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Expanding the notion of ‘benefit’: comparing public, parent, and professional attitudes towards whole genome sequencing in newborns

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Expanding the notion of ‘benefit’: comparing public, parent, and professional attitudes towards whole genome sequencing in newborns

Whole genome sequencing (WGS) is being considered as a tool to deliver newborn screening (NBS) internationally. Its use would dramatically increase the number of genetic variants identified, presenting a host of ethical, social, and practical considerations. A scoping review was conducted to examine the acceptability of WGS-NBS among parents, the public, and health professionals. Parent/public groups were enthusiastic about WGS-NBS, holding panoramic views of current/future benefits, incorporating family and wider society. While actionable early-onset findings were prioritised, non-actionable and uncertain results were still viewed as empowering. Conversely, professionals preferred selective results disclosure, prioritised by clinical need. They emphasised the need for meaningful consent and protection of the child’s autonomy. All groups outlined the importance of properly considered implementation (e.g. resources, governance) to minimise harms and prevent a reduction in NBS participation. As genomic medicine integrates into healthcare, divergent conceptualisations of ‘harms’ and ‘benefits’ across social groups must be considered.

Keywords: public and parent views, healthcare professionals, newborn screening, genomics

Introduction

Technological advances and decreasing costs mean that whole genome sequencing (WGS) is increasingly being incorporated into healthcare, with the promise of personalised medicine, targeted treatments, earlier diagnoses and cost savings (Brittain et al. 2017; Saunders et al. 2012). In the UK, the embedding of genomics into healthcare was signalled through the creation of the 100K genomes project (2012), and the establishment of the NHS Genomic Medicine Service. As part of this expansion of genomics, the Newborn Genomes Programme—a pilot study with the aim of sequencing the genomes of 200,000 babies, was launched in 2022 (Newborn Genomes Programme,

2022). The pilot was preceded by a public dialogue designed to explore public attitudes towards this unprecedented use of WGS-NBS (Hopkins Van Mil 2021), and this paper originates from the literature review conducted to inform this dialogue.

Newborn screening's (NBS) primary purpose is to detect serious conditions where outcomes can be significantly improved through early diagnosis and treatment. Nine genetic conditions are currently screened for in the UK (Guthrie heel prick test) with over 96% of babies undergoing screening (PHE 2018). Historically, the viability of screening programmes has been assessed against criteria proposed by Wilson and Jungner in 1968 (Pitt 2010), which focus on important, well-understood, treatable health problems. However, as interpretation of these guidelines varies considerably between countries, so does the number of conditions screened for. The UK NBS panel, for example, is conservative compared to European countries (Loeber et al. 2021) and the USA, which currently lists 61 conditions on the Recommended Uniform Screening Panel (ACHDNC 2020).

Through sequencing the entire genome, WGS produces swathes of data and is capable of identifying thousands of genetic variants associated (to varying degrees) with inherited conditions, predispositions to future conditions (e.g. cancer), carrier status (conditions that can be inherited by future generations), as well as many variants of unknown significance (VUS). The introduction of untargeted WGS-NBS would represent an unprecedented alteration to the scope and purpose of NBS, as well as posing ethical, practical and clinical dilemmas as to which results are relevant to the newborn and which should be returned. Whilst on the one hand, its use could increase the identification of children who would benefit from early treatment and reduce diagnostic delays (Saunders et al. 2012), it would also produce many poorly understood results, and those with highly uncertain predictability and pathogenicity. This poses

interpretive dilemmas for clinicians and can lead to children becoming ‘patients-in-waiting’, creating more—not less—diagnostic uncertainty (Timmermans and Buchbinder 2010). Results relating to untreatable conditions, those with late onsets, as well as those relevant to the wider family’s health and reproductive decision-making, raise questions as to whose benefit NBS is being conducted for.

Ethical questions include how potential harms (e.g. anxiety, overdiagnosis) are balanced against possible benefits (e.g. early intervention), whether parents will be able to understand/ adequately consent to receiving such complex information with life-long consequences, and whether parents should have access to information which only becomes relevant to the child when they are themselves old enough to consent to receiving it (e.g. carrier status, adult-onset conditions). Any reduction in (currently high) levels of participation in NBS, resulting from parental confusion/ anxiety about WGS, could also lead to treatable conditions going undetected with consequences for childhood morbidity and mortality. Endorsement by the public—parents in particular—is therefore critical if WGS is to be successfully integrated into NBS.

