Doc Talk

# Liquid biopsy a promising breakthrough for cancer screening

**The non-invasive blood test is capable of detecting multiple cancers at the early and curable stage**

Wong Seng Weng

Liquid biopsy, a non-invasive blood test capable of detecting multiple deadly cancers at the early and curable stage, might be the real deal for cancer screening.

In the 1960s, scientists believed that they had discovered the holy grail of the screening of colorectal cancer (cancer of the large bowel). They discovered a cancer marker in the blood, carcinoembryonic antigen (CEA), that was purported to have a 100 per cent accuracy in the early detection of colorectal cancer.

This proved to be a false dawn.

Upon close examination, not only was CEA not specific for a particular type of cancer such as colorectal cancer, but other non-cancer related conditions such as stomach ulcer, inflammation of the colon, gallbladder or pancreas could also lead to an elevated level of CEA. Even heavy smoking could trigger a rise.

Though tests for blood cancer markers such as CEA, CA 19-9, CA 125 and CA 15-3 are commercially available for use and are frequently offered to the public as part of a health screening package for early cancer detection, no health authority, including Singapore's Ministry of Health, recommends their use in cancer screening. These cancer marker tests are associated with unacceptably high false-positive (elevated cancer markers without the presence of cancer) and false-negative (normal cancer marker level in the presence of actual cancer) rates.

Are there any problems sticking to the decades-old cancer screening techniques?

Standard-of-care cancer screening recommendations around the world today revolve around the use of colonoscopy (colorectal cancer), mammography (breast cancer), pap smear (cervical cancer) and CT scan (lung cancer).

While these recommendations are evidence-based and worthwhile for the population to adopt, there are significant drawbacks. These tests can be invasive. Colonoscopy, for instance, involves inserting a camera-bearing instrument through the anus into the large intestine. Several, such as mammography and CT scans, involve exposure to radiation, which has health hazards.

Such consideration sometimes generates fear in the public, thus limiting the take-up rate. Furthermore, a successful cancer screening programme requires the individuals being screened to follow through with repeat testing at predetermined time intervals. Some of the risks and discomfort associated with many screening techniques may reduce compliance over time.

Even if individuals are fully committed to do whatever it takes to protect themselves from death arising from advanced-stage cancer, many deadly cancers, such as those of the pancreas and ovary, do not have a recommended screening strategy to begin with.

Small wonder that even in a society with advanced medical facilities such as the United States, data showed that only 14 per cent of all cancers diagnosed were detected through screening.

Scientists, however, have not given up on the quest for a non-invasive blood test capable of detecting multiple deadly cancers at the early and curable stage. Liquid biopsy could be it.

In a nutshell, liquid biopsy detects cancer cells in the body by picking up the presence of cancer DNA in the blood.

Abnormal alteration of cellular DNA sequences, known as genetic mutation, is the driving force behind the process of transformation of normal cells into cancer cells. There are many such known cancer mutations. To complete the process of cancer transformation, normal cells need to accumulate a certain number of mutations that confer on them the ability to multiply rapidly, attain immortality, spread to different parts of the body and all while evading detection by the body's immune system.

Cancers that originate from different parts of the body have different assemblages of mutations. In short, cancers of different origins have different DNA signatures. Breast cancer, for instance, has a different signature from lung cancer.

Cancer cells, if present in the body, will have a certain cell turnover. That is to say, even as they multiply rapidly, some cancer cells will die and break down – a process known as apoptosis. The DNA of these apoptotic cells will leach into the blood circulation. The medical community has mastered how to recover such cell-free DNA (cfDNA) from blood samples. It has also mastered the technique of analysing a huge number of nucleotide sequences of such cfDNA rapidly and with high fidelity using a technology known as next-generation sequencing.

The technique of isolating cfDNA and analysing it using next-generation sequencing is also known as liquid biopsy. The name came from the fact that a chunk of the cancer genetic material (which in the past required the needling of the cancer through a biopsy) can be obtained by using just a blood sample (blood being a liquid, in contrast to a solid cancerous tumour).

