Attitudes of health care professionals toward carrier screening for cystic fibrosis. A review of the literature

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Received: 1 February 2012 / Accepted: 12 December 2012 / Published online: 29 December 2012
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Abstract Recent technological developments in molecular genetics facilitate the large-scale detection of inherited genetic disorders and allow an increasing number of genetic conditions to be screened for (American College of Medical Genetics 2012). This technological evolution creates the background which makes reflection necessary about the desirability to offer community-based (preconception) carrier screening in the healthcare system. A positive attitude of potential providers is vital to the success of a screening program. Therefore, the objective of this article is to elaborate a review of the attitudes of healthcare professionals toward carrier screening. Examination of existing carrier screening programs could provide such information. The literature review will be focused on the attitudes toward carrier screening for cystic fibrosis (CF). The databases Pubmed and Web of Science, as well as the interface Google Scholar, were searched using the keywords for the period 1990–2011. Studies were selected if they were published in a peer-reviewed journal in English and described the attitudes of potential providers toward carrier screening. Eleven studies were retrieved describing the attitudes toward carrier screening for CF. In total, seven studies reported attitudes toward the best time for carrier screening; four studies described opinions toward the best setting to offer CF carrier screening; six studies investigated the

willingness to be involved in a carrier screening program, and in total 11 articles reported the concerns about offering carrier screening. Ten papers described a general attitude toward carrier screening. We can conclude that health care providers state willingness to be involved in a carrier screening program, but there is need for appropriate education as well as adequate support given the time constraints already present in consultation. The prospect of an increasing number of genetic disorders for which screening becomes possible, and the potential increasing demand for such screening in the future calls for the need for further debate on the desirability of carrier screening and relevant questions such as the conditions screened, the providers involved, the information provision, and counseling.

Keywords Carrier · Screening · Genetic · Testing · Attitude

Introduction

Knowledge of carrier status enables prospective parents to make informed reproductive choices. Two approaches of the identification of carriers exist: carrier testing and carrier screening. Carrier screening is defined as the detection of carrier persons who do not have an a priori increased risk for being a carrier of a certain disease, whereas carrier testing is aimed at persons who have a higher a priori risk based on their personal or family history (Castellani et al. 2010).

The most common settings for genetic screening are the newborn period and the reproductive setting (preconception and prenatal screening). Preconception care has been recognized as a crucial component of health care for women of reproductive age. The main goal of preconception care has been defined as to “provide health promotion, screening, and interventions for women of reproductive age to reduce risk factors that might affect future pregnancies” (Johnson et al.

For special issue "Predictive Genetic Testing, Risk Communication and Risk Perception"

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2006). As part of preconception care, various associations (American College of Obstetricians and Gynecologists (ACOG) Committee ACOG The American College of Obstetricians and Gynecologists 2011; Human Genetics Commission 2011) have recommended that preconception screening for some heritable disorders should be offered to couples planning a pregnancy. Based on this information, couples can get more information about their risk of having a child born with a certain autosomal recessive or X-linked disorder. As the Human Genetics Commission has pointed out, “there are good reasons why earlier testing is favored over later testing, as it facilitates wider patient choice and improved access to information supporting reproductive decision making” (Human Genetics Commission 2011). These options include prenatal diagnosis (followed or not by abortion), accepting the risk, refraining from having children, adoption, gamete donation, or pre-implantation genetic diagnosis. In contrast to most screening programs (where the aim is reducing morbidity or mortality from disease by detecting diseases in their earliest stages), the goal of preconception carrier screening is informed reproductive decision making. Unlike preconception carrier screening, prenatal carrier screening leaves only a limited number of reproductive options open for carrier couples and may impose time constraints when decisions about prenatal diagnosis have to be made (Raeburn 1994). However, studies have demonstrated a greater uptake of screening during pregnancy because this target group is highly receptive to the idea of screening and easy to reach and because most women contact their general practitioner or visit an antenatal clinic (Levenkron et al. 1997; Loader et al. 1996; Witt et al. 1996).

Beside the offer of carrier testing to individuals at an increased risk of being carrier of a certain disease because of a personal or family history of this condition, recommendations have been made to offer carrier screening in couples without family history of certain heritable disorders. For example, guidelines in favor of carrier screening for CF were developed by the American College of Medical genetics (ACMG) and the American College of Obstetricians and Gynecologists (ACOG) (ACOG Committee ACOG The American College of Obstetricians and Gynecologists 2005, ACOG The American College of Obstetricians and Gynecologists 2011; Grody et al. 2001). CF is the most common severe (life-limiting) autosomal recessive disorder in Caucasians affecting 1 in 2,500–4,000 live births (Rommens et al. 1989).

In different countries, various carrier screening program pilot studies for CF and/or hemoglobinopathies have been elaborated (Axworthy et al. 1996; Bekker et al. 1994; Bekker et al. 1993; Bruni et al. 2012; Giordano et al. 2006; Henneman et al. 2001; Henneman et al. 2003; Lakeman et al. 2008, 2009; Payne et al. 1997). In general, the majority of those invited to participate in a preconception carrier screening showed positive attitudes toward offering this kind of screening and positive

intentions to participate in carrier screening for both disorders (Lakeman et al. 2009). However, apart from some specific regions (e.g., thalassemia carrier screening in Cyprus and Sardinia (Angastiniotis et al. 1988; Angastiniotis and Hadjiminis 1981) and specific communities (e.g., carrier screening for Ashkenazi Jews (Childs et al. 1976), carrier screening programs for the entire population or for couples planning a pregnancy have hardly been implemented. At this moment, carrier testing for disorders such as CF and/or hemoglobinopathies is often restricted to families of patients with these conditions and to the partners of patients and carriers. Most carriers remain undiagnosed in this situation because they are healthy and most often do not have knowledge of any relatives with the conditions screened for (Lakeman et al. 2006).

