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Genetic Counselling for Familial Conditions during Pregnancy: A Review of the Literature Published during the Years 1989–2004

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Key Words
Genetic counselling · Pregnancy · Prenatal diagnosis

Abstract
Background: Genetic counselling for familial conditions during pregnancy may have some disadvantages, such as time pressure and induced worry. However, little is known about the reasons for and consequences of this timing of genetic counselling. ***Objective:*** The objective of this study was to provide an overview of research aimed at the counselee's reasons for seeking genetic counselling during pregnancy and the medical-technical and procedural consequences thereof. ***Methods:*** We searched the databases Medline and PsycINFO for primary research papers, reviews and case reports, published from 1989 to June 2004. ***Results:*** No papers could be retrieved which explicitly addressed our research questions. However, 34 papers, out of a total of 399 papers, covered issues with some relevance to our research questions. Limited knowledge and alertness towards genetics and a greater apparent relevance of genetic issues during pregnancy seemed to explain, at least partly, the timing of referral during pregnancy. Literature on the consequences of this timing for the quality of the genetic counselling process appeared to be scarce. These consequences, therefore, remain unclear. ***Conclusion:*** In the literature, little attention is paid to the various aspects of the timing of genetic counselling for familial conditions during pregnancy. More research on this issue is important, with a view to improving the care of pregnant women and their children.

Introduction

In 2002, approximately 15,000 people with a family history of genetic conditions attended one of the eight departments of clinical genetics in the Netherlands for genetic counselling. During the last few years, this number has increased annually by around 10%. Of these people, 10–20% attend a department of clinical genetics for the first time while being pregnant (unpubl. data). This figure does not include women who undergo prenatal screening, for example because of age-related risk factors, or women who first underwent an invasive prenatal diagnosis procedure and who subsequently are referred by their gynaecologist to discuss the implications of an adverse outcome. If questions about reproduction are part of the genetic counselling, the so-called reproductive genetic counselling, referral for familial genetic conditions during pregnancy seems to have several important disadvantages.

First, it may be too late for invasive prenatal diagnosis and the number of preventive and therapeutic options is

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limited. An adverse outcome at prenatal diagnosis should enable women to make choices about their pregnancy. This means that, in principle, they have to be able to opt for selective abortion. In the Netherlands, abortion can take place legally until 24 weeks of gestation [1]. In a group of pregnant women with a familial genetic condition, the mean gestational age at the time of the first consultation was 12 weeks [2]. This means that in most cases it will be too late for an optimal timing of a chorionic villus sampling and there are only a few weeks left to prepare and carry out an amniocentesis. Ultrasound examination at 18–20 weeks of gestation can be useful, but will not always be sufficient. If prenatal diagnosis requires DNA analysis, the precise molecular defect in the index patient has to be established first, either by direct mutation or by linkage analysis. Often, this requires cooperation of the index patient and other family members. DNA analysis for an unknown mutation takes at least a few weeks to months, and consequently, molecular prenatal diagnosis will not always be possible if the first consultation takes place after conception. Prenatal diagnosis for complex chromosomal rearrangements with fluorescence in situ hybridization also needs to be prepared by the laboratory. Obviously, the accessibility of alternative reproductive options, like pre-implantation genetic diagnosis or donor insemination, has become impossible after conception.

Second, the time pressure as a result of pregnancy may lead to adverse feelings of both the counselee and the counsellor, which may decrease the quality of the genetic counselling process. The experience with prenatal screening programs, for example, has shown that some women find it difficult to decline the offer of genetic tests during pregnancy, suggesting a degree of, probably unintended, coercion [3–5]. Furthermore, Santalahti et al. [6] found that half of the women considered participation in prenatal screening as a routine or obvious procedure; only a minority described that they actively decided about participation. Although these studies involved screening programs, coercion may be felt in a diagnostic setting too.

Furthermore, referral for prenatal genetic counselling may enhance or even induce worry and anxiety [7–9], especially if unexpected (minor) abnormalities are revealed by additional investigations. This is in contrast to the reason for which many women with an age-related risk factor seek prenatal screening, namely reassurance [6]. Finally, important decisions regarding the pregnancy have to be made within a short period of time.

Imaginably, time pressure may be felt by the genetic counsellor too. It is known that if little time is available for the medical encounter, the medical-technical exchange is given priority in most cases and less attention is paid to the psychosocial aspects [10]. In addition, discussion of important, but less urgent issues, like recurrence risks in family members may be neglected. Furthermore, it is conceivable that counsellors may experience feelings of irritation about the late timing of the referral and feelings of ambivalence about an eventual therapeutic abortion in the specific situation of the counselee, which may lead to countertransference reactions [11]. If these reactions are not recognized by the counsellor, he or she is liable to become judgmental, patronizing or otherwise not accepting the women's feelings [12]. Non-directiveness and autonomy of counselees, important tenets in genetic counselling, may be undermined by these countertransference issues [13–16].

