

# MEDICAL NEWS

A SingHealth Newsletter for Medical Practitioners MCI (P) 117/11/2018



## FOCUS: CANCER

**Current Management of Advanced Prostate Cancer**

**Cancer Survivorship – More Than Just Surviving Cancer**

**Genetic Testing for Your Patients: Understanding the Complexities**



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# Current Management of Advanced Prostate Cancer

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Prostate cancer is the 3<sup>rd</sup> most common cancer diagnosed in males in Singapore and accounts for 12% of all male cancers diagnosed from 2008 to 2018.<sup>1</sup> According to the Singapore Cancer Registry report from 2015, the incidence has been increasing from 9.7 per 100,000 previously to 28.5 per 100,000 in 2008-2012.<sup>1</sup>

Males in Singapore have a higher rate of prostate cancer than their counterparts in Asia, for example, China, Japan and India, but the rates are still much lower than those in the US, UK and Australia.<sup>1</sup> Locally, Malay and Indian men appear to have a lower risk of prostate cancer as compared to Chinese men at about 15.9-17.9 per 100,000 as compared to 25.6 per 100,000.<sup>1</sup>

The current MOH guidelines<sup>2</sup> published in 2010 suggest that men who are between 50-75 years of age with an expected life expectancy of more than 10 years may be offered screening for prostate cancer after a discussion of both the potential benefits and harm associated with cancer screening. In the absence of a strong family history, routine screening for men should not be offered for men under 50 years of age. High risk men such as African-American men or men with a strong family history of prostate cancer (one or more first-degree relatives (father/brothers)) diagnosed before 65 years old, may be offered screening at a younger age.

## NOMENCLATURE OF METASTATIC PROSTATE CANCER

Metastatic Prostate cancer can occur in several scenarios; initial localised disease that had curative treatment but recurred either biochemically and/or with radiographic evidence; de novo metastatic disease.<sup>3</sup>

The mainstay of treatment for metastatic prostate cancer involves suppression of the male hormone testosterone either surgically or chemically.<sup>3</sup> Bilateral Orchiectomy or Androgen Deprivation Therapy (ADT) in the form of gonadotropin-releasing hormone antagonist or agonist have been shown to be equally as good in achieving castration levels of testosterone.<sup>4</sup>

As patients are often sensitive to hormonal manipulation, this phase of treatment is often known as hormone-sensitive prostate cancer.

## HORMONE-SENSITIVE PROSTATE CANCER (HSPC)

In addition to ADT or surgical castration, there have been several new developments in the treatment of hormone-sensitive prostate cancer.

### High Volume/High Risk Patients

In patients who have high volume/high risk disease defined by the number of bony metastasis and/or presence of visceral disease and/or a pre-existing Gleason score, a novel anti-androgen like **Abiraterone**, a CYP17 antagonist, has shown improvement in Overall Survival (OS) in the LATITUDE<sup>5</sup> study, with a Hazard Ratio of 0.62 and a 3-year survival rate of 66% compared to 49% with ADT alone.

**Docetaxel**, a taxane chemotherapy that binds to tubulin and stabilises microtubules, thereby inhibiting mitosis, has also been shown to have an OS benefit.

A recent meta-analysis<sup>6</sup> comparing Docetaxel and ADT with ADT alone in the HSPC state showed a significant survival benefit favouring the combination. The earliest study to show this, the CHAARTED<sup>7</sup> study, showed most of the benefit of Docetaxel was obtained in the high volume HSPC cohort.

### Docetaxel vs Abiraterone/Prednisolone

Although the effectiveness of Docetaxel and Abiraterone/Prednisolone appears to be similar based on the STAMPEDE<sup>8</sup> trial, there are clear differences between the 2 treatment regimens.

### Docetaxel Treatment Regimen

The Docetaxel regimen is a 3-weekly intravenous treatment regimen for a total of 18 weeks, while Abiraterone/Prednisolone regimen is taken orally at 1000mg/10mg every day until disease progression which may result in a prolonged period of drug exposure. In the local context, the cost of treatment of Abiraterone/Prednisolone is much higher compared to the cost of chemotherapy (which is generic).

### **Differing Side Effects**

Apart from duration of treatment, the side effects of Docetaxel differ from Abiraterone/Prednisolone with chemotherapy associated with myelosuppression, febrile neutropenia, alopecia and neuropathy. Abiraterone/Prednisolone can cause an elevated liver function test and mineralocorticoid-associated side effects of hypertension, hypokalaemia and oedema.

### **Low Volume/Low Risk Patients**

In patients with low volume/low disease burden HSPC, the evidence for Docetaxel is conflicting with the meta-analysis<sup>6</sup> and STAMPEDE<sup>9</sup> showing a benefit from chemotherapy in all metastatic HSPC patients, while CHAARTED<sup>6</sup> clearly showed no benefit in the low volume burden HSPC patients.

Locally, most physicians would tend to offer chemotherapy to the high disease burden patients as defined by CHAARTED.

### **CASTRATE-RESISTANT PROSTATE CANCER (CRPC) CRPC state occurs once the patient has progressed either biochemically or with radiographic evidence, following initial treatment in HSPC setting.**

In patients with castrate-resistant prostate cancer, it is still important to continue on the existing ADT. Often, treatment options of CRPC are heavily dependent on the previous treatments that had been offered.

**In non-metastatic CRPC patients who have biochemical recurrence with no evidence of metastatic disease** based on the CT (Computed Tomography) scan and bone scan, novel agents like Enzalutamide and Apalutamide has been shown to delay metastasis-free interval as compared to placebo in PROSPER<sup>10</sup> and SPARTAN<sup>11</sup> respectively. Both treatments have received FDA approval for this indication.

**In patients who have had Abiraterone/Prednisolone in the HSPC setting,** Docetaxel is a suitable option based on the TAX 327 trial which showed an improvement in OS for patients treated with the 75mg/m<sup>2</sup> of Docetaxel.<sup>12</sup> Local retrospective data in this setting shows that an attenuated dose of 60mg/m<sup>2</sup> 3-weekly has similar efficacy to the standard of 75mg/m<sup>2</sup> with acceptable toxicity profile, and that weekly Docetaxel at 20mg/m<sup>2</sup> to 35mg/m<sup>2</sup> has significant palliative benefits in patients who are symptomatic from the cancer, despite a lower OS.<sup>13</sup>

**Likewise, in patients who had Docetaxel in the HSPC setting,** novel anti-androgens such as Abiraterone/Prednisolone and Enzalutamide are both suitable agents in the CRPC setting. COU-AA trials<sup>14,15</sup> and AFFIRM/PREVAIL<sup>16,17</sup> trials have showed similar efficacy with the absolute improvement in median OS by 4 months in respective trials. Both novel anti-androgens are oral agents with different side effect profiles. Patients on Enzalutamide experience more fatigue and seizures were reported in a small proportion of patients on it (<1%).





