme morbidity, such as chronic radiation pneumonitis (an inflammation of the lung tissue that manifests with a chronic cough and even breathlessness) and pulmonary fibrosis (scar tissue of variable extent developing in the lungs).

Prostate cancer by no means offers a less complicated clinical journey than breast cancer. With the first prostatectomy being

only 20 years younger than the first mastectomy, this historical procedure has been refined through the years in attempt to improve its benefit to complication ratio. Since the prostate gland wraps around the urethra, the surgical excision of the gland invariably requires cutting through the urethra. The healing process thereafter can potentially result in the development of a urethral stricture (narrowing of the urethra from scar tissue). This can result in considerable difficulty passing urine, and complicates almost one tenth of radical prostatectomies. It is not uncommon for affected men to undergo recurrent urethrotomies (a procedure whereby the narrowed diameter of the urethral lumen is expanded by various techniques) in order to alleviate this medical dysfunction. At the other end of the spectrum is the loss of voluntary bladder control, better known as urinary incontinence, and although it accounts for a low proportion (< 10%) of post-surgical complications, it can cause considerable disability in men with on-going symptoms. It is equally common in men treated with radiation therapy, either in the form of external beam radiation (where the radiation is emitted from outside the body toward the prostate zone) or brachytherapy (localised radioactive seeds implanted into the prostate bed).

The majority of men suffering from urinary incontinence have the stress incontinence type – a form of incontinence that only manifests during times of increased intra-abdominal pressure (for example when straining, coughing or even standing up from a seated position). This form of incontinence resolves within one year in most sufferers, and can probably be attributed to the effects of a neurapraxia (a temporary loss of nerve function) that has arisen from the prostatectomy. Only a very small minority of men have total urinary incontinence as a complication.

Much attention has recently been given in men's wellness programmes, magazines and sexual health campaigns to the previously hushed issue of erectile dysfunction (ED). While there are other, more common causes of ED (e.g. smoking), it remains a much feared complication that can result from prostate cancer in its own right as well as from the definitive treatments thereof (both surgical and non-surgical). ED is more likely to present in advanced stages of prostate cancer where the tumour may invade the nerve bundles. A unilateral nerve sparing procedure is done with the aim to preserve the surrounding nerves on only one side of the prostate

9 Worden JW, Weisman AD. The fallacy in postmastectomy depression. *Am J Med Sci.* 1977 Mar-Apr;273(2):169-75

during the prostatectomy. It ultimately tends to have a higher risk of ED compared to a bilateral nerve sparing procedure (where the nerve bundles on both sides of the prostate are preserved).

After a radical prostatectomy (depending on whether a unilateral or bilateral nerve sparing procedure had been performed), 13 – 68% of men present with ED, according to a cohort study done by Ong et al, it was 59% for brachytherapy. Interestingly it has been shown that while many factors play a role, the risk of developing ED post-brachytherapy is directly proportional to the increase in the Gleason Score. A Gleason Score of less than 7 holds a 3.7 increased likelihood of erectile function preservation compared with a Gleason Score of 7¹⁰.

- **Gleason Score:** Each core biopsy (usually 6-12 are submitted for assessment) that confirms cancerous prostate cells is graded from 1-5, with 1 being assigned to cells that fully resemble normal prostate cells and 5 being assigned to cells that least resemble normal prostate cells. The sum of the two worst grades constitutes the Gleason Score and reflects the aggressiveness of the tumour.

Breast and prostate cancer can lead to stress, anxiety and depression (including loss of self-esteem). This psychological burden is not only from the fear of the diagnosis, but also from the treatments and their complications. The psychological burden that these may have on affected individuals should be considered in the medical risk assessment, both as short- and potentially long-term problems. Furthermore, although the risk of recurrence of either of these tumours remains rare (1 in 1,000 cases), it should be remembered that other secondary cancers can still occur (typically after radiotherapy) even as far as 10 - 20 years down the line. These include lymphomas, tumours of the muscle or bone, and even certain skin cancers. This medical risk consideration is important when assessing the risk for critical illness and even disability insurance products.

10 Ong WL, et al. Long-term erectile function following permanent seed brachytherapy treatment for localized prostate cancer. *Radiother Oncol*, Aug 2014

The money is on pink



Funding for breast cancer far exceeds that for prostate cancer.

The total research funding budget for all cancers in South Africa is a mere R32 million (around \$2.6 million) and is relatively paltry, being the equivalent of 0.7% of the R4 billion (around \$335 million) budget offered in the USA for cancer research and funding¹¹. Within the USA's cancer budget, there is remarkable difference between the total funds allocated towards research on breast cancer relative to prostate cancer. Funding for breast cancer research and development is by far the greatest in value (over \$115 million in the USA) and remains two to three times more generous than the funding allocated towards prostate cancer research efforts (just over \$46 million)¹². This trend is mirrored in both the UK as well as South Africa. With prevalence being so similar between breast and prostate cancer, one may wonder why there is such a predilection for breast cancer funding. While the age-adjusted death rates from breast cancer and prostate cancer are identical as already mentioned, the actual ages at which deaths typically occur differ remarkably (see Table 2 below).

