AOGS
ACTA Obstetricia et Gynecologica Scandinavica

AOGS REVIEW ARTICLE

# Does screening for Down's syndrome cause anxiety in pregnant women? A systematic review

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**Key words**
Pregnancy, antenatal care and diagnosis, screening, down's syndrome, anxiety

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**Conflict of interest**
All authors have explicitly stated that there are no conflicts of interests in connection with this article.

Please cite this article as: Lou S, Mikkelsen L, Hvidman L, Petersen OB, Nielsen CP. Does screening for Down's syndrome cause anxiety in pregnant women? A systematic review. Acta Obstet Gynecol Scand 2015; 94: 15–27.

Received: 19 December 2013
Accepted: 13 August 2014

DOI: 10.1111/aogs.12482

## Abstract

*Background.* Prenatal screening for Down's syndrome and other chromosomal abnormalities is included in prenatal care programs in many countries. However, the potential association between prenatal screening and maternal anxiety remains an issue of debate. *Objective.* To systematically review and summarize the current scientific evidence on whether screening for Down's syndrome might cause anxiety in pregnant women with a negative or a false-positive screening result. *Methods.* Five databases (PubMed, Embase, Cinahl, PsychInfo and Cochrane) were systematically searched for randomized controlled trials or cohort studies comparing screening and no screening, or comparing different types of screening for Down's syndrome. The search was limited to studies published between September 2001 and April 2013. In all, 316 studies were identified through search of databases and 40 were included for full-text assessment. Two observers independently screened the articles and seven studies satisfied the inclusion criteria. They were subsequently assessed for risk of bias and level of evidence. *Main outcome measures.* Quantitative measurements of maternal anxiety or worry. *Results.* Two studies compared anxiety in pregnant women who accepted or declined screening and showed no difference between groups. All studies described a decrease in anxiety following a screen-negative result. Four studies reported that women's anxiety levels increased significantly upon receiving a screen-positive result. However, after a normal diagnostic result, anxiety levels declined to the same level as for screen-negative women. *Conclusion.* Studies using quantitative, validated measures to estimate anxiety showed no association between screening and residual anxiety.

**Abbreviations:** CEBM, Oxford Centre for Evidence-based Medicine
HADS, Hospital Anxiety and Depression Scale; NTM, nuchal translucency measurement; PRAQ-R, Pregnancy Related Anxiety Questionnaire-Revised; STAI, Spielberger's State-Trait Anxiety Inventory.

## Introduction

In many countries, pregnant women are offered prenatal screening for Down's syndrome and other chromosomal abnormalities. However, the advantages and shortcomings of screening for Down's syndrome remain issues of debate in the media, in academia, and among clinicians.

### Key Message

There does not appear to be any evidence to suggest that screening for Down's syndrome causes anxiety in screen-negative women. Screen-positive results increase anxiety but the anxiety returns to normal levels following a normal diagnostic result.

 

Proponents stress the right of pregnant women to have access to information about their fetus and to make reproductive choices (1,2). Opponents are concerned with the ethical implications of screening for a condition that cannot be prevented or cured (3–5). Often, it is asserted that screening causes unnecessary worry or anxiety in women because it introduces or underscores the possibility that there might be something wrong with the fetus (6–8). It is argued that this anxiety may linger throughout the pregnancy, even after a normal screening and/or diagnostic result has been obtained (9,10).

Since the late 1980s, extensive research has been conducted on the potential emotional consequences of prenatal testing. In 2004, the NHS Research and Development, Health Technology Assessment program published a systematic review by Green et al. (11) on the psychosocial aspects of genetic screening in pregnant women and newborns. That review presented a thorough, robust assessment and discussion of the published literature on screening for Down's syndrome and the associated anxiety. Based on 24 qualitative and quantitative studies, the review concluded that there was no evidence of increased anxiety among screen-negative women (11, p. 26). The authors also found some evidence that anxiety was raised in women that received a positive screening result, but anxiety decreased when subsequent diagnostic testing showed a normal result (11, p. 28). They found insufficient evidence to determine whether residual anxiety remained. However, the authors expressed substantial methodological concerns regarding many of the publications; thus, their ability to make robust conclusions was limited. Consequently, further research was recommended.

Currently, a decade later, it may be relevant to ask whether the recommendations of Green et al. have been addressed with further research. What is the current scientific evidence on psychosocial aspects of prenatal screening for Down's syndrome? In the continuously expanding and advancing field of prenatal screening, we chose to narrow our focus to a core area of debate among clinicians, administrators and ethical commentators – the association between prenatal screening and anxiety. Since the majority of women who undergo screening receive either a negative or a false-positive screening result, we decided to limit the investigation to these two groups. Anxiety is a complex concept and we decided to focus solely on studies using quantifiable measures of anxiety. Accordingly, the aim of this review was to summarize the scientific, quantitative evidence that points to whether screening for Down's syndrome causes anxiety in pregnant women, and we address specifically (i) differences in anxiety between women who accept screening and women who either decline screening or are not offered screening, and (ii) differences in anxiety before and after screening in women who accept screening.

## Material and methods

### *Search strategy*

We used the PRISMA guidelines (12) to structure our review process. In an initial scoping of the literature, we specified the search strategy accordingly, based on PICOS:

- **P**opulation: Pregnant women.
- **I**ntervention: Maternal serum, nuchal translucency or combined screening for Down's syndrome.
- **C**omparison: screening vs. no screening, or pre-screening vs. post-screening.
- **O**utcome: Maternal anxiety.
- **S**tudy design: Quantitative studies: randomized controlled trials and cohorts.

To investigate current practices and technologies in screening for Down's syndrome, the search was limited to studies published after Green et al. (11) completed their literature search. Thus, this review includes only studies published between 1 August 2001 and 1 April 2013.

Based on the PICOS, search terms were formulated, and test searches were performed to develop the final search strategy. The search terms agreed on are presented in Table 1. In April and May 2013, we performed a systematic search in five databases (PubMed, Embase, Cinahl, PsychInfo, and Cochrane). When possible, we used thesaurus terms (such as terms included in the Medical Subject Headings index, MeSH). Because each database uses slightly different thesaurus terms, the terms were adapted accordingly, without changing the meaning of the search terms in the search protocol. The full search strategy can be obtained from the authors on request.

