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Original Article

International approaches for delivery of positive newborn bloodspot screening results for CF☆

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ABSTRACT

Background: Newborn bloodspot screening (NBS) for cystic fibrosis (CF) is a well-established public health strategy with international standards. A European survey demonstrated considerable variability in approach to delivering a positive NBS result. We used a mixed methods approach to explore healthcare systems and beliefs around this process.

Methods: We used semi-structured interviews and online questionnaires with a purposive, international sample of health professionals involved in communicating positive NBS results to parents. Data were analysed using thematic analysis and Qualtrics Survey Software.

Results: In total, 63 healthcare professionals were approached; 25 interviews were conducted with delegates at the 2017 ECFS conference, 4 online questionnaires were subsequently completed by participants in the EU, 1 from Australia and 33 from the US. Methods used to communicate positive NBS results to families varied considerably. This influenced the quality and quantity of information provided which had the potential to heighten anxiety and affect timely diagnostic testing. Participants identified positive practices including systems to improve the timeliness of screening and processing of results, as well as areas for improvement. Respondents stated that knowledge of CF and familiarity with the family were both important when deciding who should communicate positive NBS results.

Conclusions: Guidance and practice regarding communication of positive NBS results for CF to families varies considerably internationally. Further research is needed to ensure information received is accurate, up-to-date and from the most appropriate person. Also, that all children are followed up in a timely manner to minimise potential negative outcomes for the child and family.

1. Introduction

The introduction of newborn bloodspot screening (NBS) programmes internationally over the last 50 years for a range of inherited conditions has been an important public health initiative [1,2]. Screening for cystic fibrosis (CF) has been incorporated into most of these programmes. The rationale for NBS for CF is well established [3] however, there continues to be challenges in terms of its implementation [4]. One of these challenges relates to the way positive NBS for CF are communicated to families. The clinical spectrum in screen positive cases varies enormously and consequently the message to parents needs to be accurately presented for a range of outcomes. Communication of positive NBS results is a challenging task which requires preparation and evidence to minimise potentially harmful negative sequelae [5–9].

The consent process for NBS varies internationally. In the UK, NBS is offered on a voluntary basis. Parents are required to provide informed consent (but not written) and 'opt in' to the screening programme. This is different to most of the United States (US) and Canada where an 'opt out' approach is taken. Recent findings from a review of the expansion and performance of national newborn screening programmes for cystic fibrosis in Europe [10] found that written informed consent was mandatory in six (38%) countries. The consent process will influence parents' knowledge and expectations regarding the communication of positive NBS results.

Abbreviations: NBS, newborn bloodspot screening; CF, Cystic Fibrosis; CFSPID, Cystic Fibrosis Screen Positive, Inconclusive Diagnosis; EU, European Union; ECFS, European CF Society; IRT, Immunoreactive trypsinogen; NSWG, Neonatal Screening Working Group; SCD, Sickle Cell Disease; US, United States of America.

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Previous studies indicate variation in the way positive NBS results are communicated to families. In the US, qualitative interviews with 28 parents following their child's positive NBS result for CF demonstrated communication of the positive NBS result resulted in parental uncertainty and emotional distress. This was influenced by the approach to informing parents of the result with face-to-face communication (as opposed to use of the telephone) and the physician having time and knowledge to explain the results in detail being preferable [11]. These findings were supported by another study which consisted of telephone interviews with 270 parents following communication of carrier status after NBS for CF and sickle cell disease (SCD). The findings indicated that content and knowledge of the person imparting the result, was important in terms of the parental experience of the process [12]. A more recent study in Switzerland exploring parents' perspective of NBS for CF found that parental dissatisfaction with the communication of the NBS result was associated with poor information provision about the screening result and the actual disease, again demonstrating the importance of ensuring the information is delivered by someone who is well-informed [13].

A study of NBS in Europe [10] reported 17 national programmes, 4 countries with regional programmes and 25 countries not screening for CF. The screening algorithms in these countries differed; further details of the individual algorithms are described in the paper [10]. Briefly, all programmes used measurement of immunoreactive trypsinogen (IRT) for first tier testing. However, second tier testing differed considerably with four programme using repeat IRT, two programmes using pancreatitis-associated protein, ten programmes using DNA analysis with panel sizes ranging from 4 to 644 mutations. Four used further IRT testing at day 21 for infants with one mutation recognised and three programmes used extended gene sequencing for infants with one recognised mutation. Ten used a "safety net" with infants with a high IRT but no mutation recognised being referred for further testing. National programmes were also found to employ different protocols, regarding processes used to communicate positive NBS results to families. A positive NBS result was most often reported by the CF centre, and in most cases, by telephone. It was also found that the result may be reported to the family by a CF Physician, a specialist CF nurse, a community Nurse or a Family Doctor. Two countries reported the result being communicated to the family directly by the NBS laboratory. The details of the different approaches, and the health service beliefs underpinning these approaches have not been explored. We aimed to explore international healthcare systems and beliefs around the NBS process.