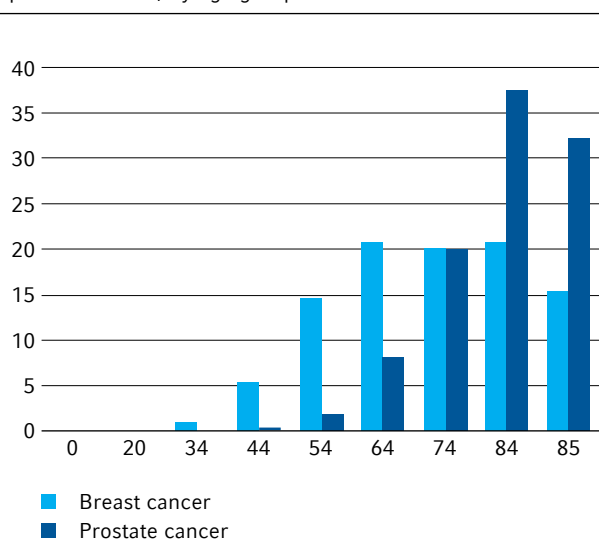
This trend explains the reasons behind the significant imbalance between funding for breast cancer versus prostate cancer each year, in that breast cancer typically affects younger women and mothers while their children are young. This societal impact, through higher mortality at younger ages, drives the increase in funding towards breast cancer research.

11 Albrecht C. Overview of the South African Cancer Research Environment as a basis for discussions concerning the activation of CARISA (Cancer Research Initiative of South Africa), Aug 2006. Available online: <http://www.sahealthinfo.co.za/cancer/overviewdocument.pdf>

12 <http://www.cancer.org/research/currentlyfundedcancerresearch/grants-by-cancer-type>

Prostate cancer, on the other hand, mostly affects men older than 45; these men more often than not die ‘with’ and not ‘from’ prostate cancer.

Table 2: Percentage of deaths attributable to breast and prostate cancer, by age group (2006-2010)



Back in the training ring ... what new moves are being learnt?

Acknowledging these large research funds, we are constantly awaiting the special breakthrough of a ‘wonder-drug’, ‘miracle cure’ or ‘protective vaccine’. While advances in therapies are constantly being made, a great deal of attention is also given to identifying potential risk factors for breast and prostate cancer, ranging from dietary intake to cancerous genes. In addition, diagnostic strategies that could help identify breast or prostate cancer with a high level of accuracy as well as a high detection capability are equally important in order to ensure that these cancers get diagnosed early and effectively in order to optimise treatment outcomes. Although potentially costly, the insurance industry could benefit greatly by making use of screening and diagnostic advances in the future in order to maximise the scientific assessment of these two cancer risks.

The recent news frenzy around the infamous hereditary ‘breast cancer genes’ – better known as the abnormal “BRCA1

and BRCA2” genes resulted in much awareness of these genes, and saw many women following in celebrity footsteps in order to get tested for the presence of them. Women testing positive for an abnormal BRCA gene can have up to an 80% risk of being diagnosed with breast cancer during their lifetimes. Scientists are studying the best use of these genetic tests, considering that they come at a hefty price (around R1,600 per test). Attracting the attention of many clinicians (and potentially the insurance industry) are the developments around the detection of circulating breast cancer cells, suggesting that we are probably closer to having a blood test for breast cancer than we realise. However, the real ado is around the SmartBra – a brassiere in its fourth and final clinical trial that is said to detect breast cancer up to six years earlier than a mammogram could. It consists of several thermo-sensors in a brassiere, that when worn for a 24 hour period, can detect an underlying tumour based on an assessment of the micro-thermal changes within the breast tissue. So far, it exhibits a 92.1% level of accuracy at correctly classifying the tumours.

Although allocated a proportionately smaller budget, prostate cancer research certainly does not need to shy away from the enormous advances being made on all levels. Particular mention should be made regarding diagnostic radiological advances. The Colour Doppler Ultrasound is a specialised type of sonar that can detect the increased blood supply around a prostate tumour, and ensure that a prostate biopsy is done in this ‘hot zone’ (ultimately increasing the chance of accurately biopsying the tumour). Magnetic Resonance Imagings (MRIs) are also being studied based on their ability to detect tumours more readily and could be useful in cases where the prostatic specific antigen (PSA), a blood marker used for screening for prostate cancer, is persistently elevated in the face of normal prostate biopsies and normal clinical assessment of the prostate.

Defend, defend, defend, ATTACK!

The 5 year survival rates for both breast and prostate cancer plummet dramatically as the tumour stage progresses from Stage 3 to Stage 4 (72% to 22% for breast cancer and 100% to 28% for prostate cancer)¹³.

13 www.cancer.org

When either of these tumours involves extensive lymph node or distant organ metastases, the possibility of cure becomes significantly more challenging and sufferers of either cancer potentially endure extreme morbidity such as chronic pain, depression and ultimately organ failure from metastases.