### *Study selection*

The systematic search identified 383 candidate publications (Figure 1). After removal of duplicates, two of the authors (S.L. and L.M.) independently screened the

**Table 1.** MeSH terms used in PubMed search.

| Patient | | Intervention | | Outcome |
|---|---|---|---|---|
| Pregnancy<br>or<br>Pregnant women | AND | (Mass Screening<br>or<br>Prenatal diagnosis)<br>and<br>(Chromosomal disorders<br>or<br>Down Syndrome) | AND | Behavior<br>or<br>Emotions |

  

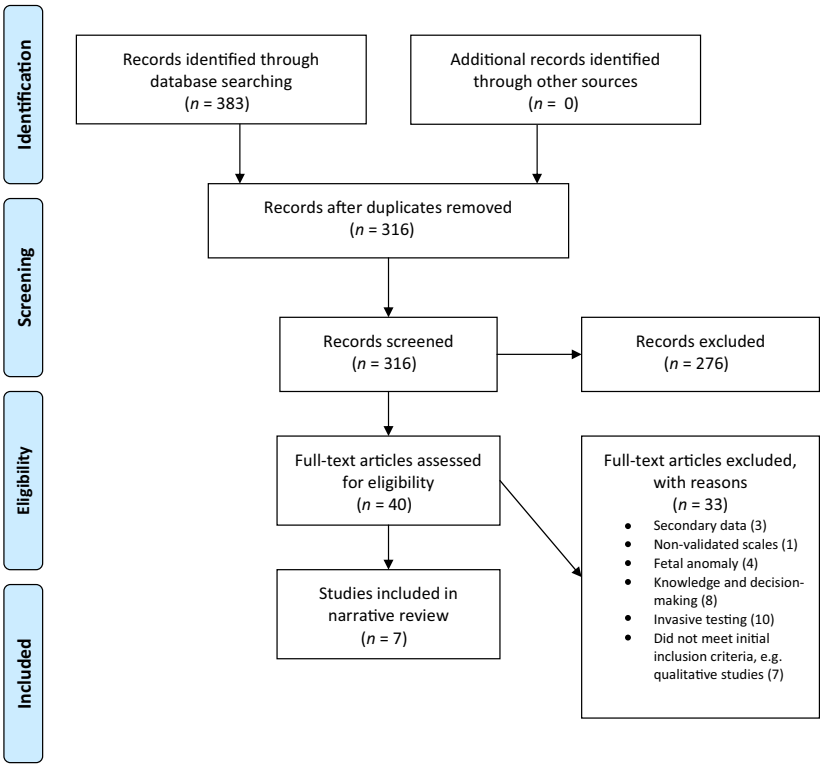


**Figure 1.** PRISMA 2009 flow diagram.

remaining 316 publications for eligibility by title, abstract and full-text, when necessary. Criteria for inclusion at this point were quantitative studies that investigated screening for Down's syndrome and emotional responses from pregnant women.

As a result, 40 publications were identified for potential inclusion. All studies were read in full by authors S.L. and L.M. independently, and assessed for eligibility according to PICOS and exclusion criteria. A search of reference lists and Science Citation Index did not identify additional studies.

Criteria for excluding publications were:

- Studies that presented only secondary data, such as reviews.
- Studies that used non-validated scales developed specifically for the study in question.
- Studies on fetal anomalies detected during the screening process.
- Studies on parental knowledge and decision-making regarding screening.
- Studies on anxiety during invasive testing.

Consequently, another 33 publications were excluded. The seven eligible publications are listed in Table 2. Study relevance and validity, including risk of bias, was assessed independently by authors S.L. and C.P.N. using checklists developed by the Danish National Board of Health (13), and assessments were compared and discussed between the authors.

Studies were subsequently ranked according to the Oxford Centre for Evidence-based Medicine (CEBM) guidelines (14). Based on the assessment of the individual study, grades of recommendation (A–D) of the overall evidence on relevant outcomes were given according to the CEBM guidelines (14). For the evidence to be graded with recommendation A, consistent level 1 studies (randomized controlled trials and cohorts) are required: recommendation A thus indicates high level of evidence, whereas a recommendation D reflects level 5 studies (such as expert opinion) or troubling inconsistent studies of any level, and thus poor level of evidence.

Due to the heterogeneity of aims and designs of the included studies, we decided to present a narrative review and thus no meta-analysis was done.

## Results

### *Characteristics of included studies*

Table 2 displays the main characteristics of the studies included. The studies were ranked as 1b to 2b level of evidence according to CEMB guidelines. The studies

