# Aneuploidy screening in women of advanced age in the public healthcare setting of a low- to middle-income country – an observational cohort study

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**Background.** Screening and termination of pregnancy (TOP) for Down syndrome (DS) are both available in South Africa (SA), but DS is infrequently diagnosed prenatally in the public sector (7% in 2008), resulting in a high live-birth prevalence (1.33 - 2.1 per 1 000). In the SA public sector, DS screening and confirmatory genetic testing are fully state subsidised for women of advanced maternal age (AMA) but, owing to the low positive predictive value of AMA-based screening, ultrasound-based screening is also offered. Given the limited resources and the steady increase in the number of pregnant women of AMA, the value of DS screening in altering pregnancy outcome needs to be critically assessed.

**Objectives.** To determine the uptake of prenatal screening for DS, invasive testing and TOP in pregnant women of AMA, as well as factors influencing maternal decisions.

**Methods.** This retrospective cohort study, based on prospectively captured data, includes all women of AMA (>37 years at conception) seen at a regional fetal medicine unit in Cape Town offering fully state subsidised DS screening and testing for a geographically defined area, including mostly women of African or mixed ancestry. Screening was age- and ultrasound-based, and DS risks were calculated using published algorithms. Non-directive genetic counselling was provided to all women ≥40 years old (pre-screen if feasible), women with a relevant history, a fetal anomaly or DS risk higher than that of a woman aged 37 years. Participant characteristics, results, decisions and reasons to decline testing were recorded prospectively, and compared between women <40 completed years and ≥40 years old, and between women accepting or declining invasive testing or TOP.

**Results.** During the study period, 1 196 women of AMA were seen. Ninety-three received pre-screen counselling, and 44 of these declined DS screening (47.3% (95% confidence interval (CI) 36.9 - 57.9)). Uptake of invasive testing after screening was low (18.1% (CI 15.2 - 21.3)). Age category was not an independent confounder for this, but uptake was lower after previous miscarriage(s), higher after high-risk screening results and highest with a fetal anomaly. The most common reason for declining testing was opposition to TOP. The uptake of TOP for DS, when offered to those who were screened and had accepted invasive testing, was 65.8% (48.7 - 80.4).

**Conclusion.** The uptake of screening and/or testing was low, and this reflected strong views on TOP for DS. As uptake of testing and/or TOP was higher with abnormal ultrasound findings, a prenatal screening programme addressing structural anomalies and aneuploidies simultaneously (i.e. ultrasound) is preferred over other DS screening tools that target DS specifically.

**Keywords:** ultrasound, Down syndrome, aneuploidy, prenatal screening, LMIC, Africa.

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Screening and termination of pregnancy (TOP) for Down syndrome (DS) are both available in South Africa (SA), where DS is the most common congenital abnormality.[1] As invasive genetic testing is costly and carries risks, it is generally reserved for pregnancies at high risk, hence the existence of screening protocols. These have evolved from screening based on advanced maternal age (AMA, with different age-cutoffs in different settings) to increasingly complex and expensive programmes,[2] including ultrasound, serum biochemistry (based on circulating levels of biochemical markers) and non-invasive prenatal testing (NIPT) based on cell-free fetal DNA in the maternal circulation.[2-5] Internationally, prenatal genetic screening has become an integral part of antenatal care, and this has created complex ethical and social dilemmas.[6,7] It should be an autonomous informed choice, consistent with the woman's values, requiring pre-screen genetic counselling to promote preference-based decision-making.[8] Programme design[9] or suboptimal counselling[6,10-12] influence this process, and lack of preference-concordant decision-making persists[13-16] and may be worsened by language barriers, low health literacy or numeracy or socioeconomic status.[14,17,18]