Recent technological developments in molecular genetics facilitate the large-scale detection of inherited genetic disorders and allow an increasing number of genetic conditions to be screened for (American College of Medical Genetics ACMG The American College of Medical Genetics 2012). Bell et al. report that it is technical feasible to undertake a comprehensive preconception carrier screening for 448 recessive childhood diseases, although it would be necessary to establish a reference disease mutation database (Bell et al. 2011). This will not only create a huge bioinformatics costs but will require time-consuming individual genetic counseling for a large number of people (Bell et al. 2011; Jackson and Pyeritz 2011). Moreover, commercial companies have started to offer preconceptional carrier tests directly to consumers. Although DTC genetic testing has mainly remained focused on the commercial offer of individual risk assessments for common disorders and nutrigenomic tests (Howard 2008), more and more companies also started to sell carrier tests for autosomal recessive or X-linked disorders (Borry et al. 2011). This created concerns about the current offer of preconception carrier tests through online commercial companies, especially with regard to the provision of information, the implications for the informed consent, the lack of medical supervision, and the impact on the healthcare system (Borry et al. 2011).

In this perspective, it is important to understand better why healthcare systems have failed to implement preconception carrier screening programs. Researchers have referred to concerns related to the psychosocial impact of carrier test results (Axworthy et al. 1996), stigmatisation (McQueen 2002), coercion, or medicalization (Verweij 2008). However, the lack of implementation of preconception carrier screening programs might also be linked to pragmatic considerations, such as the difficulty to reach couples before conception (Lakeman et al. 2009) or provider-related barriers (Morgan et al. 2004). Therefore, the objective of this article is to elaborate a review of the attitudes of healthcare professionals toward carrier screening. Although public policy with respect to carrier screening ought not to be based solely on the opinions of

relevant physicians and genetics professionals, it would be imprudent to proceed with a policy of widespread screening in the absence of professional support. A positive attitude of potential providers is vital to the success of a preconception screening program. In contrast, an important barrier for implementation of a screening program might be a negative attitude of potential providers toward such screening. A review of healthcare professionals' views toward carrier screening might bring clarity in general attitudes of healthcare professionals toward carrier screening, their views on the best timing and most appropriate setting, their willingness to be involved, as well as their concerns and perceived barriers toward implementation of a preconception carrier screening program. Because carrier screening for CF has already been studied extensively and is likely to provide a model for screening for other conditions if implemented, we decided to limit the scope of this review to studies focused on the attitudes toward carrier screening for CF.

Method

Data sources

We searched the databases Pubmed and Web of Science, as well as the interface Google Scholar, using one of the following keywords (attitude*, view*, survey, questionnaire, response*, opinion*, belief*, perspective*, reasoning, “focus group”, conviction*, idea*, emotion*, thought*, feeling*) in combination with the terms carrier, screening, or genetic. Relevant references within an article were also consulted. The search was limited to the period 1990–2011.

Study selection

The search in Pubmed (in title and abstract), Web of science (in title), and Google scholar (in title), using all of the above-mentioned search terms, revealed in total 6,288, 789, and 887 articles, respectively. Titles and abstracts of papers identified by the electronic searches were screened by SJ. Studies were included if they were published in a peer-reviewed journal in English and reported the attitudes of health care professionals toward carrier screening on a population based perspective. Qualitative as well as quantitative studies were included. Eighty-nine were selected, of which full-text copies were screened and reviewed. Ultimately, only 14 papers were retrieved that reported about the attitudes of healthcare professionals toward cystic fibrosis carrier screening (Table 1) (Fig. 1; Moher et al. 2009). Two papers of Poppelaars et al. (2004, 2003a) describe results of one study, as well as the papers of Boulton et al. (1996, 1995). Also, Rowley et al. (1993) and Loader et al. (1996) render the results of the same study.

Data extraction and synthesis

As there is considerable heterogeneity in populations studies and measures used, it would be inappropriate to pool the data in a meta-analysis. The data are presented here in a summary form.

Results

The results are presented in relation to following questions: General attitudes toward carrier screening (ten papers); attitude toward the best time for carrier screening (target population) (seven papers); attitudes about the appropriate setting toward carrier screening (four papers); willingness to be involved in carrier screening programs (six papers); and concerns about offering carrier screening (11 papers).

General attitudes toward carrier screening

In general, various respondents in the studies reported held positive attitudes toward carrier screening for CF. However, also critical positions could be observed.

In the studies of Watson et al. (1991), Boulton and Williamson (1995), and Mennie et al. (1998) general practitioners (and family planning clinic staff) held essentially positive attitudes toward CF carrier screening. However, when prioritizing screening programs, only 2 % rated CF screening as most important in relation to four other screening programs with over half rating it as least important (Mennie et al. 1998).

Rowley et al. (1993) reported that at least two thirds somewhat or strongly agreed that screening should be offered to all women of reproductive age, if screening is free. However, many providers withdrew from the study because of the anticipated time commitment. At the end of the trial in which CF carrier screening was offered to female patients of reproductive age, Loader et al. (1996) re-evaluated the attitudes of those professionals who actually submitted samples. Obstetrician gynecologists who submitted samples had a significantly more favorable attitude toward CF carrier screening for all women of reproductive age than they had at the information session explaining the project.

We retrieved three papers in which participants generally had a positive attitude toward preconception CF carrier screening but were more reserved when considering routinely offering screening (Baars et al. 2004; Faden et al. 1994; McClaren et al. 2008). Specialties most involved in provision of genetic services (genetic counselors, obstetricians, medical geneticists, and family physicians that practice obstetrics) most opposed to the routine use of the available test, but they were most supportive of the routine use of an error-free test (Faden et al. 1994). The results from the survey of Baars et al.