**Table 2.** Description of included studies (in order of year of publishing).

| Reference | Intervention | Study | *n* | Stated aim of the article | Design | Outcome measures | Study group(s) | Results | Level of evidence |
|---|---|---|---|---|---|---|---|---|---|
| (21) | Maternal serum test | Lai et al. (2004) Singapore | 109 | To assess anxiety levels in mothers with low-risk pregnancies before and after offering routine serum screening | Cohort | Anxiety – Spielberger's STAI<br>• T1: Before serum counseling<br>• T2: After counseling but before screening<br>• T3: On day of 20-week scan (screening results known)<br>• T4: 4–6 weeks after scan | Routine maternal serum screening at 15–20 gws | No difference between pregnant women and reference population at baseline<br>Significant decrease in S-anxiety from T1 to T4 | 2b |
| (17) | Nuchal translucency measurement | Öhman et al. (2004) Sweden | 2026 | To evaluate the effect of ultrasound screening for Down's syndrome on women's anxiety in mid- pregnancy and 2 months after delivery | Randomized controlled trial | Anxiety – Spielberger's STAI<br>Cambridge Worry Scale<br>Edinburgh Postnatal depression scale<br>• T1: Early pregnancy (at inclusion, before randomization)<br>• T2: At 24 gws<br>• T3: 2 months postpartum | Intervention: Offered NTM at 12–14 gws ($n$ = 1030)<br>Control: Standard care, no screening offered ($n$ = 996) | No statistically difference between groups.<br>In both groups, women's worries decreased from baseline over mid-pregnancy to 2 months after delivery | 1b |
| (15) | Nuchal translucency measurement or maternal serum test | Kleinveld et al. (2006) The Netherlands | 2879 | (i) Does offering prenatal screening increase anxiety? (ii) Does receiving a negative screening result make women less anxious and does a positive screening result make women more anxious? (iii) What are the long-term consequences for anxiety of offering screening and receiving a screening result? | Randomized controlled trial | Anxiety – STAI-form Y<br>Child-related anxiety – PRAQ-R<br>• T1: Before information about screening<br>• T2: After information<br>• T3: After test result was known<br>• T4: At 24 gws<br>• T5: Postpartum (not included in this study) | Intervention 1: Offered NTM screening ($n$ = 686)<br>Intervention 2: Offered MST screening ($n$ = 648)<br>Control: Standard care, no screening offered ($n$ = 512) | Generally, offering screening and receiving test result do not adversely affect anxiety.<br>Women who screened positively had the highest general anxiety, however, at T4 this had returned to normal | 1b |
| (16) | Nuchal translucency measurement | Müller et al. (2006) The Netherlands | 687 | (i) To compare anxiety and depression during pregnancy and puerperium between woman who are offered NTM and women who are not, and (ii) to compare levels between women | Cohort | Anxiety – Hospital anxiety and depression scale (HADS)<br>• T1: Intervention group: After information, but before screening (11–14 gws)/Control group: 12 gws | Intervention: Information and offer to undergo NTM screening ($n$ = 527)<br>Control: Standard care, no screening offered ($n$ = 160) | Offering screening does not increase anxiety or depression levels.<br>Women who were offered screening (accepting/declining) had significantly lower HADS-levels at T2 and T3 | 2b |

**Table 2.** Continued

| Reference | Intervention | Study | *n* | Stated aim of the article | Design | Outcome measures | Study group(s) | Results | Level of evidence |
|---|---|---|---|---|---|---|---|---|---|
| | | | | accepting and declining screening. | | • T2: Both groups: 20 gws<br>• T3: Both groups: 6 weeks postpartum | | | |
| (19) | Nuchal translucency measurement | Chueh et al. (2007) Taiwan | 352 | To assess pre- and post-procedural maternal anxiety when screening for Down's syndrome, and the psychological impact of a positive screening result. | Cohort | Anxiety – Spielberger's STAI<br>• T1: Before screening<br>• T2: 1 week after screening<br>• T3: At 22 gws (invasive testing complete and<br>• T4: 6 weeks postpartum | Intervention: NTM screen-positive result (*n* = 172)<br>Control: Normal screening result (*n* = 180) | Women with positive screening result did not have sustained increase in anxiety. | 2b |
| (20) | Maternal serum test | Cheng et al. (2008) Taiwan | 2782 | To study the effect of fast reporting by mobile phone SMS on anxiety levels in women undergoing prenatal biochemical screening for Down's syndrome. | Randomized controlled trial | Anxiety – Spielberger 's STAI<br>• T1: At inclusion, before screening<br>• T2: Before appointment at clinic (when SMS had already been given to intervention group)<br>• T3: 3 days after appointment. | Intervention: Fast reporting by SMS (*n* = 1422)<br>Control: No mobile phone reporting (*n* = 1360) | Fast reporting by SMS significantly alleviates anxiety for screen-negative women while waiting for appointed clinical visit | 1b |
| (18) | Nuchal translucency measurement | Öhman et al. (2009) Sweden | 620[a] | To explore how information about being at risk for Down's syndrome was understood and whether the actual risk and the woman's perception of risk was associated with worry or depressive symptoms during and after pregnancy. | Cohort | Worry – Cambridge Worry Scale<br>Edinburgh postnatal depression scale<br>• T1: Early pregnancy (at inclusion, before randomization)<br>• T2: At 24 gws<br>• T3: 2 months postpartum | Women undergoing risk assessment for Down's syndrome 26 women were high-risk (all false-positive) 582 women were low risk | No significant relation between high risk and worry/depressive symptoms during or after pregnancy.<br>Women perceiving as being at high-risk were slightly more worried in mid-pregnancy, but this abated to the same levels 2 months postpartum. | 2b |

CEBM, Oxford Centre for Evidence-based Medicine; gws, gestational weeks; HADS, Hospital Anxiety and Depression Scale; NTM, nuchal translucency measurement; PRAQ-R, Pregnancy Related Anxiety Questionnaire-Revised; STAI, Spielberger's State-Trait Anxiety Inventory.

[a]Öhman et al. (18) included 620 women in their study but only reported results from 608 women.