Given the emergent nature of this topic, no previous studies have compiled and contrasted public, parent, and professional views on WGS-NBS. By drawing on international literature, this review highlights the social and ethical consequences of WGS-NBS, by presenting harms and benefits as perceived from public, parent, and health professional (HP) perspectives. From this, core areas of convergence and divergence are delineated and the complexities of views around the use of WGS-NBS outlined.

Methodology

Due to the time-limited nature of this study, the emergent nature of the topic, and lack of previous reviews, a scoping-review methodology was adopted. Scoping reviews are

appropriate when there is a need to map the landscape of current research evidence, including the extent, nature, and range of studies conducted on a topic (Cacchione 2016).

Searches of published and grey literature were conducted (August-September 2020) using PubMed MEDLINE, ISI Web of Science, Embase, CINAHL and Google Scholar. Synonyms of the following terms (connected by 'AND') were used: *parent* or *public* or *health professional*; *views*; *attitudes*; *whole genome sequencing*; *next-generation sequencing*; *newborn screening*; *neonatal screening*. Qualitative, quantitative and mixed methods studies directly reporting public/parent/HP attitudes towards WGS-NBS were searched for. Whilst there were no geographical or temporal limits, only papers written in English and reporting empirical data were included (commentaries and opinion pieces were excluded). No limitations were placed on HP field, with studies reporting the views of genetics specialists (e.g. counsellors, clinical and laboratory geneticists, researchers, specialist nurses) and genetics non-specialists (e.g. midwives, general practitioners, obstetricians, paediatricians) included. Backwards and forwards bibliography checking of all relevant studies was also undertaken.

As initial searches returned a small number of papers (n=9) meeting our inclusion criteria, searches were broadened iteratively by including:

- (1) studies of WGS outside of NBS (e.g. WGS in adults)
- (2) studies exploring the expansion of NBS (with/without genetic testing)
- (3) the views of genetic services patients, including research participants (e.g. BabySeq project) and parents of critically ill newborns undergoing clinical WGS.

Additional search terms were *patient*; *neonate*; *expanded*; *paediatric*; *genetics*; *heel*

prick; bloodspot.

As is typical for scoping reviews, both authors read all included papers and relevant findings were ‘charted’ (Peters et al. 2015) (see Supplemental Information), which is the process of developing a descriptive tabulated summary of relevant extracted data, along with key information about the paper (e.g. year, methods, sample size). This was followed by a thematic analysis to synthesise key findings. Broad meta-themes that cut across studies were firstly identified by one author (FB) before being refined into sub-themes through fine coding by both authors independently. Analysis meetings were conducted to discuss sub-themes and resolve discrepancies in coding (although these were few). Theoretical saturation was achieved when no new themes were being generated and the coding framework accounted for the entire dataset. The results are presented around the core meta-themes, with sub-themes discussed within each one. Studies cited in the results section have been selected because they clearly demonstrate the theme under discussion, however all 103 included studies contributed to the core meta-themes and sub-themes.

Results

Only nine studies directly focused on attitudes towards WGS-NBS. Findings from the UK public dialogue (Hopkins Van Mil 2021) have since been incorporated, bringing the number of directly relevant studies to ten. Of these, six examined parental perspectives, two the general public’s, and two HP attitudes. With the relevant surrounding literature, a total of 103 papers were included in the review, with some overlap between groups (52 public, 46 parents, 25 HPs).

Support amongst parents and the public

There was widespread support for WGS amongst parents and the general public; over

half of US adults were interested in having their own—or their child’s—genome sequenced (Dodson et al. 2015), and attitudes were generally supportive of clinical applications (Etchegary et al. 2020), including for NBS (Hopkins Van Mil 2021). In one quantitative public-attitudes study, 80% of US participants would choose to participate in WGS-NBS (Bombard et al. 2014). Support was generally high in the studies directly exploring parental views; for example, 82.2% of US parents (surveyed following their child’s birth) were interested in WGS, with 46.1% ‘very/extremely’ interested (Waisbren et al. 2015).

Support for WGS-NBS was motivated by the wide-ranging benefits parent/public groups envisaged the technology providing, summarised below.

Direct clinical benefit to the child

Public/parent groups overwhelmingly wanted to receive findings relating to early-onset conditions, particularly when an intervention could prevent it or modify its severity (Goldenberg et al. 2014; Hopkins Van Mil 2021). This included pharmacogenomic findings where, for example, parents imagined their child could be helped more swiftly in an emergency (Joseph et al. 2016).