The value of DS screening needs to be critically assessed in healthcare settings with limited resources. The public healthcare sector in SA provides fully state-subsidised antenatal care for >85% of all pregnancies, including fully state-subsidised prenatal genetic screening and testing. Aneuploidy screening is mostly AMA-based (i.e. invasive genetic testing is offered to all woman older than a specific age) and could potentially result in a 43% prenatal detection rate,[19] yet it is performed ineffectively,[20,21] resulting in few prenatal diagnoses of DS (7% in 2008) and a high live-birth prevalence (1.33 - 2.1 per 1000).[1,22] Maternal age has increased over time[23-27] and in 2016, 14.7% of pregnant SA women were >35

at delivery.[28] Owing to the low positive predictive value of AMA-based screening (the lower age limit for women to obtain routine access to genetic testing in the region is 37 years of age at the time of conception)[5,19,27,29] ultrasound-based screening is offered for all pregnancies of AMA in the eastern half of the Western Cape Province. In 2016, Tygerberg Academic Hospital (TAH) was the only facility providing genetic counselling, aneuploidy screening and invasive testing for pregnant women receiving public healthcare in the eastern half of the Western Cape Province (including 47 550 births, 57.3% in urban districts).[30]

The primary aim of the present study was to determine the proportion of pregnant women of AMA accepting prenatal DS screening, invasive genetic testing, or TOP. Secondary aims included the identification of factors influencing maternal decisions.

## Methods

This retrospective cohort study is based on prospectively collected data, and includes all women of AMA (regionally defined as >37 completed years at the time of conception) seen in 2016 at the Fetal Medicine Unit (FMU) of TAH. TAH is an academic hospital in Cape Town, SA, responsible for referrals from low-income communities in rural and urban districts, mainly of African or mixed ancestry. Women screened or tested in the private sector or pregnancies from younger donor oocytes were excluded.

All women who were aged ≥40 years at the time of conception, and seen before 23 weeks or with fetal anomalies, received genetic counselling and were offered invasive testing, as their risk with the previous algorithm of second-trimester soft markers was always higher than the risk of a 37-year-old woman. Women fluent in English or Afrikaans received pre-screening counselling when feasible, allowing them to opt in or out of screening or testing. For the remainder of women who were ≥40 years, genetic counselling was provided after ultrasound assessment, incorporating the background risk (based on maternal age, gestational age and previous history of an autosomal trisomy) and the ultrasound findings. For women of AMA but <40 years of age at conception, genetic counselling was only offered after ultrasound assessment and for specific genetic risk factors, fetal anomalies, or an adjusted DS risk higher than that of a woman 37 years of age without screening (>1:165 in the first and >1:200 in the second trimester). Women <37 years only have access to opportunistic screening as they are referred from peripheral healthcare institutions whenever soft markers, amniotic fluid volume abnormalities or fetal anomalies are seen or suspected, either by qualified sonographers or on point-of-care scans by clinicians. Women <37 years at the time of conception do not form part of this study. All formal counselling was provided by medical geneticists or qualified genetic counsellors, and basic information on the counselling sessions was captured prospectively. As a visual medium is easier to understand for people with low scientific literacy[31] and little awareness of DS, prenatal screening and testing,[21] we used a 15-minute video followed by individual face-to-face counselling. The video was developed following focus group discussions and in-depth interviews with several stakeholders, and it provides salient clinical information in a non-directive way (in the three official languages of this province), with a balanced view of DS[11] and test options, but without paralysing over-disclosure.[32] The video includes factual information, shared experiences and visual representation of risk in different formats.

Apart from maternal age and structural anomalies, DS risk assessment was based on first trimester nuchal translucency measurement with additional markers when feasible,[2] and/or the second trimester algorithm for soft markers[33] (both available in the Astraia software program (NEXUS/ASTRAIA GmbH, Germany)). NIPT screening is not available in the public sector, serum screening is not feasible, as pregnancy dating using recall of the first day of the last menstruation is very inaccurate in this population, many women initiate antenatal care after 20 weeks, and effective serum screening would therefore require universal ultrasound dating, which is currently not feasible.

The primary aim of the present study was to determine the proportion of pregnant women of AMA accepting prenatal DS screening, invasive testing, or TOP. Secondary aims included identification of factors influencing maternal decisions. Due to differences in screening and counselling policies for women ≥40 years and <40 years of age, both groups were compared.

Data were collected from electronic medical records (OpenText ECM system (Open Text Corporation, Canada)), and prospectively recorded data from the Astraia program and the genetic counselling database, entered in Excel 365 (Microsoft, USA) and analysed using Statistica Software (TIBCO Software Inc., USA)). As race is a sensitive issue and ethnic differences would not justify differential policies, this information was not captured or analysed. Continuous data with a normal distribution were expressed as means and standard deviations, and non-normally distributed data or categorical data as medians and P5-95. Appropriate parametric and non-parametric tests were used for comparisons between women who were ≥40 years and <40 years of age at the time of conception, and between women who accepted or declined invasive testing or TOP. A $p$-value <0.05 was regarded as significant. Ethical approval was obtained from the Stellenbosch University Health and Research Ethics Committee (ref. no. S18/05/101), with a waiver for individual informed consent.