We explored the experience of delivering positive NBS results to families to examine existing practices in more detail. We approached countries with established NBS programmes.

2. Methods

This was a mixed methods study using semi-structured interviews and online questionnaires with a purposive, international sample of health professionals involved in communicating positive NBS results to parents. For the purposes of this study, a positive NBS result referred to the initial result prior to second tier testing [10]. Ethical approval was granted by the Research Ethics Committee at City, University of London (Staff/16-17/25).

Members of the European CF Society (ECFS) Neonatal Screening Working Group (NSWG) were contacted via email prior to the ECFS Conference in June 2017 (n = circa400, it is not known how many of these met the eligibility criteria). Information about the proposed study was included as well as contact details of the research team. Members of the NSWG were considered eligible and advised to contact the study team to discuss inclusion in the study if they were involved in communicating positive NBS results to families, attending the ECFS conference and willing to be interviewed.

Members of the NSWG who responded to the email and expressed an interest in the proposed study were sent an invitation via Doodle Poll which allowed them to select dates and times during the 2017 ECFS conference that would be convenient for them to participate in a face-to-face interview. Once the Doodle Poll had been completed by all interested parties, each potential participant was sent a final invitation via email including a date and time to be interviewed at the ECFS conference.

Semi-structured interviews were conducted at the 2017 ECFS conference in a separate room in the conference venue. Prior to the interview taking place, written, informed consent was obtained from study participants. Interview prompts were derived from the literature and agreed by the research team. Interviews were audio-recorded and transcribed verbatim.

Prior to and following the 2017 ECFS conference, members of the NSWG who were not at the conference, contacted the research team and expressed an interest in being involved in the study. Therefore, the interview prompts were developed into an online questionnaire using Qualtrics Survey Software. This was circulated to members of the NSWG who were not present at the 2017 ECFS conference. To gather data from the US, an adapted version of the online survey was circulated to all US Centre Directors ($n = 50$).

Similar questions were used for the interview guide and the questionnaire. Each started with questions aimed at gathering demographic data such as; country of work, job title, number of years involved in the NBS process. This was followed by questions related to their role in communication of positive NBS results and the NBS programme in their country including the age at which the bloodspot is taken, who takes the bloodspot, the NBS algorithm used, consent procedures and what is considered a positive NBS result. Next participants were asked specific questions related to how results are communicated to parents such as timing, people involved and the process and content of the communication. Also, what second tier testing is undertaken, how and by whom and how the results of the second tier testing are communicated to the family? Following this, participants were asked their opinions regarding these processes such as who they thought the most appropriate person was to communicate the result, how this should be done, what they thought worked well about their NBS programme and any improvements they might like to see.

2.1. Data analysis

Quantitative (demographic) data from the interviews and questionnaires were analysed initially using simple descriptive statistics and are presented in Figs. 1–3. Following this, qualitative data from the semi-structured interviews and the open-ended questions in the online questionnaire were analysed thematically [14]. This process consisted of six phases; familiarisation with the data, generating initial codes, searching for themes, reviewing the themes, defining and naming the themes and producing the report.

3. Results

Twenty-five interviews were conducted at the 2017 ECFS conference lasting on average 30 min (range 15–47 min). Four questionnaires were completed by participants in the EU, 1 from Australia and 33 from the US (see Fig. 1). As responses from Australia and New Zealand were low, these were grouped with the EU responses due to similarities in health care structure and organisation. Data from the US were analysed separately. Health care professionals involved in the study comprised centre directors, doctors, nurses, professors, research scientists, genetic counsellors and NBS co-ordinators (see Fig. 2).

Responses indicated there are differences in terms of who communicates the initial positive NBS result to families. In the US, this was primarily the Primary Care Physician (PCP) but in the EU/Australia/New Zealand, this varied widely and included a range of professionals (see Fig. 3).

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Origin	Interviews	Questionnaires	Total
Europe	**21**	**4**	**25**
Czech Republic	1		
Denmark	2		
England	5		
France		1	
Germany	3		
Italy	3	1	
Netherlands	1		
Norway	1		
Scotland	1		
Serbia	1		
Spain	1	1	
Switzerland		1	
Turkey	2		
Australia		**1**	**3**
New Zealand	**2**		
United States	**2**	**33**	**35**

Fig. 1. Number of interviews and questionnaires conducted in each group.

Thematic analysis revealed three main themes, (i) positive practices, (ii) challenges and (iii) areas for improvement each of which contained subthemes. Managing communication of the positive NBS result was influenced by structure, provision and availability of services and this influenced the care families were perceived to receive.