**Table 3.** Timepoints and anxiety scores (with standard deviations).

| Reference | Study | Scales | Baseline | Screening | Late pregnancy | Postpartum |
|---|---|---|---|---|---|---|
| (21) | Lai et al. (2004) Singapore | STAI[a] | 15–20 gws<br>Before counseling:<br>S-Anxiety: 36.73 (±6.99)<br>T-Anxiety: 39.73 (±6.53)<br>After counseling (same day):<br>S-Anxiety: 35.50 (±7.78)<br>T-Anxiety: 39.25 (±6.84) | On day of screening, before screening (20 gws)<br>S-Anxiety: 35.46 (±7.34)<br>T-Anxiety: 38.96 (±6.57) | 24–26 gws<br>S-anxiety: 30.61 (±5.66)<br>T-anxiety: 38.55 (±6.55) | |
| (17) | Ohman et al. (2004) Sweden | STAI<br>EPDS[b] | | | 24 gws<br>Screening:<br>S-Anxiety: 32.8 (±8.7)<br>T-anxiety: 34 (±8.6)<br>EPDS: 11.8<br>No screening (control):<br>S-Anxiety: 32.9 (±8.8)<br>T-anxiety: 34 (±8.5)<br>EDPS: 13.3 | 2 months postpartum<br>Screening:<br>S-Anxiety: 30.2 (±8.4)<br>T-anxiety: 32 (±8.8)<br>EPDS: 8.2<br>No screening:<br>S-Anxiety: 31 (±8.2)<br>T-anxiety: 32.1 (±8.4)<br>EDPS: 9.0 |
| (15) | Kleinveld et al. (2006)[c] The Netherlands | STAI<br>PRAQ-R[d] | <16 gws<br>STAI (S-anxiety)<br>Before/after information<br>Screening accepted: 37/36<br>Screening declined: 37/35<br>No screening (control): 37/36<br>PRAQ-R<br>After information<br>Screening accepted: 2.5<br>Screening declined: 2.4<br>No screening (control): 2.4 | After test result (or comparable time)<br>STAI (S-anxiety)<br>High risk: 42<br>Normal risk: 33<br>Screening declined: 33<br>No screening: 35<br>PRAQ-R<br>High risk: 2.8<br>Normal risk: 2.2<br>Screening declined: 2.3<br>No screening: 2.3 | 28 gws<br>STAI (S-anxiety)<br>High risk (false-positive): 37<br>Normal risk: 35<br>Screening declined: 34<br>No screening: 36<br>PRAQ-R<br>High risk (false-positive): 2.7<br>Normal risk: 2.2<br>Screening declined: 2.3<br>No screening: 2.2 | |
| (16) | Muller et al. (2006) The Netherlands | HADS[e] | <11 gws<br>Screening: 7.55 (±5.18)<br>No screening (control): 8.63 (±4.07) | | 20 gws<br>Screening: 5.66 (±4.07)<br>No screening: 7.50 (±5.69) | 6 weeks postpartum<br>Screening: 6.97 (±6.08)<br>No screening: 8.91 (±6.05) |
| (19) | Chueh et al. (2007) Taiwan | STAI | 11–14 gws<br>High-risk screening result<br>S-anxiety: 39.2 (±9.8)<br>T-anxiety: 40.1 (±17.2)<br>Control<br>S-anxiety: 41.2 (±11.3)<br>T-anxiety: 41.7 (±13.9) | 1 week after NTM result<br>High-risk screening result<br>S-anxiety: 44.3 (±14.4)<br>T-anxiety: 42.6 (±9.2)<br>Control<br>S-anxiety: 37.3 (±10.8)<br>T-anxiety: 40.9 (±11.3) | 22 gws<br>False-positive screening result<br>S-anxiety: 36.9 (±8.8)<br>T-anxiety: 39.7 (±11.7)<br>Control<br>S-anxiety: 37.1 (±12.1)<br>T-anxiety: 41.5 (±8.9) | 6 weeks postpartum<br>False-positive screening result<br>S-anxiety: 38.5 (±9.9)<br>T-anxiety: 39.6 (±10.2)<br>Control<br>S-anxiety: 37.1 (±12.1)<br>T-anxiety: 41.5 (±8.9) |

**Table 3.** Continued

| Reference | Study | Scales | Baseline | Screening | Late pregnancy | Postpartum |
|---|---|---|---|---|---|---|
| (20) | Cheng et al. (2008)<br>Taiwan | STAI | <14–18 gws<br>Normal risk screening result<br>Intervention<br>S-anxiety: 38.9 (±9.9)<br>T-anxiety: 39.8 (±11.2)<br>Control<br>S-anxiety: 37.8 (±11.3)<br>T-anxiety: 38.4 (±10.9)<br>High-risk screening result<br>Intervention<br>S-anxiety: 39.2 (±11.4)<br>T-anxiety: 38.7 (±8.8)<br>Controligh-risk<br>S-anxiety: 39.9 (±9.4)<br>T-anxiety: 40.1 (±13.2) | At day of clinical follow-up[f]<br>Normal screening result<br>Intervention<br>S-anxiety: 33.8 (±7.9)<br>Control<br>S-anxiety: 39.1 (±10.1)<br>High-risk screening result<br>Intervention<br>S-anxiety: 44.1 (±13.4)<br>Control<br>S-anxiety: 42.9 (±11.5) | 3 days after clinical follow-up<br>Normal screening result<br>Intervention<br>S-anxiety: 35.3 (±12.5)<br>Control<br>S-anxiety: 34.9 (±10.1)<br>High-risk screening result<br>Intervention<br>S-anxiety: 43.4 (±9.6)<br>Control<br>S-anxiety: 43.1 (±10.6) | |
| (18) | Öhman et al. (2009)[g]<br>Sweden | EPDS SCWS[h] | 11–14 gws<br>High-risk screening result<br>EDPS: 5.6<br>SCWS: 3.2<br>Normal risk screening result<br>EDPS: 5.8<br>SCWS: 3.1 | | 24 gws<br>High-risk screening result<br>(false-positive)<br>EDPS: 7.2<br>SCWS: 2.7<br>Normal risk screening result<br>EDPS: 5.4<br>SCWS: 2.6 | 2 months postpartum<br>High-risk screening result<br>(false positive)<br>EDPS: 5.6<br>SCWS: 1.5<br>Normal risk screening result<br>EDPS: 4.9<br>SCWS: 1.1 |

gws, gestational weeks.

[a]The State Trait Anxiety Inventory (STAI) scores respondents on a scale of 20–80. Scores of 35 are considered normal anxiety and scores of 50–61 are considered an acute anxiety response (11,24).

[b]The Edinburgh Postnatal Depression Scale (EDPS) scores respondents on a scale of 0–30. Scores of ≥13 indicate probable minor depression in the antenatal period (49).

[c]Kleinveld et al. (15) did not supply T-anxiety scores or information on standard deviations.

[d]The Pregnancy-related Anxiety Questionnaire-Revised (PRAQ-R) consists of three subscales, but only "fear of bearing a physically or mentally handicapped child" is included in the present study. Scores range from 1 (low anxiety) to 5 (high anxiety) (15).

[e]The Hospital Anxiety and Depression Scale (HADS) scores respondents on a scale of 0–56, where values of 8–11 define possible and values of 11 or more definite probable cases of anxiety or depression (16).

[f]Results of screening known by intervention group and high-risk group.

[g]Öhman et al. (18) did not provide information on standard deviations.

