ORIGINAL ARTICLE

Prospective assessment of the Hong Kong Hospital Authority universal Down syndrome screening programme

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Objective To evaluate the performance of the locally developed universal Down syndrome screening programme.

Design Population-based cohort study in the period July 2010 to June 2011 inclusive.

Setting Four Hong Kong Hospital Authority Departments of Obstetrics and Gynaecology and a central university-based laboratory for maternal serum processing and risk determination.

Participants Women were offered either a first-trimester combined test (nuchal translucency, free beta human chorionic gonadotropin, and pregnancy-associated plasma protein-A) or nuchal-translucency-only test, or a second-trimester double test (alpha-fetoprotein and total human chorionic gonadotropin) for detection of Down syndrome according to their gestational age. Those with a trisomy 21 term risk of 1:250 or higher were offered a diagnostic test.

Results A total of 16 205 pregnancies were screened of which 13 331 (82.3%) had a first-trimester combined test, 125 (0.8%) had a nuchal-translucency test only, and 2749 (17.0%) had a second-trimester double test. There were 38 pregnancies affected by Down syndrome. The first-trimester screening tests had a 91.2% (31/34) detection rate with a screen-positive rate of 5.1% (690/13 456). The second-trimester test had a 100% (4/4) detection rate with a screen-positive rate of 6.3% (172/2749). There were seven (0.9%) pregnancies that miscarried following an invasive diagnostic test. There were two Down syndrome–affected live births, both with an estimated first-trimester trisomy 21 term risk lower than 1:250.

Conclusion The universal screening programme offered at the four units was effective and achieved the expected detection rates and low false-positive rates, and to maintain these, the current emphasis on training, quality control, and regular auditing must continue.

New knowledge added by this study

- Locally developed trisomy 21 risk screening (based on maternal/pregnancy characteristics) achieved or exceeded expected performance predicted for population screening models.

Implications for clinical practice or policy

- Both public and private screening centres and laboratories should report annual detection and false-positive rates to ensure expected performance is actually achieved.
- A centralised cytogenetic registry is urgently needed, so that pregnancy outcomes of those undergoing screening and/or diagnostic tests are recorded for purposes of quality assurance.
- Assessment of nuchal translucency within a universal screening programme should only be performed by credentialed sonographers.

Key words
Down syndrome; First trimester screening; Second trimester screening; Nuchal translucency; Quality control

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Introduction

In July 2010 the Hong Kong Hospital Authority (HA) instituted a universal Down syndrome screening programme under which pregnant women were offered either the first-trimester combined test (nuchal translucency [NT], free beta human chorionic gonadotropin (free β-hCG), and pregnancy-associated plasma protein-A [PAPPA]) or the existing second-

香港醫院管理局產前唐氏綜合症篩查的前瞻性評估

目的 評估本地產前唐氏綜合症篩查的表現。

設計 2010年7月至2011年6月期間進行以人口為基礎的隊列研究。

安排 四家香港醫院管理局轄下的婦產科部門和一所以大學為中心的實驗室作母體血清處理和風險確定。

參與者 根據胎齡，產婦可選擇於妊娠前期接受「聯合篩查」測試（即頸後半透明帶、游離絨毛膜促性腺激素及妊娠相關蛋白A）或「頸後半透明帶」的單項測試，或於妊娠中期接受「二聯篩查」（即甲胎蛋白及人絨毛膜促性腺激素）以檢測唐氏綜合症。如果檢測結果顯示染色體21三體症比率達至1:250或以上，會為產婦提供一個診斷測試。

結果 共有16 205位產婦接受唐氏綜合症篩選檢測，其中13 331（82.3%）人接受了妊娠前期「聯合篩查」測試，125（0.8%）人接受了「頸後半透明帶」的單項測試，另2749（17.0%）人於妊娠中期接受「二聯篩查」。研究對象中有38人受唐氏綜合症影響。妊娠前期測試有91.2%（31/34）偵測率，其中5.1%（690/13 456）呈陽性反應。妊娠中期測試有100%（4/4）偵測率，其中6.3%（172/2749）呈陽性反應。有7位產婦（0.9%）在接受侵入性診斷測試後流產。最終有兩名嬰兒患有唐氏綜合症，他們妊娠前期的染色體21三體症比率均為1:250以下。