3.1. Positive practices

Many positive practices were identified by participants. These have been divided into the following subthemes, communication and co-ordination, timeliness and the multi-professional team.

3.1.1. Communication and co-ordination

Several respondents from the US highlighted effective communication between the screening laboratory, the PCP and the CF centre as a positive aspect of their NBS programme and commented on how this had improved over time. This enabled professionals to provide appropriate information to families during the process from screening to diagnosis. This also made respondents feel that they were unlikely to have any missed cases.

Similar responses were obtained from health professionals from the EU/Australia/New Zealand. However, often this was a perception of how important good communication is and the detrimental effect of poor communication practices.

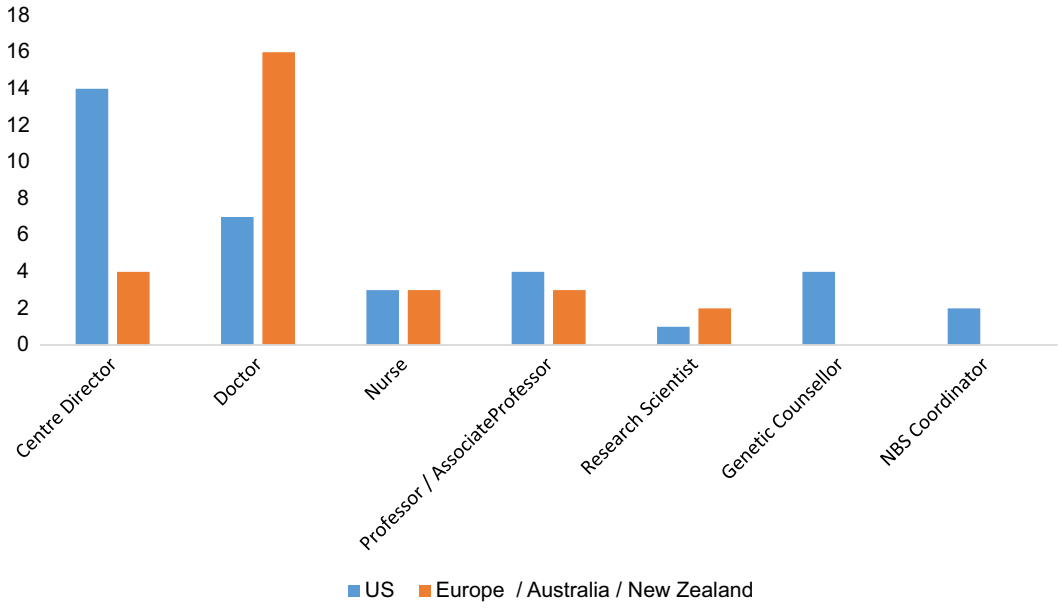

Fig. 2. Health care professionals involved in the study.

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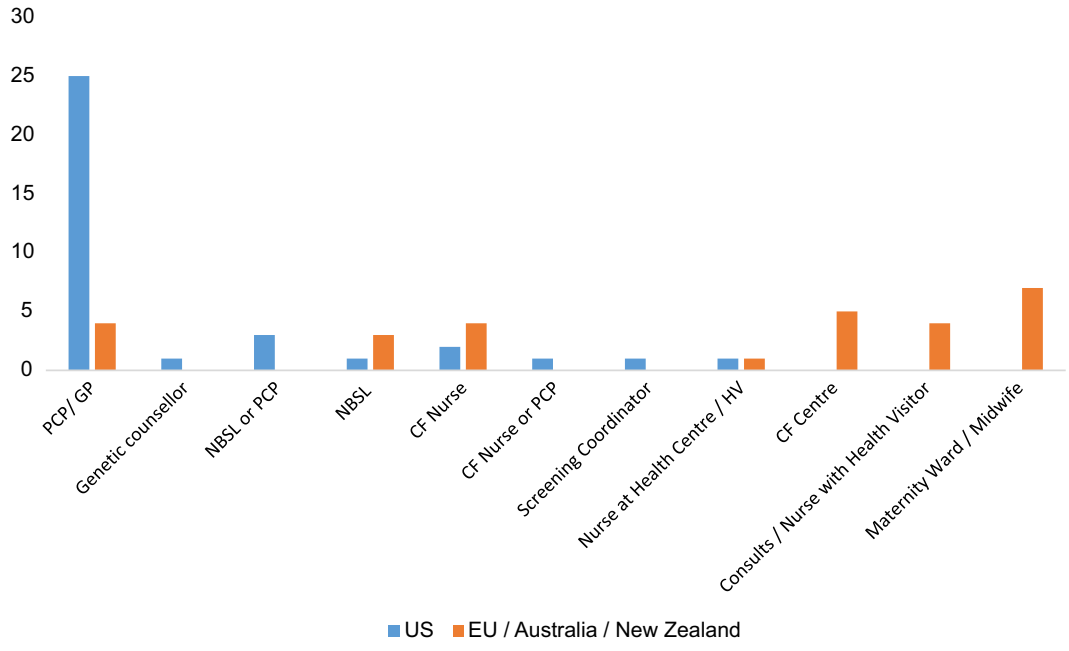

Fig. 3. Professional who communicates the initial positive NBS result to families.