The scientific reasoning goes: If we can detect cancer DNA in the blood, we should be fairly confident that a cancer is hiding somewhere in the body. Since we can detect multiple cancers using the same technique, we do not need different tests to screen for different cancers. And since cancers of different origins have different DNA signatures, we can figure out where it is hiding and direct further medical investigation in that direction. And all these achieved through a simple and risk-free blood test.

So, does liquid biopsy live up to its hype?

There are two objective measures of how good a cancer screening technique is – sensitivity and specificity. This has to do with the false-positive and false-negative rates. Based on published trial results from different laboratories in this field, the forerunners are reporting test sensitivity and specificity rates of 90 per cent and above.

A sensitivity rate of 90 per cent means that 90 per cent of the targeted cancers present in the body are picked up. Conversely, 10 per cent of the targeted cancers are missed and the individual screened was given a false reassurance that everything was fine.

A specificity of 90 per cent means that if the test showed a positive result, 90 per cent of the time, a cancer exists. In 10 per cent of the cases, it was a false alarm. These figures are considered fairly robust from a scientific point of view.

Is liquid biopsy ready for the prime time?

Even though this technology is commercially available for use by doctors, for multi-cancer detection liquid biopsy tests to be widely adopted, this technique needs to jump through three hoops.

First, it needs regulatory approval for efficacy and safety. In the United States, the Food and Drug Administration (FDA) needs to give its nod. At least one American laboratory, CellMax Life, was given an FDA breakthrough device designation. This means that the preliminary assessment deemed it to be good enough for the FDA to streamline the application and review process towards accelerated approval. The equivalent regulatory hurdle in Singapore would be approval by the Health Sciences Authority.

The second bar to be cleared will be for the test to receive public funding. In the US, the Centres for Medicare & Medicaid Services (CMS) have to judge that the use of public monies to fund the test is justified. The CMS has set the approval threshold at a sensitivity level of at least 75 per cent and specificity level of at least 90 per cent. The leading laboratories have cleared that bar. The equivalent in Singapore will be to gain MediSave reimbursement for the test.

Finally, physicians usually consult the national guidelines of their respective countries when deciding screening strategies for their patients. The US guidelines are set by the US Preventive Services Task Force. The equivalent recommendations in Singapore are usually detailed in the Ministry of Health's practice guidelines.

These national guidelines go beyond the assessment of efficacy, safety and cost-effectiveness, and make actual recommendations of how physicians should integrate new technology into pre-existing norms. Where different methods of screening are available, these guidelines may analyse the pros and cons of each, and rank the options in order of preference, or recommend how to adapt the screening strategies in accordance with the varying risk-profile of different segments of the population.

The technology for liquid biopsy for cancer screening has arrived. In the days ahead, this technique for cancer screening is likely to gain wider acceptance. Coming soon to a clinic near you.

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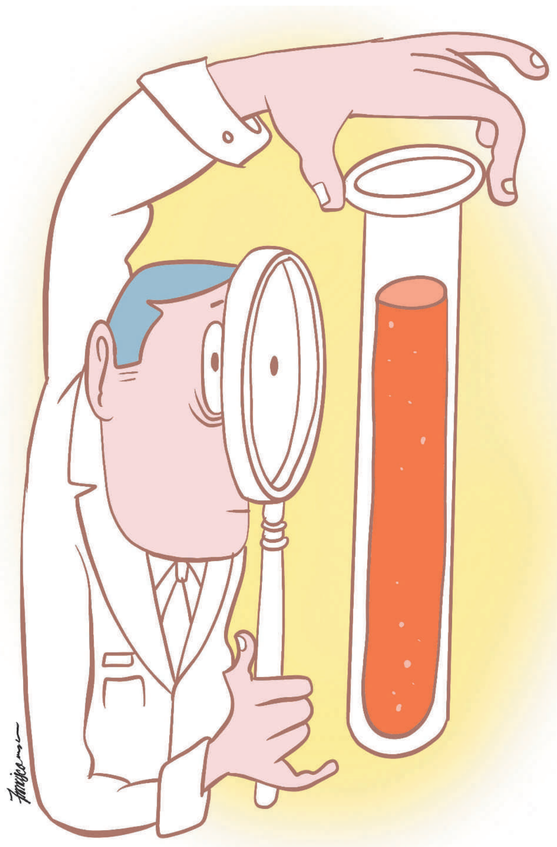
• Dr Wong Seng Weng is the medical director and consultant medical oncologist at The Cancer Centre.



