

# Screening for Down syndrome - The Odds are with you.



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"providing obstetric support"

## INTRODUCTION

SAMSAS has been involved in multi-analyte screening for Down syndrome since 1990, now possessing one of the largest data sets in Australia. SAMSAS develops and manages its own software and algorithms which are based on local populations being screened and confirms its performance with yearly audits published in The South Australian Birth Defects Register Reports. SAMSAS validates its risk calculations using published methods as described by Wald, 1996 and Spencer, 2002. SAMSAS provides screening services to hospitals and private health practitioners in South Australia, Tasmania and Northern Territory.

Both 1<sup>st</sup> and 2<sup>nd</sup> trimester screening services are offered.

**The 1<sup>st</sup> trimester screen** (10wks to 13wks6days) involves a risk calculation derived from the combination of two biochemical placental markers - free beta hCG and Papp-A, with the ultrasound marker nuchal translucency thickness. This service is offered through collaboration between SAMSAS and a number of ultrasonology practices that can offer nuchal translucency measurements. SAMSAS offers these practices feedback on nuchal translucency measurements for the purposes of quality assurance and program performance. **The 2<sup>nd</sup> trimester screen** (14wks to 20wks6days) uses biochemical markers only - alpha-fetoprotein, free beta hCG and unconjugated estriol.

**The likelihood ratio (LR)** derived from the marker combinations is independent of maternal age. The LR in 1<sup>st</sup> or 2<sup>nd</sup> trimester screens is used to adjust the maternal age related risk at delivery resulting in a **calculated risk** which is reported. For both screens a risk cut off 1:300 is used to categorise the pregnancy as either "at increased risk" or "not at increased risk". The cut off of 1:300 determines the percentage of pregnancies screened at increased risk (recall rate, RR) and the percentage of affected pregnancies which can be detected (detection rate, DR). For a 5% recall rate, we would expect to detect 75 - 90% of all affected pregnancies with Down syndrome in the first trimester, and 60-75% in the second trimester.

The calculated risk and the classifying of a pregnancy as either "at increased risk" or "not at increased risk" forms the basis for offering women diagnostic testing such as CVS or amniocentesis. Half of all affected pregnancies with Down syndrome have calculated risks of 1:20 or greater, most couples choose diagnostic tests at these levels but that decision becomes more difficult when risks are near the cut off level of 1:300 or near the fetal loss rates following either chorionic villus sampling or amniocentesis.

Maternal age risk in the risk odds calculation leads to different performance across age groups. There is also a difference in performance between 1<sup>st</sup> and 2<sup>nd</sup> trimester screens.

## AIM

To determine the risk odds of having an affected fetus with Down syndrome following both a "high" and "low" risk first or second trimester maternal screen result for women at different ages.

## METHOD

The likelihood ratios derived for 65 1<sup>st</sup> trimester and 80 2<sup>nd</sup> trimester marker profiles from Down syndrome affected pregnancies and over 1000 marker profiles from unaffected pregnancies were used to determine the % of affected cases detected (DR) and the % of cases screened at increased risk (RR) for each maternal age group.

The risk odds of detecting and missing a pregnancy affected with Down syndrome were calculated using the relationship between DR, RR and prevalence as described by the following equations.

Risk Odds of having a Down syndrome fetus following an "At increased risk" report = 1: (Prevalence x RR) / DR

Risk Odds of having a Down syndrome fetus following a "Not at increased risk" report = 1: (Prevalence x (1-RR)) / (1-DR)

Prevalence at the time of screen was calculated from the maternal age risk of having a baby with Down syndrome at delivery, adjusted for expected fetal loss after the time of screening from both 1<sup>st</sup> and 2<sup>nd</sup> trimesters as described by Morris *et al.*, 1999.

## DISCUSSION

Yearly audits show that the % of women screened at increased risks and the detection of affected pregnancies with Down syndrome is higher in older women compared to younger women. This observation is true for both 1<sup>st</sup> and 2<sup>nd</sup> trimester screening modalities.

**Figure 1** shows the relationship between advancing maternal age, RR and DR and the comparative performance of 1<sup>st</sup> versus 2<sup>nd</sup> trimester screening. Figure 1 shows that 1<sup>st</sup> trimester screening improves detection of affected pregnancies in younger mums and reduces the recall rate for older mums.

**Figure 2** shows that if screened at increased risk using the 1<sup>st</sup> trimester screen compared to the 2<sup>nd</sup> trimester screen the risk odds of having an affected fetus are higher as less diagnostic tests are required to detect one case of Down syndrome. In addition the risk odds increase with advancing age.

**Figure 3** shows that missing an affected pregnancy following a not at increased risk report is less likely with the 1<sup>st</sup> trimester screen compared to the 2<sup>nd</sup> trimester screen.

**Figures 1, 2 and 3 show the improved sensitivity and specificity of the 1<sup>st</sup> trimester screen versus the 2<sup>nd</sup> trimester screen for the detection of Down syndrome.**

**The odds are with you to use during pre-test and post-test counselling as they provide information which reflects outcome for women at different ages.**

## RESULTS

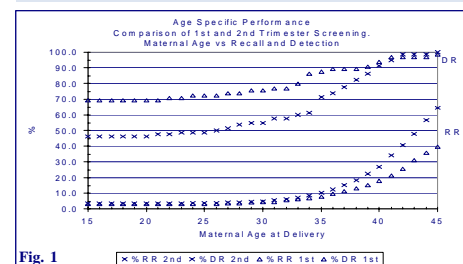


Fig. 1

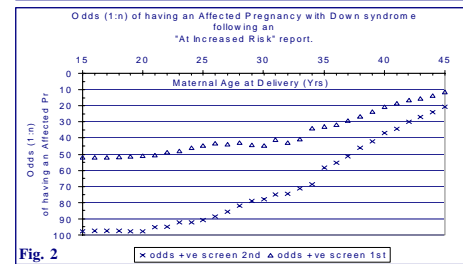


Fig. 2

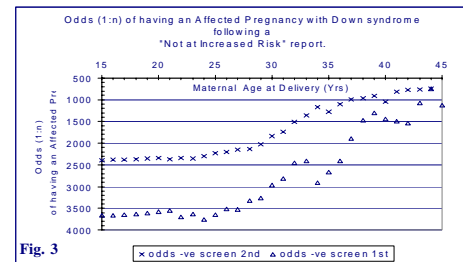


Fig. 3