Experiencing disadvantages of genetic counselling for familial conditions during pregnancy in daily practice, and given the literature on the disadvantages of prenatal screening, we searched the literature for data to gain insight into any beneficial or detrimental consequences of the counselling process for pregnancy.

Two research questions were formulated:

- First, why do people with a familial genetic condition seek genetic counselling during pregnancy? Gaining insight into their motives is important for the evaluation of whether genetic counselling during pregnancy is desirable or should be mandatory, at least in some cases.
- Second, what are the effects of this timing of genetic counselling on (1) the medical-technical aspects of the process, such as the possibilities of prenatal diagnosis and pregnancy outcome, and on (2) the counselling part of the process, such as the quality of the doctor-patient interaction and the autonomy of the patients?

Methods

Search Strategy

The databases Medline and PsycINFO were searched for literature from 1989 to June 2004. We chose to include only the relatively recent literature from the last 15 years, because the field of clinical genetics develops quickly and, in our opinion, current attitudes and views towards genetic counselling are covered by this period. We combined sets of terms from the MeSH database as follows: (1) genetic counselling and prenatal diagnosis (with both terms restricted to major topic headings in the Medline database), (2) genetic counselling and prenatal care, and (3) genetic counselling and preconception care. The search revealed 316, 55 and 28 papers, respectively. Titles and abstracts were screened by one of the authors (C.M.A.) and 118 abstracts were selected. Selec-

tion of the papers was based on the apparent relevance to our research questions. The full text copies of 94 potentially relevant papers could be retrieved. Full text copies of 24 papers could not be retrieved within a reasonable period of time, for example because they were not available in the Netherlands. Reference lists from all potentially relevant papers were examined for additional papers, excluding papers which were published before 1989.

Inclusion Criteria and Data Extraction

Primary research papers, reviews and case reports that investigated any aspect related to our research questions as defined were included. Papers written in English, German, French and Dutch were considered. The papers retrieved were heterogeneous in their focus, methods and outcomes. In order to avoid excluding relevant papers, all papers with some relevance were included, instead of applying a strict set of methodological exclusion criteria. Papers dealing exclusively with prenatal screening were not included, because issues in screening differ from diagnostic issues. Opinion articles, editorials and other commentaries were excluded, because it seemed unlikely that these would contain relevant empirical data.

Results

A total of 34 papers were included in our review. None of the retrieved studies specifically addressed one of our three research questions. Most of the selected studies were essentially descriptive in nature (see table 1). In the research papers, data were collected by self-report, including self-created data collection forms in nine studies [17–25] and semi-structured interviews in five studies [26–30] and by studying medical records in six studies [31–36]. Furthermore, we included seven literature reviews [37–43], six case reports [44–49] and one study, in which a mathematical model was used [50].

For each research question, the papers were divided according to different emerging themes, which are described in table 1. Some articles addressed more than one theme and are therefore mentioned twice in table 1.

Reasons for Attending Genetic Counselling during Pregnancy

Twenty-three papers were considered relevant to the question as to why people attend counselling whilst pregnant. Five main themes could be identified: 'knowledge about genetics', 'alertness towards genetic risk factors', 'attitudes towards genetic and prenatal testing', 'pregnancy planning' and 'financial aspects' (table 1).

Concerning the first theme, inadequate knowledge about genetics and preconceptional measures in professionals and in women may lead to referral only during pregnancy. Knowledge about genetic risk factors among both professional health workers and lay people was found to be moderate to poor in most papers. Obstetricians' knowledge about the genetics of single gene disorders, for example, was limited [25] and Dutch general practitioners considered their knowledge about genetics as insufficient [20]. In the general population, knowledge about the use of folic acid in order to reduce the risk on neural tube defects was insufficient [40]. Moderate to poor knowledge about genetic aspects was reported for specific disorders in particular patient groups, for insulin-dependent diabetes patients [27], family members of cystic fibrosis patients [24] and parents of a child with a genetic disorder [30]. In contrast, in a group of neurofibromatosis patients and their families [19] and a group of parents who had at least one child with cystic fibrosis [33], knowledge about the genetic aspects of the disease was good.

Limited alertness towards genetic risk factors before pregnancy, the second theme, may also lead to referral only after conception. Generally, alertness among physicians is considered to be limited. Inadequate genetic risk assessment, especially by primary care providers, was described in three studies [31, 34, 35]. By obtaining a three-generation pedigree in women referred for amniocentesis because of advanced maternal age or abnormal maternal serum α-fetoprotein findings, Cohn et al. [31] identified a significant extra genetic risk in 36% of the pedigrees that had not been noted by the referring physician. In a similar setting Meschede et al. [35] identified in 11% of the cases a 'significant and previously unknown genetic or teratologic risk factor', of which '55% could be recommended a specific prenatal test'. Langer and Kudart [34] reported that in a pre-amniocentesis counselling session at least one condition, other than those for which the patient was referred, could be identified in 72% of the pedigrees.