"…if you have a bad start to begin…the whole diagnosis process starts off on the bad foot that they [the parents] are influenced very lengthily." Germany.

In the EU/Australia/New Zealand, positive communication practices more commonly referred to communication with the family and co-ordination of care after the family had been seen in the CF clinic as opposed to communication of the initial positive NBS result (e.g. Germany).

"Starting that day quickly from the result of the sweat test, we have a very structured plan that we will talk about once they have a positive diagnosis, how the admission works, what they will learn during the admission, that we have an on call service that they call and we really encourage that and I think that from that time on they do feel that you know there is someone regardless of what happens that they can address their question to." Germany.

In the EU/Australia/New Zealand, there was an appreciation of the importance of good communication at all stages when communicating positive NBS results from the laboratory to parents. This was demonstrated in communication between health professionals and families once the child and family had been referred to and/or seen at the CF clinic. However, it was often felt that the initial communication of the positive results could be performed better.

3.1.2. Timeliness

Ensuring that children and their families were seen in a timely manner after receiving the initial positive NBS result was deemed very important. Many respondents from the US commented on this in relation to children being seen quickly in the CF clinic following the positive screening result.

"*Most patients seen before 2 weeks of age." US.*

"Timeliness in specimen collection, shipping, reporting and follow-up" US.

Similarly, respondents from the EU/Australia/New Zealand commented on the importance of timeliness in terms of communicating with the families.

"..it's good that we get onto it quickly, it's good that the midwife and the family know to contact us almost immediately…and I think it's good that we can get them in within 24 hours." New Zealand.

"*What I think works well is that we do not leave too much time between the initial message that screening is positive and the first visit in the hospital, so I think it's very important that you don't leave too much time between that. So, because otherwise parents have too much time to think, and to be worried, and for uncertainty." Netherlands.*

Many respondents from the US commented on the timeliness of the sweat test and availability of results.

"Sweat test results [are available] the same day." US.

"Time to sweat test and time to diagnosis when family can be found and has PCP goes very well." US.

Timeliness of the sweat test was variable in the EU/Australia/New Zealand. In Italy and Germany for instance the result of the sweat test is available the same day, indeed in Germany it is almost instant.

"…you get the results if you do it immediately after the sweat was collected and you have, five minutes later" Germany.

In some countries, the sweat test is done separately after the parents have been told the child has a positive NBS result but before they were seen by the CF team. Therefore, the intention is for the results to be available when the child is seen for the first time by the CF team. In other places such as the UK and New Zealand, the results of the sweat test were commonly not available the same day, and were then given to parents over the telephone the following day. This was commonly due to the availability of services to undertake and report the sweat test.

3.1.3. Multi-professional team

Internationally, the importance of involvement of members of the multi-professional team and effective team work in the care of children with CF and their families after they had received the initial positive NBS result was highlighted. However, there was variations in terms of when different members of the team became involved and the composition of the team. In most instances the CF doctor and CF nurse were the first members of the team who were involved with the family. In the US, involvement of a genetic counsellor early in in the families' journey was viewed favourably.

"The presence of a genetic counsellor has been reported to be very helpful by families as they are professionals who are used to provision of information at a variety of educational levels to families under stress. The use of the genetic counsellor while the sweat test is going on provides a distraction from "going to the bad places" while also providing reassurance about the relatively low risk of their child having CF and the importance of early detection should the test be positive" US.

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However, inclusion of a genetic counsellor in the CF team in the EU/Australia/New Zealand was rare and in Italy this was viewed less favourably.

"The problem is that we don't have a geneticist inside the CF centre." Italy.

Early involvement of members of the multi-professional team was deemed valuable by all while acknowledging the importance of not overwhelming the family.

"We try to call the whole team, or different members from the whole team… if you are alone it is also not good, but if we are two or sometimes three, then that is very helpful…. Most of the time we are only two, but this is already okay because on the other side you have also two people. You know, if you would come with five this is probably scary." Germany.

3.2. Challenges

Several challenges of the NBS process were identified and have been grouped into three subthemes; sweat test, professional roles, and genetic mutations.