Table 1 Location, methods, sample size, response rate, measures, results, and limitations of studies assessing the attitude toward carrier screening for cystic fibrosis (CF)

Authors and year	Location	Methods	Sample size	Response rate (RR)	Measures	Results	Limitations
Watson et al. (1991)	North Thames (West) Region, UK	Questionnaires were sent to all GPs in two districts and FPCS in three districts	All GPs and FPCS in the selected districts	227 (52 %), 178 GPs and 49 FPCS (GPs and nurses)	Attitude toward CF carrier screening, the best time to offer screening; competence to counsel; willingness to participate in pilot studies	About 75 % thought that introduction of CF carrier screening was appropriate, less than 10 % opposed. No agreement as to the best time to screen. 70 % GPs and 57 % FPCS felt competent to counsel. 50 % GPs and 76 % FPCS were willing to participate in pilot studies.	High proportion of GPs who did not respond to the questionnaire
Rowley et al. (1993)	Rochester, NY, US	Questionnaires were given to attendees at the information session of a trial to offer CF carrier screening to all their female patients of reproductive age, pregnant or not, if testing and genetic counseling are for free, hold at obstetrical staffs of all five Rochester hospitals having obstetric services	124 prenatal care providers (111 OBs and 13 family practitioners)	81/124 (65 %) attended information session and completed questionnaire; 79/124 (63 %) fulfilled attitude questionnaire; 68/79 (86 %) were willing to participate in the trial	Attitude toward CF carrier screening of all women of reproductive age; willingness to participate in the trial; knowledge about CF	At least two third agreed that, if CF carrier screening is for free, it should be offered to all women of reproductive age, pregnant or not. Of those completing the attitude questionnaire 86 % was willing to offer screening to all their patients if testing and all related activities were for free. Familiarity and knowledge of CF was a concern. The imperfect test sensitivity was not mentioned as a matter of concern.	
Loader et al. (1996)	Rochester, NY, US	Providers, willing to participate in the trial to offer CF carrier screening to all female patients of reproductive age, if testing and genetic counseling are for free, that had submitted samples, were interviewed at the end of the study	Prenatal care providers (OBs)	See Rowley et al. (1993) 37/68 prenatal care providers willing to offer testing, actually submitted patient samples	Attitude toward CF carrier screening of all women of reproductive age; sample characteristics	Attitudes of providers agreeing to participate in the trial differed from those not agreeing to participate in several ways. The providers who submitted samples had a significantly more favorable attitude toward CF carrier screening for all women of reproductive age than they had at the trial's inception.	If a charge had been made for testing or for genetic counseling of all carriers, participation likely would have been lower
Faden et al. (1994)	US	Questionnaires. PCPs and psychiatrists were selected from the American Medical Association Physician Masterfile from 10 states. For comparison medical	1795 PCPs (358 family physicians, 360 internists, 360 OBGYNs, 359 PEDs) and 358 psychiatrists. Comparison: 180 medical geneticists	PCPs and psychiatrists, 64.8 % (from 61 % for OBGYNs to 72.6 % for PEDs) Medical geneticists and genetic counselors: 79.1 %	Attitude toward preconception CF carrier screening under 3 conditions: actively offering a hypothetical error-free test, offering a CF test available	Although 92 % of respondents believed that a couple asking about a test that detected 80 % of carriers should be tested, only 43.9 % believed such test should be offered	

Table 1 (continued)

Authors and year	Location	Methods	Sample size	Response rate (RR)	Measures	Results	Limitations
		geneticists and genetic counselors in the same states were selected from the American Board of Medical Geneticists	and 180 genetic counselors		(80 % sensitivity) on individual or routine basis; perceived variables associated with that attitude; knowledge about CF; sample characteristics	routinely. The majority in all specialties favored routine offering of the error-free test. Knowledge of CF was associated with favoring an error-free test. Specialists predominantly concerned with the provision of genetic services were most opposed against routine screening, the main concern against routine screening was that the available test archived only an 80 % detection rate. 'High perceived risk' and innovativeness were associated with being in favor of routine CF carrier screening.	
Boulton and Williamson (1995)	North Thames (West) Region, UK	Questionnaires were sent to all GPs of four areas. A list of GPs was obtained from the Family Health Service Authority	616 GPs of which 602 were eligible	388/602 (64 %)	Attitude toward CF carrier screening; willingness to provide CF carrier screening; knowledge about CF; sample characteristics	Majority supported community carrier identifying carrier couples prior to conception was important and 84 % felt that identifying pregnant women at risk was important to offer prenatal diagnosis. 45 % said to be willing to provide carrier screening, only 15 % did not. Majority had limited understanding of epidemiology and population genetics of CF.	Underrepresentation (12 %) of single-handed practices and overrepresentation of female respondents
Boulton et al. (1996)	North Thames (West) Region, UK	Questionnaires were sent to all GPs of four areas. A list of GPs was obtained from the Family Health Service Authority	616 GPs of which 602 were eligible	388/602 (64 %)	Attitude toward CF carrier screening; the best time to screen, the best setting to offer screening; willingness to provide CF carrier screening; sample characteristics;	About two third had a positive attitude toward CF carrier screening. When a close relative has been diagnosed (65 %) and when seeking family planning (63 %) were seen as the best times to screen. General practice was believed to be an appropriate place (67 %) to offer screening. 45 % said to be willing to	Underrepresentation (12 %) of single-handed practices and overrepresentation of female respondents

Table 1 (continued)