結論 如果能保持當前的重點培訓、質量控制和定期審查，四個部門所提供的產前唐氏綜合症篩查均為有效，它們都可達至預期的檢測率以及低假陽性率。

trimester double test (alpha-fetoprotein [AFP] and total human chorionic gonadotropin [hCG]) irrespective of their age. Prior to the start of the universal programme, the double test and a direct diagnostic test were only offered to women of advanced maternal age (≥35 years at delivery). The combined screening test was not previously available under the Hong Kong HA but was available within the territory as a pay-per-service test performed within the private health care sector.

Published studies from our unit and elsewhere using commercial software and screening model parameters developed at other screening centres have demonstrated that the first-trimester combined test has a detection rate (DR) of approximately 90% and a 5% false-positive rate (FPR).[1-4] Published population parameters derived specifically from Hong Kong Chinese women determined over the preceding 5 years are now available.[5] These population model parameters have now been incorporated into a locally developed screening software (www.obsscreening.hk).

The objective of the current study was to evaluate and report the performance of the universal screening programme using locally derived population risk model parameters of pregnancies jointly screened by four Hong Kong HA obstetric sites.

Methods

Subjects

This was an analysis of all pregnancies that were screened under the universal screening programme for Down syndrome at the Kwong Wah, Prince of Wales, Princess Margaret, and United Christian hospitals between July 2010 and June 2011 inclusive. The four units provide obstetric services to over 2 million residents of the New Territories East, Kowloon East, and West regions of the Hong Kong Special Administrative Region (HKSAR). Women were offered either a first- or second-trimester screening test according to their gestational age at initial booking and subject to availability of ultrasonography (US) within the optimum gestational window for the assessment of the NT. Women booking after 13 weeks of gestation or for whom US could not be conducted between 11 and 13 weeks of gestation were offered the second-trimester double test.

Maternal demographic characteristics, US findings, and maternal serum samples were obtained at the time of screening by staff at each hospital. Serum samples were centrally processed and analysed by the Obstetrics Screening Laboratory of the Chinese University of Hong Kong. Maternal serum concentrations of AFP, hCG, free β-hCG and PAPPA were assessed using either the Kryptor (Brahms Diagnostica GmbH, Berlin, Germany), DELFIA Xpress (PerkinElmer, Waltham, United States), or Roche Cobas e411 (Roche Diagnostics, Rotkreuz, Switzerland) analysers. Measured serum levels were converted to multiples of the expected gestational median (MoM) values. In women undergoing the combined test, gestational age at blood taking was estimated based on the fetal crown-rump length (CRL).[6] In those who underwent the double test, the gestational age was estimated based on the reported expected date of delivery and date of blood sampling. All serum MoM values were further standardised for pregnancy, and maternal and analyser characteristics, using locally derived and published adjustment factors.[5] Fetal NT and CRL were measured using standardised techniques by sonographers. The latter were midwives and doctors, who were all accredited and annually recertified to assess the fetal NT by the Fetal Medicine Foundation (FMF, London, United Kingdom). All NT measurements were converted to their equivalent MoM value using the expected median NT for CRL.[5] The NT measurements were carried out for CRLs between 42 and 84 mm, a

gestation age equivalent to 11 to 14^{+1} weeks (using a local CRL dating formula).[6]

Internal and external quality assurance

Individual marker MoM values were assessed on a weekly and monthly basis to determine the central tendency (median) and dispersion (standard deviation [SD]), as part of the laboratories internal quality control (QC) programme. The medians were checked to ensure that they remained within 10% (0.9-1.1 MoM) of the expected value of 1 MoM in unaffected pregnancies. The $\log_{10}$ SDs of AFP, hCG, free β-hCG, and PAPPA were compared to the expected reference values of 0.23, 0.14, 0.26, and 0.22 respectively. Daily QC samples with known low, intermediate, and high concentrations were measured and monitored on all analysers to determine inter-day variations. In addition, the laboratory participated in the United Kingdom National External Quality Assurance Scheme for laboratories providing aneuploidy screening. As part of the laboratories quality assurance programme, sonographers and supervisors at each hospital site received monthly quality assurance feedback reports on each active participant. All the sonographers and screening co-ordinators at each hospital received a monthly audit report indicating whether their individual NT measurements and overall NT measurements of their unit's central tendency and dispersion were within permitted limits.[7,8] Screening requests were not accepted from sonographers not accredited to measure fetal NT at the time the US scan was performed.