## Results

In 2016, 1 196 women of AMA were seen in the FMU (representing 24% of the total caseload). The general breakdown of prenatal findings and decisions is presented in Fig. 1, separately for women who were ≥40 years and <40 years completed years at conception.

A total of 322 women (26.9% of the overall total) were counselled for a high-risk genetic screening result or fetal anomaly (Table 1). Urban women (71%) were overrepresented in this cohort ($p$<0.001).[30] Women aged >40 had higher gravidity and parity and were less likely to have a previous perinatal death, to access first-trimester screening or to live in an urban area (Table 1).

Of the 93 women receiving pre-screen counselling (all >40 years old), only 42 accepted screening for DS (45.2% (95% confidence interval (CI) 35.1 - 55.3), while 44 (47.3% (CI 37.2 - 57.5)) declined screening or testing because they would not consider TOP, and 7 (7.5% (CI 2.2 - 12.9)) had testing without screening (all normal). The decision regarding screening was not influenced by maternal characteristics, obstetric history, or timing of counselling. Women aged >40 were more likely to receive genetic counselling and undergo invasive testing, and they had a higher background and adjusted risk, and a higher chance of a high or very high-risk screening result (≥1:10) (Table 1).

Ten patients opted for TOP without genetic testing (one was not offered invasive testing), and 115 of the remaining 631 women who were offered testing accepted (18.2% (CI 15.2 - 21.2)). The yield of prenatal karyotyping was 15.7% (CI 9.0 - 22.3), and 21 genetic conditions were identified (1.76% (CI 1.01 - 2.50) of all patients), including 18 autosomal trisomies (9 DS), all with a high-risk screening result and/or fetal anomaly. The overall uptake of invasive testing by women >40 years was lower than for younger women, but it was similar in both age groups when there was a high-risk screening result or a fetal anomaly (28.8% and 28.1%, respectively; $p$=0.8) (Fig. 1, Table 1).