Our local data on Abiraterone/Prednisolone in the CRPC setting is comparable with other clinical data overseas reflecting a lower OS in patients, likely due to patients selection factors i.e. poorer performance status, shorter response to ADT of less than 12 months, high burden of disease and prior use of older anti-androgens.<sup>18</sup>

**In patients who have disease that have progressed post Docetaxel**, Cabazitaxel at the dose of 20mg/m<sup>2</sup> can be considered as 2<sup>nd</sup> line chemotherapy.

Cabazitaxel is a taxane designed specifically for anti-tumour activity in the Docetaxel-resistant patients. The TROPIC<sup>19</sup> study evaluated Cabazitaxel at 25mg/m<sup>2</sup> given every 3 weeks against the control Mitoxantrone, showing an OS favouring Cabazitaxel. PROSELICA<sup>20</sup> subsequently showed that Cabazitaxel at 20mg/m<sup>2</sup> was non-inferior to 25mg/m<sup>2</sup> with respect to OS with decreased toxicity compared to 25mg/m<sup>2</sup>.

Side effects are similar to Docetaxel including chemotherapy-related cytopenias, febrile neutropenia and GI toxicities.

Radium-223, an alpha particle emitting radionuclide that binds to the hydroxyapatite in osteoblastic bone metastatic has been shown to improve overall survival in **CRPC patients who have bone-only metastasis and without nodal metastasis** of more than 3 cm as noted in the ALSYMPCA study.<sup>21</sup> The OS was prolonged in the radium 223 group median OS 14.9 versus 11.3 months in the control group.

Side effects include diarrhoea and thrombocytopenia.

Lastly, bone modifying agents in the form of Bisphosphonates<sup>22</sup> and Rank Ligand antibody Denosumab<sup>23</sup>, have been shown to reduce the risk of skeletal-related adverse events such as pathological fractures, spinal cord compression and symptomatic bony pain requiring palliative radiation or surgery.

The potential side effects are hypocalcaemia or a small risk of osteonecrosis of the jaw in patients.

### THE FUTURE

The future management of advanced prostate cancer remains bright with several upcoming trials that are on the horizon. We look forward to the studies on PARP (Poly (Adp-Ribose) Polymerase) inhibitors and its role in patients with germline or somatic alterations in homologous recombination repair genes.

The ENZAMET study which investigates the role of Enzalutamide and chemotherapy in the high risk HSPC setting could answer the question on a combination of novel anti-androgens and chemotherapy.

In addition, we eagerly await results from PSMA Lu177 therapy, a very promising approach known as theranostics, in the treatment of advanced prostate cancer. There are also a number of genomic-related treatment strategies that are being investigated now that will pave the way for what will be truly personalised medicine.

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# Cancer Survivorship – More Than Just Surviving Cancer

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## CASE STUDY 1



Claire is a 52-year-old executive whose youngest daughter has just completed her pre-university studies and is now applying for university.

As she looked forward to the next stage of her life, she was horrified to feel a new breast lump while in the shower. She saw her GP and was promptly referred to a breast surgeon. After a series of tests and a biopsy, she was unfortunately but fortunately diagnosed with curable early stage breast cancer. Claire, being the positive and proactive person she was, bravely underwent surgery and subsequently adjuvant chemotherapy, radiotherapy and endocrine therapy to improve her chances of cure.

Although currently free of cancer, she was plagued by persistent numbness of her feet and noticed difficulties in her memory and ability to concentrate. She was gripped with the fear of recurrence, slept poorly and often felt emotionally down. For the first time, she was also physically disconnected from her husband as

she felt uncomfortable with her post-cancer body image. Claire tried her best to remain positive and wanted to adopt any lifestyle measures that could aid her recovery and further reduce her risk of recurrences or any new cancers, but was disappointed and confused with the lack of reliable information on this. She initially wanted to confide in her oncologists regarding her problems and concerns, but the consultation time was often too short and almost entirely focused on screening for cancer recurrence. Claire turned to her usual GP, but she felt cancer was a highly specialised field and was not confident to advise her. Adding to this, there was also little to no communication with her GP regarding her cancer diagnosis and treatment.

It was strange and unexpected that she was experiencing such immense suffering despite being cancer free. She was supposed to be transitioning towards a better health state, but instead, she feels the worst she has ever been, confused and abandoned.

### CANCER SURVIVORSHIP AND ITS IMPORTANCE

Claire’s story represents the journey of many cancer survivors in Singapore, being cancer free but still plagued with a multitude of physical and psychosocial issues from the cancer or as a result of its treatments. This results in not only a poor quality of life for survivors and their families, but also a detriment to society and the nation due to the loss of human capital and productivity. As such, care for cancer patients does not stop with anti-cancer treatments and early diagnosis, but must also encompass care to aid and promote holistic post-treatment recovery and wellness.

#### What Is Survivorship?

Cancer survivorship commonly relates to “Living with, through and beyond cancer”. This means that cancer survivorship begins at diagnosis and encompasses patients across the entire survivorship continuum, from early curable to long term survivorship or advance incurable states. The American Society of Clinical Oncology (ASCO) describes 3 distinct phases of survivorship<sup>2</sup> (Refer to Figure 1):

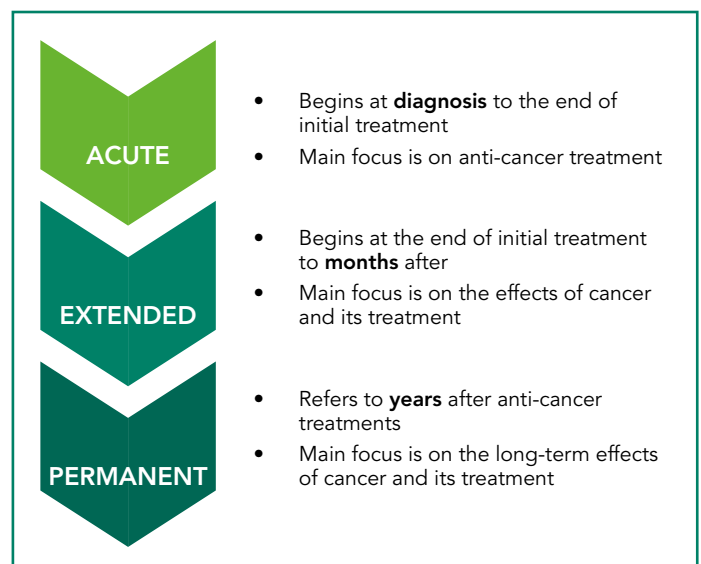


Figure 1

The United States Institute of Medicine (IOM) highlighted the importance of dedicated cancer survivorship programmes to effectively address the supportive and survivorship care needs of all cancer survivors. The IOM, in its landmark publication, "From Cancer Patient to Cancer Survivor: Lost in Transition" highlighted 4 essential components of a cancer survivorship programme.<sup>3</sup>

