

## Achieving universal and comprehensive publicly funded prenatal screening and diagnostic algorithms in Hong Kong: an interview with Dr Wing-cheong Leung

Dr Leung and three other members of the FMPRG voting team: (from left to right) Dr Anita Kan (Tsan Yuk Hospital Prenatal Diagnosis Laboratory), Dr WC Leung, Dr Elaine Kan (Hong Kong Children's Hospital Radiology), and Dr HM Luk (Hong Kong Children's Hospital Clinical Genetics) at the Hospital Authority Convention 2024

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In the field of obstetrics and gynaecology (O&G), Dr Wing-cheong Leung is a distinguished leader whose contributions have greatly advanced maternal health. As Hong Kong's first accredited subspecialist in maternal fetal medicine (MFM), Dr Leung served as the Chief of Service of the Department of O&G at Kwong Wah Hospital from 2010 to 2021 and as the President of the Hong Kong College of Obstetricians and Gynaecologists (HKCOG) from 2016 to 2018. His unwavering dedication to the public sector and substantial contributions to O&G—encompassing areas ranging from prenatal diagnosis and postpartum haemorrhage to perinatal mental health (including domestic violence)—earned him the title of Honorary Fellow of the HKCOG in 2022 and the Outstanding Staff Award of the Hospital Authority (HA) in 2024.

Dr Leung's journey in MFM began in 1999, when he undertook overseas training in the subspecialty at the Perinatal Centre of the University of Toronto, Canada. An unexpected encounter with the thesis topic of rapid aneuploidy testing ignited his passion for prenatal diagnosis. He subsequently earned his MD with a thesis *Rapid aneuploidy*

*testing or traditional karyotyping, or both, in prenatal diagnosis* and developed a novel algorithm for prenatal diagnosis. This innovative work laid the foundation for his current project, the FMPRG platform (Fetal Medicine, Pathology, Radiology, and Genetics/Genomics), which is transforming the landscape of prenatal diagnosis in Hong Kong.

The concept of prenatal diagnosis for trisomy 21, widely known as Down syndrome, was first introduced in the 1960s. At that time, only pregnant women aged 35 years and older were eligible for amniocentesis in the public sector because the likelihood of having a child with Down syndrome increases with maternal age. Although this represented a substantial advancement in prenatal diagnosis, the approach had important limitations. Women aged 35 years and older faced the unsettling risk of miscarriage associated with amniocentesis, whereas those younger than 35 years were excluded from screening. This exclusion was a considerable oversight, considering that most expectant mothers at the time were younger than 35 years. Among women ineligible for public-sector screening, the financial burden of self-financing tests in the private