Risk determination

The estimated adjusted risk at term was determined using a multivariate model and the maternal a priori background risk of having Down syndrome. Details and descriptions of the theoretical background by which the estimated background risk, likelihood ratios, and adjusted risks were derived are provided at www.obsscreening.hk. Women undertaking the test were screened 'negative' or 'positive' if their risk of having Down syndrome at term exceeded a predefined cut-off value. In public hospitals, women screened 'positive' were offered a detailed morphology scan and/or a diagnostic test by chorionic villus sampling (CVS) or amniocentesis. Alternatively they could seek the same diagnostic tests, or non-invasive fetal trisomy (NIFTY) testing to ascertain chromosomal status as a pay-per-service procedure from a private specialist.[9] Fetal structural abnormalities as well as soft markers associated with aneuploidy, such as the nasal bone, nuchal fold, heart, bowel and bladder, were assessed using a detailed morphology scan. The term risk threshold adopted to indicate a 'negative' or 'positive' test result was 1:250, the level used by the HA Prenatal Diagnostic Laboratory at Tsan Yuk Hospital prior to the start of the screening programme.

Determination of pregnancy outcome

Details on pregnancy outcome and Down syndrome out-patient clinic attendance were obtained from the HA's Clinical Data Analysis and Reporting System. Chromosomal status of screened 'positive' pregnancies were recorded in the screening registry, based on: (1) test results supplied by the Prenatal Diagnostic Laboratory at Tsan Yuk Hospital on a monthly basis, or (2) directly self-reported private test results, ascertained from the Antenatal Record System for patients. Delivery records of births from the four hospitals were cross-matched with the pregnancy number and gravida. Hospitals were asked to inform the screening laboratory whenever a pregnancy with a 'negative' screening test resulted in a birth of a Down syndrome baby (false-negative case). Fetuses of screened pregnancies were considered to be phenotypically 'normal' at birth, if (1) the pregnancy was not reported as a false-negative case; (2) the fetus did not have any congenital abnormalities at birth; or (3) diagnostic test results in cases screened positive indicated that the pregnancy was euploidy (46XX/46XY) or had a karyotype considered to be a normal variant (balanced translocation, inherited maternal/paternal).

Determination of expected screening performance

Monte Carlo methods were used to simulate the individual marker MoMs distributions for 100 000 euploid and 100 000 trisomy 21 pregnancies at 12 weeks for the combined test, and at 16 weeks for the double test.[10] Standardised DR and FPR were calculated by taking the proportions with risks above a given threshold after adjustment for maternal age according to the maternal age distribution of pregnancies in the 2004 penta-annual Hong Kong territory-wide audit conducted by the Hong Kong College of Obstetricians and Gynaecologists (HKCOG).[11] The expected DR and FPR rates were also estimated for the previous HA policy under which the double test was only offered to women of advanced maternal age (≥35 years at delivery).

Results

A total of 16 205 pregnancies were screened, of which 13 331 (82.3%) had a first-trimester combined test and 2749 (17.0%) a second-trimester double test. The remaining 125 (0.8%) pregnancies underwent a first-trimester NT screening test only, primarily for