- (1) Prevention and detection of new cancers and recurrent cancer
- (2) Surveillance for cancer spread, recurrence, or second cancers
- (3) Intervention for the consequences of cancer and its treatment and
- (4) Coordination between specialists and Primary Care Providers (PCPs) to ensure that all of the survivor's health needs are met.

#### Why Is Survivorship Care Important?

##### 1. Increasing cancer survival rates

Based on Singapore's Cancer Registry, the estimated lifetime risk for developing cancer is about 1 in every 4-5 people. Worryingly, the incidence of cancer has increased and is likely to continue to rise with an ageing population. The crude incidence rates of all cancers in

males and females between 2011-2015 were 330.7 and 338.5 per 100,000 person-years respectively. Although the Age-Standardised Incidence Rate (ASIR) for cancer in males has largely been stable between 1973 and 2012, the rate for females displays a consistent rising trend. On the whole, the ASIR in female cancers for 2008-2012 was 31.7% higher than in 1973-1977 which amounted to an average annual change of 0.8%.<sup>5</sup>

Moreover, with earlier diagnoses through screening measures and constantly improving anti-cancer treatments, the number of people surviving cancer will also increase. This is evident by improving survival rates of many cancer types in Singapore over the years.<sup>5</sup>

##### 2. Multiple and complex needs of cancer survivors

Cancer survivors can experience a multitude of unique physical and psychosocial issues associated with cancer and its treatments. In addition to the direct physical and psychosocial toxicities of cancer and its treatments, indirect consequences of increased chronic comorbidities and second primary cancers can also occur. Adding to this complexity is the likely lack of awareness of the general medical community of the unique care needs of cancer survivors, despite cancer now being the primary source of mortality in Singapore.<sup>5</sup> This can be illustrated in the case example below.

## CASE STUDY

# 2

A 35-year-old woman presents to her primary care physician with an ischaemic-like chest pain. She was previously treated with chest irradiation for Hodgkin's Lymphoma when she was 15. Many doctors would not be aware of chest irradiation being a risk factor for an earlier diagnosis of ischaemic heart disease and may have inadvertently treated her chest pain as musculoskeletal or anxiety in source. Her risk of a myocardial infarction would actually be similar to a 55-year-old man. This emphasises the need for greater awareness amongst the general medical community of the potential issues faced by cancer survivors.<sup>6</sup>





### What Defines High Quality Survivorship Care?

The ASCO describes the key components as follows<sup>4</sup>:

- (1) Surveillance for recurrence
- (2) Monitoring for and managing psychosocial and medical late effects
- (3) Screening recommendations for second cancers
- (4) Providing health education to survivors regarding their diagnoses, treatment exposures, and potential late- and long-term effects
- (5) Providing referrals to specialists and resources as indicated
- (6) Familial genetic risk assessment (as appropriate)
- (7) Guidance about diet, exercise and health promotion activities
- (8) Providing resources to assist with financial and insurance issues
- (9) Empowering survivors to advocate for their own health-care needs

Many of these components can be provided across both tertiary and primary care settings, but has to be tailored according to the unique care needs of each cancer survivor. A risk-stratified approach is commonly adopted where cancer survivors with more complex survivorship needs remain

within the tertiary system for specialty survivorship care, and those who are more stable can receive ongoing survivorship and wellness care in the community. Such an approach would not only be more cost-effective but also allow greater personalisation of survivorship care.