An increased awareness among people about genetic risk factors may be present during pregnancy, as has been stated by Lubin et al. [39] and Wilkins-Haug et al. [25]. In addition, Gibb et al. [27] found in a group of insulin-dependent diabetic women that they were all aware of the importance of good blood glucose control during pregnancy.

Negative attitudes towards genetic and prenatal testing and its consequences, the third theme, may also lead to inadequate timing of the referral. Most papers, however, reported a generally favourable view towards these issues among both lay people and professional health workers [18, 19, 21–24, 26].

Table 1. Overview of 34 selected papers divided according to the research questions and subdivided according to some relevant themes (some articles address more than one theme)

Authors and year of publication	Design of the study	Genetic disorder involved	Subjects involved
Why do people with a familial genetic condition ask for genetic counselling during instead of before pregnancy?			
Knowledge about genetics			
Cnossen et al., 1997 [19]	Research Qualitative – Questionnaires	Neurofibromatosis	68 parents of affected children and 24 affected parents
Gaytant et al., 1998 [20]	Research Qualitative – Self-reporting questionnaire	Various disorders, relevant for preconception counselling	86 general practitioners
Gibb et al., 1994 [27]	Research Qualitative – Structured face to face interview	Insulin-dependent diabetes mellitus	124 female patients
Janes et al., 1990 [22]	Research Qualitative – Self-reporting questionnaires	Cystic fibrosis	217 parents of affected children and 88 affected adults
Kim et al., 1989 [32]	Research Qualitative – Review of delivery records – Patient interviews	Various disorders	126 women with an indication for prenatal cytogenetic diagnosis
Lafayette et al., 1999 [24]	Research Qualitative – Self-reporting questionnaire	Cystic fibrosis	173 relatives of cystic fibrosis patients
Lane et al., 1997 [33]	Research Qualitative – Retrospective review of case notes	Cystic fibrosis	46 families with a second affected child
Schrander-Stumpel, 1999 [40]	Review – Non-systematic	Unspecified	
Wilkins-Haug et al., 1999 [25]	Research Qualitative – Self-reporting questionnaires	Various genetic diseases	554 obstetricians
Zahed et al., 1999 [30]	Research Qualitative – Face to face interviews	Various genetic disorders	90 couples with genetic disorders
Awareness about genetic risk factors			
Gibb et al., 1994[a] [27]	Research Qualitative – Structured face to face interview	Insulin-dependent diabetes mellitus	124 female patients
Cohn et al., 1996 [31]	Research Qualitative – Pedigree information from charts	Advanced maternal age and abnormal maternal serum α-fetoprotein	275 women with advanced maternal age and 103 women with abnormal maternal serum α-fetoprotein
Langer and Kudart, 1990 [34]	Research Quantitative – Retrospective review of records	Various	1,131 women who were referred for amniocentesis
Lubin et al., 1990 [39]	Review – Not systematic	Common familial disorders of adulthood	
Meschede et al., 2000 [35]	Research Quantitative – Review of patient files	Various disorders relevant for prenatal diagnosis	1,356 referred for advanced maternal age or abnormal serum screening
Wilkins-Haug et al., 1999[a] [25]	Research Qualitative – Self-reporting questionnaires	Various genetic diseases	554 obstetricians

Table 1 (continued)