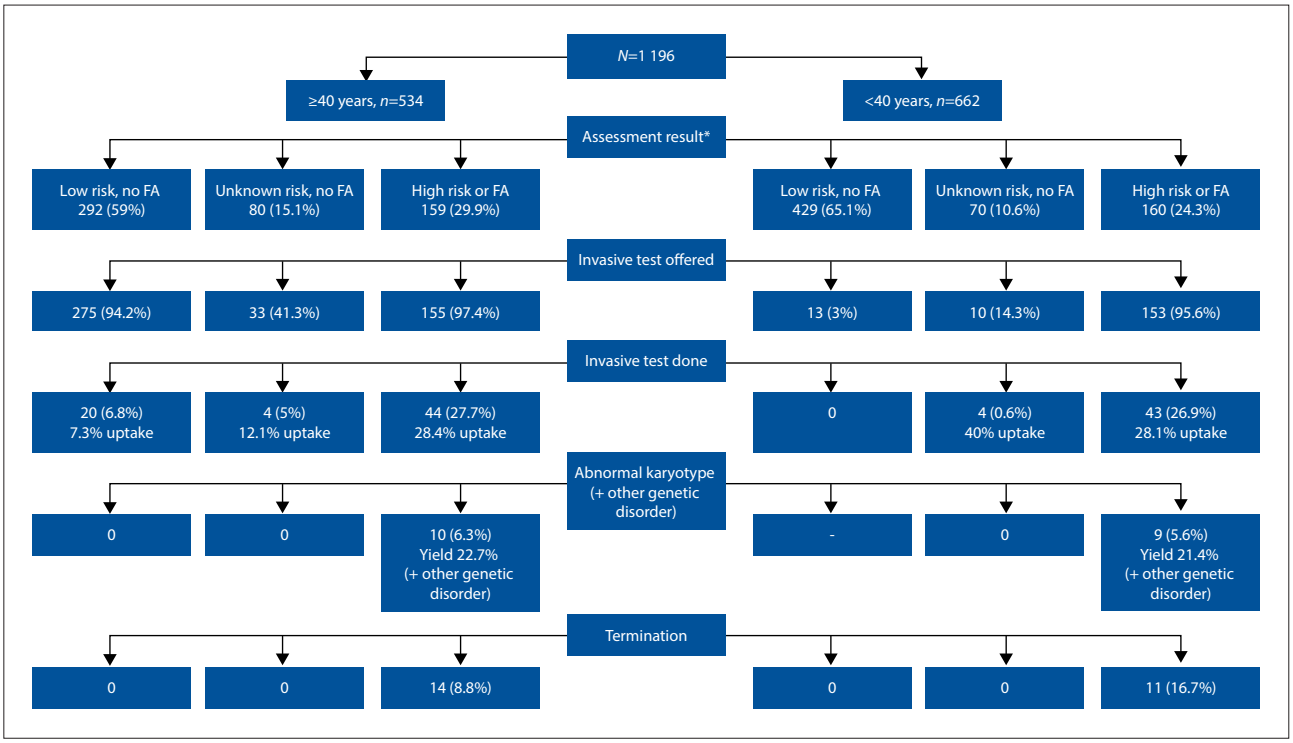


*Fig. 1. Breakdown of decisions and results among women of advanced maternal age (≥37 years at the time of conception) according to age group (≥40 years) compared with <40 years at conception), and ultrasound findings. *Excluding three miscarriages in women ≥40 years; one miscarriage, one extrauterine pregnancy and one termination for anhydramnios, severe growth restriction and pre-eclampsia in women <40 years. (FA = fetal anomaly.)*

Most women who declined invasive testing stated that they would not consider TOP for DS (75.5% (CI 71.7 - 79.4)) (Table 1). Uptake was not influenced by gravidity, parity, rural residence, or presence of a companion, but more of the women who declined were ≥40 years, and had previous miscarriages, pre-screen counselling and first trimester assessment (Table 2). Acceptance was significantly higher with a high-risk result or an increase in the risk, but it was highest when a fetal anomaly was detected (26/55, 47.3% (CI 33.7 - 61.2)), followed by a risk ≥1:10 (24/74, 32.4% (CI 22.0 - 44.3)) (Table 2).

TOP was offered to 38 women (3.2%), of whom 25 (65.8% (CI 48.7 - 80.4)) accepted (including 5 of 8 with DS (62.5% (24.5 - 91.5)), with no influence of gravidity, parity, place of residence, timing of assessment, presence of a companion, background, or adjusted risk (Table 3). Marginally more women aged >40 accepted TOP when offered ($p$=0.07), and more women with a previous early miscarriage declined ($p$=0.02). The decision was not influenced by a confirmed genetic diagnosis (64.7% (CI 38.3 - 85.8), acceptance for aneuploidy (11/17) or structural defects (62.5% (CI 43.7 - 78.9) acceptance (20/32).

## Discussion

Uptake of DS screening and of invasive testing by women of AMA was low in this region (47% (CI 36.9 - 57.39) and 18.1% (CI 15.2 - 21.3), respectively).

DS screening uptake varies greatly,[19,29,32-36] and reasons to decline screening include (perceived) risk and severity, aversion to procedure-related miscarriage or TOP, acceptance of DS, avoidance of anxiety, etc.[7,9,34,35,37,38] Acceptance of DS or aversion to TOP was common in this cohort.