3.2.1. Sweat test

While some respondents in the US commented on the timeliness of sweat testing and receiving the results, others raised concerns about the sweat testing process. One of these appeared to be with the way sweat testing is recorded particularly for patients where only one mutation is identified.

"We have delays if there is a positive NBS but 1 mutation because we don't have a good way to track if/when the sweat tests are ordered/scheduled" US.

Another issue identified was the timing and success of performing a successful sweat test. Many respondents commented on being unable to get a definitive result due to the quantity of sweat collected being insufficient presumably due to the weight of the child.

"I wish we could perform the sweat test sooner after the positive screen, but the high QNS [quantity not sufficient] rate necessitates waiting for 2–4 weeks before performing the confirmatory test" US.

Similarly, in the EU/Australia/New Zealand, issues related to the timeliness and success of sweat testing were also raised. In Turkey and Germany, parents are expected to arrange the sweat test after they had been informed that their child has a positive NBS result. In Germany, this was due to legal requirements that meant the CF centre could not be sent patient details. This raised concerns for clinicians in terms of ensuring that babies who have a positive NBS result are followed up in terms of the sweat test and being seen by the CF team in a timely manner.

"*I think what's very difficult is the tracking. Who comes at which time? Because, you know, if the parent stays at home, we have no information. In the legal way [of] how things should happen." Germany.*

"*It decrease their urgency to coming to see us because many families reject to come and so there are delays in that diagnosis… they say ok the baby is fine, there is no need to come because sometimes they come to the hospital and they couldn't find out and then they say ok he or she is not ill" Turkey.*

This can have serious consequences

"I learned that the family rejected to come to the university…He had a positive screening test but unfortunately the baby died. The family, I learned, rejected to come to the university for a sweat chloride test…I didn't learn about that positivity until that patient had died." Turkey.

3.2.2. Professional roles

Professional roles did not appear to be an issue in the US perhaps due to the fact that it was most commonly the PCP who communicated the initial positive NBS result to families. However, in some countries in the EU/Australia/New Zealand there are issues related to who is seen to 'own' the screening result. In Germany, it is usual practice for the positive screening result to be communicated back to the maternity ward were the screening was performed. Indeed, the maternity ward are not allowed by law, to contact the CF centre and give them personal data about the patient. Therefore, the positive NBS results is given by an obstetrician (Germany) or a General Practitioner (Turkey) who is not perceived to have expert knowledge of CF which impacts on the message given to parents:

"…most of them cannot get any information from the GP and they were so curious and some were just very anxious… most of them were not informed by the GP about CF." Turkey.

This was also the case in New Zealand where midwives were responsible for the care of mothers when the result of NBS became available and so they were considered to be best placed to communicate the positive NBS result.

"…the midwife then delivers the information to the family she, not owns the family but she is the one that has been responsible for the care to that point so…she delivers the information to the family… it's sort of almost who owns the information in the healthcare at that point." New Zealand.

This is also the case in the Netherlands:

"Officially, we are not allowed to contact the parents, because we do not have a relationship with them yet…the GP has the relationship with the family." Netherlands.

Conversely, in the UK, there were issues in terms of people who were not CF specialists feeling it was not their job to deliver the initial positive NBS result.

"*Some [health professionals] say 'well that's not really our job to do'. Well? Okay, well, whose job is it?" UK.*

Perceptions of the roles of different health professionals in terms of both job description and information ownership therefore also complicates communication of positive NBS results.

3.2.3. Genetic mutations

The choice of DNA panel was mentioned by some states in America as having implications in terms of identification of those patients considered to have CF or CF screen positive, inconclusive diagnosis (CFSPID).

"Our state has elected to go with a very narrow panel of 23 genes. This is not commensurate with our diverse and ethnic population." US.

In some parts of Turkey, because of the wide range of CF mutations, it has not been possible to find a cost-effective DNA panel and therefore commonly DNA analysis is only undertaken after diagnosis i.e. after a positive sweat test. However, in other areas of Turkey, the high rates of consanguinity mean if relevant, the child may undergo advanced genetic analysis.

Issues were also raised in terms of the importance placed on the identified mutations during the screening process. One respondent in the UK explained the difficult position the CF expert can be put in when giving a screening rather than diagnostic result i.e. prior to second tier testing particularly if they are aware of the genetic mutations.

"…it felt quite uncomfortable, in some situations we knew the diagnosis, but we weren't there to give the diagnosis, and we were then saying 'you need to come to the hospital this afternoon', we had a few patients say to us…'well you knew this result, and you were sat in our house this morning, but you-'. They kind of get why I suppose you didn't tell them…we started getting embroiled in lots of conversations about CF, and what it means, without them actually having a full on diagnosis and that felt uncomfortable …" UK.