Authors and year of publication	Design of the study	Genetic disorder involved	Subjects involved
Attitudes towards genetic and prenatal testing			
Campbell and Ross, 2003 [26]	Research Qualitative – Semi-structured interviews	Phenylketonuria, Duchenne muscular dystrophy, familiar adenomatosis coli, breast cancer, Apoε4	12 paediatricians, 13 geneticists
Chen and Schiffman, 2000 [18]	Research Qualitative – Questionnaire	Various genetic and acquired disorders	15 people with a physical disability
Cnossen et al. 1997[a] [19]	Research Qualitative – Questionnaire	Neurofibromatosis	68 parents of affected children and 24 affected parents
Jallinoja et al., 1998 [21]	Research Qualitative – Self-reporting questionnaire	Unspecified	Stratified sample of 1,169 Finnish people
Janes et al., 1990[a] [22]	Research Qualitative – Self-reporting questionnaire	Cystic fibrosis	217 parents of affected children and 88 affected adults
Jayasekara, 1989 [23]	Research Qualitative – Self-reporting questionnaire	Unspecified	302 practising doctors and 143 final-year medical students from Sri Lanka
Lafayette et al., 1999[a] [24]	Research Qualitative – Self-reporting questionnaire	Cystic fibrosis	173 relatives of cystic fibrosis patients
Marfatia et al., 1990 [47]	Case report	Cleft lip/palate, Coffin-Lowry syndrome, spina bifida, advanced maternal age	4 women who were referred for genetic counselling
Schover et al., 1998 [28]	Research Qualitative – Face to face semi-structured interview		55 couples undergoing IVF
Zahed et al., 1999[b] [30]	Research Qualitative – Face to face interviews	Various genetic disorders	90 couples with genetic disorders
Pregnancy planning			
Schrander-Stumpel, 1999[a] [40]	Review – Non-systematic	Unspecified	
Wille et al., 2004 [43]	Review – Non-systematic	Unspecified	
Financial aspects			
Bernhardt, 1993 [17]	Research Qualitative – Questionnaire	Cystic fibrosis	216 people who had cystic fibrosis testing performed
Van der Riet et al., 1997 [50]	Mathematical model on costs and benefits of DNA analysis	Cystic fibrosis, Duchenne muscular dystrophy, myotonic dystrophy, fragile X syndrome	
What are the effects of this timing of genetic counselling on the medical-technical aspects of the process?			
Preventive measures			
Fonda-Allen and Mulhauser, 1995 [44]	Case report Descriptive	Various adverse outcome at prenatal diagnosis	6 women who underwent prenatal diagnosis for various reasons
Jack and Culpepper, 1991 [38]	Review – Non–systematic	Unspecified	
Salize et al., 1992 [36]	Research Quantitative – Review of patient records	Phenylketonuria	731 women with phenylketonuria

Table 1 (continued)

Authors and year of publication	Design of the study	Genetic disorder involved	Subjects involved
Performance of prenatal diagnosis			
Garagiola et al., 2003 [45]	Case report Descriptive	Factor VII deficiency	One family with two children who died of factor VII deficiency
Kim et al., 1989[a] [32]	Research Qualitative – Review of delivery records – Patient interviews	Advanced maternal age, chromosomal abnormality in the family, previous child with anomalies	126 women with an indication for prenatal cytogenetic diagnosis
Lea, 1999 [46]	Case report	Retinoblastoma	Pregnant woman, whose husband had had a retinoblastoma
Marfatia et al., 1990[a] [47]	Case report	Cleft lip/palate, Coffin-Lowry syndrome, spina bifida, advanced maternal age	4 women who were referred for genetic counselling
Sutton, 2002 [41]	Review – Non–systematic	Tay-Sachs disease	
Tverskaya et al., 1997 [48]	Case report	Ataxia teleangiectasia	Pregnant woman with a son with ataxia teleangiectasia
Ward, 1991 [49]	Case report	Phenylketonuria, polycystic kidney disease, Duchenne muscular dystrophy	3 pregnant women referred for genetic counselling and prenatal diagnosis
Pregnancy outcome			
Cohn et al., 1996[a] [31]	Research Qualitative – Pedigree information from charts	Advanced maternal age and abnormal maternal serum a-fetoprotein	275 women with advanced maternal age and 103 women with abnormal maternal serum α-fetoprotein
Lane et al., 1997[a] [33]	Research Qualitative – Retrospective review of case notes	Cystic fibrosis	46 families with a second affected child
Langer and Kudart, 1990 [34]	Research Quantitative – Retrospective review of records	Various	1,131 women who were referred for amniocentesis
Van der Riet et al., 1997[a] [50]	Mathematical model on costs and benefits of DNA analysis	Cystic fibrosis, Duchenne dystrophy, myotonic dystrophy, fragile X syndrome	
What are the effects of this timing on the counselling aspects of the process?			
Non-directiveness			
Williams et al., 2002 [29]	Research Qualitative – Individual interviews – Group discussions	Unspecified	70 diverse practitioners (e.g. midwives, gynaecologists, genetic counsellors, psychologists)
Reproductive choices			
Frets and Niermeijer, 1990 [37]	Review – Studies from the last decade on factors influencing reproductive planning after genetic counselling	Unspecified	
Lafayette et al., 1999[b] [24]	Research Qualitative – Self reporting questionnaire	Cystic fibrosis	173 relatives of cystic fibrosis patients
Van der Riet et al., 1997[b] [50]	Mathematical model on the costs and benefits of DNA analysis	Cystic fibrosis, Duchenne dystrophy, myotonic dystrophy, fragile X syndrome	
Schrander-Stumpel, 1999[b] [40]	Review – Non–systematic	Not specified	
Wallerstedt et al., 2003 [42]	Review – Non–systematic	Unspecified	
Wille et al., 2004[a] [43]	Review – Non–systematic	Unspecified	

If available, the genetic disorder and number of people involved are mentioned.
[a] Second time a paper is mentioned. [b] Third time a paper is mentioned.