Authors and year	Location	Methods	Sample size	Response rate (RR)	Measures	Results	Limitations
Mennie et al. (1998)	Lothian Health Board area, UK	Questionnaires were sent to GPs. The list of fundholding GPs was taken from the NHS in Scotland Directory (1996)	532 GPs	361/532 (68 %) responded of which 25 declined, leaving 334/532 (63 %)	Attitude toward CF carrier screening; the best time to offer screening; the best setting to offer screening; willingness to provide CF carrier screening; sample characteristics	provide screening, only 15 % did not. 87 % supported the concept of CF carrier screening, only 3 % opposed. However 55 % gave it the lowest priority when ranking it with other screening programs. Only 13 % thought it right to offer screening to those without family history. Antenatal clinics, GP surgeries, family planning clinics and genetic clinics were preferred screening sites. Most were in favor to be involved in a screening program, yet would need support. Only 23 % had no experience with CF and 77 % were aware of the existing screening program.	
Poppelaars et al. (2003)	The Netherlands	Questionnaires were sent to GPs and MHS workers. GPs were selected by the Netherlands Institute of Primary Care Research and MHS workers were selected by inquiry with the directors of all 45 MHS in The Netherlands	200 GPs of which 197 eligible and 134 MHS workers	GPs: 102/197 (52 %) MHS workers: 113/134 (84 %)	Attitude toward preconception CF carrier screening; the best setting to offer screening; screening strategies; concerns to offer screening; competence to provide screening; sample characteristics	55 % GPs and 73 % MHS workers favored routine offering of preconception CF carrier screening. Preferred methods to inform the target population were by leaflets, during GP consultation and sending personal invitation letters. 74 % GPs believed they were able to counsel carrier couples. Perceived obstacles were high workload, costs and absence of a preconception care setting.	Modest response rate of GPs. Focus on health care providers in The Netherlands
Poppelaars et al. (2003)	The Netherlands	Sessions were held with 2 focus groups of potential providers of screening (GPs and MHS workers). Sessions were tape-recorded. At the end	13 GPs and 9 MHS workers		Attitude toward preconception CF carrier screening; the best setting to offer screening; concerns to offer screening; willingness to provide	In general there was a positive attitude toward CF carrier screening. Most participants in both care provider groups were willing to contribute to the preconception CF carrier	Sampling method: for care-providers having time to participate in the study, lack of time may be a less important barrier, however CME accreditation was

Table 1 (continued)

Authors and year	Location	Methods	Sample size	Response rate (RR)	Measures	Results	Limitations
		participants completed a questionnaire			CF carrier screening; sample characteristics	screening, but lack the time and relevant knowledge. Barriers in implementation include absence of a preconception care setting, problem to reach the target population, heavy workload of GPs and limited knowledge about CF in general population.	provided. Focus on Dutch health care providers
Poppelaars et al. (2004)	The Netherlands	Questionnaires starting with information about CF and the CF carrier test were sent to GPs and MHS workers. GPs and MHS workers were analysed together as appeared that type of care provider was not an important predictor of attitude	200 GPs (197, 3 excluded) and 134 MHS workers	GPs: 102/197 (52 %) MHS workers: 113/134 (84 %)	Attitude toward preconception CF carrier screening and perceived variables associates with that attitude; sample characteristics	55 % GPs and 73 % MHS workers favored routine offering of preconception CF carrier screening. 89 % GPs and 83 % MHS workers were in favor of informing the target population about the possibility of having a CF carrier test. The strongest association with a positive attitude was found for perceived severity for CF, perceived lower barriers, high perceived test sensitivity and religion (reformed providers more opposed).	
Baars et al. (2004)	The Netherlands	Questionnaire developed by the American researchers (Faden et al. 1994) was adapted to the Dutch health care situation. GPs were selected by the Netherlands Institute of Health Services research, obstetricians by a random sample of the Dutch Society of Obstetrics and Gynecology, PEDs were active members of The Netherlands Pediatric Association	200 (195, 5 excluded) GPs, 300 (285, 15 excluded) GYNs and 265 (247, 18 excluded) PEDs	GPs: 124/195 (64 %), GYNs: 198/285 (69 %), PEDs: 177/247 (72 %)	Attitude toward preconception CF carrier screening under 3 conditions: actively offering a hypothetical error-free test, offering a CF test available (95 % sensitivity) on individual or routine basis; perceived variables associated with that attitude; sample characteristics	63 % GPs, 69 % GYNs and 72 % PEDs supported preconception carrier screening for CF if a couple request the test. 16 %, 19 % and 25 % respectively were in favor of actively offering a test with 95 % sensitivity to all couples planning a pregnancy. A positive opinion toward routine CF carrier screening was associated with 'high perceived risk of having a child with CF' (GYNs), considering test sensitivity less important (GPs, GYNs), 'providing genetic counseling in own practice'	

Table 1 (continued)

Authors and year	Location	Methods	Sample size	Response rate (RR)	Measures	Results	Limitations
Morgan et al. (2004)	US, Puerto Rico, Canada	Questionnaires were sent to members of the ACOG. Except for demographics, statistical analysis was limited to those whose primary specialty was gynecology (GYNs only) or Obstetrics and gynecology (OBGYNs)	1165 ACOG fellows (1,143, 22 excluded)	731/1143 (64 %) 632/731 respondents were GYNs only (85) or OBGYNs (547)	Practice patterns regarding CF screening in pregnant and non pregnant women; opinions/concerns about CF carrier screening; sample characteristics	(PEDs) and 'reassurance when both partners test negative' (PEDs) were correlated with a positive opinion toward routinely use. Almost half of the physicians never specifically asked non pregnant patients about family history of CF (45.3 %) or routinely provided them with info regarding CF and CF screening (46.5 %). Concerning pregnant patients the vast majority asked about family history of CF (88.7 %) and provided information of screening (86.6 %). 65.8 % offered screening to all pregnant patients, only 2.2 % never did. For those screening only in specific situations patient request followed by family history were the most frequently selected options. Concerns were the liability from not offering screening, the ability to interpret a positive screening test and familiarity with CF.	
McClaren et al. (2008)	Victoria, Australia	Open-ended questions were used in semi-structured focus groups. Potential providers were selected from telephone directory listing practices in local metropolitan Melbourne area. In addition staff at the Royal Children's Hospital was invited to participate. Victorian health professionals involved in CF care attending the sixth Australian and New	12 health professionals: 2 GPs, 2 OBs, 2 midwives, 4 physiotherapists, 1 social worker, 1 genetic counselor		Attitude toward CF carrier screening: the best time to offer screening; the best setting for screening; concerns to offer screening	Participants were in agreement that CF carrier screening should be made available to everyone. The best time for screening was considered to be the one individually chosen by the persons to be screened. An information brochure was seen as useful. Potential psychological harms to patients and time constraints negatively influenced the willingness	