[h]The Swedish version of the Cambridge Worry Scale (SCWS) only include one item ("worry about the possibility of something being wrong with the baby") scoring on a 0–5 scale. Values of 4–5 are defined as "major worry" (18).

include a total of 8835 participants. Two studies were conducted in the Netherlands (15,16), two in Sweden (17,18), two in Taiwan (19,20) and one in Singapore (21). All studies had a stated aim to assess anxiety or worry in pregnant women undergoing screening for Down's syndrome, but the study designs varied considerably. Three studies were randomized controlled trials and four were cohort studies. The studies included 109–2782 participants. The screening tests investigated were maternal serum test (20,21), nuchal translucency measurement (NTM) (16–19), or both (15). Three studies compared a group of women who were offered screening with a control group of pregnant women who were not offered screening (15–17). Three studies compared interventions in a cohort where both the intervention and control groups underwent screening (18–20). One study did not include a control group (21).

All studies used self-administered questionnaires to measure respondents' anxiety levels at several points during pregnancy. All studies included a baseline anxiety measurement and a mid-pregnancy, post-screening measurement at approximately 20–28 gestational weeks, thus allowing for comparisons across studies. Four studies also included anxiety measurements at 6–8 weeks postpartum (16–19). Table 3 displays numerical results and standard deviations (where available) of the individual measurements in the included studies. Statistical significance is reported under Results where relevant.

Five studies, including the three randomized controlled trials, used Spielberger's State-Trait Anxiety Inventory (STAI). STAI is a validated (22), 40-item scale that differentiates between the temporary condition of "state anxiety" (S-anxiety) and the more general, long-standing quality of "trait anxiety" (T-anxiety) (23). Thus, S-anxiety fluctuates over time, whereas T-anxiety is more stable. Respondents are scored on a scale of 20–80, where the higher scores are positively correlated to higher levels of anxiety. A STAI score of 35 is considered normal anxiety, and STAI scores of 50–61 are considered acute anxiety responses (11,24). The widespread use of STAI facilitates comparisons across studies. The remaining studies also used validated scales; for example the Cambridge Worry Scale (25) and the Hospital Anxiety and Depression Scale (HADS) (26).

In the following presentation of results, the Green et al. (11) review is used as frame of reference to compare previous and current scientific evidence on screening and anxiety. We emphasize that the results of the present review are autonomous and can be read independently of Green et al (11).

### *Anxiety before screening*

Green et al. (11) reported mean anxiety scores of 33–36 (27) and 38 (28) on the STAI for pregnant women that chose screening. Green et al. considered a STAI score of 34 as "normal", and they suggested that pregnant women had slightly increased anxiety levels compared with a non-pregnant population (11). Due to significant drop-out in the included studies, the authors recommended that those scores should be interpreted with caution.

In the present review, all studies included anxiety measures in early pregnancy prior to any randomization and/or intervention (at 8–16 gws). For the five studies using the STAI, the mean scores ranged from 36.7 (21) to 41.7 (19). We found moderate to good evidence (CEBM recommendation B) that the mean anxiety scores for women in early pregnancy were within this range; however, these studies did not report a comparable anxiety score for the background population or a matched non-pregnant group.

Müller et al. (16) included a reference to a Dutch validation study of the HADS-scale providing a mean score for the general population (29). The authors concluded that there was no significant difference between Dutch subjects and pregnant women. However, on the basis of the present review, we could not conclude whether pregnant women were more or less anxious at baseline than the general population.

### *Anxiety in women who are offered screening compared with women who are not*

Green et al. (11) did not address the issue of anxiety in women who are offered screening compared with women who are not. In the present review, two randomized controlled trials (15,17) and one cohort study (16) addressed this question. In the Swedish randomized controlled trial by Öhman et al. (17), 2026 pregnant women were randomized to either a 12–14 gestational weeks (gws) ultrasound examination including screening for Down's syndrome or to standard prenatal care (routine scan at 15–20 gestational weeks with no screening for Down's syndrome). The results showed no statistical difference between the intervention and the control group regarding anxiety or depressive symptoms during pregnancy or postpartum.

In the study by Kleinveld et al. (15), pregnant women were randomized to three groups: one was offered a maternal serum test, the second was offered NTM, and the third received standard care (no screening). In the two groups randomized to screening ($n = 1471$), the pregnant women received information and decided for or against screening; 694 declined the offer. The results showed that S-anxiety levels in women who declined screening were lower than in women who were not offered screening at all. This led the authors to conclude that allowing women to have a choice regarding prenatal

  

screening may have a small favorable effect on general feelings of anxiety. This result was supported by the findings of Müller et al. (16) who showed that women who were offered screening (acceptors as well as decliners) had significantly lower HADS scores at 20 gestational weeks and postpartum than women who had not been offered screening at all.

Thus, with one study showing no difference between groups, and two studies showing lower anxiety levels in women who were offered screening compared with women who were not, we found low to moderate evidence (CEMB recommendation C) that allowing women to have a choice regarding prenatal screening had a positive effect on general feelings of anxiety.

### *Anxiety among pregnant women who decline screening*

Green et al. (11) found three studies that compared women who accepted screening with women who were offered, but subsequently declined, a maternal serum test or NTM screening (30–32). However, the drop-out rates were 47–78% among women who declined screening. Therefore, the authors could not conclude whether anxiety differed between women who chose and those who declined screening.

In the present review, the two Dutch studies included pregnant women who declined an offer of prenatal screening. Müller et al. (16) found no statistically significant difference in anxiety between women who accepted or declined screening, at 12 gestational weeks, 20 gestational weeks or at six weeks after birth. Kleinveld et al. (15) found that after having received information about the offer of prenatal screening, women who declined screening had lower child-related anxiety [Pregnancy Related Anxiety Questionnaire-Revised ((PRAQ-R)] than women who accepted; however, the authors found no significant difference in STAI scores between women accepting and women declining screening. This lack of difference between groups continued throughout the pregnancy, both immediately after screening (or at a comparable time for decliners), and in the last trimester of pregnancy. Based on the Müller et al. and the Kleinveld et al. studies, we found low to moderate evidence (CEBM recommendation C) that anxiety levels did not differ between pregnant women who accepted and pregnant women who declined the offer of screening for Down's syndrome.

### *Anxiety after a screen-negative result*

Green et al. (11) found that anxiety before a screening test was slightly elevated compared with STAI norms, but anxiety returned to normal levels after a negative result had been obtained.