However, less favourable views have been reported as well. Three papers, which focussed on neurofibromatosis [19] and cystic fibrosis [22, 24], respectively, reported that few people would actually terminate an affected pregnancy. In a group of 55 couples undergoing in vitro fertilization, in which about half had a genetic risk factor other than maternal age, 71% of the couples had no interest in receiving formal genetic counselling and only a minority would undergo amniocentesis or chorion villus sampling. Finally, social cultures differ in their degree of acceptance of genetic and prenatal testing [47, 30]. Zahed et al. [30], for example, found that the main reason for refusal of prenatal diagnosis among at risk couples in Lebanon was the religious conviction against pregnancy termination.

Unplanned pregnancies, the fourth theme, obviously make a referral before pregnancy impossible. The importance of unplanned pregnancies in preconception genetic counselling has been mentioned by Schrander-Stumpel [40] and Wille et al. [43]. In the Netherlands, over 80% of the pregnancies are planned, but in the United States this number is estimated at around 50% and in the United Kingdom at around 65% [40].

Finally, financial aspects might influence the timing of genetic counselling. Bernhardt [17] found that in individuals with a positive family history for cystic fibrosis who were tested in the Mid-Atlantic region of the United States, coverage by health insurances was better during than before pregnancy (93 vs. 52%, respectively).

Medical-Technical Consequences of the Counselling Process during Pregnancy

Fourteen papers were relevant with regard to the medical-technical aspects of counselling, and three different topics could be deduced: 'preventive measures', 'performance of prenatal diagnosis' and 'pregnancy outcome' (table 1).

With respect to preventive measures, Salize et al. [36] found that the treatment of elevated maternal plasma phenylalanine levels in 18 pregnant women with phenylketonuria in order to prevent embryofetopathy was inadequate; in 10 of these women, treatment started after conception or not at all. Jack and Culpepper [38] reviewed several articles which described the negative effect of inadequate treatment of pregnant women with, respectively, phenylketonuria and diabetes mellitus on the health of their children. The importance of adequate dexamethasone treatment in a woman pregnant with a girl affected with 21-hydroxylase deficiency is illustrated by a case report [44]. Had these women been counselled properly before their pregnancies, the treatment would most likely have been better.

Regarding the performance of prenatal diagnosis, several authors describe the problems which can arise if prenatal DNA, cytogenetic or metabolic diagnosis has not been prepared before pregnancy. Technical difficulties arose in these situations [32, 41, 45–49]. Three case reports described situations in which adequate prenatal diagnosis could not be performed at all because of the late timing [32, 46, 47]. In one case report, prenatal testing was not performed because it took too much time to obtain the insurance company's guarantee that they would cover the expensive testing [46].

Clearly, it is important to know whether pregnancy outcome is influenced by a late timing of the consultation. However, only 4 papers addressed this issue. Cohn et al. [31] estimated that of all live-born children, the birth of 0.2% affected children might have been prevented if standard genetic counselling before amniocentesis was performed. In a group of 1,131 pregnant women, however, no diagnosis of a fetal genetic condition was made based on unexpected information obtained from the pedigree in a pre-amniocentesis counselling session [34]. Lane et al. [33] found that not offering prenatal diagnosis during pregnancy led to the birth of a second child with cystic fibrosis in 3% of the families with a prior sibling with cystic fibrosis. By creating a mathematical model on the costs and benefits of DNA diagnosis, Van der Riet et al. [50] showed that DNA diagnosis during pregnancy for different genetic diseases under different circumstances in a high-risk population will lead to a decrease in the number of affected children, which, consequently, results in considerable savings.

All 4 papers assume counselling early in pregnancy. We found no papers about the effect on pregnancy outcome if preconception counselling had been performed. Hence, it remains unclear whether the timing of the counselling before conception would make a difference.

Effects of Pregnancy on the Counselling Aspects of the Process

Seven papers dealt with issues which we consider relevant to the quality of the counselling: 1 paper addressed 'non-directiveness' and 6 papers addressed 'reproductive choices' (see table 1).

Williams et al. [29] argue that the tenet of non-directiveness may be undermined because of a shortage of time and less familiarity with this principle by midwives and obstetricians, who increasingly carry out genetic counselling during pregnancy, instead of specialized genetic workers.

The aim of genetic counselling is to enable reproductive choices. Indeed, several papers describe how preconception counselling affects reproductive decision making. Relatives of cystic fibrosis patients indicated that they would use the information of preconception carrier testing in family planning decisions [24]. Frets and Niermeijer [37] in their review concluded that reproductive planning was determined by whether a risk was interpreted to be high or low, instead of by the actual risk provided during counselling, and by the desire to have children. Wallerstedt et al. [42] point at the importance of interconception counselling after perinatal loss in order to enable parents to 're-establish mental, emotional, physical and spiritual balance in their lives'. Wille et al. [43] and Schrander-Strumpel [40] mention the possibility of alternative reproductive options, like adoption, pre-implantation genetic diagnosis and avoidance of pregnancy, as an advantage of preconception counselling. Finally, Van der Riet et al. [50] predict an increase in the number of couples choosing further offspring, if it is indicated that DNA diagnosis during pregnancy is possible.