The uptake of invasive testing was much lower than in previous studies in this region (74% in 1992 - 1994;[40] 52.3% in 2006 - 2007;[19] 31% in 2008 - 2009).[20] The first reduction followed the incorporation of ultrasound-based risk adjustment during counselling,[19] in line with reported lower uptake after normal ultrasound findings.[27] The even lower rate in the current cohort was unanticipated as, to reduce the number of invasive tests for AMA, invasive testing is now restricted to women with a relevant previous history, women >40 years and fetuses with soft markers or fetal anomalies.[5,29] A gradually decreasing uptake of invasive testing for AMA has been noted almost universally,[7,31,37] and is strongly linked to the introduction of any additional screening.[27,31,34,36,41-46] Locally, counselling by specialised professionals, increased confidence in ultrasound-based screening, increasing empowerment of women, change in demographics and improved social services may have contributed to this decreasing trend. Gravidity, parity, presence of a companion and place of residence had no influence, but lower uptake by women residing in rural areas has been previously reported.[47,48] Age group was not an independent confounder, as uptake for high-risk screening results was similar, but previous miscarriage(s) reduced invasive testing uptake.[49] We did not assess the impact of ethnicity,[37,40,50] but others have shown that family and social context are far more important.[51] We did not investigate the effect of lower education (or health literacy) or socioeconomic status, but in women of all ages these have been associated with poorer understanding,[17,52] potentially resulting in decisions that are not truly aligned with the patient's personal preferences and values.[14,37,39] In this study, invasive testing uptake was higher with a risk increase, a (very) high-risk screening result or the presence of a structural fetal anomaly. These trends are in line with others[27,31,36,41-45,53-56] but only 29% of women of AMA with high-risk screening results accepted invasive testing. Others have also found confirmation rates of <50%,[45] although many report much higher rates.[43,50] Decision-making is more complex than balancing actual (or rather perceived) risks of DS and miscarriage.[37,50,57] Women's prior attitude toward DS, disability in general, miscarriage or TOP are strong determinants of choice,[7,9,35,37-39,50,57-59] while the need for reassurance or preparation,[9,39,57] intolerance toward uncertainty or

**Table 1. Descriptive data of all women of advanced maternal age (>37 years at the time of conception) assessed in 2016, with comparison between those ≥40 and those <40 completed years at conception**