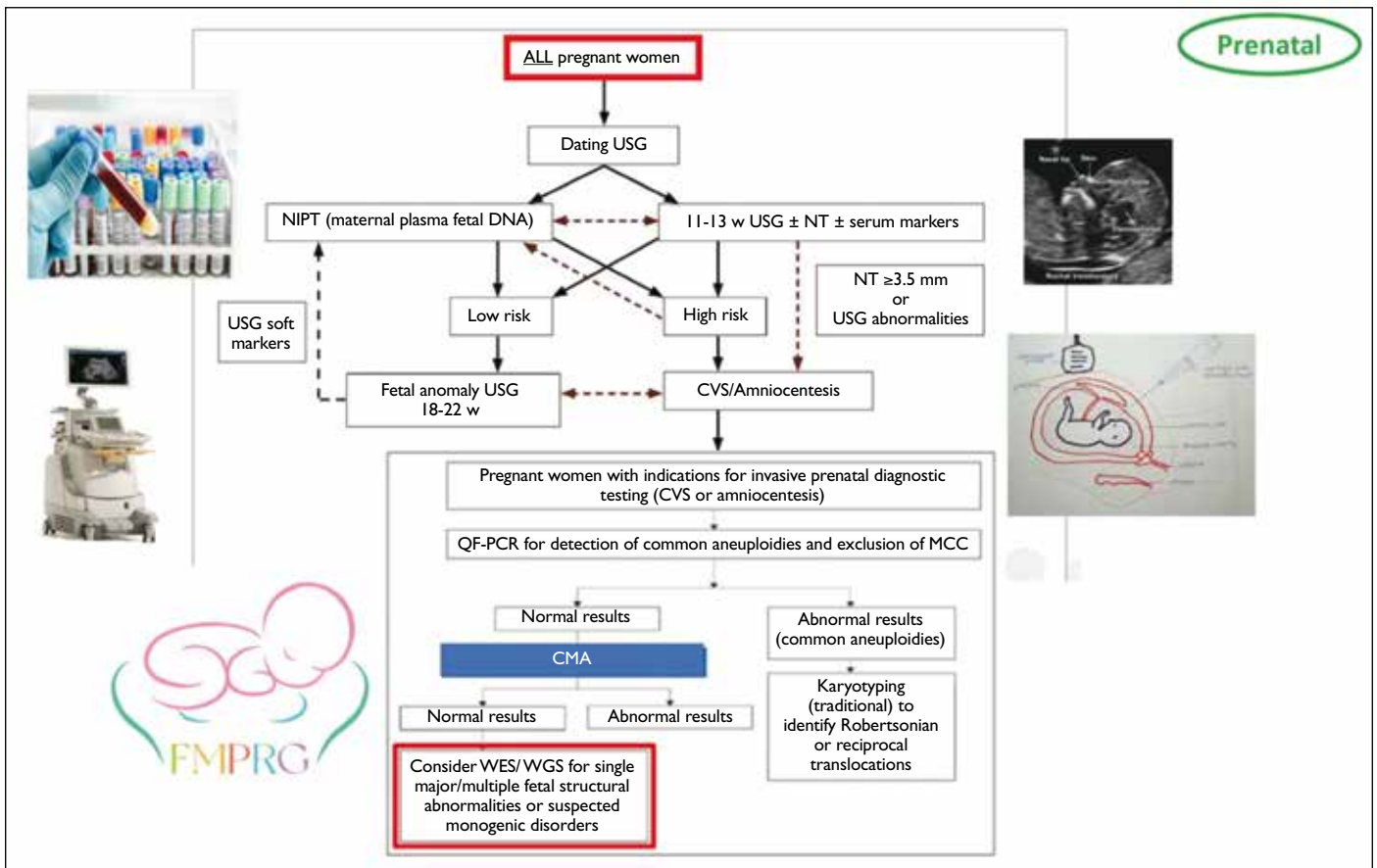


FIG. Publicly funded Hospital Authority prenatal screening and diagnosis algorithm

Abbreviations: CMA = chromosomal microarray; CVS = chorionic villus sampling; MCC = maternal cell contamination; NIPT = non-invasive prenatal testing; NT = nuchal translucency; QF-PCR = quantitative fluorescent-polymerase chain reaction; USG = ultrasonography; WES = whole-exome sequencing; WGS = whole-genome sequencing



Dr Leung with student reporters Asta and Nicholas

sector further exacerbated the stress associated with prenatal diagnosis.

Recognising these inequities, Dr Leung and his MFM seniors and colleagues developed a new algorithm (Fig) to screen for Down syndrome in all pregnant women, reserving amniocentesis for those who met specific criteria. This strategy significantly reduced the number of women exposed to the risk of miscarriage associated with amniocentesis. The initial screening process involves non-invasive methods, including maternal serum markers and fetal nuchal translucency measurements; amniocentesis is required only if these methods show Down syndrome positivity. To further refine the selection process, a second tier comprising non-invasive prenatal testing (ie, maternal plasma cell-free DNA analysis with higher sensitivity and specificity) is used for evaluation prior to amniocentesis. There is also the potential to offer non-invasive prenatal testing as a first-tier screening method if its cost decreases and public funding becomes available.