Clearly, the aforementioned choices are significantly reduced in case of an already present pregnancy.

Discussion

The aim of our review was to shed more light on possible consequences of the process of genetic counselling for pregnancy. None of the papers retrieved explicitly addressed one of our questions concerning counselees' reasons to attend during pregnancy and the medical-technical and procedural consequences thereof. However, 34 papers were retrieved that did cover issues related to our questions. From these papers the following picture emerges.

Limited knowledge of and alertness towards genetic risk factors, both of practitioners and counselees, and unplanned pregnancies partly explain late referrals. Genetic risks and tests seem to gain relevance for women and health care workers once the women are pregnant. In addition, one research paper [17] illustrates that coverage of the costs of the genetic counselling by health insurances may be better during than before pregnancy. We do not know if these financial aspects are of substantial or only incidental importance in the timing of the referral.

The impact of initiating genetic counselling during pregnancy on medical-technical aspects of the counselling process has clearly not been investigated systematically. Inadequate preventive measures and the inability to perform optimal prenatal diagnosis because of the late timing have been illustrated mainly by a few case reports. We found no figures about the magnitude and implication of these seeming disadvantages of genetic counselling during pregnancy. Most importantly, the consequences for the pregnancy outcome remain unclear. Although there were some estimates about the number of affected children which would be born after inadequate genetic counselling [31, 50], there was only 1 paper which actually assessed outcomes. No additional affected children were observed among a group of 1,131 women, based on unexpected information obtained from the pedigree in a pre-amniotic counselling session [34]. The lack of randomized studies that demonstrate outcomes with diminished morbidity, prevention of mental retardation and reduced costs is surprising, especially since at present preconception care is propagated all over the world.

The consequences of genetic counselling during pregnancy for the quality of this counselling remain unclear. The possible effects of time pressure during pregnancy on, for example, the doctor-patient interaction and the tenet of non-directiveness in genetic counselling have not been studied, as far as we know. Findings on the consequences of genetic counselling for family planning are contradictory, but clearly during pregnancy family planning issues are less relevant.

Overall, our search illustrates that in the medical literature little attention is paid to various aspects of the timing of genetic counselling. It may be that the group of pregnant counselees is too small to attract much attention. Indeed, women who attend genetic counselling in the context of screening, for example because of advanced maternal age or in the light of preconception screening, deserve more attention because of the much larger numbers involved. On the other hand, 10–20% of our total population of around 15,000 people, who attend for genetic counselling in a diagnostic setting, is pregnant, which is still a substantial number of people. Worldwide figures on the percentage of pregnant counselees are lacking, to the best of our knowledge. Regardless of their number, however, this group of counselees, too, deserves adequate and optimal genetic counselling.

Another factor which may account for the limited attention to the timing of counselling is that in general studies addressing the ethical, legal and societal (ELSA) implications of genetic counselling, screening and prenatal diagnosis are scarce, as compared to the total number of publications on applied human genetics [51]. Obviously, priority is given to the 'technical' data in human genetics, instead of the 'quality' data. As a consequence, the

allocation of financial resources to studies addressing the ELSA aspects of human genetics appears to be minimal.

Finally, genetic counselling for a familial genetic condition during pregnancy may be perceived as unavoidable, for example because of the number of unplanned pregnancies. Indeed, most likely there will always be a group of women attending diagnostic genetic counselling for the first time during their pregnancy. However, the implications of this timing for the genetic counselling process deserve attention in order to ensure optimal care for these counselees.

Obviously, we may have missed some data because of our search strategy. Since none of the papers directly addressed our research questions, some misinterpretation as a result of the selection of papers cannot be completely ruled out. In addition, literature focussing on prenatal screening issues may contain relevant aspects, which were not included in our search. However, the scarceness of relatively recent literature related to our questions seems evident, leading us to conclude that so far, little attention has been paid to the causes and consequences of initiating genetic counselling during pregnancy. Hopefully our review will generate interest in researching these quality aspects of genetic counselling in this specific group of counselees, which may be relevant especially in the discussion on the importance of preconception care.