| Characteristic | Total | Age ≥40 years | Age <40 years | *p*-value |
|---|---|---|---|---|
| *n* (%) | 1 196 (100) | 534 (44.6) | 662 (55.4) | |
| Rural residence, *n* (%) | 347 (29.1) | 182 (34.1) | 165 (24.9) | <0.001 |
| Age (years), mean (SD) | 39.9 (1.97) | 41.7 (1.4) | 38.5 (0.9) | <0.001 |
| Gravidity, median (P5 - 95) | 4 (2 - 6) | 4 (2 - 7) | 4 (2 - 6) | 0.005 |
| Primigravida, *n* (%) | 37 (3.1) | 16 (3.0) | 21 (3.1) | 0.9 |
| Parity, median (P5 - 95) | 2 (0 - 5) | 2 (0 - 5) | 2 (0 - 4) | <0.001 |
| Nullipara, *n* (%) | 65 (5.4) | 27 (5.1) | 38 (5.7) | 0.6 |
| Previous obstetric history | | | | |
| Perinatal mortality | 105/1 193 (8.8) | 37/532 (7.0) | 68/661 (10.3) | 0.04 |
| Miscarriage | 342 (28.7) | 147 (27.6) | 195 (29.5) | 0.5 |
| TOP | 46 (3.9) | 17 (3.2) | 29 (4.4) | 0.6 |
| Genetic counselling provided | | | | |
| All (%) | 645 (54.0) | 465 (87.1) | 180 (27.2) | <0.001 |
| Indication known | | | | <0.001 |
| Low risk | 269 (41.7) | 263 (56.6) | 6 (3.3) | |
| High risk | 263 (40.8) | 123 (26.5) | 140 (77.8) | |
| Fetal anomaly | 59 (9.0) | 29 (6.1) | 30 (16.0) | |
| Age alone | 50 (7.8) | 50 (10.8) | 0 | |
| Previous history | 4 (0.6) | 0 | 4 (2.1) | |
| First trimester assessment | | | | |
| Scanned | 455 (38.0) | 186 (34.8) | 269 (40.6) | 0.04 |
| Risk calculated | 436/1 196 (36.5) | 177/534 (33.1) | 259/662 (39.1) | 0.03 |
| Background risk, median (P5 - 95) | 86 (46 - 139) | 56 (30 - 72) | 114 (86 - 151) | <0.001 |
| Adjusted risk, median (P5 - 95) | 1 064 (223 - 2832) | 643 (135 - 1291) | 1 607 (422 - 2646) | <0.001 |
| Second trimester assessment | | | | |
| Scanned | 1 033 (86.4) | 481 (90.1) | 552 (83.4) | <0.001 |
| Risk calculated | 855/1 196 (71.5) | 382/534 (71.4) | 473/662 (71.5) | 1.0 |
| Background risk, median (P5 - 95) | 124 (41 - 1 742) | 73 (33 - 1 227) | 154 (98 - 2 375) | <0.001 |
| Adjusted risk, median (P5 - 95) | 654 (10 - 11 786) | 423 (7 - 8 980) | 999 (16 - 18 060) | <0.001 |
| Screening result | | | | |
| High risk | 301/1 040 (28.9) | 149/451 (33.0) | 152/589 (25.8) | 0.01 |
| Risk ≥1:10 | 79/1 035 (7.4) | 48/449 (10.7) | 31/586 (5.3) | 0.001 |
| Fetal anomaly | 69/1 196 (5.8) | 36/534 (6.7) | 33/662 (5.0) | 0.2 |
| High risk or anomaly | 319/1 040 (30.7) | 159/451 (35.3) | 160/589 (27.2) | 0.005 |
| Risk ≥1:10 or anomaly | 117/1 039 (11.3) | 67/450 (14.9) | 50/589 (8.5) | 0.001 |
| Invasive testing | | | | |
| Offered, *n* (%), (95% CI) | 640 (53.5), (50.7 - 56.3) | 464 (86.9), (84.0 - 89.8) | 176 (26.6), (23.2 - 30.0) | <0.001 |
| Accepted | 115 | 68 | 47 | |
| % of all | 9.6 | 12.7 | 7.1 | <0.001 |
| % of those offered | 18.0 | 14.7 | 26.7 | <0.001 |
| Invasive test or TOP | 124 | 73 | 51 | |
| % of all | 9.9 | 13.7 | 7.7 | <0.001 |
| % of those offered | 18.4 | 15.7 | 29.0 | <0.00 |
| Reason to decline known | 482/531 (90.8) | 361/401 (90.0) | 121/130 (93.1) | 0.3 |
| Would not terminate | 364 (75.5) | 277 (76.0) | 87 (69.6) | 0.03 |
| Fear of miscarriage | 50 (10.4) | 33 (9.1) | 17 (13.6) | |
| Risk acceptable | 28 (5.8) | 26 (7.7) | 2 (1.6) | |
| TOP (without test) | 9 (1.9) | 5 (1.4) | 4 (4.0) | |
| Need partner's opinion | 31 (6.4) | 20 (5.8) | 11 (11.2) | |
| Genetic diagnosis | 21 (1.7) | 11 (2.1) | 10 (1.5) | 0.8 |
| Abnormal karyotype | 19 (18 prenatal) | 10 | 9 (8 prenatal) | |
| Total, % of all | 1 196 (1.6) | 534 (1.9) | 662 (1.4) | 0.5 |
| *n*/*n* % of prenatal tests (yield) | 18/115 (15.7) | 10/68 (14.7) | 8/47 (17.0) | 0.7 |
| TOP | | | | |
| Offered/all, *n* (%) | 38 (3.2) | 19 (3.6) | 19 (2.9) | 0.5 |
| Performed/all, *n* (%) | 25 (2.1) | 14 (2.6) | 11 (1.7) | 0.2 |
| Uptake rate, *n* (%) | 25/38 (65.8) | 14/19 (73.7) | 11/19 (57.9) | 0.3 |

P = percentile; SD = standard deviation; CI = confidence interval; TOP = termination of pregnancy.

**Table 2. Comparison between women who were offered invasive testing and accepted v. declined (excluding 9 pregnancy terminations without preceding genetic testing)**