There are also legal considerations with respect to the DNA component of NBS. In Germany, mutations will only be released to the physician upon request and after the child has received a positive sweat test. Therefore, carriers will not be identified or told about their status as carrier screening is not allowed but parents should be made aware of this when the NBS is performed. Similarly, in Norway, due to law, carrier results are not reported. Additionally, in Germany, midwives are not allowed to perform the bloodspot for CF because it identifies genetic information and in German law only doctors can give information about genetic diseases. Therefore, those children who are born outside of

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hospital will often not have their CF screening performed either at all or on time.

3.3. Areas for improvement

Respondents identified many areas for improvement which were encompassed in the subthemes; provision of services and information giving.

3.3.1. Provision of services

In the US, in some states, geography hampered the perceived efficacy of the NBS programme.

"We are really challenged by geography. The nearest other CF Center to us is a 5 hour drive away. We have some patients who drive 6+ hours to come see us." US.

This was also seen as an issue in some parts of Turkey where families could have a considerable distance to travel which could even involve an overnight stay in order to obtain the sweat test. This was felt to be another barrier to parents ensuring their child is followed up following a positive NBS result.

3.3.2. Information giving

Agreement in terms of the right person to communicate the initial positive NBS result to families was a contentious issue. Communication between the screening laboratory, the PCP and the CF centre was viewed positively in the US. However, many respondents in the US were concerned with the information parents received from the PCP who was the most common person to communicate the initial positive NBS result to parents.

"Some PCP's do not do as recommended - some call families with results and give vague if not outright incorrect information." US.

"Education for PCP so that they are more knowledgeable and improve communication with parents" US.

Respondents commented that when incorrect information was given by the PCP during the initial communication, this created complications later on in terms of ensuring parents had a good understanding of CF and its treatment. This was also reflected in Turkey where misinformation from the GP could impact on parents seeking confirmatory testing.

"I don't know what they [GP] tell to patients, but I know some bad stories about the knowledge taught by GPs. Sometimes they can say that it's a very bad disease, and you can't do anything to your baby, it's a very bad disease. Sometimes, they [the parents] don't want to come to the University in that case. I think the education of the GPs is very important." Turkey.

This was also reflected in responses from the UK where more commonly, the positive NBS result is given by a member of the CF team (CF nurse or less commonly the CF doctor). Respondents generally expressed a preference to deal with the initial communication for fear of the GP or health visitor not being well equipped in terms of their knowledge of CF to deliver accurate information to the family.

"Well [other health professionals] don't know a lot about CF I don't think and I it's not really very fair on them to ask them to do that…they don't have a background of CF…sometimes you get asked a lot of questions and obviously, they would keep saying I don't know I don't know which I don't think would be particularly good for families…I don't think it's appropriate really it needs to be somebody with a background of CF." UK.

The importance of the most appropriate professional giving the news to families was also recognised by respondents in New Zealand.

"…given the number of midwives and children its very common that this will be the first child that she delivers this information to and she won't know much about cystic fibrosis and so the conversation [with the CF nurse] before she talks to the family is very important it gives her confidence and she kind of runs through what she is going to say or if there is any questions. It also means that if the family asks something that she doesn't know that is unexpected she doesn't feel at a loose end" New Zealand.

However, it was also felt that the person communicating the initial positive NBS result should also be known to the family.

"…the midwife is the first person to contact them because they don't know us, you can't call somebody you haven't seen in your life…The midwife, or the person who is looking after the parents the whole time would call the parents and give the results… it makes much more sense if someone who knows the people actually tells them the results." New Zealand.

Currently in Germany, the screening laboratory informs the birth clinic, the birth clinic informs the parents, and the parents have to organise their diagnostic confirmation themselves. However, this was not seen to be ideal by the CF health professionals interviewed.

"I personally think it's the communication from the CF centre [that] is more important, because these are the persons you want to work together with for the next 18 years, or even longer, whatever you build up as a connection to the family, if you are the first one to discuss it with the family, you have some additional advantage. The maternal department… they're not well trained to do this type of communication, and to be able to answer every question related to cystic fibrosis." Germany.

The importance of both parents being present when communicating the initial positive NBS was acknowledged by most participants. However, the logistics of ensuring this happened was seen as a challenge.

"I tell them [the parents] they can go on the speakerphone so we can talk. Everyone can hear it. But usually when you call them when they're two weeks, in Denmark, the Dad has two weeks paternity leave, and then he usually goes back to work. So…only the mother has been at home". Denmark.

"…if there's a dad, partner or husband, they've probably just gone back to work after their paternity leave. It's, you know, bad timing. But, [we] are very mindful of that and they'll quite often, the mums will call a grandma, or a partner or husband, or a friend to come round with them." UK.

In Europe, the general consensus was that parents should be deterred from looking at the internet to find out more about CF prior to being seen in the CF Centre.