## Vaccines and booster shots can reduce risk of developing long Covid

FROM C1

WHO recommends taking vaccines and booster shots, when offered, to reduce the risk of developing long Covid. But who should take these booster shots?

**SHOULD YOU GET A BOOSTER SHOT?**

An MOH spokesman says, from Jan 1 to July 15, more than 683,400 doses of Covid-19 vaccine were administered under the National Vaccination Programme.

With 81 per cent of the population achieving the minimum protection, the national recommendation now is for individuals aged 60 years and above, as well as medically vulnerable persons, to receive an additional booster dose in 2023, around one year from their last dose, after achieving minimum protection.

Younger people may also get a booster after the same interval of time if they wish. However, the spokesman says: "People aged 12 to 59 years who are healthy have a lower risk of severe disease when infected with Covid-19, compared with people aged 60 years and above, or those who are medically vulnerable."

Why is a seasonal Covid-19 shot not on the National Immunisation Schedule? The spokesman says: "Vaccinations under the national immunisation schedules are stable long-term recommendations for the population. Influenza vaccinations have been developed and administered for many years, and meet this standard. Further study is needed on the Covid-19 disease characteristics and vaccines before the latter can be considered for the national immunisation schedules."

From Jan 1 to July 15, more than 683,400 doses of Covid-19 vaccine were administered under the National Vaccination Programme, says a Ministry of Health spokesman. PHOTO: ST FILE

Infectious diseases specialist Leong Hoe Nam urges younger people to complete the minimum protection doses and to consider a booster shot if they have family members who are medically vulnerable or aged 65 and older. Younger people who get boosters can reduce the risk of transmitting Covid-19 to their vulnerable family members.

Young people who are immunocompromised or otherwise medically vulnerable will also benefit from a booster, but should consult their doctors.

Ms A. Aw, 25, is waiting for her health to stabilise before taking another Covid-19 vaccine.

She finished the minimum protection vaccine doses in January 2022, tested positive for Covid-19 in February and August the same year, developing long Covid after the second infection.

Her symptoms include insomnia and disturbed sleep, heart palpitations while walking and brain fog. She is on medication and taking a break after completing her bachelor's in psychology at a local university.

"It's 'watch and see' because my long Covid symptoms haven't settled down," she says. "There's a risk of me developing other symptoms."

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# Should my son be circumcised?

**Paediatric surgeon Ong Lin Yin answers questions about penile hygiene, caring for your son's foreskin and circumcision**

Proper care of your son's foreskin can help prevent infection. PHOTO: GETTY IMAGES

The foreskin is a sheath of skin that covers the head of the penis (glans). In most baby boys, it is stuck to the glans and cannot be pulled back (retracted). As they grow older, the foreskin can be retracted back over the glans, exposing the hole where the pee comes out (urinary meatus). This is a gradual process, and may only be complete after puberty.

Paediatric surgeon Ong Lin Yin shares more on how parents can care for their baby's foreskin to prevent infection and inflammation.

**Q How should I care for my son's foreskin and what if it can't be fully retracted?**

Good penile hygiene is important as it is common for small amounts of urine to remain within the foreskin after a pee, causing irritation and infection.

If your son's foreskin can be retracted, it should be done gently when showering to expose the glans for cleaning. After this, the foreskin should be returned to its original position, covering the glans.

