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The how (and why) of disease registers

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ABSTRACT

A disease register is central to the understanding of clinical outcomes but the principles underpinning register design are not always apparent. My group developed, implemented and analysed outcomes using cystic fibrosis (CF) registers in Scotland (~500 patients, 1992–1995), the UK (~7000 patients, 1995–2006) and more recently across Europe (~30 000 patients, 2006–2009). The key design principles are summarised and exemplified using the process required to add new diseases such as CF to neonatal screening programmes to illustrate pitfalls in the complex path from screening to timely entry into specialist CF care. The disciplines of screening and specialist CF disease therapy are very different and our findings may be relevant for the evaluation of the fragile links in the complex patient journey. Should these links fail, they have the potential to delay the entry of a screened baby into therapy after testing positive for a preventable disease.

1. Introduction

When considering the design of any new disease register, there are broadly two areas to be addressed: the 'high-level' principles necessary to establish the infrastructure of a sustainable registry project and the technical/software framework within which the actual data are gathered and analysed.

This paper deals with the requirements of establishing the project infrastructure based on our experience since 1992 with national and international registries [1]. We propose that there are four key principles: firstly, the aim or mission of the registry should be carefully defined at the outset. Is the registry to be purely demographic [2,3] or are additional clinical and outcome data to be collected and analysed [4]? The former requires a simple registry of few fields (see www.eurocarecf.eu) whereas the latter would necessitate a more sophisticated approach, ideally incorporating a clinic management system that is integrated into routine care pathways. An accurate mission statement facilitates informed consent from each patient as an essential second principle. To comply with national laws and European directives, the consent form must comprehensively describe all potential uses of the registry as envisaged in the mission statement. A third obvious but sometimes overlooked principle is that the output from the registry should be of assistance to personnel charged with providing the data. This improves data quality. Finally, it is advisable to implement a pilot phase of about 12 months to test the registry design and its protocols. As we show in an example described herein, no matter how detailed the original planning, changes are often identified in the pilot phase which may necessitate changes to the original aims of the registry and its software design. Following the principles outlined above (as for example in www.cystic-fibrosis.org.uk) should help create a high quality registry consistent with standards proposed by experts in the field [5].

2. Data quality and coverage

The resultant disease register (synonyms registry or database) will require certain immutable principles for sustainability. One of the most important is that the data output has to be useful to members of the team charged with providing the data. Where the registry includes clinical data, monitoring output, audit and research should ideally fall out of the design axiomatically. Obtaining data from clinical staff who have no interest in its quality leads to 'garbage in garbage out'. This 'multi-data use' principle empowers the data suppliers who see the advantage of undertaking the onerous task of data entry because they see a benefit for their daily work. For example, in cystic fibrosis (CF), a simple graph of height, weight, body mass index and percent predicted lung function plotted automatically by a clinic management system creates a motivating real time feedback tool. Simultaneously, the same data can feed a secondary design aim, namely, that longitudinal research (into outcomes) should be facilitated. The input data are only reliable if the staff use them routinely, making them more likely to be correct, with the research caveat that often, surrogates of outcome have to be gathered such as FEV_1 in CF outcome because the actual drivers of premature death are complex [1,2,6,7]. Finally, since one purpose of all registries is outcome analysis, an analysis of social class (because of its well recognised relationship to deprivation [8,9]) should be integral in the design by including

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the first 4 digits of the postcode (UK) or its equivalent (in other countries).

Unfortunately, it is a common occurrence that very little resource is available to support good registry practice. Too often, the data suppliers to the registry receive no incentives. A failure to prune potential data fields to a minimum usually leads to poor completion by demotivated local teams who see it as just another chore. As a general rule, data fields should be in single figures for start up registries, particularly when there is no funding for data collection. The best type of 'pruned data' is collectable in a short time, binary (male or female, alive or dead), quantitative with high precision (genetic type, height weight, etc.) and predictive of outcome. We recently applied the 'pruned data' principle to gather demographic data in CF across thirty five countries in Europe [1]. Initially, all 'desired' variables were ranked in order of importance, ease of collection and meaningful analysis based on unambiguous definitions. For example, weight is insufficient and weight without external clothing is a better definition; since length is difficult to measure in newborn babies, it was ranked lower than weight. Further, frequency of data collection was minimised pragmatically with respect to the timescale of changes in outcome (over a few years in our case, because CF outcomes only change over decades) and by constraints imposed by the length of guaranteed funding.