Inoperable tumours in their own capacity contribute to localised invasion of surrounding tissue, nerve impingements (and damage) and treatment failure. These complications of advanced breast or prostate cancer emphasise the importance of an early diagnosis being made whereby treatment intentions are curative and not palliative.

How long until the 12th round?



A range of different therapies can be used to treat both types of cancer.

In order to implement the most effective therapeutic strategies for breast and prostate cancer, fully understanding their behaviours as well as the reasons for their occurrences can help design treatments that target the cancer specifically, and hence have little to no impact on normal surrounding tissues. Knowing which tumours will respond to certain treatments (e.g. chemotherapeutic agents) spares some patients from being treated unnecessarily and enduring the adverse effects with no real treatment benefit.

While there is effective treatment available for both breast and prostate cancer, some revolutionary treatment options are becoming available. ‘Target drug therapies’ – a group of cancer treatments that we are seeing more and more frequently at underwriting – are already extensively being used with excellent clinical outcomes.

This group of formulated drugs are scientifically designed to treat various cancers at a genetic level (where genes play an important role in the development of certain cancers) as well as the progression and growth of tumours. Herceptin (trastuzumab) is a targeted drug therapy that specifically targets a growth receptor in breast tissue and, by blocking this receptor, prevents further tumour growth. Only about 25% of breast cancers express the associated receptor in adequate amounts for Herceptin to work effectively. These drugs are not typically used in isolation, but rather as part of a greater treatment strategy. Similarly, drugs that target and block the development of blood vessels around a tumour could effectively ‘starve’ the tumour by depriving it of its nourishment. Some studies suggest that breast tumours with more extensive blood supplies are likely to be more aggressive, thus this treatment strategy could prove to be highly effective against high grade tumours.

The technological advances being made for prostate cancer treatment are dramatic and although they require skill, are showing promising results. A new form of sonar, known as High-Intensity Focused Ultrasound (HIFU), is currently being assessed on its ability to destroy prostate cancer cells by heating them with highly focused ultrasound beams. While already being used in Europe, further clinical trials are underway to determine its safety and effectiveness. Special mention should also be made of the 4 Da Vinci’s, the famous robotic devices that arrived in South Africa in late 2013. These devices are currently being used for robotic-assisted radical prostatectomies and although highly user-dependent, are effective, safe, and reduce hospital stay substantially.

Immunotherapy makes use of one’s immune system in order to mount an attack on cancer cells. An FDA-approved vaccine (Provenge®) is a special type of vaccine that boosts the body’s immune system, not to prevent infections, but rather to get it to attack prostate cancer cells in the body. It typically gets used to treat advanced prostate cancer that is refractory to other treatment options, but is not yet available in South Africa. Although not a cure, it has been shown to extend life expectancy by several months. Acting in a similar way (activating the cancer-destroying cells of the immune system) is Oxaliplatin (Eloxatin), a drug that recently made headlines in ‘The Telegraph’, which used a similar therapeutic action to that of the vaccine and reportedly showed signs of human

tumours being ‘almost completely destroyed’ by the animal’s own immune system in a trial. This has led to the hope that this treatment option could potentially eradicate advanced prostate cancer. A cure, however, does not imply a lack of morbidity or adverse effects¹⁴.

Conclusion

When comparing breast cancer with prostate cancer, it is clear that they share a surprising number of characteristics. With identical lifetime risks, incidences, prevalence and age-adjusted mortality rates, it is understandable that many may feel these two cancers deserve equal attention. Breast cancer is associated with genetic and environmental factors, some identical to prostate cancer and others different but equally apparent, and in both cancers these predispositions remain at the forefront of research – the aim being to maximise our understanding of these two cancers.

It is probably not reasonable to think of breast cancer as ‘worse’ than prostate cancer but sadly, breast cancer does tend to affect women at relatively young ages. This impact generally affects society more profoundly than that seen in men affected by prostate cancer, not only through emotional burden but also from treatment morbidity and even death. This substantial societal impact influences the channelling

14 Prostate cancer could be ‘wiped out’ by new treatment . The Telegraph. Available online: <http://www.telegraph.co.uk/news/health/news/11571730/Prostate-cancer-could-be-wiped-out-by-new-treatment.html>

of significantly increased funds towards understanding the nature of breast cancers. This ultimately drives the chances of improved prevention, screening, diagnostic outcomes and treatment in a more favourable direction.

Interestingly enough, the advances made in prostate cancer developments do not lurk in the shadows of breast cancer, despite a significantly more conservative spending budget. We have come a long way in our struggle against both of these cancers and where once we had grossly labelled them as ‘The Big Cs’, the survival rates experienced for both cancers fuel the hope of not only possibly beating these cancers entirely one day, but also minimising suffering and morbidity. Can our insurance industry keep up with these developments and will our current cautious risk assessment be cushioned as we increasingly understand these two cancers? Our perceptions of both of these cancers should probably be reviewed sooner than we thought necessary.

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