If the foreskin is only partially retractile, parents may aid the separation process by gently retracting the foreskin on a regular basis. Do not forcibly retract the foreskin if it remains tight or if the child complains of pain when doing so.

**Q How are some common problems with my son's foreskin treated?**

Some common potential problems include:

- **Phimosis:** A condition where the foreskin is very tight and cannot be retracted. This is normal in younger boys, and only requires treatment if it is causing persistent irritation, infection such as balanitis, or a condition called paraphimosis. Your son may be prescribed a cream to help with retraction of the foreskin.
- **Balanitis or balanoposthitis:** Infection or inflammation of the glans or foreskin. Your son may experience pain from passing urine, redness of the foreskin and swelling. There may also be pus discharge. This is usually treated with antibiotics.
- **Balanitis xerotica obliterans:** A long-term infection of the foreskin. Left untreated, it can scar the glans and lead to narrowing of the meatus. Your child is likely to experience frequent pain and bleeding of the foreskin, as well as difficulty peeing. An early circumcision is recommended in order to minimise complications.
- **Paraphimosis:** A condition where the foreskin is retracted over the glans, gets stuck and cannot be returned to its original position. This causes pain and swelling of the glans. If the foreskin is not reduced urgently, the blood supply to the glans can be also be affected.

**Q Is it necessary to circumcise my son and what are the possible complications?**

Circumcision is an irreversible procedure to remove the foreskin, leaving the glans permanently uncovered. Medical indications, religion or cultural beliefs are common reasons for circumcision.

Should you wish to circumcise your son, it's best to first discuss it with your surgeon as there are still risks and complications, though uncommon. There are also different techniques of circumcision, and the final appearance of the penis may differ depending on the technique and your son's penile anatomy.



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ask the experts

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# All-in-one skincare for men

**Suntory Wellness Research Centre's product researcher Tatsuo Matsuoka shares how its patented technology combines lotion, serum and cream in one product and simplifies your grooming regime**

It's important for men to prioritise their skin health and prevent dry, irritated skin from years of shaving. PHOTO: GETTY IMAGES

For many men, navigating the world of skincare may get difficult and confusing, especially when department store shelves are stocked with rows of different products for different needs. Product researcher at Suntory Wellness Research Centre, Tatsuo Matsuoka, helps to demystify the topic for men and shares what to look for in a facial product.

**Q I have always been using soap and water to cleanse my skin. Isn't that enough?**

Skincare isn't limited to women; it's equally important for men to prioritise their skin health. Despite producing more oil, men's skin tends to be naturally drier compared to women's, emphasising the need for skincare routines designed to address both oily and dry skin concerns.

One common issue men encounter is dry and irritated facial skin. This is often due to years of shaving, adversely affecting the skin's lipid layer, which plays a crucial role in retaining moisture. The skin becomes dry, susceptible to irritation, and appears lacklustre.

**Q Why can't I use the same skincare products as my wife instead of a separate range for men?**

Men's facial skin typically exhibits higher sebum production and lower moisture content compared to women's skin. Therefore, it is logical that skincare approaches should vary between genders. Suntory Varon is specifically designed to cater to the unique skin concerns of men, taking into account their distinct needs such as moisture retention and sebum reduction.

**Q What is a good skincare regimen for men and what products should I use?**

To maintain healthy skin, it is essential to follow a few key steps. Firstly, ensure you wash your face twice daily, once in the morning and once before bed. Opt for a gentle facial cleanser and use lukewarm water for best results.

Secondly, incorporate a moisturiser into your skincare routine to protect your skin from external pollutants in the air. It helps your skin look brighter, smoother, and younger. Consider Suntory Varon, which controls sebum and helps give your skin intense moisture.

Lastly, do not forget to apply sunscreen to minimise the damaging effects of UV rays, which can accelerate the development of wrinkles and age spots.

**Q What makes Suntory Varon a unique skincare product for time-strapped men?**

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