A number of technical and legal issues are also important. The first is measurement precision: that a given data field is either quantitative, semi-quantitative (i.e. has a scale associated with it) or qualitative. Next, that field should be internally tagged as public or private to the patient (or semi-private). The legal principle here is that if the data can be used to identify the patient then these are private data (day of birth), if the data cannot be used to identify the patient, these are public data (year of birth) but if the data can with a combination of other pieces of information be used to identify the patient (such as month and year of birth), but this is unlikely in practice, then these are semi-private data. Regulatory agencies should be informed, partly through ethical approval and partly through the relevant Data Protection Authority. Data protection law at country versus European level is often different and if the registry is transnational, the patient approval and consent should follow an agreed template such as the example in the supplementary material of our recent paper [1].

Ultimately, disease coverage is dependent on 'buy in' from those charged with doing the work such as referral centres and who does what (and when), should be agreed up front; where relevant, 'buy in' from the specialist patient and medical organisations should also be agreed up front. The registry will then 'march' at the pace of the slowest. Hence, pilot phases are essential to identify the levers of adherence:

- In the pilot phase, it is unrealistic to expect more than 50% to 70% coverage; we found that high accuracy in $\ll 50\%$ coverage is better than potential errors in higher coverage [4].
- In the pilot phase, returned data will be of unknown quality and our experience suggests that if the registry team is responsive and always checks and returns the received data within 2 weeks of receipt, then clinics sending high quality data rapidly identify themselves. We found that this two week window lies within current working memory for data suppliers to correct errors (i.e. before clinic notes go back to filing). We suggest that pilot resources are initially targeted to those clinics returning data with few errors. The next focus in the short window of the pilot should be on helping data suppliers who are not meticulous in their attention to detail with feedback letters stating that 'our records show you have z% of data that is missing or erroneous'. Only then will the audit, outcome and research capability of the registry be empowered.
- After the pilot, we found that training days instigated a competitive element in poor-responders by our decision to award bronze silver or gold status to each data supply centre based on their data quality calculated from errors on first submission. We found that local clinic directors were unwilling to admit to their peers that they were bronze and rapidly attained silver or gold by the next annual feedback session. Coverage of good quality data in our registry was thus facilitated by the public award of gold silver and bronze certificates in sealed envelopes on an annual basis.

3. Consent and management

A patient information sheet written in clear lay language describing the uses of the data, the steps to guarantee their anonymity and the process of management control of the data should be sent for ethical approval. It is good practice also to obtain approval from data protection officers. These patient information sheets must explain the function of the registry, which should enable patient-relevant outcomes to be easily measured. If outcome parameters are unknown, then surrogates for those outcomes must be established at the outset and patients must be informed. The data uses must be clearly specified such as measuring compliance against standards of care if these are agreed but if these are not available and need to be established, then this should be an aim stated in the consent. Great care is needed in the wording because the uses of the data cannot go beyond that stated on the consent form signed by the patient. This form must also state who controls the data, who can gain access and under what circumstances access is granted. The role of a person called a trusted third party in this process cannot be over emphasised because he/she is the point of contact for all participants inside and outside the registry project and is the sole person with access to all the patient-named data on a confidential basis that is needed to administer the registry. The role of this trusted third party must be specified in the consent stating that their remit is to ensure data accuracy (a legal requirement) and confidentiality. This 'trusted' person must in turn be authorised by a legal guardian (in the UK this is called a Caldicott Guardian, an eponymous designation for a person under the law who guarantees anonymity for patients through restricted access to their data).