Familial current and future benefits

Family relationships and responsibilities were critical to parent/public views, with ‘family legacy’ being the most common analogy used by the UK public to describe genomic data (Ballard et al. 2020). Public/parent groups often perceived the decision to engage with WGS as a ‘familial’ decision (Dodson et al. 2015; Etchegary et al. 2020), benefitting current and future family members through the identification of health risks (Tolusso et al. 2017), and aiding diagnoses (Middleton et al. 2020). Carrier status results (often de-prioritised within existing NBS) were viewed as important for guiding their

own/wider family's/child's future reproductive decisions (Mackley et al. 2018; Sapp et al. 2014) and were explicitly referred to as "reproductive risk information" in Miller et al. (2015). UK dialogue participants, presented with Familial Hypercholesterolaemia as a case study, saw indirect benefits to the child from their parent becoming aware of their own risk status through the child's NBS result, as they could take steps to avoid a potentially fatal condition (Hopkins Van Mil 2021). Screening results were also seen as a springboard for accessing family support (Hasegawa et al. 2011), highlighting the relevance of the social and cultural positioning of the family unit in responses to WGS-NBS.

Knowledge is power

Parent and public groups valued 'knowledge for the sake of knowledge' (Pereira et al. 2019), believing that 'knowledge is power' (Hasegawa et al. 2011; Ryan et al. 2017). This theme surfaced frequently when considering untreatable and/or late-onset conditions and uncertain findings. For example, 67% of parents whose child was enrolled in a prospective WGS study wanted results for adult-onset conditions (Groisman et al. 2019). Similarly, the majority of parents in DeLuca (2018) thought the maximum conditions possible should be screened for (regardless of treatability/onset), and several studies illustrated a desire amongst public/parents to receive all findings (Fernandez et al. 2014; Harris et al. 2012; Sapp et al. 2014; Starr 2015). The desire for results affording no current clinical benefit was often linked to a sense of taking ownership of one's own/family's health, with the hope that future clinical interventions (Bollinger et al. 2012) or changes in lifestyle (McGuire et al. 2009) could bring benefits across the life-course and for subsequent generations. The information was also seen as enabling mental and practical preparation, through accessing support networks, education, advocacy, the prevention of diagnostic odysseys and guiding the child in

their life decisions (e.g. career) to allow for anticipated future health (Bollinger et al. 2012; Hopkins Van Mil 2021; Pereira et al. 2019; Ryan et al. 2017).

Societal benefits – altruism and scientific progress

Public/parent groups, including parents of children with rare diseases, identified altruistic benefits to future generations and wider society from genomic data-sharing, with many willing to share their own/child's data for research purposes (Middleton et al. 2020; Moultrie et al. 2020; Sapp et al. 2014; Starr 2015). Data-sharing was seen as enhancing the value of WGS through increased efficiency, accelerating research, improving healthcare, and serving 'a greater good' (GAUK 2019; Goldenberg et al. 2014; Starr 2015; Shabani et al. 2014). Trust in, and support for, scientific progress frequently underpinned altruistic motivations, with WGS aligned with 'information' and 'progress' in the UK public's imagination (Ballard et al. 2020).

Support amongst health professionals

HP views were notably different to those of parent/public groups. In the two studies directly analysing HPs views, 65% (Iskrov et al. 2017) and 85% (Ulm et al. 2015) of genetics professionals opposed WGS-NBS. Despite this, 75.7% of ACMG members saw the introduction of WGS as 'inevitable' (Ulm et al. 2015), and 65% of geneticists and 74% of paediatricians would consent to WGS-NBS for their own child (Iskrov et al. 2017). Most favoured targeted use of WGS, focussing on clinically actionable childhood-onset conditions (Lohn et al. 2013, Ulm et al. 2015), or to improve the sensitivity/specificity of existing NBS (Iskrov et al., 2017; McCullough et al. 2016). HPs were more supportive of WGS for critically/chronically ill and high-risk newborns/children, than for healthy children (Hiraki et al. 2006). Differences between professions were noted, with genetics-specialists least in favour of WGS-NBS (Iskrov et

al. 2017) and the use of WGS more widely, compared with non-genetics HPs. This was particularly pronounced where results concerned untreatable conditions, non-serious conditions, risk/predispositions, and VUS (Middleton et al. 2016).