References

1 Leschot NJ, Vjerslev LO: Proceedings of the EUROMIC workshop on prenatal diagnosis. Eur J Hum Genet 1997;5:1–6.
2 Aalfs CM, Mollema ED, Oort FJ, De Haes HCJM, Smets EMA: Genetic counseling for familial conditions during pregnancy: an analysis of patient characteristics. Clin Genet 2004;66:112–121.
3 Clausen H, Brandt NJ, Schwartz M, Skovby F: Psychological and social impact of carrier screening for cystic fibrosis among pregnant woman – a pilot study. Clin Genet 1996;49:200–205.
4 Hartley NE, Scotcher D, Harris H, Williamson P, Wallace A, Craufurd D, Harris R: The uptake and acceptability to patients of cystic fibrosis carrier testing offered in pregnancy by the GP. J Med Genet 1997;34:459–464.
5 Henneman L, Bramsen I, Van der Ploeg HM, Ader HJ, Van der Horst HE, Gille JJ, Ten Kate LP: Participation in preconceptional carrier couple screening: characteristics, attitudes, and knowledge of both partners. J Med Genet 2001;38:695–703.
6 Santalahti P, Aro AR, Hemminki E, Helenius H, Ryynanen M: On what grounds do women participate in prenatal screening? Prenat Diagn 1998;18:153–165.
7 Brisch KH, Munz D, Bemmerer-Mayer K, Terinde R, Kreienberg R, Kachele H: Coping styles of pregnant women after prenatal ultrasound screening for fetal malformation. J Psychosom Res 2003;55:91–97.
8 Cederholm M, Sjoden PO, Axelsson O: Psychological distress before and after prenatal invasive karyotyping. Acta Obstet Gynecol Scand 2001;80:539–545.
9 Gotzmann L, Schonholzer SM, Kolble N, Klaghofer R, Scheuer E, Zimmermann R, Huch R, Buddeberg C: Suspected fetal malformation in ultrasound examination: effects on the psychological well-being of pregnant women (in German, English summary). Ultraschall Med 2002;23:33–40.
10 Goedhuys J, Rethans JJ: On the relationship between the efficiency and the quality of the consultation. A validity study. Fam Pract 2001;18:592–596.
11 Heimler A, Greendale K, Phelps L, Callanan N, Resta R: Workshop: countertransference and the genetic counselor. Birth Defects Orig Artic Ser 1990;26:133–135.
12 Kessler S: 12. The genetic counselor as psychotherapist. Birth Defects Orig Artic Ser 1979;15:187–200.
13 Bartels DM, LeRoy BS, McCarthy P, Caplan AL: Nondirectiveness in genetic counseling: a survey of practitioners. Am J Med Genet 1997;72:172–179.
14 Clarke A: Is non-directive genetic counselling possible? Lancet 1991;338:998–1001.
15 Fineman RM, Walton MT: Should genetic health care providers attempt to influence reproductive outcome using directive counseling techniques? A public health prospective. Women Health 2000;30:39–47.
16 Kessler S: Psychological aspects of genetic counseling. XI. Nondirectiveness revisited. Am J Med Genet 1997;72:164–171.
17 Bernhardt BA: A survey of reimbursement for cystic fibrosis carrier testing. J Genet Couns 1993;2:69–76.
18 Chen EA, Schiffman JF: Attitudes toward genetic counseling and prenatal diagnosis among a group of individuals with physical disabilities. J Genet Couns 2000;9:137–152.
19 Cnossen MH, Smit FJ, Goede-Bolder A, Frets PG, Duivenvoorden HJ, Niermeijer MF: Diagnostic delay in neurofibromatosis type 1. Eur J Pediatr 1997;156:482–487.
20 Gaytant MA, Cikot RJ, Braspenning JC, Grol RP, Merkus JM, Steegers EA: Preconception counseling in family practice; a survey of 100 family physicians (in Dutch, English summary). Ned Tijdschr Geneeskd 1998;142:1206–1210.
21 Jallinoja P, Hakonen A, Aro AR, Niemela P, Hietala M, Lonnqvist J, Peltonen L, Aula P: Attitudes towards genetic testing: analysis of contradictions. Soc Sci Med 1998;46:1367–1374.
22 Janes SR, Rosenfield JM, Wertz DC, Erbe RW: DNA diagnosis of cystic fibrosis: utilization of genetic counseling. Birth Defects Orig Artic Ser 1990;26:254–257.
23 Jayasekara RW: The attitudes of doctors and students towards a genetic service in an Asian country: Sri Lanka. Asia Oceania J Obstet Gynaecol 1989;15:267–270.
24 Lafayette D, Abuelo D, Passero MA, Tantravahi U: Attitudes toward cystic fibrosis carrier and prenatal testing and utilization of carrier testing among relatives of individuals with cystic fibrosis. J Genet Couns 1999;8:17–36.
25 Wilkins-Haug L, Hill L, Schmidt L, Holzman GB, Schulkin J: Genetics in obstetricians' offices: a survey study. Obstet Gynecol 1999;93:642–647.
26 Campbell E, Ross LF: Professional and personal attitudes about access and confidentiality in the genetic testing of children: a pilot study. Genet Test 2003;7:123–130.