"…don't go on the internet and look everything up, because you'll see the worst cases." Netherlands.

"So I would actually have the maternity ward communicate that they shouldn't look…at the internet" Germany.

"We tell them [health visitors] to suggest that families don't get on the internet…but of course most of them do…" UK.

There was wide variation regarding whether the genetic mutations should be disclosed to the parents during the initial communication of the positive NBS result. In some parts of Italy, this information is provided in writing to the parents before they are seen in the CF centre. In the UK, the Netherlands and Denmark, some respondents stated that if they knew the mutations, they would disclose them to parents during the initial conversation. However, this seemed to be based on personal choice rather than relying on relevant protocols.

"So I know the guidance is not to tell them the genetics…but I do say… they've found two mutations" UK.

"So, if the baby is, for example, homozygous for 508, they [the laboratory] will report that. For us, that is diagnostic. I know that it's a screening tool, but our experience is, we've taken it as diagnostic and, therefore, we will deliver that result as diagnostic… I think that's morally wrong [to not tell the parents their child has CF] because the baby has got cystic fibrosis..." UK.

"We've tended to give a diagnosis based on the mutations and the IRTs, so the sweat test hasn't been a make-or-break thing." UK.

In Turkey, the diagnosis was given following a variety of outcomes:

"Some of our patients get the diagnosis with only the genetic-test positivity. Some of them, both genetic-test positivity and sweat chloride test positivity. Some of them have only sweat chloride test positivity." Turkey.

In other countries such as New Zealand, Switzerland and Serbia, these would not be available until after the sweat test and in Germany only if requested. In Italy, the Czech Republic and Norway, even if the mutations were known, they would not be discussed with the parents until after the sweat test.

To summarise, thematic analysis led to the identification of 3 main themes regarding communication of positive NBS results to

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families (i) positive practices, (ii) challenges and (iii) areas for improvement. Positive practices included interagency communication when processing the NBS result, the timeliness of processing the result and communicating the positive NBS to the family and involvement of the multi-professional team early in the families' journey. Challenges included obtaining the sweat test, the role of different health professionals in the NBS process and communication of genetic information to families. Areas for improvement included provision of services both in terms of geography and availability of services such as sweat testing and information giving. The latter highlighted the importance of efficient, accurate and reliable information being given the family by a health professional with knowledge of the relevant NBS algorithm as well as condition specific knowledge.

4. Discussion

This piece of work confirms the findings of extreme variants across the globe in the delivery of positive NBS results. This variation was due to many factors including geographical/logistical, legal, financial and cultural constraints. Processing and communicating positive NBS results for CF well, is challenging and requires training and experience.

We have identified three key elements of the NBS process for CF; (i) interagency communication between the laboratory and relevant health professionals such as PCPs or the CF team, (ii) the first interface with the family and (iii) the diagnostic process.

A key element is how the positive NBS result is processed. For most countries, interagency communication and co-ordination between the laboratory and relevant health professionals such as the PCP or the CF team was viewed as a positive aspect of the NBS programme. The importance of this being done efficiently and reliably was acknowledged.

The first interface with the family was often viewed less favourably than interagency communication. There was a lack of consensus in terms of who is the most appropriate person to inform the family with responses indicating knowledge and familiarity are both considered important. The importance of knowledge is consistent with previous research [11–13] but familiarity has not been considered previously.

In the US, communication with families is most commonly undertaken by the PCP. However, the findings of this study support the findings of previous work [11,12] and suggest that PCPs continue to be inadequately prepared to undertake this role. In the EU/Australia/New Zealand, a range of professionals are responsible for communicating the positive newborn screening result to families. Provision of complete and accurate information was considered to be associated with reduced parental anxiety and better decision making regarding seeking diagnostic testing and support from the CF team. In some countries in Europe such as Turkey, regulations regarding who 'owns' the information about the positive NBS result and therefore who communicated the result to the family had the potential to influence their perceptions of the urgency and/or necessity for their child to be followed up by the CF team. The key element is that the information parents received during the initial communication of the positive NBS result is accurate and up to date. There may be a tension between trying to achieve familiarity i.e. someone the family knows and someone that has the knowledge. However, someone who only communicates positive NBS results once or twice in their career is going to find this challenging and it is perhaps better to have someone who is not known to the family but does know about the condition and is therefore able to alleviate parental anxiety.