There was some evidence of HPs adopting a wider view beyond immediate clinical benefit to the newborn; for example, parents' discovery of their own carrier status (Leppert et al. 2018). They did not, however, emphasise the range of non-clinical benefits—or perceive the same level of clinical benefits—as parent/public groups, and were more likely to highlight potential harms (Pereira et al. 2019).

Ambivalence and Decision-Making

Despite generally positive views towards WGS-NBS, public/parent support was not universal. Only 33% of parents enrolled on the BabySeq WGS-NBS project thought that all newborns should be offered WGS, compared with 93% for standard NBS (Pereira et al. 2019). Similarly, a greater proportion of the public would consent to using current targeted-NBS technologies than WGS, leading Bombard et al. (2014) to question whether introducing WGS might reduce NBS participation. Several subthemes emerged in relation to decision-making and reticence, summarised below as those associated with return of WGS results and those allied with the practical implementation of WGS.

WGS Results

Psychosocial harm

Immediate psychosocial harms, such as postpartum stress, anxiety/overwhelm, the loss of 'normal' time with the child whilst asymptomatic, and possible difficulties with parent/child bonding, were prominent parental concerns (Campbell and Ross 2005; Detmar et al. 2008; Hasegawa et al. 2011; Kerruish 2016; Nicholls et al. 2013). In Blom et al. (2019), despite 81% of parents supporting WGS-NBS, 57% thought that delaying

identification of an untreatable late-onset condition would allow for some 'golden/happy' years before symptom onset. Families who received a diagnosis from NBS have described the difficulties in reconciling the contradictions between an abnormal result and a seemingly healthy child (Grob 2008). Parents in Detmar et al. (2008) highlighted the potential for families to experience the 'loss of normal life' following early diagnosis, and for 'disturbed' identity development in the child, who may find themselves occupying a liminal space between health and illness during the latent period of their condition (Timmermans and Buchbinder 2010).

A sense of guilt and responsibility was evident within some parents/public views. Diagnosis of a genetic condition can elicit unique forms of parental guilt and responsibility amongst family members (Quinlivan and Suriadi 2006). Indeed, some felt obligated to screen in anticipation of guilt if they forwent an opportunity to detect a treatable condition in their child (Moultrie et al. 2020), even if this meant receiving potentially unwanted information (McCullough et al. 2016). A participant in Ryan et al. (2017) spoke of a societal obligation to accept medically actionable results to reduce/prevent the need for later medical intervention. This notion of obligation also emerged in the UK Public dialogue, where there was concern that parents may feel pressured to use WGS (Hopkins Van Mil 2021), highlighting the possibility of a future 'technological imperative' (Markens et al. 2010).

Weighing up benefits compared to risks

Parents/public expressed near-universal enthusiasm for immediately actionable results, where early intervention could cure or modify the course of a disease, as this was viewed as unequivocally beneficial to the child (Hopkins Van Mil 2021). Even modest clinical benefit was perceived to outweigh potential harms (e.g. overdiagnosis, false positives) (Miller et al. 2015). Beyond this point, however, there was no clear consensus

amongst lay groups on ‘where to draw the line’ in terms of which results should be returned (Joseph et al. 2016).

Similar to HPs, lay groups prioritised the importance of findings by condition severity, preventability/treatability, and the reliability/predictability of the result (Middleton et al. 2016). Parents were, for example, less interested in conditions seen as ‘liveable’ (Kerruish 2016) compared to those they considered more ‘serious’ (Detmar et al. 2008). For serious, but incurable conditions, parents prioritised non-clinical benefits (e.g. faster diagnosis, mental preparation) over the harm of receiving unanticipated and ‘devastating’ news (Blom et al. 2019). It was evident that when assessing potential harms, lay groups offset them against their panoramic view of benefits (e.g. familial/non-clinical benefits), which could be dispersed throughout the child’s lifetime and beyond (Hasegwa 2011). This positivity towards WGS, seen by some as a ‘leap forward’ in medicine (Hopkins Van Mil 2021), meant accepting a certain level of harm to achieve a perceived overarching good.