27 Gibb D, Hockey S, Brown LJ, Lunt H: Attitudes and knowledge regarding contraception and prepregnancy counselling in insulin dependent diabetes. NZ Med J 1994;107: 484–486.
28 Schover LR, Thomas AJ, Falcone T, Attaran M, Goldberg J: Attitudes about genetic risk of couples undergoing in-vitro fertilization. Hum Reprod 1998;13:862–866.
29 Williams C, Alderson P, Farsides B: Is nondirectiveness possible within the context of antenatal screening and testing? Soc Sci Med 2002;54:339–347.
30 Zahed L, Nabulsi M, Bou-Ghanim M, Usta I: Acceptance of prenatal diagnosis for genetic disorders in Lebanon. Prenat Diagn 1999;19: 1109–1112.
31 Cohn GM, Gould M, Miller RC, Habecker-Green J, Macri CJ, Gimovsky ML: The importance of genetic counseling before amniocentesis. J Perinatol 1996;16:352–357.
32 Kim SK, Kim IK, Kim CK, Yang YH, Park TK, Kim KY: The effect of genetic counseling on performance of prenatal cytogenetic diagnosis. Yonsei Med J 1989;30:16–22.
33 Lane B, Williamson P, Dodge JA, Harris H, Super M, Harris R: Confidential inquiry into families with two siblings with cystic fibrosis. Arch Dis Child 1997;77:501–503.
34 Langer A, Kudart E: Construction of a family pedigree in genetic counseling before amniocentesis. J Reprod Med 1990;35:715–718.
35 Meschede D, Albersmann S, Horst J: The practical importance of pedigree analysis in women considering invasive prenatal diagnosis for advanced maternal age or abnormal serum screening tests. Prenat Diagn 2000; 20:865–869.
36 Salize HJ, Funders-Bucker B, Knorrek U, Kolbe S, Pietsch V, Seidlitz G, Ullrich K, Trefz FK: Maternal phenylketonuria: problems in detecting and risk educating identified females. Monatsschr Kinderheilkd 1992;140: 42–46.
37 Frets PG, Niermeijer MF: Reproductive planning after genetic counselling: a perspective from the last decade. Clin Genet 1990;38:295–306.
38 Jack BW, Culpepper L: Preconception care. J Fam Pract 1991;32:306–315.
39 Lubin MB, Lin HJ, Vadheim CM, Rotter JI: Genetics of common diseases of adulthood. Implications for prenatal counseling and diagnosis. Clin Perinatol 1990;17:889–910.
40 Schrander-Stumpel C: Preconception care: challenge of the new millennium? Am J Med Genet 1999;9:58–61.
41 Sutton VR: Tay-Sachs disease screening and counseling families at risk for metabolic disease. Obstet Gynecol Clin North Am 2002; 29:287–296.
42 Wallerstedt C, Lilley M, Baldwin K: Interconceptional counseling after perinatal and infant loss. J Obstet Gynecol Neonatal Nurs 2003;32:533–542.
43 Wille MC, Weitz B, Kerper P, Frazier S: Advances in preconception genetic counseling. J Perinat Neonatal Nurs 2004;18:28–40.
44 Fonda-Allen JS, Mulhauser LC: Genetic counseling after abnormal prenatal diagnosis: facilitating coping in families who continue their pregnancies. J Genet Couns 1995; 4:251–265.
45 Garagiola I, Palla R, Peyvandi F: Pitfalls in molecular diagnosis in a family with severe factor VII (FVII) deficiency – misdiagnosis by direct sequence analysis using a PCR product. Prenat Diagn 2003;23:731–734.
46 Lea DH: Client advocacy and collaboration with insurance and laboratory testing agencies: a case study illustrating genetic counselor roles. J Genet Couns 1999;8:175–181.
47 Marfatia L, Punales-Morejon D, Rapp R: Counseling the underserved: when an old reproductive technology becomes a new reproductive technology. Birth Defects Orig Artic Ser 1990;26:109–126.
48 Tverskaya SM, Dadali EL, Evgrafov OV: Prenatal DNA diagnosis on demand – a possible new approach to DNA service provision. Prenat Diagn 1997;17:989–990.
49 Ward PA: Applications of molecular genetics technology for prenatal diagnosis of genetic disease. Clin Lab Sci 1991;4:287–290.
50 Van der Riet AA, Van Hout BA, Rutten FF: Cost effectiveness of DNA diagnosis for four monogenic diseases. J Med Genet 1997;34: 741–745.
51 Lippman A: Research studies in applied human genetics: a quantitative analysis and critical review of recent literature. Am J Med Genet 1991;41:105–111.