The studies in the present review show similar results. Three studies reported mean S-anxiety scores between 33 and 37.3 for screen-negative women (15,19,20). Two studies showed that post-result anxiety scores were significantly lower than pre-screening anxiety scores (15,20). Two other studies reported a numerical decrease in scores, but this was not statistically significant (19,21). All studies found that, in screen-negative women, anxiety continually decreased over time, from pre-screening to mid- and late pregnancy (20–28 gestational weeks) where mean STAI scores ranging from 30.6 to 37.1 were reported (16,17,19–21). Kleinveld et al. (15) reported HADS anxiety and depression scores of screen-negative women to be 35 after screening, compared with 37 at baseline. Furthermore, after test results were known, screen-negative women had significantly lower PRAQ-R scores than women who declined screening. Three studies measured anxiety postpartum, and all reported the lowest anxiety levels at this point (16,17,19). Thus, we found no evidence (CEBM recommendation B) to support an assumption of residual anxiety in screen-negative women.

### *Anxiety after a screen-positive result*

Green et al. (11) found that women experienced an acute response when they received a positive screening result. STAI scores rose to about 55 points upon receiving a positive screening result (30,33,34). Nevertheless, the findings also suggested that anxiety scores returned to normal levels after diagnostic testing showed normal results (33,35).

In the present review, three studies included screen-positive women. All three reported significantly higher levels of anxiety compared with screen-negative women. The S-anxiety scores reported were 42 (15), 42.9–44.1 (20) and 44.3 (19); thus, these scores were numerically much lower than those reported in the studies reviewed by Green et al. (11).

For example, Chueh et al. (19) compared two groups of pregnant women; one was a group with positive screening results (NTM screening, $n = 172$) and the other was an age-matched control group with negative screening results ($n = 180$). One week after screening, women with positive screening results scored significantly higher than controls for S-anxiety. However, at 22 weeks' gestation and at six weeks after delivery, STAI scores did not differ between the groups. Chueh et al. concluded that screening does not induce a sustained increase in anxiety. Though much smaller in sample size, the findings by Kleinveld et al. (15), and Müller et al. (16) ($n = 20$ and $n = 8$, respectively) supported this conclusion. By 28

gestational weeks, Kleinveld et al. (15) found a numerical difference in PRAQ-R Child-related anxiety between women with a normal screening result (2.2) and women with a false-positive screening result (2.7). However, this difference was not statistically significant.

Öhman et al. (18) found that a woman's perception of being at high-risk for Down's syndrome (regardless of the actual risk score) was associated with worry and depression. In contrast, the actual risk score was not associated with worry or depression. However, two months after delivery, Öhman et al. found no association between the level of worry and either the actual or perceived risk.

Based on the included studies, we found moderate to good evidence (CEBM recommendation B) that anxiety levels increased upon receipt of a screen-positive result. However, upon receipt of a normal diagnostic result, in the third trimester, and after delivery, we found no significant difference in anxiety levels between women with negative and positive screening results. Therefore, the present review did not support the hypothesis of residual anxiety. On the contrary, we found moderate to good evidence (CEBM recommendation B) that anxiety levels declined to normal levels after receiving a normal diagnostic result.

## Discussion

In this article, we reviewed and summarized very different studies in different countries with different traditions regarding prenatal care and screening. Interestingly, across all studies, anxiety in screen-negative women consistently decreased from baseline to the third trimester and postpartum. All four studies measuring screen-positive women's anxiety after screening found a statistically significant increase in anxiety (15,16,19,20). However, by the third trimester, anxiety levels in false-positive women returned to the same level as for screen-negative women (15,16,19). Thus, our results contribute to the current base of evidence for understanding anxiety in relation to screening for Downs' syndrome in pregnant women.

There are some methodological challenges pertaining to most of the study designs which may limit the generalizability of the results. First, there is risk of selection bias in the inclusion of pregnant women in the studies. For example, in the Swedish study by Öhman et al. (17) the inclusion rate was only 23%, and compared with the background population, the sample population included fewer women of non-Swedish decent and larger proportions of older women, nulliparous women, women who were married/cohabiting, and women with a relatively higher level of education. The only other study providing demographic statistics, Kleinveld et al. (15), similarly reported women in the study population to be of higher education than the general population of pregnant women. Studies have shown a positive correlation between educational level and knowledge about prenatal screening (36,37), and making an informed decision regarding prenatal screening has been shown to decrease decisional conflict (38) and increase satisfaction later in pregnancy (39). Consequently, the included women might be better at coping with screen-associated anxiety, and thus, the anxiety levels in these studies could be biased towards lower values of anxiety.

Secondly, the drop-out rates must be taken into consideration. Only Müller et al. (16) analyzed data according to intention-to-treat and thus included scores for all participants in the analysis – including the drop-outs. All the other studies selectively analyzed only data from participants who completed all the questionnaires. Because dropping out of a study is known to be proportionally larger in sections of the population with relatively low resources, these attrition rates potentially added to the selection bias already present at inclusion. Öhman et al. (17) reported that drop-outs did not skew the socio-demographic distribution of women in their final study group. Similarly, Müller et al. (16) reported no significant difference in socio-demographic or obstetric background between completers and drop-outs. However, drop-out levels in the other studies might potentially influence the validity of the results in the present review. Similar to the selection bias, we hypothesize that drop-out might lead to an underestimation of the anxiety levels.

Despite these limitations, we argue that our findings address important aspects of prenatal screening. The pros and the cons of prenatal screening have been an ongoing debate; currently, there remain professionals, academics and decision-makers who question the benefits of prenatal screening, primarily due to the assumption that it induces harmful anxiety (3). One concern is the general anxiety and medicalization of pregnancy that prenatal screening might increase by making pregnant women aware of the risk that something might be wrong with the fetus. Green et al. (11) referred to a few studies that indicated that prenatal screening could result in residual anxiety lingering throughout the pregnancy and postpartum period (10,40,41); however, they concluded that this relation was yet to be confirmed. In the present review, we did not find any evidence to support the hypothesis of residual anxiety. On the contrary, there was a continual decrease in anxiety throughout the pregnancy for women participating in screening.