| Characteristic | Declined | Accepted | *p*-value |
|---|---|---|---|
| *n* (%) of those offered | 516 (81.8) | 115 (18.2) | |
| Rural residence, *n* (%) | 165 (32.0) | 42 (36.5) | 0.3 |
| Age (years), mean (SD) | 40.9 (1.9) | 40.4 (1.9) | 0.02 |
| ≥40 years old, *n* (%) | 391 (75.8) | 68 (59.6) | 0.005 |
| Gravidity, median (P5 - 95) | 4 (2 - 7) | 3 (1 - 6) | 0.06 |
| Parity, median (P5 - 95) | 2 (1 - 5) | 2 (0 - 5) | 0.8 |
| Previous obstetric history, *n* (%) | | | |
| Perinatal loss | 47 (9.1) | 8 (7.0) | 0.5 |
| Miscarriage | 155 (30.0) | 22 (19.1) | 0.02 |
| Termination | 22 (4.3) | 3 (2.6) | 0.4 |
| Genetic counselling, *n* (%) | | | |
| Pre-screen | 84/516 (16.3) | 9/115 (7.8) | 0.02 |
| Accepts risk assessment | 39 (46.4) | 2 (22.2) | 0.2 |
| Accepts any test | 41 (48.8) | 7 (77.8) | 0.7 |
| Counselling provided to | | | 0.7 |
| Woman | 404 (78.3) | 88 (76.3) | |
| Couple | 99 (19.2) | 27 (23.7) | |
| Woman with other | 13 (2.5) | | |
| First trimester assessment | | | |
| Scanned, *n* (%) | 203 (39.3) | 23 (20.2) | < 0.001 |
| Risk calculated, *n* (%) | 192 (37.2) | 23 (20.2) | 0.005 |
| Background risk, median (P5 - 95) | 61 (22 - 133) | 65 (25 - 146) | 0.1 |
| Adjusted risk, median (P5 - 95) | 632 (19 - 1 473) | 178 (2 - 1 729) | 0.04 |
| Risk increased, *n* (%) of scanned | 22/203 (10.8) | 7/23 (30.4) | 0.008 |
| *n* (%) of risk calculations | 22/192 (11.5) | 7/23 (30.4) | 0.01 |
| Second trimester assessment | | | |
| Scanned, *n* (%) | 470 (91.1) | 102 (88.7) | 0.4 |
| Risk calculated, *n* (%) | 415 (80.4) | 92 (80.0) | 0.9 |
| Background risk, median (P5 - 95) | 88.0 (30 - 1270) | 88.5 (34 - 174) | 0.1 |
| Adjusted risk, median (P5 - 95) | 354 (3 - 9 934) | 64 (2 - 669) | < 0.001 |
| Risk increased, *n* (%) of scanned | 88/470 (18.7) | 40/102 (39.2) | < 0.001 |
| *n* (%) of risk calculations | 88/415 (21.2) | 40/92 (43.5) | <0.001 |
| Any trimester, *n* (%) | | | |
| Fetal anomaly | 29/516 (5.6) | 30 (26.1) | < 0.001 |
| Risk calculated | 478 (92.6) | 107 (93.0) | 1.0 |
| Very high risk ≥1:10 | 48/478 (10.0) | 24/107 (22.4) | < 0.001 |
| High risk | 203/478 (42.5) | 80/107 (74.8) | < 0.001 |
| High risk or anomaly | 212/480 (44.2) | 87/107 (81.3) | < 0.001 |
| Very high risk or anomaly | 65/479 (13.6) | 40/107 (37.4) | < 0.001 |
| Increase in risk | 103/516 (20.0) | 47 (46.1) | < 0.001 |

SD = standard deviation; P = percentile.

loss of control,[35,37,38] influence of others, available support, etc., also play a role.[60] In the present study, women of AMA declined invasive genetic testing mostly because they were opposed to TOP for DS.

TOP acceptance was 65%, with no influence of adjusted risk, the severity of the diagnosed conditions or maternal characteristics, with the exception of previous miscarriage.[61-64] The 62.5% TOP rate for DS only applies to the few women accepting invasive testing. In many high-income countries, the overall TOP rate for DS is very high.[23,58,61-64] In combination with high uptake of screening and testing, the live-birth prevalence of DS has decreased or stabilised[23] over time, but the impact of DS screening is limited by parental choice.[58,59] TOP rates for DS may be lower in lower socioeconomic settings,[61,65] and in a recent local study, reasons to decline TOP for fetal anomalies mainly reflected hope and religious faith.[66] Apart from later diagnosis, different attitudes toward DS or TOP may contribute to the higher DS live-birth rate in more deprived communities.[47,48,67] There is concern, however, that factors other than truly preference-based decision-making are at play in these settings, including late initiation of antenatal care, limited or late access to prenatal diagnostic services, late diagnosis,[62,64,67] poor referral systems and poor understanding.[14,17,52] Uptake of screening and testing is affected by the degree to which parents understand the issues,[37] and ideally, all women should receive adequate information about DS and tests, adapted to their culture and educational level,[37] to improve knowledge and reduce decisional conflict.[8] Various approaches to facilitate values-based decision-making exist,[8,68,69] and we used a visual medium (video) followed by individual face-to-face counselling. As information on prior intent or knowledge was not