The greatest divergence of opinions occurred when considering results of lower/unknown predictive value or uncertain penetrance (e.g. risk of disease, VUS), and those linked to late-onset conditions, particularly when untreatable. Here, benefits were less tangible and parent/public groups were conflicted between “knowledge is power” and “ignorance is bliss” (Joseph et al. 2016). Some viewed results as giving the opportunity to encourage protective health behaviours (e.g. diet, exercise, vigilance); for others, however, they risked parental overload and anxiety, and the child experiencing stigma and discrimination for a condition that may never materialise (Campbell and Ross 2005; Joseph et al. 2016; Quinlivan and Suriadi 2006; Ryan et al. 2017; Van Mil et al. 2017).

Experience with health conditions or genetic screening

Parents of children with health conditions were more interested than other parents in WGS-NBS for subsequent children (Goldberg et al. 2014). Disease propensity findings, although not prioritised by parents of healthy children (Goldenberg et al. 2014), were supported by parents of children already participating in research or diagnostic WGS (Fernandez et al. 2014; Groisman et al. 2019). These parents were also keen to receive carrier results (Hopkins Van Mil 2021; Mackley et al. 2018; Sapp et al. 2014) and showed high levels of support for receiving all (including uncertain) findings (Fernandez et al. 2014; Harris et al. 2012; Sapp et al. 2014). Levenseller (2014) and McCullough (2016) suggest that these parents are more supportive of WGS than those of healthy children because they are more familiar with medical uncertainty and, in their search for diagnosis/treatment, weigh the relative risks and benefits differently.

Rare disease patients/parents in Mackley et al. (2018), however, highlighted the contradiction between the ‘huge’ potential benefits of achieving a diagnosis, and the generation of additional uncertainty through equivocal results. For some, this meant not wanting information that could provide an ‘additional burden’ (Mackley et al. 2018). Similarly, parents—potentially at the start of a diagnostic odyssey—showed less enthusiasm for WGS in case it increased their already high anxieties and feelings of overwhelm (Waisbren et al. 2015).

Choice versus the rights of the parent, family, and child

These deliberations and ‘risk analyses’ were viewed by parent/public groups as personal decisions, not to be determined by professionals, or suiting a ‘one-size-fits-all’ approach (Hopkins Van Mil 2021; Townsend et al. 2012). HPs, however, preferred patient choice “up to a point” (Townsend et al. 2012), or using patient choice to ‘guide’, rather than

determine, information returned (Yu et al. 2014). Many HPs conveyed tensions between balancing the parents' right to know versus protecting the child's 'right to an open future' (Lohn et al. 2013). This reasoning was frequently cited by HPs as justification for not disclosing results, or at least delaying disclosure until a point that the child could consent themselves (Barajas and Ross 2015; Lohn et al. 2013).

Parents, however, saw themselves as custodians of their child's genome (Daack-Hirsch et al. 2013; Ryan et al. 2017), with some planning to filter the information passed to their child, even as adults (Mackley et al. 2017). Many did, nevertheless, express conflict between their right/duty to hold this information, versus their child's rights, particularly the right not to know. For example, carrier status, which could have immediate reproductive implications for parents, but would only be relevant to the child when they themselves are of reproductive age and could provide their own consent (Moultrie et al. 2020; Sapp et al. 2014). In this regard, some thought it more appropriate for parents to undergo pre-conception screening rather than receiving carrier information through NBS (Hopkins Van Mil 2021). Participants in the UK dialogue suggested a 'dynamic' consent model, whereby the child can 'opt-out' in the future (Hopkins Van Mil 2021). However, the child would still be the 'last to know' about health information already divulged to parents, and potentially other family members (Hopkins Van Mil 2021).

Concerns around the practical implementation of WGS-NBS

Public, parent, and HP groups frequently raised concerns over whether current infrastructure is adequate to implement WGS, e.g., resources to support families, systems for data access/storage, and governance to protect against data misuse. A clear conclusion from the UK public dialogue was that these practical barriers must be overcome before WGS could be integrated into UK healthcare (Hopkins Van Mil 2021).