TABLE. Characteristics of the 16 205 pregnancies screened at the four hospitals

Parameter	No. (%) or median (range)	
	First trimester (n=13 456)	Second trimester (n=2749)
Screening hospital		
Kwong Wah	3522 (26.2%)	1138 (41.4%)
Prince of Wales	4024 (29.9%)	823 (29.9%)
Princess Margaret	3611 (26.8%)	521 (19.0%)
United Christian (Jul 2010 to Apr 2011)	2299 (17.1%)	267 (9.7%)
Maternal characteristics		
Age at delivery (years)	32.5 (16.7-48.2)	31.3 (16.9-45.7)
Advanced maternal age (≥35 years)	4004 (29.8%)	730 (26.6%)
Weight (kg)	54.92 (33.7-166.0)	55 (36.0-158.0)
Smoker	402 (3.0%)	125 (4.5%)
Nulliparous	7643 (56.8%)	1256 (45.7%)
Spontaneous conception	13 151 (97.7%)	2726 (99.2%)
Singleton pregnancy	13 331 (99.1%)	2749 (100.0%)
Ethnicity		
East Asian	12 999 (96.6%)	2598 (94.5%)
South Asian	162 (1.2%)	79 (2.9%)
South-East Asian	142 (1.1%)	66 (2.4%)
Caucasian, Afro-Caribbean	37 (0.3%)	6 (0.2%)
Gestational age at testing (days)	88 (77-99)	120 (102-143)

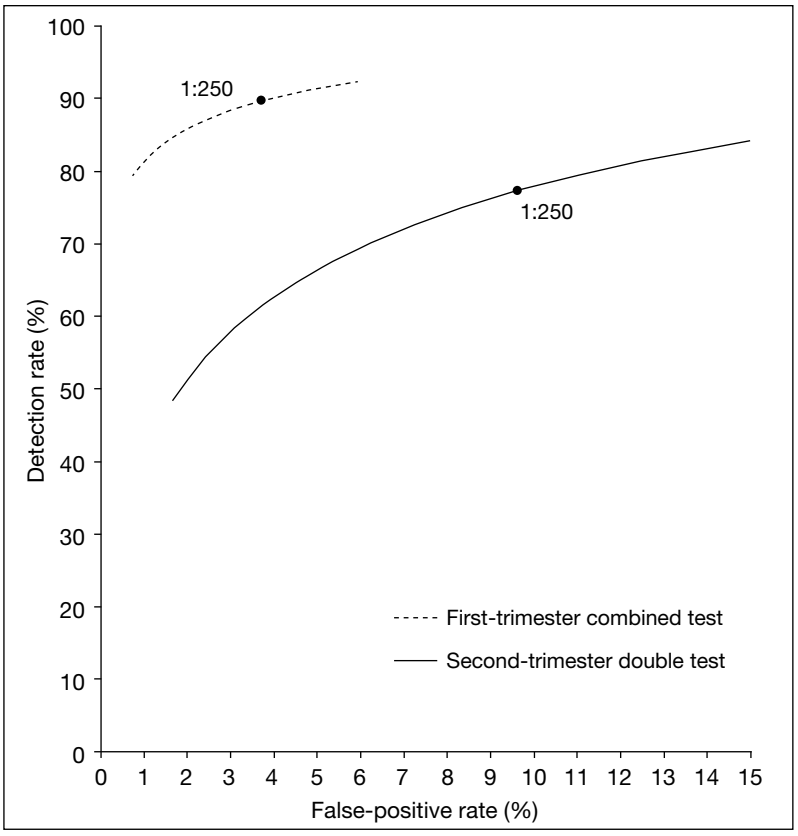

FIG. Expected detection rates of trisomy 21 for increasing false-positive rate (based on Gaussian distribution models after adjustment for maternal age according to the distribution of pregnancies in Hong Kong in 2004). The expected performance of the Hospital Authority screening programme using a risk cut-off threshold of 1:250 or higher is indicated on the chart

multiple pregnancy (twin pregnancies: 101; triplet pregnancies: 5). The Table summarises the maternal and pregnancy characteristics of those undergoing screening in the first and second trimesters. Thirty-nine (0.24%) of the women had a history of having a pregnancy affected by a chromosomal abnormality. Outcome of the pregnancy could not be determined in 2690 (16.6%) instances as these women did not deliver or seek further antenatal care at a HA hospital. Therefore, there was no accessible information to allow determination of pregnancy outcomes in these subjects.