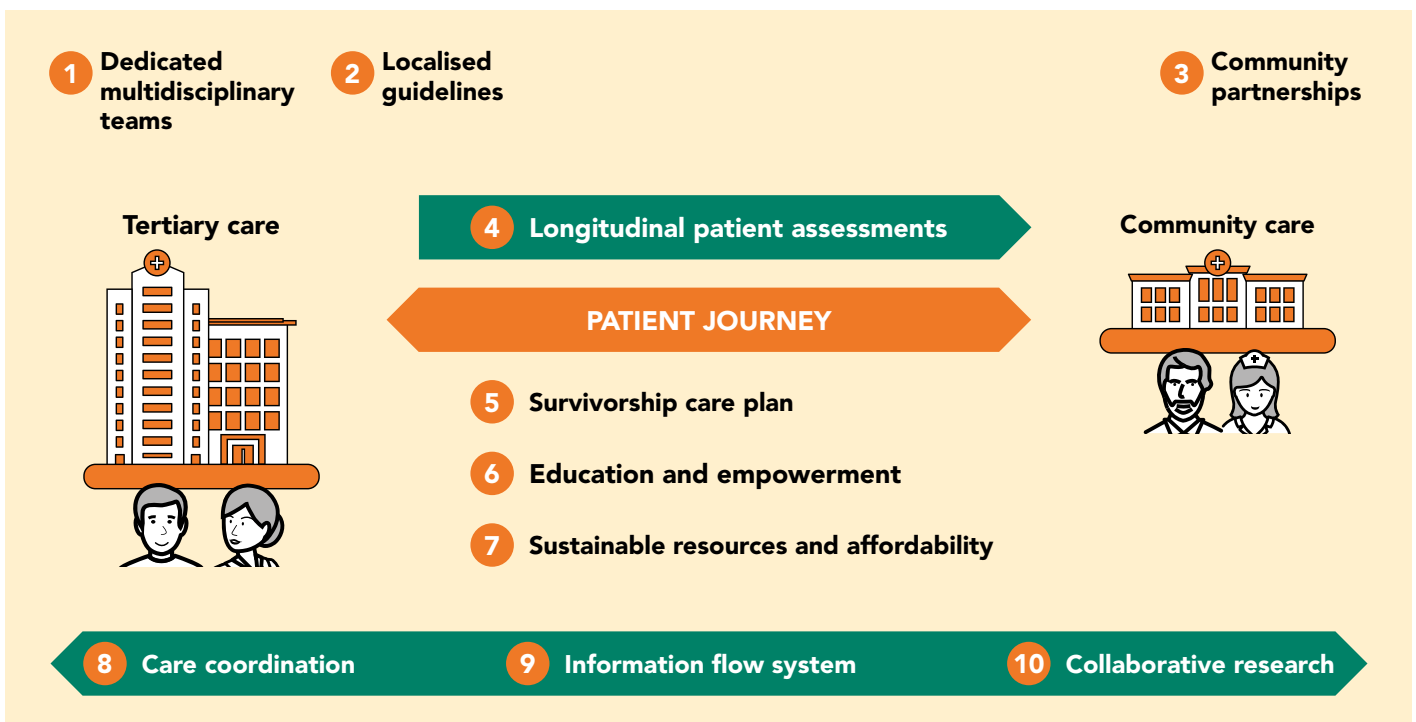
### CURRENT AND FUTURE LANDSCAPE OF CANCER SURVIVORSHIP IN SINGAPORE

Despite Singapore's excellence in oncological care evident by comparable cancer survival rates to first world countries, significant gaps in cancer survivorship care exist. These mainly pertain to care fragmentation and the lack of skillsets and resources for optimal survivorship care within the tertiary and primary healthcare care system.

In December 2016, NCCS launched Singapore's first Cancer Survivorship Forum, bringing together 70 oncology practitioners and researchers across Singapore, to raise awareness and discuss the future landscape of cancer survivorship care in Singapore. This culminated in a proposed cancer survivorship care model that is integrated, survivor-centric, coordinated, accessible and affordable. It also embraces the importance of collaboration between the survivor, as an active and empowered partner, and tertiary and community care providers.

The proposed model highlights the key components needed for excellent survivorship care in Singapore (Refer to Figure 2).<sup>8</sup> NCCS in response, has reorganised its services and resources to allow a new focus on optimal survivorship care, starting with a pilot study to test the feasibility and effectiveness of this new model of care, expected to commence in 2019.

Figure 2 Key components for Optimal Survivorship Care in Singapore





## COMMUNITY CANCER SURVIVORSHIP AND THE ROLE OF PRIMARY CARE

Primary Care Practitioners (PCP) have played pivotal roles in cancer survivorship in the community in first world settings in North America, Europe, and Australia. Current evidence suggest that PCPs can provide more cost-effective and equally safe surveillance care to cancer survivors with no difference in recurrence rates, time to detection of recurrence, mortality and health-related quality of life, compared to specialists.<sup>9-12</sup>

Nonetheless, a collaborative approach is still recommended for cancer survivors to tap on the preventive and wellness care skills of PCPs and cancer-specific and survivorship skills of specialists.

### POSITIVE IMPACT OF PCPs

Many PCPs hold strong relationships with their patients and families and thus can positively impact them through **education and motivation on lifestyle measures**, such as exercise and healthy diets, that have been shown to promote recovery and even lower the risk of cancer.

PCPs can also use their therapeutic alliance with patients and families to promote **compliance to treatments, follow-ups, and evidence-based screening** for cancers and common comorbidities.

Besides preventive and wellness care, the PCP can also play a vital role in **cancer surveillance** as well as the monitoring and **co-management of toxicities** from cancer and its treatments.

Indeed, if well supported through good communication, clear guidance and routes back to specialist, general prac-



tice may be a preferable place for cancer follow-up for many cancer survivors who would benefit from a broader generalist perspective.<sup>7</sup>

### BETTER RECOVERY IN COMMUNITY

From a survivor's perspective, **returning to the community allows for better recovery** due to more familiar and supported surroundings and promotes a wellness rather than sickness mindset as they move further on from institution-based acute care.

The push for community survivorship care is also very much in line with Singapore's mission to empower and engage PCPs in the delivery of holistic, quality and continuing care for patients with chronic health issues and the vision of building a sustainable healthcare for the future with the 3 frameworks of "Beyond Healthcare to Health, Hospital to Community and Quality to Value".<sup>14</sup>

### GOING FORWARD WITH NCCS

NCCS's model for optimal survivorship care (*Refer to Figure 2*) places great importance on community partnerships.<sup>8</sup> For years, NCCS has been supporting this initiative through PCP education programmes and more recently, have taken steps towards understanding the barriers for PCP involvement in community survivorship care through focus group sessions with PCPs.<sup>15</sup>

Whilst discussions with key stakeholders are ongoing to address key logistical, administrative and financial issues, the next logical step would be the creation of a formal cancer survivorship training programme for interested PCPs, of which is currently being planned.



## CONCLUSION

Survivorship care is an essential component of high quality cancer care due to rising cancer incidence, survival and the recognition of unique health challenges cancer survivors face. Although significant gaps still exist in survivorship care, there is an emerging focus and movement towards the development of high quality survivorship care in Singapore. High quality survivorship care is best delivered using a collaborative approach between tertiary-based specialists and community-based PCPs.



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# Genetic Testing for Your Patients: Understanding the Complexities

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From the vantage point of 2018, it is difficult to imagine a time when cancer was not widely accepted as a genetic disease, in the most basic sense of being caused by alterations in the structure and function of genes. Indeed, it was not until the second half of the 20th century that the heritable nature of common cancers started to be widely accepted. Over the decades since then, genealogic and epidemiologic observations set the stage for a burst of scientific activity in the 1990s, when the discovery of genes responsible for cancer predisposition syndromes was made.

These discoveries provided valuable insights to the biology of cancers, paved the way for integration of genetics in cancer risk assessment and realising the potential of gene-directed management and treatment.

Currently, over 400 hereditary cancer susceptibility syndromes have been described, most of which feature an autosomal dominant inheritance pattern. Although many of these are rare syndromes, they account for at least 5–10% of all cancer incidences (Refer to Figure 1).