A named steering committee, defined in the consent, should be elected whose job is to approve any changes to the software and additional items outside the scope of the consent can only be added by re-consent. Once the project starts and timelines are agreed, to avoid fatal 'mission creep' (a military term for going beyond the remit), no further changes should generally be permitted to the software until the deliverables agreed at the outset are met. The steering committee should not be named as individuals, rather by the functions they perform to avoid re-consent when members leave the committee. Finally, the identity of the party known as the data controller needs to be specified on the patient consent form as required by national law and European Directive.

To help those thinking of setting up a registry, we have designed a generic patient information sheet that is compatible with European law and should be given to each patient participant in order to obtain truly informed consent. These are available online in the supplementary material from our recent paper [1]. It should be remembered that this design is intimately related to the type and rank of the data to be collected which must be such that the anonymity of the patient is preserved (see types of data above).

Additional management matters relevant to consent include:

- The brief of the project manager who runs the registry needs to be specified. For example, post-pilot, essential changes need to be project planned (version control) and a helpdesk with swift feedback for data definition problems must be established by the manager.
- The software shelf life should be defined at the beginning. The relationship between any paper records and web-based or local computer-based data collection approaches should be evaluated

from the outset (length of storage, charges, dispute management, non-consent and withdrawing consent after initial consent, insolvency matters relating to the software code).
- It is helpful to have a minimum of 3 years of funding at the beginning (year 1 is the pilot) but preferably a 5 year funding cycle should be established once the first two years have passed.

4. An example

To illustrate the principles outlined above, an example of a pilot which is familiar to all neonatologists is presented to highlight an emerging clinical problem and a proposed registry solution. We describe a systems analysis approach (computer jargon for a project plan to answer the question posed by the problem) and finally, we discuss how the pilot refines the questions to be answered by the registry. We hope that the analysis reported here could act a 'process paradigm' for audit, outcome and research into screened diseases in general. We recognise that our example is one that adds on to an established registry but this does not matter because the example is 'stand alone' in the sense that it is perfectly possible to take our analysis and apply it to pilot a paper trail suitable for any screened disease.

4.1. The journey from screening for cystic fibrosis to specialist care

One of the aims of any National Health Service (NHS) is to prevent disease by timely screening. However, benefit only accrues if screening facilitates timely entry into specialist care. We define the term 'process' as the links in the chain connecting these very different disciplines of screening and patient care. A good example is the expansion of many neonatal blood spot programmes to additionally screen for a number rare diseases such as inherited disorders of metabolism or severe genetic disease. Here, we focus on one such disease, cystic fibrosis (CF) but the principles apply across the spectrum of screened diseases. In resource constrained times, NHS monitoring systems must be able to demonstrate the efficacy of the chosen screening process to an independent auditor or face the risk of closure. Since we had already invested many years of effort in setting up a UK-wide CF database (www.cystic-fibrosis.org.uk), which was operational across all UK CF Specialist Centres prior to the inclusion of CF into the screened panel of diseases in 2003, we carried out a systems analysis of the potential problems in auditing the efficacy of the new CF screening process. We used the newly introduced CF screening programme in Scotland as our test bed.

4.2. Process analysis: a pilot approach using a paper trail

Let us consider the *in utero* baby of two healthy parents. At around 36 weeks of gestation, Scottish parents receive an NHS leaflet explaining that a screening programme exists so that otherwise healthy babies such as theirs can be prevented from developing severe handicap. If the parents consent, and in our experience much less than 1% refuse, then their newborn baby is screened shortly after birth with a blood spot test that is sufficiently powerful to rule-out the screened-for disease in most cases (>95% of 'normals' have a primary screening test result below a pre-agreed cut off value; in this case immunoreactive trypsinogen for CF). Conversely, should any potentially positive screening test result occur, then in combination with the addition of a DNA or another type of test applied to a different blood spot on the card, the 'confirmed' positive result is sufficiently informative to rule-in CF disease (in >90%). That 'true' result must be matched with 'safeguard' re-testing on a clinic blood sample from the baby (in case of a card-induced mistaken identity) and clinical assessment (which captures almost all true CF positives). These principles apply to all screened diseases with the aim of timely entry into specialist care. Such a CF test was introduced in Scotland in 2003 but no outcome monitoring procedure was in place to ensure timely entry into care. We decided to test the robustness of the process leading to entry to care as a primary aim (mission) recognising that merely entering care in due time was simply a necessary first step (short term outcome) to facilitate a subsequent analysis on the degree to which screening ameliorated poor nutritional indices that characterise naturally presenting CF disease (long term mission). For the latter reason, we attempted data capture on growth parameters at birth as a prerequisite towards determining long term nutritional outcomes captured by the UK CF database. Here, we concentrate on the primary aim.