Table 1 (continued)

Authors and year	Location	Methods	Sample size	Response rate (RR)	Measures	Results	Limitations
Darcy et al. (2011)	US	Zealand CF conference in 2005 were also invited. Questionnaires were mailed to obstetricians, perinatologists and those offering equivalent services (such as GPs). Email list was purchased from Lakeshore Media group, in addition 130 addresses were obtained from affiliations with local hospitals	2044 obstetricians, perinatologists and their equivalent (such as GPs who provide obstetric services)	156/2,044 (7.6 %)143/156 completing all questions	Awareness of ACOG guidelines for CF carrier screening; knowledge of CF; concerns to offer screening; sample characteristics	to offer CF carrier screening. 88.2 % of obstetricians offer CF carrier screening according the ACOG guidelines. 12.3 % were not aware of the guidelines. Mainstream were knowledgeable about CF and considered themselves capable to interpret and explain screening results, however 17.7 % did not have these skills. There is room for education, especially for non-academic working physicians.	Potential non-response bias due to low RR

FPSCS family planning clinic staff; *GPs* general practitioners; *PCPs* primary care physicians; *GYNs* gynecologists; *OBs* obstetricians; *OBGYNs* obstetrician-gynecologists; *PEDs* pediatricians; *MHS* Municipal Health Service; *ACOG* American College of Obstetricians and Gynecologists

(2004) were in line with the findings among physicians in the US; however, physicians in The Netherlands are less in favor of preconception CF carrier screening in all situations. Overall, only 16 % of the general practitioners were in favor of routinely offering CF carrier screening to all couples planning a pregnancy with the available test.

This is in contrast with the findings of Poppelaars et al. (2003a), who reported that 55 % of the Dutch general practitioners and 73 % of the Municipal Health Service workers favored routinely offering carrier screening to couples planning a pregnancy. The proportion of general practitioners (89 %) and Municipal Health service workers (83 %) in favor of informing the target population about the possibility of having a carrier test for CF was even higher (Poppelaars et al. 2004). In the focus group study of Poppelaars et al. (2003b), respect of the autonomy of the individual was mentioned as the main reason for offering screening by some of the participants.

Attitude toward the best time for carrier screening (target population)

The surveys from the UK (Boulton et al. 1996; Mennie et al. 1998; Watson et al. 1991) showed little support for screening during pregnancy, although at the time the studies were performed, community carrier screening was most commonly conducted that way (Boulton et al. 1996). In the survey of Watson et al. (1991), only 3 % supported screening during pregnancy. Seeking advice before pregnancy was supported by Boulton et al. (1996) (63 %) and Mennie et al. (78 %) (1998). In the study of Boulton et al., only few respondents saw pregnancy as an appropriate time for screening. Moreover, in the study of Mennie et al. (1998), only 13 % thought that screening should be offered to those with a negative family history.

In the study of McClaren et al. (2008) (Australia), a variety of settings that provide an opportunity for people to make a personal choice about screening when they felt they were ready was considered most appropriate. Screening prior to pregnancy was supported given at that time maximum reproductive choices are available, and there is no time constraint. Screening during pregnancy was said to be too late; however, they felt it was the most practical time. Also, in the paper of Rowley et al. (1993) (US), some were more resistant to offering screening to non-pregnant patients, not because they believe timing is less appropriate but because non-pregnant patients are more difficult to reach.

Four studies specifically investigated the attitude toward carrier screening for CF in the preconception period (Baars et al. 2004; Faden et al. 1994; Poppelaars et al. 2003a, b, 2004). Faden et al. (US) (1994) and Baars et al. (The Netherlands) (2004) investigated physician's opinions regarding offering CF carrier testing under three different

Fig. 1 Study selection: flow diagram adapted from PRISMA (Moher et al. 2009)

conditions: a hypothetical error-free test, a carrier test with current sensitivity at that time on an individual basis and on a routine basis. Overall, there was more support offering testing if couples request the test themselves (test with current sensitivity on an individual basis).

Attitudes about the appropriate setting (place) to offer carrier screening

We retrieved only a few studies describing opinions regarding the appropriate setting to offer carrier screening for CF. In two studies conducted among general practitioners (and

family planning clinic staff) in the UK (Boulton et al. 1996; Mennie et al. 1998), general practice was a preferred screening site; schools and workplace were less favored. In the paper of Mennie et al. (1998), antenatal clinics (65 %), family planning clinics (61 %), and genetic clinics (54 %) were also found an appropriate place, unlike the study of Boulton et al. (1996) where these locations enjoyed less preference. In the survey of Watson et al. (1991), there was equal support for screening at school, at birth, before marriage/family planning. In the focus group study of Poppelaars et al. (2003b), some participants suggested testing school children of 16 years would result in a high uptake rate as was stated by some in the study of McClaren et al. (2008) that screening at high school would enable population to be reached en masse.

In the survey of Poppelaars et al. (2003a), most providers thought that the target population should be informed by means of leaflets and/or during a general practitioner's consultation if couples seek advice before pregnancy. Forty percent of the general practitioners and 58 % of the municipal health service workers considered the general practitioner the most appropriate person to offer pre-test counseling. A preconception consultation setting to provide pre-test counseling was another possibility mentioned by more than 30 % of the participants. In the focus group study from Poppelaars et al. (2003b), such a standard general preconception consultation was also suggested. There was no consensus whether such setting should be the general practice or a new preconception consultation center.