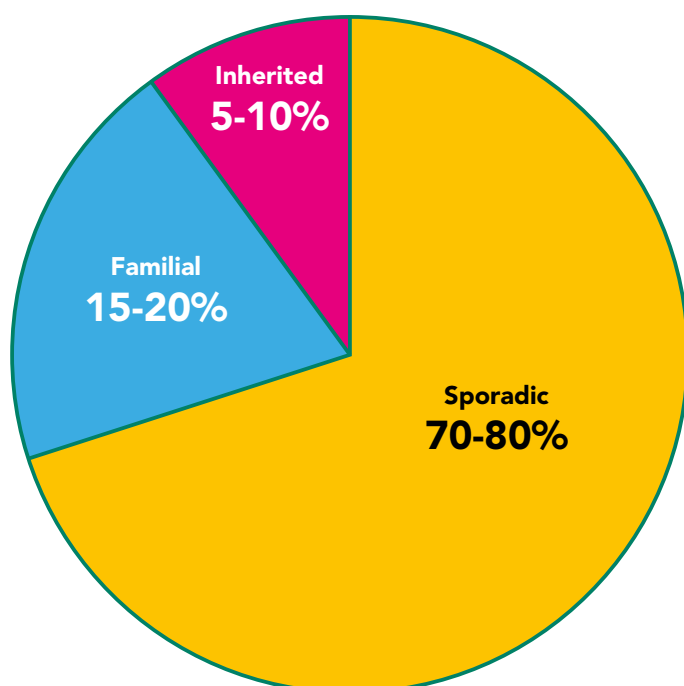


Figure 1 Inherited Cancers Account for About 10% of All Cancers

An inherited cancer susceptibility syndrome is usually suspected in families with the following characteristics:

- Two or more relatives with the same type of cancer on the same side of the family
- Several generations affected
- Earlier age of cancer diagnosis than typically seen for that cancer type
- Individuals with multiple primary cancers
- The occurrence of cancers in one family, which are known to be genetically-related (such as breast and ovarian cancer, or colon and uterine cancer) and
- The occurrence of non-malignant conditions and cancer in the same person and/or family (Refer to Figure 2)

However, due to phenotypic variability, age-related penetrance, and gender-specific cancer risks, many families with an inherited cancer syndrome will not meet these criteria and may be missed by clinicians.

**Cancers that arise as a result of a germline predisposition are typically managed differently from those that arise sporadically.** Patients may undergo more extensive local therapy if they are at increased risk for metachronous malignancy.

Obvious examples include the consideration of bilateral mastectomy instead of breast conservation in patients with breast cancer carrying a germline BRCA1 or BRCA2 mutation, and subtotal colectomy instead of limited resection in patients with colorectal cancer who have Lynch syndrome. Furthermore, germline mutations have also been shown to be predictive of differential response to treatment approaches.

Perhaps the most important application of genetic testing is in individual cancer risk assessment. In addition to enabling successful risk reduction strategies for the at risk patient, identification of germline mutations in cancer-associated genes also informs family members of their individual cancer risks such that appropriate intervention can be offered

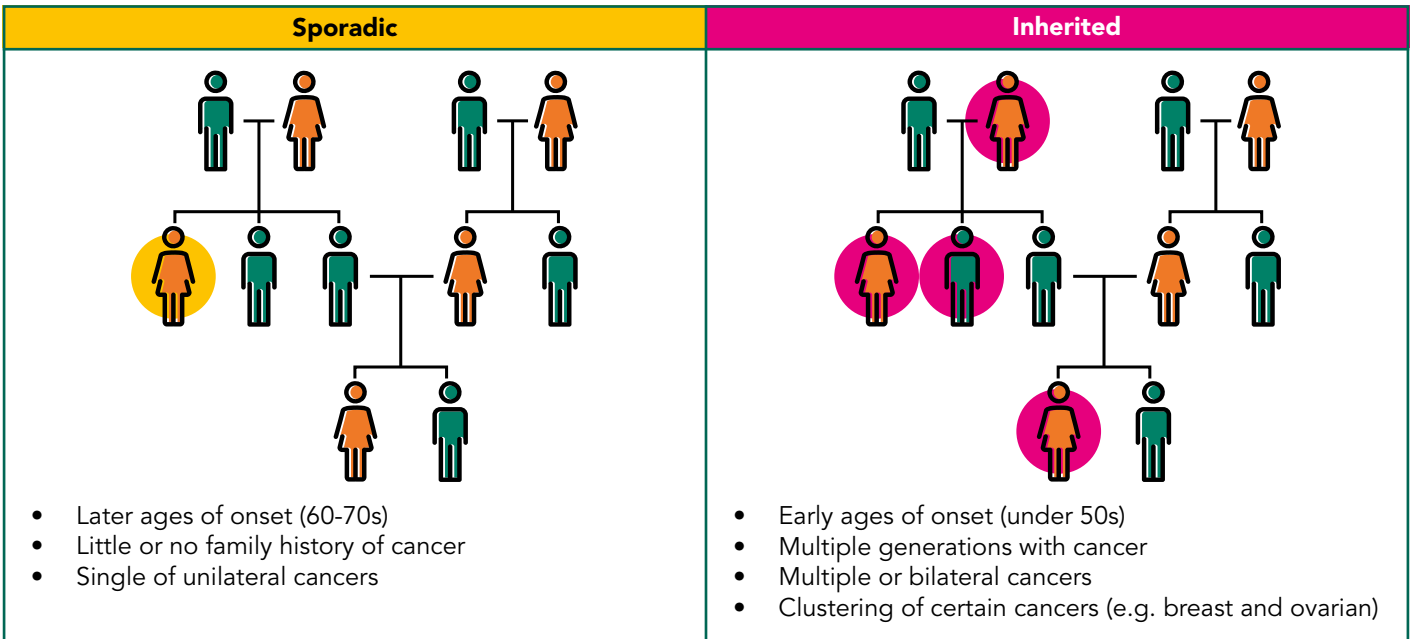


Figure 2 Red-Flags for Hereditary Cancers

for affected family members or unwarranted surveillance can be avoided in those unaffected. Knowing who is at high-risk allows us to intensify screening to those who will benefit from the surveillance, resulting in earlier cancer detection and overall cost-savings (Refer to Figure 3).

The Cancer Genetics Service (CGS) at the National Cancer Centre Singapore investigates genetic diseases caused by germ-line (inherited) mutations, and provides comprehensive clinical genetic services, education and support to patients

and family members. Our team of clinical cancer geneticists and genetic counsellors work closely with primary care providers and specialists to help incorporate genetic information into a patient's overall healthcare plan.

Throughout the CGS's defined four-step genetic testing process, our highly trained and compassionate genetic counsellors help patients navigate the complexities of genetic testing, translating complicated data into information patients can readily understand.