Technology and governance

The potential for a 'loss of privacy', including issues around data security/access, was identified by all groups (Goldenberg et al. 2014; Joseph et al. 2016; Nicholls et al. 2013; Pereira et al. 2019); specifically, profiteering by pharmaceutical companies (Starr 2015), employment or health/life insurance discrimination (Campbell and Ross 2005; Detmar et al. 2008; Harris et al. 2012; Quinlivan and Suriadi 2006; Shabani et al. 2014; Van Mil et al. 2017), and accidental/malicious data leaks (Hassan et al. 2020; Hopkins Van Mil 2021). The importance of governance and technology to prevent data misuse and discrimination was repeatedly highlighted (GAUK 2019; Iskrov et al. 2017; Van Mil et al. 2017). Although HPs raised these issues more frequently than parent/public groups (Iskrov et al. 2017; Pereira et al. 2019; Yu et al. 2014), when questions were framed within the context of the commercial value of genomic data, public support for data-sharing reduced (Briscoe et al. 2020), highlighting the importance of non-commercialisation amongst lay groups. Even within the context of data-sharing for medical purposes—which was well supported—concerns were nevertheless raised about 'mission creep' with changes in government, legislation, or medical knowledge (Hassan et al. 2020). Indeed, 49% of Bionews readers (people with personal/professional interest in reproductive technologies) thought WGS results could alter their ability to obtain health/life insurance, despite a moratorium in the UK to prevent this (Starr 2015), suggesting a lack of awareness of, or trust in, the moratorium.

Resourcing

WGS was seen as ushering in an entirely new approach to genetic counselling, with the removal of pre-test counselling, and a dramatic rise in the number and complexity of results (Nardini et al. 2014). Genetics professionals questioned the ability of parents and

other HPs to interpret results (Hiraki et al, 2006; Leppert et al. 2018), and genetic counsellors reported seeing unnecessary treatments/interventions resulting from misunderstood screening results (Leppert et al, 2018; Mighton et al. 2020).

A considerable proportion of HPs did not consider themselves to have a high level of knowledge of either NBS or WGS (Iskrov et al. 2017): only 45% of genetic counsellors (Lohn et al. 2013) and 32% of ACMG members (Ulm et al. 2015) reported having the highest levels of knowledge/familiarity with WGS. The need for a dramatic increase in training and education for all HPs was noted by genetic counsellors in Nardini et al. (2014), with the majority feeling unprepared to counsel patients on WGS-NBS results.

The perceived lack of staff to provide adequate follow-up care and counselling was a key concern (e.g. Leppert et al. 2018). The possibility of re-interpretation of results over time could mean that repeated consent, disclosure, and counselling would require ongoing resources (Ulm et al. 2015). Genetic counsellors expressed fears of unmanageable workloads (due to the possibility of at least one abnormal result for every newborn screened), the potential for 'marathon' counselling sessions, and increased time pressures due to the possibility of clinically actionable findings (Nardini et al. 2014). One genetic counsellor referred to their role as becoming one of 'damage control', assisting parents to navigate a swathe of uncertain and unclear results (Nardini et al. 2014).

The 'huge' resource implications of integrating WGS into healthcare was also noted by public/parent groups (Etchegary et al. 2021; Mackley et al. 2018). Participants in the UK dialogue questioned whether the NHS could afford the implications of screening (e.g. treatments and life-time monitoring) and whether this would lead to

under-funding in other areas, or create a two-tier health service, with some treatment options only available via privately-funded healthcare (Hopkins Van Mil 2021).

Informed Consent

Informed voluntary consent was seen as key across all groups (Hiraki et al. 2006; Joseph et al. 2016; Quinlivan and Suriadi 2006; Ulm et al. 2015; Ulph et al. 2020); yet genetics professionals argued that there are significant challenges to obtaining it given the range/complexity of possible findings, and because the public generally have poor understanding of genomics (Levenseller et al. 2014). HPs cited pre-existing difficulties with NBS consent processes, with many parents incorrectly assuming it is compulsory (Nardini et al. 2014; Ulph et al. 2020). Indeed, concerns were raised that parents may not fully consider the impact of receiving information relevant to their own future health (Levenseller et al. 2014) carrier status (McCullough, 2016) or other potentially distressing discoveries, such as non-paternity (Leppert et al. 2018). Some feared that the sheer volume of information and ambiguity of findings could lead to anxiety and confusion (Hiracki et al. 2006, Peirera et al. 2019) with subsequent parental frustration, dissatisfaction, or mistrust, reducing NBS uptake (Leppert et al. 2018).

Whilst public/parent groups showed high levels of familiarity with broad genetic concepts (Haga et al. 2013), knowledge about current NBS and the possible consequences of WGS was low (DeLuca 2018; Etchegary et al. 2020; Haga et al. 2013). Despite this, in research/dialogue settings, parents/public groups repeatedly demonstrated an ability to balance complex equations of harms/benefits once provided with sufficient information (Hopkins Van Mill 2021; Ryan et al. 2017). They also noted that genomic information is different in character to other forms of health data (Middleton et al. 2020; Nicholls et al. 2013), therefore warranting specific consent processes (Etchegary et al. 2021).