Screening test and screening strategy

Faden et al. (1994) found that despite 92 % of respondents agreeing that a couple inquiring about availability of a CF carrier at that time (80 % sensitivity) should be tested, less than half (43.9 %) thought that the available test should be offered routinely to all couples planning a pregnancy. Majority in all specialty groups (75.9 %) favored offering a hypothetical inexpensive error-free test to all couples. The most important influencing factor against routine testing was the consequences of the 80 % detection rate. This would result in an increase on reported risk for couples in which one of the two is identified as a carrier: the so-called "one carrier couple" problem.

In the study of Baars et al. (2004), about two thirds of participants (general practitioners, pediatricians, and gynecologists) supported preconception CF carrier screening (95 % sensitivity) in couples requesting for a test. Only about one third supported routinely offering the hypothetical error-free test; even less supported routinely offering the available test with lower sensitivity (95 %). "Considering the test sensitivity less important" was associated with a positive opinion toward routinely offering preconception

CF carrier screening. Overall, despite test sensitivity had increased over the years, physicians in The Netherlands were less in favor of preconception carrier screening than physicians in the UK.

Although in the study of Poppelaars et al. (2003a) there was great variability among providers in terms of opinions about the different screening strategies (single sampling, sequential testing/double sampling, sequential testing/double testing, double testing), majority (46 % GPs and 52 % MHS workers) were in favor of the double sampling, double testing method. Reasons in favor of this screening strategy were changing relationships, possibility of informing relatives, no differentiation between partners, and the right of both partners to know.

A positive family history was the most important reason to offer carrier screening in the study of (65 %) Boulton et al. (1996) and Mennie et al. (88 %) (1998). Testing of family members after identification of an affected individual or CF carrier is called cascade testing.

Willingness to be involved in carrier screening programs

In total, seven studies discussed the willingness to provide screening and/or willingness to perform counseling. Watson et al. (1991) found that at least half (50 % of general practitioners and 76 % of the family planning clinic staff) were willing to participate in pilot studies. Equally, Boulton et al. (1996) found that nearly half of the participants were prepared to offer screening. The study of Mennie et al. (1998) showed that most general practitioners favored being involved in CF carrier screening; however, they indicated that support would be necessary for each of the screening activities, and only 28 % expressed interest in participating in a pilot trial of CF carrier screening. Also, Poppelaars et al. (2003a) reported that half of the general practitioners thought that all of the carrier screening activities could be carried out in their practice. In the focus group study conducted by Poppelaars et al. (2003b), most Municipal Health Service workers were willing to inform the population, invite, coordinate, and organize the screening. On the other hand, many providers (40 % general practitioners and 33 % of Municipal Health Care Service workers) felt that it was not their task to offer preconception carrier screening.

In the pilot study of Rowley et al. (1993), nearly half of the potential providers would not offer screening, 35 % (56/124) did not attend the explanation of the trial, and of those who attended, 86 % (68/79) were willing to participate the trial. Finally, after visiting the practices agreeing to participate, further explaining the project, many providers withdrew, leaving only 47 % (37/79) submitting samples (Loader et al. 1996).

Concerns and barriers toward offering carrier screening

The three major concerns reported in most studies are the time commitment, the need for education for possible providers, as

well as the possible psychological consequences for carriers. McClaren et al. (2008) reported that offering CF carrier screening was perceived as a burden given the time constraints already present in consultations. Also in the study of Poppelaars et al. (2003a), high workload was an expected obstacle for 82 % of general practitioners and 54 % of the Municipal Health Workers. In the focus group study of Poppelaars et al. (2003b), general practitioners mentioned lack of time as an important barrier with regard to pre-test counseling. Even when genetic counseling and educational materials were provided without charge, the major concern to participate in a CF carrier trial was the anticipated time commitment (Rowley et al. 1993). In contrast, Morgan et al. (2004) reported unreimbursed time spent on patient education for CF screening among the lowest concern ratings.

Boulton et al. (1996) noticed that the majority of general practitioners had limited understanding of the epidemiology of CF pointing to the urgent need for adequate education. Lack of knowledge was mentioned as a barrier by Poppelaars et al. (2003b). In the paper of Morgan et al. (2004), over half of the obstetrician gynecologists rated lack of the ability to interpret a positive screening test (59.5 %) and lack of familiarity with genetics and CF (58.9 %) as more than moderate concern suggesting need for education. Also in the study of Mennie et al. (1998), only 35 % showed enthusiasm for counseling those with positive results. Darcy et al. (2011) concluded that there is room for education and increasing the availability to access information about carrier rates, screening sensitivities, and residual risk, especially for non-academic working physicians.

Two studies reported the potential psychological harm and potential stigmatization for carrier patients as a matter of concern (Boulton et al. 1996; Boulton and Williamson 1995; McClaren et al. 2008).

Liability from not offering screening, if the patient has a child with CF, was more than a moderate concern for over three quarters in the study of Morgan et al. (2004).

Discussion

In the studies we retrieved that were focused on the attitude of health care professionals (potential providers) toward CF carrier screening, there was general support for such screening; nevertheless, there were major concerns about offering carrier screening especially time constraints, need for education, and possible psychological harm to carriers.

Although in many studies there was support for some form of screening such as screening on people's request, often, there was less support for routinely offering CF carrier screening (Baars et al. 2004; Faden et al. 1994; McClaren et al. 2008). In addition, a positive attitude toward routine carrier screening was often associated with certain conditions such as

a hypothetical error-free test (Baars et al. 2004; Faden et al. 1994) or if testing and counseling is without charge (Rowley et al. 1993). Taking into account the concerns and conditions for provision of screening in the studies, caution must be exercised to translate a "positive" attitude toward carrier screening as an effective readiness to participate in a screening program.

Overall, CF carrier screening meets the general criteria that justify screening (Henneman et al. 2002). CF is an important health problem; there is an effective intervention or a decision to be taken by the person screened, and there is a suitable test with known predictive value. Considering the economic criteria for CF screening, a review of literature indicated that a CF carrier screening program may result in savings to health care payers (Radhakrishnan et al. 2008). However, it is generally agreed that economic considerations should not be the intention of a screening program. The ultimate goal of CF carrier screening is to offer couples informed reproductive choice. Consequently, in addition to the basic principles of population screening (Wilson and Jungner 1968), it has been stated that appropriate education should be provided so that individuals can make an informed decision about having testing, the individuals' decision should be respected, and they should be protected from stigmatization and discrimination (Andermann et al. 2008; Khoury et al. 2003).