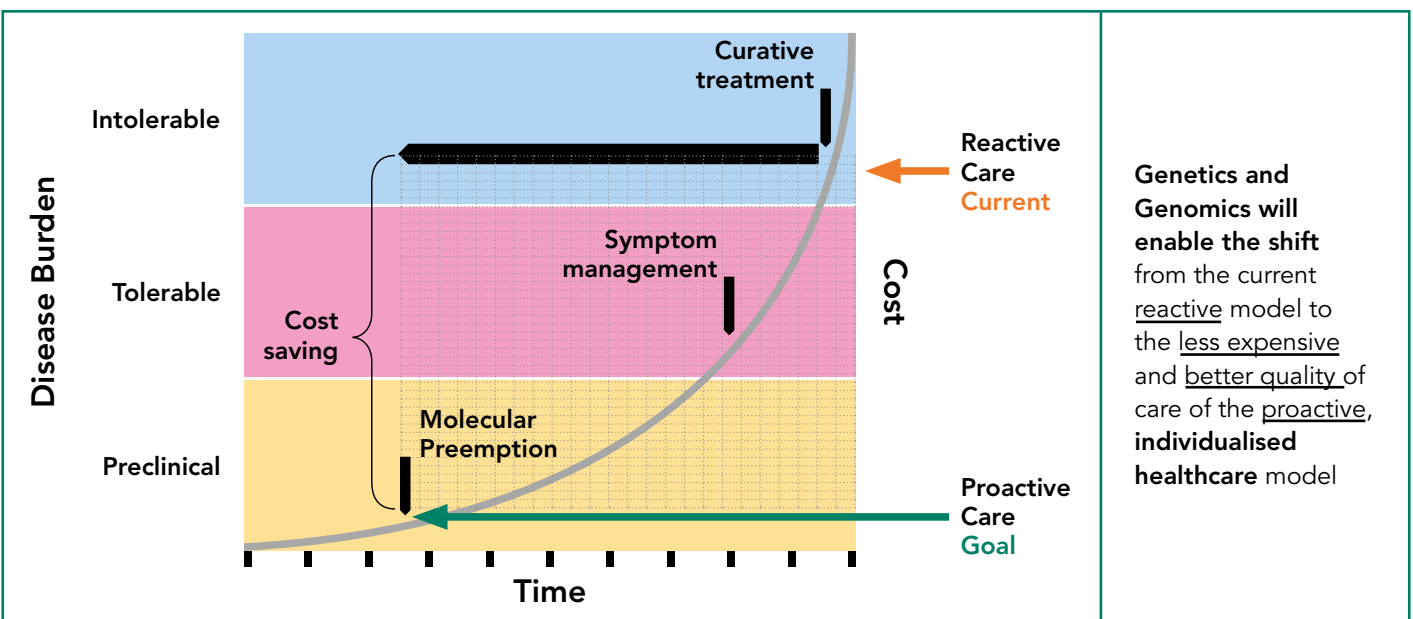


Figure 3 Genomics Allow Us to Identify High-Risk Patients Early

## WHEN REFERRAL IS INDICATED

Referrals are made when:

- a patient or family member is diagnosed with cancer or other diseases at a young age
- a patient presents with features of a genetic or inherited condition or with a family history of such a condition, or
- when a patient with a strong family history of a disease or predisposing ethnicity has questions about genetic testing.

### Step 1: Risk Assessment

**The genetic testing process at the Cancer Genetics Service (CGS) at NCCS begins prior to the first appointment.**

Patients provide detailed family health information, focusing on family members that have been diagnosed with genetic or developmental conditions, at what age and if/when family members have died from the disorder(s). The family history allows genetic counsellors to identify patterns of inheritance.

**During the initial appointment, the genetic counsellor reviews findings and completes the patient's medical history.** A physical exam may be performed by the doctor to look for syndromic features such as hand length, arm span, ear length or head circumference (*Refer to Picture 4*).

### Step 2: Consultation

With the risk assessment completed, **the genetic counsellor, often in conjunction with a cancer geneticist, determines whether a genetic testing is advised**, and the appropriate test(s) for the patient.

Genetic counsellors provide a great deal of education and counselling prior to and after testing, helping patients understand and consider their options. They explain the basics of genetics and describe the conditions being investigated. If a genetic condition is confirmed, they also walk the patients through the emotional, psychological, and social impact of the genetic results to the patient and family members.

Some patients want to know their risk, even when effective treatments for the condition do not yet exist, while other patients would rather not know in that circumstance.

Genetic counsellors are adept at communicating sensitive genetic information to patients and relatives, taking into account family dynamics and individual coping styles. They also discuss costs and insurance. The decision to pursue genetic testing is personal and genetic counsellors help guide patients and families through the difficulties in decision-making process.

### Step 3: Testing

**Generally blood is drawn on the same day or at next visit** to allow patients time to digest the information provided during consultation. Results may take 2 weeks to 4 months, depending on the extent of testing.



**Picture 4** A Cancer Genetics Service (CGS) Consultation



#### Step 4: Post-Test Genetic Counselling

**Gene test results are discussed with the patient by phone or during a follow-up appointment** with a genetic counsellor, as part of the standard of care. Next steps may include additional testing, testing of other family members and discussion of gene-informed medical management issues.

If a test result shows a genetic mutation, we carefully discuss future risks and prevention options and formulate an individualised medical management plan based on the specific mutated gene in the context of personal and family history. For example, if a patient tests positive for a BRCA1/2 breast cancer mutation, we review the statistical risk of developing breast and/or ovarian cancer and their ages of risk; discuss high-risk surveillance (e.g., breast MRI); prevention options, including surgery; and recommend that other family members be screened.

We take time to address patient concerns and answer questions from relatives. We work closely with the patient's primary physician. Like all investigations, some patients will have results which are not informative or have a result that is of uncertain significance. Our team closely reviews all such results with the clinical laboratory as well as with the patient to tailor management according to their personal and family histories.

If a research opportunity is available, we discuss the risks, benefits and limitations of participation. We also provide ongoing care for patients with genetic conditions, coordinate multidisciplinary medical appointments and help patients access resources related to their condition.

Since 2014, the Cancer Genetics Service at NCCS has seen a sharp rise in demand by patients requesting for genetic testing. Over the last 3 years, more than 1800 patients have had genetic risk assessment and clinical testing. **On average, one-fifth (20%) of the patient tested are positive for one of the cancer predisposition syndromes.**

Our team has studied and published on the local prevalence of inherited genetic mutations in breast cancers, gynaecological cancers, childhood cancers as well as in rare cancers such sarcomas and endocrine-related cancers. Prevalence varies according to cancer type, for example, about 20% of all patients with ovarian cancers and 5% of all patients with colorectal cancers have underlying genetic predisposition.