These findings are commensurate with findings of studies that have explored communication of positive NBS results for other conditions included in the NBS Programme. For instance, a study in the US which focussed on communication of carrier status for CF and sickle cell disease found that content and knowledge of the person imparting the result, was vital in terms of parental experience of the process [12]. Similarly, a study in the US which explored parental experiences of receiving a positive NBS result for a metabolic condition suggested the methods used to communicate the NBS result and the condition specific knowledge of the individual imparting the result influenced parental dissatisfaction, anxiety and distress. Results delivered over the telephone, by staff not known to the families or without condition specific knowledge were viewed less favourably [17]. More recently, a study with parents who had received a positive NBS result for a metabolic condition included in the expanded NBS programme in the UK suggested that first contact between the parent and the health professional relay the screening result left a strong lasting memory with parents and that the initial contact need to provide 'the right amount of information' but the quantity and content was difficult to define [18]. These findings support those of the present study and suggest that the need for the initial communication to be undertaken by someone with condition specific knowledge is not unique to CF.

The situation in Germany is unique and of concern to participants in this study from that country. The system for processing a positive NBS result complies well with the ethical principle of autonomy, as the family are able to decide the clinical care pathway, but it is clear that healthcare workers in Germany feel this places families at a significant risk of receiving inaccurate early information and inappropriate early CF care. Both of these would be counter to the ethical principles of beneficence (doing good) and non-maleficence (avoiding unnecessary harm). This system is not imposed because of a lack of health service resource (as is the case in some other countries). It is clear that processing a positive result through the well-established CF centres would be possible and that this State mandated process represents the impact of cultural beliefs on a health system. Some reports suggest similar pathways occur in some countries and states in the US, but the families appear to receive clearer direction in those cases.

In terms of the diagnostic process, respondents indicated differences in terms of the structure and involvement of the multi-professional team. The US viewed the inclusion of a genetic counsellor from the outset as important. However, in the EU/Australia/New Zealand, there was a distinct view that genetic counselling should not be embedded in the CF team but should be separate to allow families the opportunity to talk openly about issues such as future reproductive decisions while not feeling compromised or embarrassed.

Timeliness in terms of the period between screening and diagnosis was viewed positively by most respondents. However difficulties with the sweat testing process were expressed. These included families not understanding the importance or need for the sweat test, difficulties in accessing services due to geography as well as difficulties obtaining sufficient sweat to provide a definitive result. Worldwide, the sweat test remains a key and important part of the diagnostic process and age-related changes in sweat chloride should be taken into account [15,16]. However when a sweat test result is unavailable, a presumptive diagnosis should be made and treatment should not be delayed. In the US, many respondents acknowledged the difficulty of obtaining a sweat test in infants who were too small at the initial appointment with the CF team.

In terms of diagnosis, as mentioned above, sweat chloride concentration is considered the gold standard [15,16]. However, many respondents stated that if two CF causing variants (according to CFTR2) were identified during the screening process, they would consider this diagnostic and would often communicate this to the family before sweat testing had been attempted. Respondents provided a range of reasons for doing this including, moral judgement in terms of not wanting to deceive families or not wanting families to feel later on that they had been deceived, reassurance from personal experience that the screening results have never been inaccurate as well professional judgement based on the screening result and clinical assessment providing enough evidence that the child has CF.

These findings have implications for future research, practice and education. The most appropriate person to inform parents of their child's initial positive NBS result needs to be determined from a parental and practical perspective. The quantity and content of information provided to parents when they're informed of their child's positive

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screening result needs to be clarified in order to inform educational initiatives and ensure communication is reliable and reproducible. The findings of this study reiterate the need for the person informing the family of their child's positive NBS result to completely understand the NBS algorithm used and the meaning of the screening result. Practitioners must provide a coherent message when genetic information and/or clinical findings are indicative of a diagnosis of CF but when a sweat test is either unavailable or unachievable to ensure practice is consistent and care for families is equitable.

In terms of the study limitations it is important to consider serval factors that may have biased both data collection and study findings in the present study. These included selection bias; participants who are members of the ECFS NSWG, and who attended the ECFS meeting, may not be representative of the wider groups who care for children with CF, or communicate results of CF NBS. Equally, there may have been a bias in terms of who chose to respond to the online survey. The response rates may have also limited the generalisability of the findings. Observer bias should also be acknowledged. All study authors have prior knowledge, experience and a particular interest in CF NBS which may have influenced data collection and interpretation of study findings. To mitigate against this, interviewing and data analysis were undertaken by an experienced researcher. Respondents to this study were not always the person responsible for communication of the positive NBS result to parents. This means that these opinions may not accurately represent the views of those undertaking the initial communication.

In conclusion, guidance and practice regarding communication of positive NBS results for CF to families varies considerably internationally. The key finding of this study is that information provided to the family must be accurate, up-to-date and provided by the most appropriate person. Whatever process is established must ensure this happens consistently and in a timely manner.

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Conflict of interest

There are no conflicts of interest.

Data statement

Individual participant data that underlie the results reported in this article, after deidentification (text, figures) will be available upon reasonable request from the corresponding author.

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