Many studies have investigated the psychological impact of a CF carrier result and indicated that the short-term raised anxiety dissipated after 3 months (Bekker et al. 1994; Mennie et al. 1993; Watson et al. 1992), and at long-term, carrier status was not associated with lower self-esteem or increased anxiety (Axworthy et al. 1996; Denayer et al. 1996). Despite these results, the potential psychological harm for carrier patients was a major concern in two of the studies (Boulton et al. 1996; Boulton and Williamson 1995; McClaren et al. 2008) we retrieved.

Similarly, Gilani et al. (2007), who investigated the attitude of medical practitioners and other stakeholders toward genetic screening for thalassemia, observed that, in 26 % of those that did not accept genetic screening, fear of discrimination and, in 30 %, individual stress was the stated reason. Other studies investigating the attitude of health care practitioners toward hemoglobinopathy screening showed a fairly positive attitude mainly predicted by subjective or social norm. However, this could be explained by the reluctance toward screening which is based on ethnicity (Jans et al. 2012; Weinreich et al. 2009).

It has been shown that there is a negative correlation between knowledge level and anxiety. The study of Gason et al. (2005), in which students were offered carrier screening for Tay-Sachs disease, showed that an education session resulted in a significant increase in knowledge and a significant decrease in predicted anxiety about being a carrier.

Thus, a good pre-test and post-test counseling plays an important role in limiting the possible psychological effects of a carrier screening. In the study of Morgan et al., despite actually offering carrier testing (2004), lack of the ability to interpret a positive screening result was rated as more than moderate concern. Similarly Mennie et al. (1998) mentioned that only 35 % showed enthusiasm for counseling those with a positive test result. Three other studies (Boulton et al. 1996; Darcy et al. 2011; Poppelaars et al. 2003a) pointed to the need for education.

Lack of knowledge was also found in surveys investigating carrier screening programs for CF and/or other genetic diseases. Qureshi et al. (2006) showed that only 23 % of general practitioners felt highly confident in giving advice for either CF or thalassemia. General practitioners generally felt less confident in dealing with thalassemia than CF. Shickle and May (1989) found that general practitioners with better knowledge of communities at risk are more likely to support screening for hemoglobinopathies. Also, Ready et al. (2012) who conducted a survey at the ASRM (American Society for Reproductive Medicine) meeting to determine the attitude and knowledge toward expanded genetic screening for recessive diseases among reproductive health care providers ascertained that, despite the positive attitude toward such screening, there were misperceptions about recessive inheritance, confidentiality, and insurance discrimination necessitating for education. Given that lack of knowledge constitutes an important concern, we can assume that the need for education will increase if screening for multiple diseases would be offered. Consequently, costs for genetic counseling of carriers should be taken into account in economic evaluation of potential screening programs.

Improvement in laboratory reporting could help in interpretation of the test result. A positive test report of the first partner should include the recommendation that the other partner be tested. Since a patient with a negative test result still has a residual risk for CF heterozygosity depending on the ethnic or racial background, test reports of negative screens should define as accurate as possible the residual risk of being a carrier of an unknown or untested mutation. According to the ACMG Standards and Guidelines for Clinical Genetics Laboratories, CF reports should include the reported ethnicity of the patient and the indication for testing, as well as the mutations tested and the method of testing (Grody et al. 2001). Since various test results will generate the need for genetic counseling, referral to a genetics professional could be advised if primary care physicians do not feel comfortable to provide such counseling themselves.

Boulton et al. (1996) and Mennie et al. (1998) reported a positive family history as the most important reason to offer screening (cascade testing). This kind of testing depends on communication of test results to family members as well as the willingness of these informed family members to aim

testing themselves. Studies have not supported cascade testing as a useful approach to population screening because of its low performance (Morris 2004; Morris et al. 2004; Ormond et al. 2003), but this method may have value in identifying some carrier relatives of individuals themselves identified as carriers through population screening programs (Roberts et al. 2003).

In 2010, a European consensus document with the benchmarks for CF carrier screening was published (Castellani et al. 2010). This paper outlines the advantages and disadvantages related to CF carrier screening and presents standards for efficacious, safe, and ethical practice of such programs. This document does not imply that CF carrier screening should be implemented, which should remain a decision of the individual countries or regions in accordance with local legislation. As to the timing possibilities, preconception screening was pointed as the ideal timing, although prenatal screening was mentioned as the most common entry point. Carrier screening prior to pregnancy has ethical advantages over a screening program that targets the prenatal population because it results in more reproductive options being available. Moreover, during pregnancy, a couple often has to make difficult decisions in a short time concerning the ongoing pregnancy. In addition, when carrier screening is offered alongside other tests during pregnancy, taking an informed decision is compromised (Hartley et al. 1997). A carrier screening program that targets the preconception population might yield lower uptake, since individuals often do not consider screening until a pregnancy ensues. Moreover, if carrier screening would be offered by family physicians, people who only rarely visit their general practitioner (preconception) are not reached. As suggested by Poppelaars et al. (2003b), in order to allow for screening before pregnancy, a preconception consultation should be developed. In such consultation, also future additional genetic screening programs could be implemented. In addition, of course, an information campaign to inform the population of the existence and importance of such consultation before a possible pregnancy would be necessary.

Since multiple studies have shown a lack of knowledge in genetics, a custom training for future counselors should be provided. Another possibility would be to implement carrier screening programs within the existing genetic services. Taking into account the increasing number of genetic disorders for which screening becomes possible, in any case, additional professionals should be trained to provide genetic pre- and post-test counseling.