Scotland has a population of about five million and in a prospective audit, 41 babies were provisionally screened positive for CF from the onset of screening on 31st January 2003 through 28th January 2004. This gave rise to a CF incidence of about 1 in 2345 births. When considering this relatively low frequency of a potentially positive screening result from the point of view of a typical 'non-CF' health care professional (midwife, primary care doctor, neonatal nurse or neonatal doctor) who only sporadically engages with the blood spot screening service, the key process issue for us was the infrequent, episodic and random nature of this interaction. This low positive test frequency made it impractical to set up robust procedures that were automatic and routine in a given professional's daily practice. This problem is best illustrated by the average midwife or primary care physician who might never see a screen-positive baby in his or her working life time, even when hypothyroidism, phenylketonuria and galactosaemia are added into the screening spectrum.

From our vantage as remote auditors, this infrequent professional encounter problem was exacerbated by the fact that the patient (baby and mother) journey after any likely screen-positive result was very complicated. There were many steps that required completion by 'low encounter personnel' in finite time to maximise baby benefit. Thus 'a time running out scenario' was a great choreographic challenge because we could not be sure that everyone understood in what sequence they had to act after any baby was screened as potentially positive in order not to miss the small window of opportunity to maximise benefit. A second challenge was posed by the dispersed landscape (Scotland is served by 11 semi-autonomous Health Boards, some offshore in different Island groups). Thus, our challenge was a newly implemented CF screening process, involving thousands of babies born in different hospitals, midwifery units or at home located in widely geographically dispersed health care settings, interacting with many professionals, most of whom would be unlikely to ever be called to act on a positive result. We set up the hypothesis that a paper-based trail was needed to measure screening success (because no 'live' electronic system of data capture was available).

Our audit pilot combined systems analysis and management with data analysis/gathering and our registry team operated on the principle that in CF, delay to first therapy beyond 2 months may be detrimental to the longer term CF outcome [10]. Our 'time and motion' (systems) analysis showed that a properly executed paper trail using a multi-part form that 'followed the baby and mother journey' was a first step both to measure the awareness of the correct procedures amongst the health care professionals and to demonstrate efficacy of intervention in due time.

4.3. Ideal procedure — what should happen

We began by putting on paper our ideal chain of post-screening events compliant with the limited window of therapeutic opportunity afforded by CF screening (Fig. 1). Such time windows also apply to other diseases (phenylketonuria and hypothyroidism for example). For each potentially positive CF diagnosis, the screening laboratory (in our case in the Guthrie Institute in Glasgow) was the source of the 'red alert danger signal' for a screen-positive baby whose enzyme values lay above a cut off for potential CF and whose DNA or other test was

Newborn Screening for Cystic Fibrosis

UKCF Database

Tayside Institute of Child Health
Ninewells Hospital and Medical School
University of Dundee
Dundee DD1 9SY
Tel: 01382 632596

Screening Lab ID reference:

Category 1: Birth information – completed by unit where baby is born

- Baby's full name: _____
- Baby's NHS Number: _____ _____
- Baby's date of birth: ___/___/___
- Baby's sex: _____
- Weight at birth: _____(Kg)
- Length at birth: _____(cm)
- Head circumference: _____(cm)
- Name of Specialist CF Centre: _____

Maternal EDD (est. deliv date): ___/___/___

- Mother's full name: _____
- Town where baby was born: _____
- Mother's postcode: _____
- Name of GP: _____
- Postcode of GP:_____

Category 2: Completed by Screening Laboratory for all babies diagnosed positive / high risk

- Date of sample:
- Ethnic group:
- Name of local designated CF paediatrician:
- Any other information: _____
- Blood results:
  - IRT result 1 :
  - IRT result 2 : _____
  - Genotype: Allele 1:
    Allele 2:
  - Other genetic information: _____