To understand one's genetic profile is typically a very personal choice with many factors impacting how patients decide. A personal history and/or family history of cancer may motivate one patient to have testing but may also be the reason why another patient opt against testing.

**An in-depth interview study conducted among patients who have undergone testing showed that Singaporean patients are heavily influenced by their primary doctors' opinions on whether they should proceed with genetic testing.** It is therefore very important to elevate genetic literacy amongst clinicians and primary care doctors so that they may identify patients appropriately for a genetics referral.



*Dr Joanne Ngeow (BMedSci, MBBS, FRCP, MPH) is a Senior Consultant at the Division of Medical Oncology at the National Cancer Centre Singapore, and Associate Professor (Genomic Medicine) at the Lee Kong Chian School of Medicine, Nanyang Technological University Singapore.*

Dr Ngeow currently heads the Cancer Genetics Service at the National Cancer Centre Singapore, with an interest in caring for families with hereditary cancer syndromes. She was awarded consecutive fellowships by the National Medical Research Council and the Ambrose Monell Foundation to complete formal clinical and wet bench training in Cancer Genomic Medicine at the Genomic Medicine Institute, Cleveland Clinic, Ohio. Dr Ngeow is funded by the National Medical Research Council and Ministry of Health to explore gene-environment interactions in cancer predispose to cancer initiation and progression as well as the implementation of genomics into routine clinical care.



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# Minimal Scar Mastectomy – A Novel Nipple-Sparing Technique at KK Women’s and Children’s Hospital

Minimal Scar Mastectomy (MSM), a novel technique of nipple-sparing mastectomy without reconstruction, is enabling patients at KK Women’s and Children’s Hospital (KKH) with breast cancer to conserve their nipple-areolar complex with minimal post-surgical scarring.

Breast cancer is the top cancer affecting women worldwide, and develops when cells in the breast begin to grow out of control. **In Singapore, it is estimated that one in 14 women develop breast cancer before the age of 75.**

Pioneered by Dr Lim Geok Hoon, Senior Consultant, KK Breast Department, KKH, MSM has been introduced for select patients at KKH with breast cancer since March 2017. Arising from a combination of nipple-sparing mastectomy and the round block technique (an oncoplastic technique), MSM provides patients with an alternative to the long transverse chest scar associated with traditional mastectomy, with a more cosmetically pleasant concealed scar. MSM also enables the preservation of the nipple-areolar complex – which has been shown to improve the psychological well-being of patients.

## NIPPLE PRESERVATION MASTECTOMY WITHOUT RECONSTRUCTION

In most cases of treatable breast cancer, surgery of the breast is usually required, and would involve either breast conservation combined with radiotherapy, or a mastectomy with or without reconstruction.

Traditionally, to spare the nipple during mastectomy, reconstruction would be mandatory to support the overlying breast skin envelope after the mastectomy has been performed. This would involve the use of implants or the patient’s own tissue, usually from the back or abdomen, which increases the duration and costs associated with the surgery.

During MSM, the skin around the areola is pre-operatively outlined to estimate the amount of breast skin to be removed. Thereafter, this excess breast skin is removed and mastectomy is performed using an incision around the areola, while preserving the nipple-areolar complex. The areolar wound is then closed in the same fashion as the round block technique.

This is the first reported surgical technique that is able to preserve the nipple-areolar complex in a mastectomy without the need for reconstruction. Should the patient choose to go for reconstruction in the future, the cosmetic outcome will also be better compared to a traditional mastectomy, since the transverse scar associated with the latter is avoided.

## A PROMISING TREATMENT OPTION FOR ASIAN WOMEN

The eligibility criteria for MSM includes small breasts, with no evidence of cancer involving the nipple-areolar complex or a large area of breast skin. They would also need to have opted for mastectomy without reconstruction, and have the desire to conserve their nipple-areolar complex.

Although mastectomy with reconstruction will inevitably result in a better cosmesis as compared to without reconstruction, the decision to embark on reconstruction remains a very intimate one.

Given the high rate of patients with breast cancer who choose mastectomy without reconstruction locally, as well as a higher prevalence of women with smaller breasts in the Asian population, MSM can certainly be an option to consider for this group of breast cancer patients, allowing suitable patients to conserve their nipple-areolar complex with less scarring.



### REFER A PATIENT

Patients diagnosed with breast cancer who are considering to undergo a minimal scar mastectomy can contact KKH at **+65 6294 4050** for a consultation at the **KK Breast Centre, which is a part of the SingHealth Duke-NUS Breast Centre.**

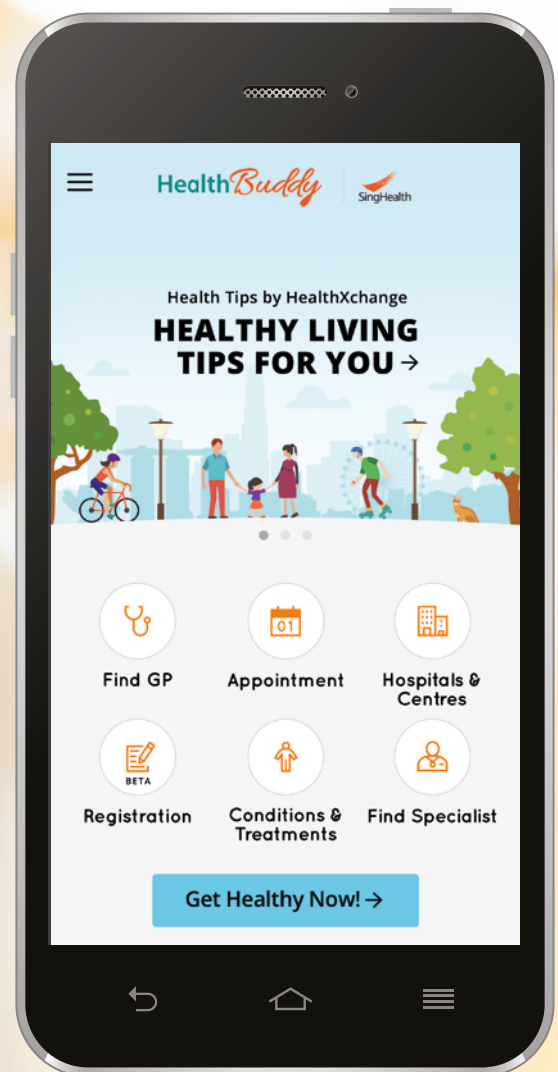


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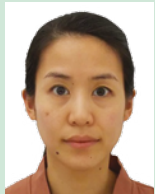
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Academic Chair, SingHealth Duke-NUS Musculoskeletal  
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**Dr Joel Lim Kian Boon**  
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**Dr Mok Wing Yan**  
Associate Consultant  
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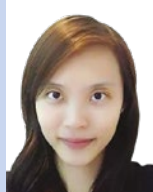
**Dr Chia Suyin Moira**  
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General Paediatrics  
Service