In the studies we retrieved, preconception screening was generally considered preferable to prenatal screening providing maximum autonomous reproductive choices. However, screening during pregnancy was performed more often or considered to be more practical. It is difficult to find differences in attitudes toward the best time or setting to offer screening with regard to profession, since most studies were

conducted among general practitioners only or a group of different specialists, and only few among obstetrician gynecologists only. Overall, general practitioners (Boulton et al. 1996; Mennie et al. 1998; Watson et al. 1991) preferred preconception screening; obstetricians preferred screening during pregnancy (Rowley et al. 1993). Morgan et al. (2004, 2005) and Darcy et al. (2011) showed that, according to the ACOG-ACMG guidelines, the majority of the obstetrician gynecologists in the US have incorporated CF carrier screening into their practice. The study of Morgan et al. (2004) confirmed that obstetrician gynecologists were indeed much more likely to offer screening to pregnant women than to non-pregnant patients. This observation applies not only to CF carrier screening but to carrier screening in general (Metcalf 2012). In the study of Riskin-Mashiah and Auslander (2007), 94 % of the Israeli gynecologists recommended genetic carrier screening at the first prenatal visit; significantly fewer (62 %) recommended genetic carrier screening in the preconception period.

Apart from offering prenatal and preconception screening in clinical settings, carrier testing can also be offered outside the clinic (high-school, workplace) (Delatycki 2008; Modra et al. 2010). Screening in non-clinic settings could provide a good pre-test education promoting autonomous decision making, and also a large percentage of the population could be reached. Genetic screening programs for Tay-Sachs disease (and β -thalassemia/CF) in high schools have proven to be successful with high rate of voluntary participation (Barlow-Stewart et al. 2003; Gason et al. 2005; Mitchell et al. 1996). Critiques that have been raised are the possibility of peer pressure and also high school students might not be mature enough (Ross 2006) to take an informed decision. Moreover, if carrier screening programs are targeted at students of particular ethnicities, screening might result in stigmatization of these groups (Ross 2006). Ioannou et al. (2010) showed that expansion of the Tay-Sachs screening program to screen for six additional conditions resulted in a decrease in knowledge levels of the high school students that participated in the study and an increase in predicted negative feelings if found to be a carrier of one of the conditions screened for. Frumkin and Zlotogora (2008) believe that school should be a place to provide genetic education about screening in order to allow students to decide when and where to have a genetic test.

Overall, we can conclude that, although there exists a positive attitude toward the idea of CF carrier screening, in most countries, the current health care system is not ready to provide such screening. Efforts should be made to train health care professionals and to give adequate support.

The need for implementation of preconception carrier screening programs into healthcare systems is likely to increase given the evolving genomic technologies which facilitates large-scale population carrier screening. Moreover, companies have started to offer preconception carrier tests

DTC. To date, there is only little information about the attitudes of health care providers toward DTC testing. The few studies that have assessed awareness and attitudes toward DCT genetic testing show limited experience with these tests (Hock et al. 2011; Kolor et al. 2009; Ohata et al. 2009; Powell et al. 2012). These studies investigated opinions toward DTC testing as personal genome tests (screening for susceptibility to certain adult onset complex diseases) and not carrier testing through DTC specifically. A recent survey of European clinical geneticists showed that 53 % strongly or somewhat agreed that preconception carrier testing offered through a DTC provider should be legally banned (Howard and Borry 2012). The most cited risks of DTC genetic testing in the described studies were potential patient anxiety, erroneous understanding of test results, weak reliability of test results, misleading advertisements, and discrimination based on genetic information. Provision of information and counseling was also a matter of concern.

As limitations to this review, we have to acknowledge that comparison of the various studies is difficult due to varying study populations, study design, study measures, and methodology. How questions have been phrased may be a possible explanation for some differences in attitudes. In the study of Poppelaars et al., when the offer was more generally formulated as “couples should be informed about the possibility of having a CF carrier test, so they can decide for themselves whether or not they want to participate” the majority of the GPs and MHS workers agreed offering screening (2004). Furthermore, studies retrieved were conducted in different countries with different legislation, different culture, and carrier frequencies. Finally, although the selection of studies and analysis of the studies has been done as systematically as possible, this was only done by one person.

To date, studies assessing attitudes of health care professionals were mainly focused on the attitude toward preconception (and prenatal) carrier screening for CF and hemoglobinopathies. With the current evolving genomic technologies, making carrier screening possible for an increasing number of genetic conditions and DTC genetic testing being available not only for prediction of susceptibility for certain diseases but also for conditions that are traditionally tested for in clinical testing such as CF carrier screening, future research should assess how health care professionals view this type of genetic testing. Attitudes toward what types of testing may be acceptable, who should be offered testing and by which means testing should be provided could help governments in decisions whether carrier screening should be implemented in health care systems.

Conclusion

Through our review, we aimed to investigate the attitudes of health care professionals toward population carrier screening

for CF. Overall, we observed a positive attitude toward population screening for CF, but we observed also major concerns. In addition, there was less support toward routinely offering CF carrier screening to all couples planning a pregnancy. It is clear that there is need for education as well as support giving the already existing time constraints in the consultation of potential providers. Moreover, a positive attitude does not automatically mean a willingness to conduct screening. As to the best time to offer carrier screening, preconception period is generally accepted as the best moment to screen; however, it seems appropriate to give individuals the opportunity for screening at different times.

The prospect of an increasing number of genetic disorders for which screening becomes possible and the potential increasing demand for such screening in the future calls for the need for further debate on the desirability of carrier screening and relevant questions such as the conditions screened, the providers involved, the information provision, and counseling. When carrier screening would be carried out, it is clear that custom education and training of health-care professionals should be organized. In addition, information campaigns should be set up in order to inform the general population about the possibility of carrier research so that everyone can take an informed decision that is completely voluntary and based on balanced information.

Conflict of interest The authors declare that they have no conflict of interest.

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