**Table 3. Comparison between women who opted for TOP and those who declined**

| Characteristic | TOP accepted | TOP declined | *p*-value |
|---|---|---|---|
| *n* (%) of TOP offered | 25 (65.8) | 13 (34.2) | |
| Rural residence, *n* (%) | 8 (32.0) | 6 (46.2) | 0.3 |
| Age (years), mean (SD) | 40.6 (2.3) | 39.9 (1.9) | 0.3 |
| Age ≥40 years, *n* (%) | 14 (56.0) | 5 (38.5) | 0.3 |
| Gravidity, median (P5 - 95) | 3 (1 - 6) | 4 (2 - 7) | 0.3 |
| Parity, median (P5 - 95) | 2 (0 - 5) | 2 (1 - 4) | 0.5 |
| Previous obstetric history, *n* (%) | | | |
| Perinatal mortality | 2 (8.0) | 2 (15.4) | 0.5 |
| Miscarriage | 6 (24) | 8 (61.5) | 0.02 |
| TOP | 0 | 0 | - |
| Any trimester, *n* (%) | | | |
| Ever high risk | 17/23 (73.9) | 11/13 (84.6) | 0.7 |
| Ever fetal anomaly | 21/25 (84.0) | 12/13 (92.3) | 0.6 |
| Ever high risk or anomaly | 24/25 (96.0) | 13/13 (100) | - |
| Genetic counselling, *n* (%) | | | |
| Indication known | 24/25 (96.0) | 13/13 (100) | 0.7 |
| Pre-screen | 1 (4.0) | 0 | 0.8 |
| Counselling provided to | | | 0.5 |
| Woman | 17/24 (70.8) | 8/13 (61.5) | |
| Couple | 4 (16.7) | 5 (38.5) | |
| Woman with other | 3 (12.5) | 0 | |
| Invasive testing, *n* (%) | | | |
| Invasive test accepted/offered | 16/24 (66.7) | 7/13 (53.8) | 0.6 |
| Prenatal aneuploidy | 11/25 (44.0) | 6/13 (46.2) | 0.9 |
| TOP without invasive testing | 9 (36.0) | 0 | - |

TOP = termination of pregnancy; SD = standard deviation.

recorded prospectively, the impact of this counselling format could not be assessed in the current study.

Strengths of the study include the substantial number of women of AMA included, a single protocol for screening, counselling and testing, and prospective recording of ultrasound findings and reasons for decision-making. The study population does not necessarily represent all women of AMA in the catchment area (only ~17%, as an estimate), as those initiating antenatal care late or those not referred for screening were not included. As formal pre-screening genetic counselling was not offered elsewhere at the time, however, selection bias based on patient choice is unlikely, and if present, would have generated a cohort more interested in prenatal screening than the background population, not less. Underrepresentation of rural women may be relevant, as their attitudes and decisions may differ from those of urban women. As pre-screening counselling was limited to women who were ≥40 years old, the results may not apply to all women of AMA. Retrospective data collection resulted in some missing data.

## Conclusion

The low uptake of screening (47%) and invasive testing (18%) indicates that, in the SA public sector, parental interest in prenatal diagnosis for DS is limited. The uptake of invasive testing was, however, four times higher for high- v. low-risk results, indicating some value of ultrasound-based risk adjustment. While DS is quite well accepted in our society,[70] and most women would not consider TOP for DS, the uptake of testing and TOP for structural anomalies was considerably higher, as also reported previously in this region.[65,71] This justifies prioritising structural anomaly detection over DS diagnosis, which can be achieved with ultrasound. We therefore argue against considering the introduction of serum screening or NIPT for DS in addition to already existing ultrasound-based screening, for reasons mentioned earlier, and owing to the significantly increased cost this would generate, with a low likelihood of substantially affecting the DS live-birth rate. Formal pre-screening counselling is an important first step to support preference-based decisions, but further research is needed to determine whether truly informed decision-making is achieved with our current counselling format.

**Data availability.** Data available from authors on reasonable request.
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