The median maternal age was 32.3 (range, 16.7-48.2) years and was consistent with that reported in the 2004 territory-wide audit report.[11,12] The Chi squared test indicated that the overall maternal age distribution did not differ significantly from that in that 2004 audit. Among those undergoing screening, the proportion of women of advanced maternal age, however, increased from 24.2% in 2004 to 29.5% in those undergoing screening between July 2010 and June 2011. Women undergoing first-trimester screening were significantly older at their estimated date of delivery in comparison with those undergoing the second-trimester test (F=179.6, P<0.0001).

The Figure shows the expected DRs and FPRs at 12 weeks of gestation for the first-trimester combined test and the second-trimester double test based on the distribution of maternal age at birth of pregnancies in 2004. Using a term risk cut-off of 1:250, the expected DR (FPR) for the combined test and double test were 89.1% (3.5%) and 76.8% (9.3%), respectively. The expected DR and FPR of the previous HA policy of only screening women aged 35 and older would be 87% and 22%, respectively.

The median number of NT scans performed by the 43 sonographers was 234 (range, 6-1425); nine (20%) of them performed fewer than 30 scans. The $\log_{10}$NT MOM distribution of all sonographers was Gaussian with a mean of 0 and SD of 0.096 (after excluding pregnancies with abnormal karyotypes). The SD was reduced by 4% compared to an expected SD of 0.1 in unaffected pregnancies previously reported.[5] The correlation (*r*) between the NT and MOM values of the 101 pairs of twins was 0.42 and was statistically significant (P<0.0001).

The median inter-assay QC coefficient of variation among the 55 different QC assays used to ensure reliable measurement of AFP, hCG, free β-hCG, and PAPPA was 3.6%. The distributions of the $\log_{10}$-transformed AFP, hCG, free β-hCG, and PAPPA MoMs after correction for pregnancy and maternal characteristics and excluding aneuploidy-affected pregnancies were Gaussian, with respective mean (SD) values of -0.029 (0.146), -0.015 (0.223), 0.002 (0.262), and 0.006 (0.211).

Of the 13 456 pregnancies screened in the first trimester, 690 (5.1%) had a term risk of trisomy 21 of 1:250 or higher, of which six (0.9%) were lost to follow-up. Regarding the remaining 684 (99.1%) pregnancies with follow-up data, 42 (6.1%) declined the diagnostic test, 2 (0.3%) had a spontaneous abortion before the procedure was performed, 233 (34.1%) had a CVS, 335 (49.0%) had an amniocentesis, 69 (10.1%) reported having either an amniocentesis or CVS by private specialists, and 5 (0.7%) had a NIFTY test. The karyotype investigation in those with a positive screening test yielded 55 pregnancies with abnormal karyotype results; 31 (56%) had trisomy 21, 8 (15%) had trisomy 18, 6 (10.9%) had trisomy 13, 5 (9.1%) were considered normal variants (balanced translocations, inherited maternal/paternal), and 5 (9.1%) were abnormal variants (Turner's, triploidy, deletion). There were no twin pregnancies in which both twins were affected. There were three pregnancies that had trisomy 21 with a negative screening test, 2 of which were live births and one was detected during the mid-trimester morphology scan (performed for all pregnancies between 18 and 22 weeks of gestation). The two trisomy 21 live births both had normal mid-trimester morphology scans. The first-trimester screening test therefore had a 91.2% (31/34; 95% confidence interval [CI], 81.6-100%) DR for trisomy 21, with a screen-positive rate (SPR) of 5.1% (690/13 456; 95% CI, 5.5-5.5%), and a FPR of 4.9% (659/13 422; 95% CI, 4.6-5.3%). The perinatal DR for trisomy 21 was 94.1% (32/34). There were two cases of trisomy 18 with a negative first-trimester test detected at the mid-trimester morphology scan. One in every 12 to 13 pregnancies (55/690) with a positive first-trimester screening test had an abnormal karyotype.

