Executive Summary

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Report issues

What are the best tests for detecting neural tube defects and Down's syndrome in a foetus during pregnancy? And what is the best way to conduct this prenatal screening? These are the central issues in this advisory report.

The aim of screening is to provide people who wish for it with information about the presence or absence of the disorder in question. This enables them to terminate the pregnancy where appropriate or to make preparations for the birth of a child with Down's syndrome or a neural tube defect.

Prenatal screening for Down's syndrome and neural tube defects was also addressed in another report, which was published by a Health Council Committee in 2001. The present report contains the findings of a Committee of the Health Council based on the most recent developments.

Background

At present, in the Netherlands, pregnant women aged 36 and above qualify for tests for Down's syndrome. Depending on the stage of the pregnancy, the test takes the form of chorionic villus sampling (from eleven weeks onwards) or amniocentesis (from sixteen weeks onwards). This invasive approach is very reliable, but it can sometimes induce a miscarriage. When women above the age of 36 are screened, the number of miscarriages after invasive diagnosis is even larger than the number of diagnoses of Down's syn-

drome (detection/miscarriage ratio: 0.7). Furthermore, this approach fails to detect more than half of the cases of Down's syndrome. This is because, although the risk of giving birth to a child with this disorder increases with age, most mothers of a child with Down's syndrome are actually younger than 36 years of age during their pregnancy.

Since the early eighties, new screening tests have been developed that involve less risk. This means that better estimates can be made of the risk of Down's syndrome than those based on age alone. In 2001, the Health Council advised that it was no longer scientifically defensible to rely solely on the screening of women aged 36 and above. It suggested making screening for Down's syndrome available to all pregnant women, whatever their age. The proposed method was the triple test – a blood test in the second trimester of pregnancy – as the most tried and tested approach at that time. In the interim, there have been further important publications on testing for Down's syndrome or neural tube defects. The Health Council believed that a new advisory report was therefore justified.

Opinion on testing for neural tube defects

There have been a number of changes in the situation relating to screening for neural tube defects since 2001. It is no longer a question of which test method is preferable: a blood test or ultrasound in the second trimester of the pregnancy. The test properties of ultrasound are better and women prefer it to a blood test. The professional organisations representing midwives, obstetricians and GPs declared their support for ultrasound in 2003.

Opinion on testing for Down's syndrome

What is the best alternative for the current policy of offering invasive testing to women aged 36 and above? On the basis of what we now know about the test's properties, acceptance by the target group and feasibility, the combined test is the best method for prenatal screening for Down's syndrome. The combined test involves a blood test and nuchal translucency measurement by means of ultrasound, both in the first trimester. The combined test is preferable to the triple test that the Health Council considered to be the best in 2001.

First of all, the combined test performs best as a test in practice. Models were used to predict sensitivity and specificity rates of the combined test for Down's syndrome. These values have now been confirmed by the results of a large number of studies. The combined test does not, incidentally, give complete certainty, but it does provide information about the risk of Down's syndrome. Chorionic villus sampling is necessary for confirmation.

Use of the combined test also greatly improves the ratio of the number of miscarriages after invasive diagnosis to the number of Down's syndrome pregnancies detected (the detection/miscarriage ratio increases from 0.7 to 3.3). At present, in women aged 36 and above, chorionic villus sampling or amniocentesis is carried out immediately. A test of this kind involves risk, and it also worries the women who undergo it. However, if the combined test gives a negative result, an invasive test is unnecessary. This drastically reduces the number of invasive tests and the number of associated miscarriages. The total number of abortions (induced abortions for Down's syndrome and miscarriages after invasive diagnosis) is also lower with screening using the combined test than with the current approach, assuming that all other things, such as participation rates, are equal. Here, a risk of 1 in 175 of a live birth involving Down's syndrome is the cut-off value for an adverse result from the combined test.

The combined test is also satisfactory from the point of view of acceptance. Women very much prefer screening early in the pregnancy. The other indications for acceptability and feasibility are also favourable. The implementation of the combined test does mean that women have to be seen by a midwife or doctor earlier in the pregnancy. To this end pregnant women must be provided with appropriate information.

The cost of screening, per detected Down's syndrome foetus, is slightly lower with the combined test than with the current test. The cost analysis does not, incidentally, include the cost of care or the social costs for people with Down's syndrome. Savings in these areas are not the purpose of screening. The pregnant women and, where appropriate, their partners must not be given the feeling that the aim of screening is to make savings.

The combined test therefore emerges as the best option. The Committee expects the risk-benefit ratio to be favourable if the quality requirements discussed in this advisory report are met.

To whom should this test be offered? The Committee notes that offering the combined test with a limit value of 1 in 175 to all pregnant women is the best conceivable combination of the minimum number of false negative and false positive test results. It concludes that, in scientific terms, there are no advantages to an age limit.

Implementation of testing for Down's syndrome and neural tube defects

The Committee recommends making screening for Down's syndrome and neural tube defects available to all pregnant women. It believes that the high quality required for implementation is feasible, on condition that there is a coordinated programme within a single organisational structure and with national management. Central control is necessary for the restructuring of the present situation of unbridled growth and for quality

control, registration and evaluation of the screening programme. Control of this kind is also needed to steer new scientific developments in the right direction.

Regional partnerships must be accountable for implementation. These associations represent all the professions involved. If the regions make agreements with the areas associated with the eight teaching centres for prenatal diagnostics, it will be possible to make the most of their know-how, experience and facilities. In order to safeguard the quality of implementation, the same organisational structure can be used for the introduction of the combined test as the one recently proposed by the three obstetric professions for the reorganisation of routine ultrasound testing.

The screening itself will have to take place in a limited number of centres with qualified ultrasound operators. These operators will have to carry out enough procedures to maintain their level of expertise. Laboratory tests also require facilities to be concentrated. Here again, quantity benefits quality. Consideration should be given to the inclusion of eight laboratories that meet quality requirements, such as participation in ring studies. One of them should act as the reference laboratory.

In addition, the Committee advises the establishment of a national committee to direct the programme. Furthermore, at the central level, an independent evaluation committee is required, as well as a training institution to be established by the professional bodies. Uniform records containing relevant data are indispensable for effective quality control and the continuous evaluation of implementation and of the results of the screening programme. Checks on the quality of screening for Down's syndrome and neural tube defects are also possible and necessary as part of the licensing procedure pursuant to the Population Screening Act.

In addition to the efficient use of facilities that safeguard quality, this centrally controlled regional structure provides an infrastructure for steering new scientific developments in prenatal screening in the right direction. This approach would also fit in with current thinking about the organisation of obstetric care and midwifery in the Netherlands. The Committee therefore advises that this organisational structure be introduced, regardless of the results of the decisions made with respect to screening.

Scientific research

The Committee also recommends that scientific research be carried out into the best way of informing pregnant women about the benefits and drawbacks of screening. Research is also required into the best way of determining whether their decision to undergo a screening or not is based on adequate information and is in accordance with their standards and values.

Further scientific investigation is also required into the best approach following an increased nuchal translucency measurement in a fetus with a normal karyotype. In these

cases, the risk of structural abnormalities (particularly of the heart), foetal death and rare genetic syndromes is higher. The question is whether a special examination with specific diagnostic techniques is better than a routine second-trimester ultrasound scan and, if so, above which limit value for a thickened neck fold. Pending the study results, routine ultrasound scanning will be adequate. Alternatively, the 99th percentile should be adopted as the limit value.

Until the value of additional ultrasound markers (nasal bone, soft markers) has been clearly demonstrated, they should not be used in screening for Down's syndrome.