We have limited the present review to quantitative studies using validated scales to address anxiety at the epidemiological level. Thus, it is important to acknowledge that for the individual woman, participation in prenatal screening might be stressful and raise anxiety and

concerns. For example, a qualitative study by Aune & Möller (42) show the complex feelings, sense of responsibility, social pressure and moral issues that women engage with when processing risk information about pregnancy and the fetus. However, that study also finds that a low-risk result increased reassurance and relief. These findings are in line with several other studies that demonstrate a reassuring affect (43,44) and increased fetal-maternal attachment (45,46) following a normal screening result.

Another often-voiced concern regarding prenatal screening is the problem of false-positive screening results, and the immediate worry and potential residual anxiety it may lead to. In all screening procedures, the risk of false-positive results is an unfortunate, but inherent, shortcoming. The studies in this review collectively stress the significant increase in anxiety following a high-risk result. Qualitative studies have described the complex information, moral dilemmas, and difficult decisions that pregnant women and their partners must deal with following a screen-positive result (7,47,48). Thus, a continual development of screening technologies to raise the level of specificity is necessary to reduce the number of false-positive women who endure emotional turmoil and risk miscarriage of a healthy fetus due to the invasive diagnostic procedures. However, a very important result of this review is that false-positive pregnant women can bounce back. We find that once a false-positive screen result is rectified by a normal diagnostic result, there is no significant difference in anxiety between women with false-positive and those with negative screening results; thus, at the epidemiological level, a false-positive screening result does not result in lingering anxiety. This finding suggests that a conclusive diagnostic result can restore the pregnant woman's faith in a healthy fetus and normal pregnancy. These findings also speak in favor of a continual optimizing of clinical practices, particularly regarding a smooth running of the diagnostic process and a fast diagnostic response to minimize undue anxiety.

This review of quantitative studies, which used validated scales, represents one perspective on prenatal screening and anxiety. Our results are consistent with the present information and refine existing knowledge. However, there are important aspects to pregnancy, screening and anxiety that are difficult to capture in randomized controlled trials and cohort studies. First, we need a better understanding of (and an ability to identify) why some women experience extremely high anxiety levels that impede effective, contemplative decision-making. Secondly, we need to investigate further the complex feelings of anxiety, excitement, nervousness and joy that inform the pregnant women's experiences with pregnancy and prenatal care. To address these complex issues, we suggest future combined studies of both epidemiological and experiential perspectives on screening.

## Funding

No special funding.

### References

1. Danish National Board of Health. Guidelines for Fetal Diagnostics – Prenatal Information, Risk Assessment, Counseling and Diagnostics. Copenhagen: Danish National Board of Health, 2004.
2. Nicolaides KH, Chervenak FA, McCullough LB, Avgidou K, Papageorghiou A. Evidence-based obstetric ethics and informed decision-making by pregnant women about invasive diagnosis after first-trimester assessment of risk for trisomy 21. Am J Obstet Gynecol. 2005;193:322–6.
3. The Danish Counsil of Ethics. The Future of Prenatal Diagnosis. Copenhagen: The Danish Council of Ethics, 2009.
4. Landsman G. Reconstructing Motherhood and Disability in an Age of "Perfect" Babies. London: Routledge, 2009.
5. Kvist M. Frasortering af syge foster er arvehygiejne [Abortion of sick foetuses is eugenic] (newspaper article). Kristeligt Dagblad 6 November 2009. Available online at: http://www.kristendom.dk/synspunkt/frasortering-af-syge-fostre-er-arvehygiejne (accessed 12 December, 2013).
6. Filly RA. Obstetric sonography: the best way to terrify a pregnant woman. J Ultrasound Med. 2000;19:1–5.
7. Williams C, Sandall J, Lewando-Hundt G, Heyman B, Spencer K, Grellier R. Women as moral pioneers? Experiences of first trimester antenatal screening. Soc Sci Med. 2005;61:1983–92.
8. Ohman SG, Saltvedt S, Waldenstrom U, Grunewald C, Olin-Lauritzen S. Pregnant women's responses to information about an increased risk of carrying a baby with Down syndrome. Birth. 2006;33:64–73.
9. Heyman B, Hundt G, Sandall J, Spencer K, Williams C, Grellier R, et al. On being at higher risk: a qualitative study of prenatal screening for chromosomal abnormalities. Soc Sci Med. 2006;62:2360–72.
10. Weinans MJN, Huijssoon AMG, Tymstra T, Gerrits MCF, Beekhuis JR, Mantingh A. How women deal with the results of serum screening for Down syndrome in the second trimester of pregnancy. Prenat Diagn. 2000;20:705–8.
11. Green JM, Hewison J, Bekker HL, Bryant LD, Cuckle HS. Psychosocial aspects of genetic screening of pregnant women and newborns: a systematic review. Health Technol Assess. 2004;8:iii, ix–x, 1–109.
12. Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: the PRISMA Statement. PLoS Med. 2009;6:e1000097.