Of the 2749 pregnancies screened in the second trimester, 172 (6.3%) had a term risk of trisomy 21 of 1:250 or higher. No pregnancies were lost to follow-up and there were no reported Down syndrome–affected live births among those with a second-trimester screening test. Twenty-four (14.0%) declined a diagnostic test, 145 (84.3%) had an amniocentesis and 3 (1.7 %) a NIFTY test. Karyotype investigation in those with a positive screening test yielded six pregnancies with abnormal karyotypes; four (66.7%) had trisomy 21 and two (33.3%) were considered normal variants. There was one case of trisomy 18 with a negative second-trimester test at the mid-trimester morphology scan. The double test had a 100% DR at the time of screening with an SPR of 6.3% (172/2749; 95% CI, 5.4-7.2%) and a FPR of 6.1% (168/2745; 95% CI, 5.2-7.0%).

In all, seven (0.9%) of the pregnancies reported to the laboratory had suffered a procedure-related miscarriage following the performance of an invasive prenatal diagnostic test. All were singletons, except that one was a twin pregnancy and only one of them had an abnormal karyotype. An amniocentesis or CVS were performed in four and three pregnancies, respectively.

Discussion

This study reports the performance of the HA's Down syndrome universal screening programme at the four hospitals. The first-trimester Down syndrome DR was 91.2%, which was within 2% of the expected rate determined from the maternal age distribution of pregnancies reported in the HKCOG 2004 territory-wide audit. In part, these performance figures are due to the emphasis placed on continued and rigorous assessment of US quality, serum median levels in affected and unaffected pregnancies, and determination of pregnancy outcomes. The audit and monitoring approach we adopted helped to continually improve the quality of the screening programme, and allowed adjustments for changes in underlying maternal and pregnancy characteristics as and when needed. All laboratories and screening centres offering a screening assessment within the HKSAR, irrespective of whether they were in the public or private health care sector, should have audit and monitoring as a central function within the screening service. This ensured that women received the best available risk evaluation and that the claimed performance was actually delivered. We were unable to find and compare our DR, FPR, and SPR from other private screening centres and laboratories performing aneuploidy screening as no published figures were available.

Numerous studies have highlighted the importance of ensuring that screening markers are consistent with the model used to determine the risk of aneuploidy. A 10% under or over estimation in a single marker can reduce or increase the DR at the expense of reduced or increased FPRs by The Quality Assurance Group of the United Kingdom National Screening Programme (UK NSP).[13,14] We have previously reported that failing to correctly adjust serum markers for maternal and pregnancy adjustment characteristics did not result in medians close to the expected value of 1 MoM.[5] In unaffected pregnancies, all serum markers in the present study had distribution parameters which were well within the UK NSP guidelines, as well as being almost identical to the expected values used within the risk calculation model. As a result the achieved DRs, SPRs, and FPRs were similar or better than those predicted by the prior simulation study. The differences between the expected and actual rates achieved can be explained by differences in the maternal age distribution assumed from the HKCOG 2004 territory-wide audit and the actual age distribution of women who had either of the screening tests. Another possible reason was that relatively few women had undergone the double test.