Category 3: Completed by Specialist CF Centre when baby is first seen

Please obtain parent's consent for details to be included on the UKCF Database and affix the patient's sticky label with the patient ID and Clinic Code

- Date of baby's first CF clinic visit at Specialist CF Centre: ___/___/___
- Baby's NHS number: _____ _____
- Father's height: _____ (feet & inches or cm)
- Mother's height: _____ (feet & inches or cm)
- Do any of the following smoke?: *(please circle)*
  Father / Mother / Other carer / Unknown / None
- Antenatal CF screening offered? Yes / No
- Older sibling with CF? Yes / No
- Is baby a twin/triplet/other multiple birth? Yes / No
- Other family history of CF? Yes / No
- Sweat test result: _____
  mmol/L chloride / mmol/L sodium *(circle one)*
- Sweat test result: _____
  mmol/L chloride / mmol/L sodium *(circle one)*

Please circle yes or no for each of the following questions:

The original of this form should "follow the baby" and be completed at each stage. As each category stage is completed a copy should be sent to the UKCF Database at the above address. To complete the audit loop, 3 copies should be received centrally at Dundee.

Fig. 1. Process analysis using a form generated by the screening centre (section 2) and sent along the patient journey post-screening. Often the data for part 1 was incomplete or unavailable. Delays in obtaining part 3 information were common. Only part 2 was 100% complete.

compatible with CF. They agreed to complete their part of our design of a pilot multi-part screening process form (they completed section 2 of the form shown in Fig. 1). This red alert form initiated a cascade of events.

- The screening laboratory sent the completed form with as much information as they could gather from the limited data on the blood spot card to both our Central CF Audit Register (acting as a trusted third party in Dundee) and to the designated paediatrician (per Health Board) who had agreed to be the initial point of contact for any screen-positive case — ideally this person was linked to the nearest CF centre specialist who might be in a different Health Board because not all Boards have CF care facilities. Thus, we, as independent auditor and the CF health care system for the potential CF baby each had copies of the same information (say by day 10 of life).

- That designated 'screen recipient' paediatrician's role was to immediately refer the potential CF baby to Regional CF centre (this may not be in their own hospital). Often, he/she was also remote from where the baby was born creating a logistical problem in gathering neonatal (part 1) information on the form.
- The nearest CF centre's remit was to see the baby immediately and then register him/her with the National Central CF Register with the first registration step being the generation of a unique identification number that would remain with that baby for life. That sticky label bearing the unique identifier was to be appended to our form. Next, that CF centre was asked to complete its section, the lowermost part of our form, that would prove that the CF baby entered the preventative care window 'in due time'.

In summary, a properly completed form should carry three essential bits of information: Information from the screening laboratory (section 2); baby's birth data from maternity/baby unit (section 1) and each CF centre's unique identifier and CF-specific, baseline data (section 3). We piloted that ideal chain via the paper form requesting that it be filled in by different links in the chain during the baby journey from birth in the community to CF care. We prospectively monitored the above ideal against the observed actuality to gather information on the rate limiting steps and how they might be overcome.

4.4. Observed problems with the operation of the existing procedure/data flow in Scotland

At the time of closure of the audit in 2004, forms were awaited for 10 of the 41 babies diagnosed in that year. Thus, we concluded that for every 4th baby who screened positive, we were unable to prove that the aspiration to prevent disease was always effective in a timely manner. This is not to say that screening failed, but entry into CF care by 2 months of age could not be proven. Given that the screening laboratory had performed in an ideal manner with 100% completion, we sought reasons from the CF centres and discovered that:

- Forms were not sent to us in time because of difficulties with the capture of birth data for example incomplete information on the baby's name (which could change for single parents, partners, etc.). This led to a great deal of time being spent chasing up missing information from maternity units. Because this birth record information was not readily available from (geographically dispersed) maternity units, we contacted the head of the Scottish Neonatal Consultants Group to explain the issues who suggested a single point of contact which helped greatly with data gathering.
- A related difficulty arose when our point of contact inside a CF centre changed due to staff turnover and a lack of a standard handover procedures meant that partially completed forms were sent to us by untrained personnel. This resulted in our having to contact the new CF clinic staff, who either could not locate our form or were unaware that these forms had to be completed. Such difficulties had to be resolved following discussions with the relevant CF Centre Director.
- Occasionally, a unique identifier label was not fixed, hence we had no means of confirming that the baby seen at CF centre was the correct screened baby.
- CF centre forms were not always returned promptly inducing a long time delay between the baby being identified by the laboratory and the baby appearing on central registry leading to more work to track "missing" babies. A key operational delay was caused by staff waiting 4–6 weeks for sweat test data. Some delay was justified because of a minority (<5%) of atypical diagnoses or babies who were found to be carriers or only subsequently diagnosed as CF positive due to a rare second mutation.

These potential deficiencies in pilot phase led us to suggest the following *Standard Operating Procedures*:

- An independent 'trusted third party' auditor in a single location remote from the service offering screening should be an essential safeguard as auditor. They should introduce a simplified version of the pilot form as their vehicle to measure the process of screening.
- With respect to the secondary aim of collecting long term outcome data, the maternity units were almost always the rate limiting step when data was missing and maternity managers should be made aware of the need to help in completing the birth information on the form e.g. baby's weight, length, head circumference, etc.
- A standard might be such that the first time a baby is seen by the CF centre, the following should happen within 1 week: The completed screening process form should be acted on by a local designated Data Manager in each CF centre so that the baby can be registered with the central CF registry. The baby should be immediately registered with the national registry by the clinic Data Manager at the first visit. A copy of the screening form along with the unique identifier sticky label should be sent to the centre responsible for audit. Any awaited test results that could delay completion of the form by the CF centre should not delay the form's return and as much information as practically available by the deadline of 1 week should be dispatched, with the rest to follow as it becomes available.

5. Conclusions

This paper sets out our standards for any high quality disease register and our procedures in the CF registry field have been cited as excellent practice by independent bodies such as the UK Data Protection Registrar (Health) and the European Rare Disease Initiative having been applied to CF projects both in the UK [11] and across Europe [12]. The underpinning protocols (www.cystic-fibrosis.org.uk; www.eurocarecf.eu) have generated many disease outcome publications and the relevant documentation is available in the supplementary material accompanying our recent paper [1]. For the UK, consent and its legal framework was undertaken as project work between 1992 and 2000. That consent, using the principles outlined in this paper, was obtained from over 7000 patients with CF before implementing our first UK register and more recently, we used a similar approach for 30000 patients across Europe. Trans-national consents applicable (with modification) to any disease have also been published [1]. In our experience, very few patients fail to consent (less than 20 amongst thousands over a decade of experience), perhaps because the explanation at a patient level is both detailed and written for maximum clarity by non-medical experts in conjunction with health care professionals. In all cases, the uses of their data are clearly spelled out.

In the example we cited, screening was implemented without formally setting up the means to monitor its effectiveness. For those contemplating a new screening process, our pilot suggests that a minimum standard should be a phone call to each centre asking for the date at which the newly screened baby was seen by the team and whether the baby entered care before 2 months of age as recommended for CF [10] and the appropriate time for other diseases. That analysis would inform government that the screening process is itself robust up to the point of entry into therapy. This is what we mean by the simple pilot approach when outcome analysis resources are almost nil as will be the case in most newly implemented screened programmes. Fortunately, we had sufficient resource to apply a paper trail, designed to mirror the patient journey. This was a simple but powerful process tool created by a registry manager and experienced data handling staff. A very similar paper form was applied in pilot phase between 1992 and 1995 (see www.cystic-fibrosis.org.uk). Indeed, that pilot led to a redesign of clinic encounter forms that facilitated an analysis of how CF centres were performing (currently

in process). In the case of the post-screening pilot form in Fig. 1, once again much valuable information was gathered to improve the screening process. To the author, who was a member of both his local area (in Tayside, Scotland) and the Scottish National Screening Implementation Groups (in Edinburgh), the insight from both sets of forms was invaluable to help improve services for screened CF babies.