Equality of access and trust

Whilst there were few consistent demographic effects on attitudes towards WGS, differences between ethnic groups emerged. In some US studies, ethnic minority participants expressed greatest concerns about genetic testing, were more suspicious of data-storage and reuse, and worried that results could increase racial discrimination (Canedo et al. 2019; Joseph et al. 2016; Shabani et al. 2014). The risk of 'racial profiling' and a general mistrust of the medical system amongst minority groups was echoed in the UK dialogue, as well as geographical and socioeconomic discrimination (Hopkins Van Mil 2021). Participants stressed the importance of ensuring equal access to the benefits of WGS-NBS, including ensuring that genomic databases are ethnically diverse (Hopkins Van Mil 2021). Education was seen as key to public cooperation and safeguarding the uptake of WGS-NBS through 'building trust' (Hopkins Van Mil 2021).

Conclusion

Public and parent groups showed greater enthusiasm than HPs for WGS-NBS as they anticipated a wider range of benefits and believed that all forms of health information were inherently valuable, even when highly uncertain. Their enthusiasm was situated within a wider endorsement of the progression of science, technology and medicine, and a valorisation of increasing amounts of health data. While they identified many of the same harms as HPs, they were more likely to see them as being offset by potential benefits. In their search for answers, parents of children with health concerns wanted as much information as possible to achieve a diagnosis or other benefits, which outweighed any harms.

The ongoing relevance of Wilson and Jungner's screening principles are currently under discussion, with questions over whether criteria centred solely around clinical utility to the child are too restrictive (Botkin 2009). This review suggests that public/parent views support this claim, as current/future family members, wider society, and scientific advancement were all recognised beneficiaries. Many parents highly value information for untreatable conditions to end diagnostic odysseys, initiate support, obtain information, and guide future reproductive decisions. The importance of non-clinical benefits to parents can be seen in other established screening programmes, such as foetal ultra-sound scanning, where visualising the foetus to support parental bonding and engage the wider family is considered a significant benefit by parents, if not by HPs (Øyen et al. 2016).

Critics, however, have problematised the public health rationale of WGS-NBS, suggesting its (untargeted) introduction would render NBS a 'fishing expedition' (Timmermans and Buchbinder 2012:21), moving beyond its original purpose, and diluting its focus from the immediate health of the newborn. Emerging evidence that WGS does not perform as well as biochemical tests as a first-tier screen for certain conditions (e.g. inborn errors of metabolism) (Adhikari et al. 2020) further weakens the argument that WGS could ever entirely replace current NBS (Downie et al. 2021). It also strengthens claims that the benefits of WGS to scientific endeavour outnumber those to the screened infant, whilst simultaneously posing significant data risks (Biesecker et al. 2021).

Despite these concerns, there was evidence that parent/public groups upheld the transformative potential of WGS-NBS. Parents of healthy and sick children alike expressed great optimism about the potential for clinical benefits, even for untreatable conditions, with the view that there was always 'something' that could be done, e.g.,

lifestyle changes or contributions to research (Mackley et al. 2018; Moultrie et al. 2020). In the early stages of the UK dialogue, a participant commented that they were ‘hard pushed to see downsides’ of WGS-NBS (Hopkins Van Mil 2021).

Research indicates the public consistently overestimate the benefits and underestimate the harms of screening (Hoffmann and Del Mar 2015). An inability to envisage harms is likely to be due—at least in part—to low levels of knowledge around the limits of genomic data and screening programmes more broadly. Patients with direct experience of genomic medicine were more likely than members of the public to be sceptical about the benefits of WGS-NBS (Pereira et al. 2019; Mackley et al. 2018). This difference carried over to HP groups, with genetics specialists less likely to support WGS-NBS than other HPs, such as paediatricians (Iskrov et al. 2017). These findings suggest that as knowledge of, and familiarity with, genomics increases, so does recognition of potential harms.