The performance of the screening programme at the four hospitals in our study cannot be extrapolated to other public or private screening laboratories or centres within the HKSAR, as the screening models and methodology used to estimate risk of aneuploidy depend on the software used at each laboratory. To ensure that claimed performances are actually achieved, the laboratories performing aneuploidy screening should determine expected DRs, FPRs and relevant screen-negative/-positive risk cut-off thresholds before offering such a screening service. Maternal age distribution varies from one population to another, and serum analysers may not function in an identical manner to that reported in other centres. The median maternal age at delivery for our pregnancies was 32 years and similar to that of all parturients in the HKCOG 2004 territory-wide audit.[11,12] The median maternal age, however, was 3 years higher than the median of 29 years in the 2002-2004 maternal age reference distribution used to assess screening performance in the UK.[15] Adopting a first-trimester cut-off of 1:300 at the time of screening (equivalent to approximately 1:450 at term) reported by Kagan et al[16] using the FMF-2009 screening model in a local Hong Kong population can result in some women undergoing unnecessary diagnostic tests. Adopting the same cut-off in Hong Kong would be expected to have a significantly higher FPR than in the UK, due to higher maternal ages at birth.[16] We have previously estimated that the gestation age-specific cut-off for a 5% FPR in Hong Kong using the FMF 2009 models would be 1:165 (approximately 1:240 at term) and that this cut-off value would yield an 88% DR.[4] Nevertheless, improvements to the current programme could be made to increase DRs and decrease SPRs. The second-trimester screening test could be improved by switching to either the triple test or Quad test by adding unconjugated oestriol (uE3) and inhibin-A.[17] In the first trimester, the NT measurement in twins should be adjusted for that of the co-twin because of the high correlation between twin NT measurements.[18] Lastly, additional US features, such as the presence or absence of the nasal bone, could be assessed at the same time as NT provided that those assessing these additional features are properly accredited.[4,19] The National Screening Committee in the UK recommends that the Quad test should be used for screening in the second trimester, because of its higher DR and a FPR equivalent to that in other second-trimester tests.[17] It has now been shown that the NT measurement in twins are correlated and not independent of each other, and failure to allow for this can result in incorrect determination of fetus-specific risks.[18]

Owing to recent developments in non-invasive prenatal tests (NIPTs), they have been advocated as being more 'advanced' because of higher DRs and lower FPRs.[9,20-22] There is currently much debate as to whether NIPTs should be an extension of prenatal screening or used for non-invasive diagnoses.[23-25] Whilst accuracy is important, other factors (cost, time taken to analyse samples, universal availability at a cost affordable to public health care services) also need to be considered. Both NIPTs and first-trimester screening require US to confirm gestational age and the number of fetuses. Current evidence suggests that apart from aneuploidy, first-trimester serum levels can also be used to screen for other complications of pregnancy such as pre-eclampsia, gestational diabetes, and growth.[26-29] Whilst NIPTs are an exciting development, our study indicates that 12 (20%) of the 61 pregnancies with abnormal karyotypes did not have trisomy 21, 18 or 13, of which five (8%) were associated with abnormal phenotypes (Turner's, triploidy). To date, NIPTs have only been performed in high-risk populations (advanced age, persons screened positive) using samples from women who are at increased risk of having Down syndrome children.[22,23] No large-scale studies involving NIPTs and close monitoring of pregnancy outcomes are currently available. It is therefore unclear whether sensitivity and specificity figures quoted in high-risk populations also apply to screening the whole population. The advantage NIPTs offer is that the majority of women who test negative could avoid having spontaneous abortions after amniocentesis or CVS. Currently, it is unclear to what extent local pregnant women would be willing to forego a definitive diagnosis through amniocentesis or CVS, and gamble on having an NIPT that has only been verified for trisomies 21, 18, and 13. Earlier, Chan et al[30] showed that Chinese women strongly preferred full karyotyping and a full chromosomal assessment.

One limitation of this study was that there were only four cases of trisomy 21 among the pregnancies that had a second-trimester test, which is insufficient for accurate determination of the long-term DR. Secondly, not all pregnancies screened could be followed until delivery, unlike in our previous single centre studies in which we were able to ascertain outcomes in over 98% of screened pregnancies.[1,2] However, the lost–to–follow-up rate of 16.6% was similar to the 19.5% reported in earlier HKSAR screening studies by Lam et al.[31] Like Lam and his colleagues, we too assumed that those lost to follow-up were phenotypically normal for the purpose of determining FPRs. More complete follow-up could only be achieved if there was a central cytogenetic registry, in which outcome of all pregnancies screened and/or having other diagnostic tests (CVS, amniocentesis, NIFTY, or safe T21) within public or private health care centres were recorded. Until that time, monitoring of false-negative cases, and invasive diagnostic procedure–associated pregnancy losses, must rely on notification of the laboratory by

individual screening and delivery centres in both the public and private health care sectors.

Conclusion

We demonstrated that the universal screening programme offered at the four units was effective and achieved expected DRs and low FPRs. The standards achieved are likely to continue, provided the current emphasis on training, QC, and regular auditing is maintained.

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