13. Danish National Board of Health. Available online at: https://sundhedsstyrelsen.dk/da/sundhed/kvalitet-og-retningslinjer/medicinsk-teknologivurdering-mtv/litteraturvurdering (accessed March 15, 2014).
14. University of Oxford. Oxford Centre for Evidence-based Medicine: Levels of Evidence. 2009. Available online at: www.cebm.net/oxford-centre-evidence-based-medicine-levels-evidence-march-2009/ (accessed 2 September, 2014).
15. Kleinveld J, Timmermans D, de Smit D, Ader H, van der Wal G, ten Kate L. Does prenatal screening influence anxiety levels of pregnant women? A longitudinal randomised controlled trial. Prenat Diagn. 2006;26:354–61.
16. Muller MA, Bleker OP, Bonsel GJ, Bilardo CM. Nuchal translucency screening and anxiety levels in pregnancy and puerperium. Ultrasound Obstet Gynecol. 2006;27:357–61.
17. Öhman SG, Saltvedt S, Grunewald C, Waldenstrom U. Does fetal screening affect women's worries about the health of their baby? A randomized controlled trial of ultrasound screening for Down's syndrome versus routine ultrasound screening. Acta Obstet Gynecol Scand. 2004;83:634–40.
18. Öhman SG, Saltvedt S, Grunewald C, Waldenstrom U. Perception of risk in relation to ultrasound screening for Down's syndrome during pregnancy. Midwifery. 2009;25:264–76.
19. Chueh HY, Cheng PJ, Shaw SW, Lin CT, Hsu JJ, Hsieh TT. Maternal anxiety about first trimester nuchal translucency screening and impact of positive screening results. Acta Obstet Gynecol Scand. 2007;86:1437–41.
20. Cheng PJ, Wu TL, Shaw SW, Chueh HY, Lin CT, Hsu JJ, et al. Anxiety levels in women undergoing prenatal maternal serum screening for Down syndrome: the effect of a fast reporting system by mobile phone short-message service. Prenat Diagn. 2008;28:417–21.
21. Lai FM, Ng CC, Yeo GS. Does maternal serum screening for Down syndrome induce anxiety in younger mothers? Singapore Med J. 2004;45:375–8.
22. Barnes LBL, Harp D, Jung WS. Reliability generalization of scores on the Speilberger State-Trait Anxiety Inventory. Educ Psychol Meas. 2002;62:603–18.
23. Spielberger B, Gorsuch RL, Lushene RE. Manual for the State-Trait Anxiety Inventory (STAI). Palo Alto: Consulting Psychologist's Press, 1970.
24. Bekker HL, Legare F, Stacey D, O'Connor A, Lemyre L. Is anxiety a suitable measure of decision aid effectiveness: a systematic review. Patient Educ Couns. 2003;50:255–62.
25. Öhman SG, Grunewald C, Waldenstrom U. Women's worries during pregnancy: testing the Cambridge Worry scale on 200 Swedish women. Scand J Caring Sci. 2003;17:148–52.
26. Murray D, Cox J. Screening for depression during pregnancy with the Edinburgh Postnatal Depression Scale. J Reprod Infant Psychol. 1990;9:99–107.
27. Ormond KE, Pergament E, Fine BA. Pre-screening education in multiple marker screening programs: the effect on patient anxiety and knowledge. J Genet Couns. 1996;5:69–80.
28. Quagliarini D, Betti S, Brambati B, Nicolini U. Coping with serum screening for Down syndrome when the result is given as a numeric value. Prenat Diagn. 1998;18:816–21.
29. Spinhoven P, Ormel J, Sloekers PP, Kempen GI, Speckens AE, Van Hermert AM. A validation study of the Hospital Anxiety and Depression scale (HADS) in different groups of Dutch subjects. Psychol Med. 1997;27:363–70.
30. Marteau TM, Cook R, Kidd J, Michie S, Johnston M, Slack J, et al. The psychological effects of false positive results in prenatal screening for fetal abnormality: a prospective study. Prenat Diag. 1992;12:205–14.
31. Michie S, Smith D, Marteau TM. Prenatal tests: how are women deciding? Prenat Diag. 1999;19:743–8.
32. Michie S, Smith D, McClennan A, Marteau TM. Patient decision making: an evaluation of two different methods of presenting information about a screening test. Br J Health Psychol. 1997;2:317–26.
33. Abuelo DN, Hopmann MR, Barsel-Bowers G, Goldstein A. Anxiety in women with low maternal serum alpha-fetoprotein screening results. Prenat Diagn. 1991;11:381–5.
34. Keenan KL, Basso D, Goldkrand J, Butler WJ. Low level of maternal alpha-fetoprotein: Its associated anxiety and the effect of genetic counseling. Am J Obstet Gynecol. 1991;164:54–6.
35. Jorgensen FS. User acceptability of an alpha-fetoprotein screening programme. Dan Med Bull. 1995;42:100–5.
36. Stefansdottir V, Skirton H, Jonasson K, Hardardottir H, Jonsson JJ. Effects of knowledge, education, and experience on acceptance of first trimester screening for chromosomal anomalies. Acta Obstet Gynecol Scand. 2010;89:931–8.
37. Dahl K, Hvidman L, Jorgensen FS, Henriques C, Olesen F, Kjaergaard H, et al. First-trimester Down syndrome screening: pregnant women's knowledge. Ultrasound Obstet Gynecol. 2011;38:145–51.
38. Dahl K, Hvidman L, Jorgensen FS, Kesmodel US. Knowledge of prenatal screening and psychological management of test decisions. Ultrasound Obstet Gynecol. 2011;38:152–7.
39. Bekker HL, Hewison J, Thornton JG. Applying decision analysis to facilitate informed decision making about prenatal diagnosis for Down syndrome: a randomised controlled trial. Prenat Diagn. 2004;24:265–75.
40. Stratham H, Green J. Serum screening for Down's syndrome: some women's experiences. BMJ. 1993;307:174–6.
41. Santalahti P, Lattika AM, Ryynanen M, Hemmiki E. Women's experiences of prenatal serum screening. Birth. 1996;23:101–7.
42. Aune I, Moller A. "I want a choice, but I don't want to decide" – a qualitative study of pregnant women's experiences regarding early ultrasound risk assessment for chromosomal anomalies. Midwifery. 2012;28:14–23.

43. Ekelin M, Crang-Svalenius E, Dykes AK. A qualitative study of mothers' and fathers' experiences of routine ultrasound examination in Sweden. Midwifery. 2004;20:335–44.
44. Da Silva EC, Silva SV, Damiao R, Fonseca EB, Garcia S, Lippi UG. Stress and anxiety in pregnant women exposed to ultrasound. J Matern Fetal Neonatal Med. 2012;25:295–8.
45. Boukydis CF, Treadwell MC, Delaney-Black V, Boyes K, King M, Robinson T, et al. Women's responses to ultrasound examinations during routine screens in an obstetric clinic. J Ultrasound Med. 2006;25:721–8.
46. Ohman SG, Waldenstrom U. Effect of first-trimester ultrasound screening for Down syndrome on maternal-fetal attachment – a randomized controlled trial. Sex Reprod Health. 2010;1:85–90.
47. Markens S, Browner CH, Preloran HM. Interrogating the dynamics between power, knowledge and pregnant bodies. Sociol Health Illness. 2010;32:37–56.
48. Rapp R. Testing Women, Testing the Fetus: The Social Impact of Amniocentesis in America. New York: Routledge, 1999.
49. Grant K-A, McMahon C, Austin M-P. Maternal anxiety during transition to parenthood: A prospective study. J Affect Disorders. 2008;108:101–11.