**Dr Tan Mui Ching Joanne**  
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Service



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Campus Director  
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*Associate Consultant*  
Division of Radiation Oncology




**Dr Saw Myat Thitsar**  
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Division of Radiation Oncology


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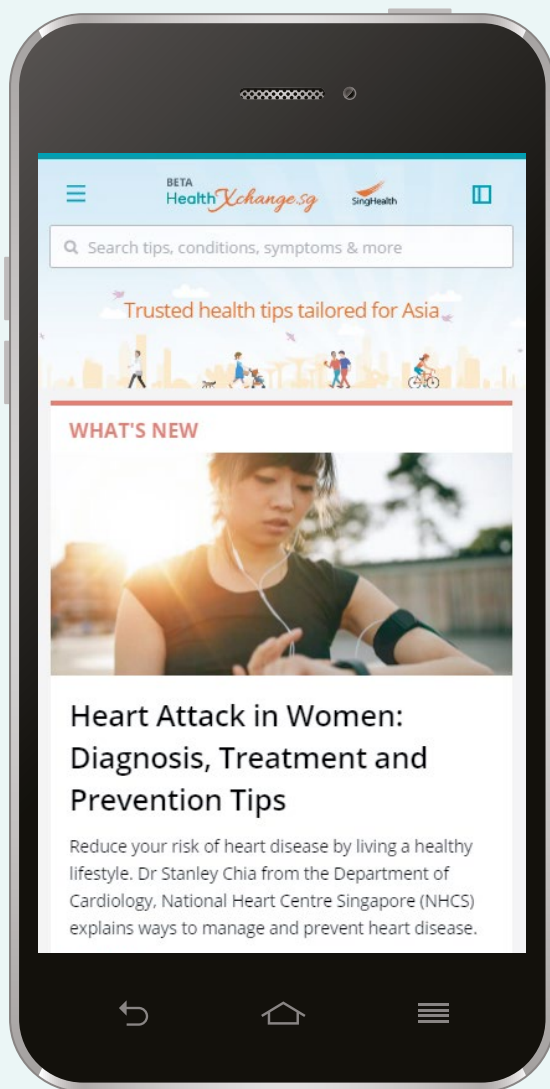
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### HEALTH SECTIONS

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-  HEART & LUNGS
-  DIGESTIVE SYSTEM
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## Courses



Forum for Healthcare Professionals

# Inaugural Paediatric Respiratory and Sleep Medicine Symposium

Venue: KKH Auditorium, Training Centre, Level 1, Women's Tower

### Paediatric Sleep Medicine Workshop

Date: 8 March 2019, Friday

Time: 8.00am to 5.00pm

CME points will be accredited

### Paediatric Respiratory Medicine Symposium

Date: 9 to 10 March 2019, Saturday to Sunday

Time: 8.00am to 5.30pm

## KEY SPEAKERS

### DR COLIN WALLIS

Division Lead and Consultant

#### Paediatric Respiratory Medicine

Great Ormond Street Hospital for Children, London, United Kingdom

### DR SADASIVAM SURESH

Consultant, Senior Staff Specialist

#### Paediatric Respiratory and Sleep Medicine

Lady Cilento Children's Hospital, Brisbane, Australia

### ASSOC PROF TEOH OON HOE

Head and Senior Consultant

#### Respiratory Medicine Service

KK Women's and Children's Hospital, Singapore

### DR MAHESH BABU RAMAMURTHY

Head and Senior Consultant

#### Paediatric Respiratory and Sleep Medicine

National University Hospital, Singapore

### DR BIJU THOMAS

Senior Consultant

#### Respiratory Medicine Service

Programme Director

#### Inaugural Paediatric Respiratory and Sleep Medicine Symposium

KK Women's and Children's Hospital, Singapore

## PROGRAMME HIGHLIGHTS

- Paediatric sleep medicine workshop
- Chronic cough
- Difficult asthma
- Bronchiectasis
- Childhood interstitial lung disease
- Pulmonary hypertension
- Congenital lung anomalies
- Aspiration-related lung disease
- Respiratory problems in children with neuromuscular diseases
- Paediatric chest imaging
- Cardiopulmonary exercise test
- Hands-on sessions on
  - Paediatric polysomnography
  - Lung function tests
  - Home ventilation for technology-dependent children

## REGISTRATION CLOSES ON 5 MARCH 2019 (TUESDAY).

Early bird registration closes on 7 January 2019 (Monday).

Pre-registration is required. For more details, please call 6394-8746 (Monday to Friday, 8.30am to 5.30pm) or log on to [www.kkh.com.sg/events](http://www.kkh.com.sg/events)

Seats are confirmed upon full payment on a first-come, first-served basis. Registration fee is non-refundable.






# SingHealth

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## GP FAST TRACK APPOINTMENT HOTLINES

 Singapore General Hospital	<b>6321 4402</b>
 Changi General Hospital	<b>6850 3333</b>
 Sengkang General Hospital	<b>6472 2000</b>
 KK Women's and Children's Hospital	<b>6294 4050</b>
 National Cancer Centre Singapore	<b>6436 8288</b>
 National Dental Centre Singapore	<b>6324 8798</b>
 National Heart Centre Singapore	<b>6704 2222</b>
 National Neuroscience Institute	<b>6330 6363</b>
 Singapore National Eye Centre	<b>6322 9399</b>

## DIRECT WARD REFERRAL CONTACT NUMBERS

 Singapore General Hospital	<b>6321 4822</b>
 Changi General Hospital	<b>6788 8833</b>
 KK Women's and Children's Hospital	<b>6394 1180</b>

## SINGHEALTH DUKE-NUS ACADEMIC MEDICAL CENTRE

 Singapore General Hospital	 Changi General Hospital
 Sengkang General Hospital	 KK Women's and Children's Hospital
 National Cancer Centre Singapore	 National Dental Centre Singapore
 National Heart Centre Singapore	 National Neuroscience Institute
 Singapore National Eye Centre	 SingHealth Community Hospitals
	 Polyclinics SingHealth