In summary, we describe a practical problem of wide relevance to neonatal screening practice that was audited in a prospective manner. The pilot paper trail from Fig. 1 can be applied to any screened disease (hearing, thyroid, metabolic, sickle cell, etc.) with appropriate modification but the pitfalls in process must be understood. Firstly, our paper trail was not seen as important. This cultural issue is a problem for many specialists who want to understand the natural history of 'their' disease but find that data gathering is the rate limiting step. Screening programme committees are usually focussed on the demanding task of getting the changes to screening protocols correctly implemented in a very short time. We suggest that proper 'buy in' of outcomes analysis by both specialists in the disease concerned and screening committees should be agreed before screening starts. Nevertheless, we believe that, provided the principles described in the first part of this paper are applied, the systems analysis that generated the form in Fig. 1 remains applicable to measure the success of any screening disease process and we hope that others will use the information we have gathered for the benefit of all individuals with preventable diseases of the newborn. Finally, a 'post-pilot' analysis of our form shows that it could be further refined in mission without jettisoning its aims. For example, parental height was included to ensure that future growth of the CF child was within expected limits but it could be equally regarded as superfluous to our primary process mission because it could be gathered later by the CF centre. This is what we refer to as keeping within the primary purpose (mission) of the paper trail and avoiding 'mission creep' in the final form. Screening is set to expand as technology improves and on a more general note, it will soon be affordable to analyse complete genomic sequences at birth for many diseases for less than $1000. Unless outcome and process measures are put in place through audit, we may fail to grasp the opportunities to show the potential benefit afforded by this powerful emergent technology actually accrues, whilst minimising unintended harm to the screened population at large.

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References

[1] McCormick J, Mehta G, Olesen HV, Viviani L, Macek Jr M, Mehta A. Comparative demographics of the European cystic fibrosis population: a cross-sectional database analysis. Lancet 2010;375(9719):1007–13.
[2] Dodge JA, Lewis PA, Stanton M, Wilsher J. Cystic fibrosis mortality and survival in the UK: 1947–2003. Eur Respir J 2007;29(3):522–6.
[3] McCormick J, Green MW, Mehta G, Culross F, Mehta A. Demographics of the UK cystic fibrosis population: implications for neonatal screening. Eur J Hum Genet 2002;10(10):583–90.
[4] Mehta G, Sims EJ, Culross F, McCormick JD, Mehta A. Potential benefits of the UK Cystic Fibrosis Database. J R Soc Med 2004;97(Suppl 44):60–71.
[5] Black N. High-quality clinical databases: breaking down barriers. Lancet 1999;353 (9160):1205–6.
[6] Sims EJ, Green MW, Mehta A. Decreased lung function in female but not male subjects with established cystic fibrosis-related diabetes. Diab Care 2005;28(7): 1581–7.
[7] Lai HJ, Cheng Y, Cho H, Kosorok MR, Farrell PM. Association between initial disease presentation, lung disease outcomes, and survival in patients with cystic fibrosis. Am J Epidemiol 2004;159(6):537–46.
[8] Schechter MS, Margolis PA. Relationship between socioeconomic status and disease severity in cystic fibrosis. J Pediatr 1998;132(2):260–4.
[9] Schechter MS, McColley SA, Silva S, Haselkorn T, Konstan MW, Wagener JS. Association of socioeconomic status with the use of chronic therapies and healthcare utilization in children with cystic fibrosis. J Pediatr 2009;155(5):634–9.
[10] Farrell PM. The meaning of "early" diagnosis in a new era of cystic fibrosis care. Pediatrics 2007;119(1):156–7.
[11] Sims EJ, Mugford M, Clark A, Aitken D, McCormick J, Mehta G, et al. Economic implications of newborn screening for cystic fibrosis: a cost of illness retrospective cohort study. Lancet 2007;369(9568):1187–95.
[12] McCormick J, Sims EJ, Green MW, Mehta G, Culross F, Mehta A. Comparative analysis of Cystic Fibrosis Registry data from the UK with USA, France and Australasia. J Cyst Fibros 2005;4(2):115–22.