After years of refinement, the approach to prenatal diagnosis has evolved to encompass a wider range of congenital conditions and genetic

disorders. The fetal anomaly ultrasound scan, typically conducted between 18 and 22 weeks of gestation, represents the next critical component of the algorithm for all pregnant women. This scan evaluates fetal development and identifies potential structural abnormalities, such as heart defects, spina bifida, and other major organ anomalies. The inclusion of the fetal anomaly ultrasound scan is particularly important in regions such as Hong Kong, where termination of pregnancy is legally permissible only within 24 weeks of gestation. By detecting major structural abnormalities within the legal timeframe, pregnant women are enabled to make informed decisions regarding their options and to prepare for any required neonatal interventions.

Within this framework, pregnant women who undergo invasive prenatal diagnostic testing, such as chorionic villus sampling or amniocentesis, are subsequently offered quantitative fluorescent polymerase chain reaction. This test detects common aneuploidies and excludes the possibility of maternal cell contamination. If the results are normal, chromosomal microarray analysis (CMA) is performed to assess microdeletions and microduplications associated with various genetic conditions, including those that may result in developmental delays and intellectual disabilities.

In each step of this comprehensive algorithm, the diagnostic yield of prenatal diagnoses increases, effectively mitigating potential risks for the expectant mother while maximising the likelihood of detecting any fetal conditions. However, it is important to note that the cost of prenatal genetic tests remains high. Although the costs of polymerase chain reaction and CMA tests are fully covered by the HA in Hong Kong, overall costs substantially increase if whole-exome sequencing (WES) or whole-genome sequencing (WGS) is indicated after the CMA test. Dr Leung and Dr WF Ng (Senior Pathologist, HA) are addressing this issue through their current initiative—the FMPRG platform.

The FMPRG platform uses a multidisciplinary approach to select complex fetal cases for publicly funded WGS or WES. The FMPRG represents the multidisciplinary team comprising specialists in fetal medicine, pathology, radiology, and genetics/genomics. The voting team currently includes 15 core members, including MFM subspecialists from all eight HA hospitals offering prenatal diagnosis

clinical services, clinical geneticists, the heads of the two university prenatal diagnosis laboratories, pathologists, and radiologists. Complex fetal cases are uploaded to the platform for online interactive discussion and voting, enabling the team to select appropriate cases for publicly funded WES or WGS in a fair and timely manner. Not only does WES or WGS increase the probability of identifying the genetic cause of complex fetal abnormalities, but the anonymised archiving of these cases on the platform also creates a valuable database for future education and research. The implications of this initiative extend beyond the laboratory. As funding expands from 20 to 60 cases annually, the initiative aims to alleviate the financial burden on eligible mothers while empowering families with critical genetic insights to guide their pregnancies.

Looking to the future, Dr Leung envisions the integration of artificial intelligence (AI) into the consultation process as a transformative advancement in prenatal care. Considering the prolonged waiting times for consultations in Hong Kong, AI chatbots could alleviate unnecessary stress and anxiety for patients by addressing common misconceptions and providing personalised information about prenatal diagnosis, including details about the algorithm and the FMPRG platform. However, Dr Leung emphasises that AI is intended to complement, rather than replace, face-to-face consultations. By thoughtfully integrating AI within prenatal care, this approach combines the efficiency of AI chatbots with the human touch of in-person interactions, resulting in a more streamlined and responsive care experience.

Dr Leung's pioneering work in MFM is setting a gold standard for equitable access to prenatal diagnoses for all expectant mothers. He is a firm advocate of the principle that financial circumstances should never jeopardise a mother's access to prenatal diagnoses. Through the development of the HA algorithms and the FMPRG platform, combined with AI-driven consultations, he is committed to ensuring equitable access to advanced prenatal screening and diagnostic options for all expectant mothers. Dr Leung's vision is to establish a 'universal safety net' for all pregnant women, regardless of their economic status, equipping them with the resources necessary to make informed decisions about their health and the health of their babies.