Currently implemented screening programmes have faced criticism for not providing a balanced view of harms, which, for some, has led to a change in emphasis from maximising participation to increasing informed decision-making (Gigerenzer 2015). Concerns already exist around the ‘proceduralisation’ of NBS (Nicholls 2012), with many parents accepting screening by default, particularly within the context of the NHS which is viewed as a trusted healthcare provider. When provided with information in a research setting, public/parent groups can reflectively weigh-up harms and benefits (e.g. Hopkins Van Mil 2021), and although many became more discerning with increasing knowledge (e.g. Ryan et al. 2017) a general sense of optimism remains.

In contrast to over-optimism, currently high levels of NBS participation could be reduced due to suspicion over who is collecting/accessing WGS-NBS data and parental anxiety/confusion (Bombard et al. 2014; Hopkins Van Mil 2021; Leppert et al. 2018).

Enabling the public to make truly informed decisions is therefore key to both managing expectations and reducing fear and suspicion. The impact of mistrust on medical practice has been starkly illuminated by the Covid-19 pandemic, where scepticism, misinformation, and fear led to reduced uptake of vaccinations, particularly amongst ethnic minorities, people of lower socioeconomic status, and those with lower levels of education (Paul et al. 2021).

The debate over which genetic conditions/variants parents should have access to will continue as part of the ongoing dialogue around WGS-NBS. Most groups supported the disclosure of immediately clinically relevant—as opposed to all—results, leaving the child to decide (at an appropriate age) whether to receive the remainder (Hopkins Van Mil 2021; Ryan et al. 2017). Some parents, however, wish to use their own deliberations of potential harms/benefits and consider it their right to access to all of their child's genetic information.

The UK NHS aims to be the first national health care system to offer routine WGS, to facilitate a personalised, efficient and cost-effective health service (DHSC 2020). Whilst this aspiration is largely welcomed by the public, all groups expressed concerns about its feasibility (Hassan et al. 2020; Hopkins Van Mil 2021; Mackley et al. 2018). Use of WGS-NBS will have ramifications across professions, for example, family doctors/GPs, who are often a preferred source of information (Mackley et al. 2018). Maintaining trust and ensuring equity of access will require investment in education and outreach. Throughout the literature, lay groups described a vision of WGS-NBS as providing a lifetime resource that could be 'dipped into' at relevant stages by themselves, authorised HPs (Hopkins Van Mil 2021; Ulph et al. 2014), and scientists for reanalysis (Daack-Hirsch et al. 2013). However, NHS systems are not currently designed with this functionality (Report of the Joint Committee on Genomics in

Medicine p15) and therefore investment will be required. Moreover, governance, in terms of data protection and disclosure, is under pressure to keep pace with the speed of genomic technological advancement. The guiding principles for consent and confidentiality in the use of genomic information (JCGM 2019), and the legislation on which they based, are open to subjective interpretation with clarity often coming from test legal cases. For example, ABC v St George's Healthcare NHS Trust, where family members asserted that their right to genetic information trumped patient confidentiality (Lucassen and Gilbar 2018). Without clear guidelines, the role of HPs in deciding which results to divulge, and to whom, is likely to become more complex with HPs under pressure to avoid legal repercussions (Miller et al. 2009).

In summary, the general public and parents supported the use of WGS-NBS in principle, as they perceive wide-ranging benefits to their child, family and society—even if those benefits were not immediately realisable. This panoramic view of benefit neutralised many of the risks they identified. However, to ensure public support and retention of (currently high) levels of NBS participation, several issues regarding practical implementation would need to be resolved before WGS-NBS could be successfully integrated into standard healthcare.

Limitations and Further Research

The scoping review methodology meant that the searches performed were not exhaustive, and quality appraisals were not conducted on included studies (Peters et al. 2015). In addition, as searches were not limited by geographical region the data were generated across a range of (contrasting) healthcare systems. This potentially limits the transferability of some findings to a UK context. However, not limiting by geographical area enabled this review to develop a broad overview of both the extent, and content, of

the literature that surrounds the use of WGS-NBS from the perspectives of public, patient, parent and HP groups. Moreover, the key meta-themes and trends identified were found to be largely consistent, with differences occurring more commonly within subthemes.

We were unable to determine from the majority of papers how WGS had been described/introduced to study participants (e.g. likelihood of inconclusive results or VUS) and this may have affected how positively participants viewed WGS. As the literature expands, future research may usefully explore the impact of information provided to participants when making their deliberations, as well as differences in attitudes across populations and contexts, for example, the role of ethnicity, reproductive status, age, and educational/socioeconomic status.

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