The public perception of the facilitators and barriers to implementing personalized medicine: a systematic review

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Abstract:

The integration of Personalized medicine (PM) into mainstream healthcare will only be successful if the public understand and support this change. The aim was to understand the public perception of the barriers and facilitators towards the use of PM. A mixed methods systematic review of the literature was conducted within six databases from 2006 to present. Twenty-one studies with 9507 participants were included. The key themes were familiarity and willingness to use PM, perceived benefits and perceived risks of PM. The review shows that, despite a limited familiarity of the underlying principles, the public is generally enthusiastic about the introduction of PM. The study defines areas where progress can be made to enhance this understanding and address legitimate concerns.

Introduction

The international Human Genome Project began in the 1990s to produce the first DNA sequence of the entire reference human genome [1, 2]. The sequencing of the human genome provides new insights that explain the causation and severity of human diseases and predict individual responses to medication [2]. The Human Genome project has provided the foundation to translate genomic information into health benefits in the form of PM. This emerging PM approach aims to deliver targeted treatments, based on an individuals' genetics aims to improve treatment efficacy and reducing the risk of adverse effects [2, 3]. Leaders of countries and large healthcare organisations are urging a rapid translation of these discoveries into benefit for patients [4, 5]. However, the conversion to "an innovative approach that takes into account individual differences in people's genes, environments, and lifestyles" [5] from the existing "one-size-fits-all" approach in healthcare will require a better understanding of this new approach by the general public and other stake-holders [6].

PM is a term which has been adopted within the literature and within clinical practice with a varied number of definitions. The subjectivity when defining PM has been recognised by Schleidgen et al, who performed a systematic literature review to produce a precise definition: "PM seeks to improve stratification and timing of health care by utilizing biological information and biomarkers on the level of molecular disease pathways, genetics, proteomics as well as metabolomics" [5]. Other publications have viewed pharmacogenetics/genomics (PGx) as the foundation of personalized medicine and thus solely focused on PGx when measuring opinion on personalized medicine. For the purpose

of this literature review the authors have followed the National Institute of Health (NIH) definition of PM as an “approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person” [7].

With an increasing appreciation that PM will only become successful with public acceptance and participation [8], there is now an extensive body of literature regarding the public’s attitude and opinion regarding PM. However, while the last decade represents a critically important period in the history of development and maturation of PM, our searches of 6 databases could not identify any systematic reviews on this subject since 2006 [9]. The last systematic review of the public perspective of PM by Nielsen and Moldrup was published in 2006 and focused mainly on pharmacogenomics [9]. This reveals a significant knowledge gap regarding the public’s views on PM. It is thus currently difficult to fully appreciate the public’s views about PM against the context of the very positive views expressed by government and opinion leaders. We do not have a holistic understanding of the concerns regarding PM within the public. Overall, this lack of knowledge makes it difficult to design public engagement activities in this field that are based on an up-to-date understanding of public opinion. There is thus a need for a detailed systematic review of publications in this area until the current date, and to produce regular updates of such a review.

Methods

Search strategy

A search of the literature was conducted in February 2018 using 6 databases (Medline, Embase, Cinhal, BNI and Psycinfo). Terms for PM were searched in conjunction with terms relating to public opinion (see appendix 1 for full search strategy). The search was restricted to papers published from 2006-2018, to capture the effect of the most recent advances in genomics and PM on public perception. Editorials, conference abstract or reviews were excluded from the review. In addition, papers were identified from references of selected articles that were relevant and met the inclusion criteria.

Inclusion and exclusion criteria

Studies were eligible if they included an aim or objective relating to the public’s opinion of PM and if at least one group of participants were members of the public. Studies with both quantitative and qualitative study designs were included. Studies were excluded from the review that were editorials, conference abstract, reviews and commentaries and if it was published before 2006. The full inclusion and exclusion criteria can be seen in appendix 2.

Study selection and data extraction

The Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) summarises the systematic review process used (see figure 1). Data was extracted using a proforma before qualitative synthesis was carried out using a thematic approach that was independently adopted by two of the authors. The methodology, including the research question, search strategy, inclusion and exclusion criteria and risk of bias assessment, was defined prior to the start of the review.

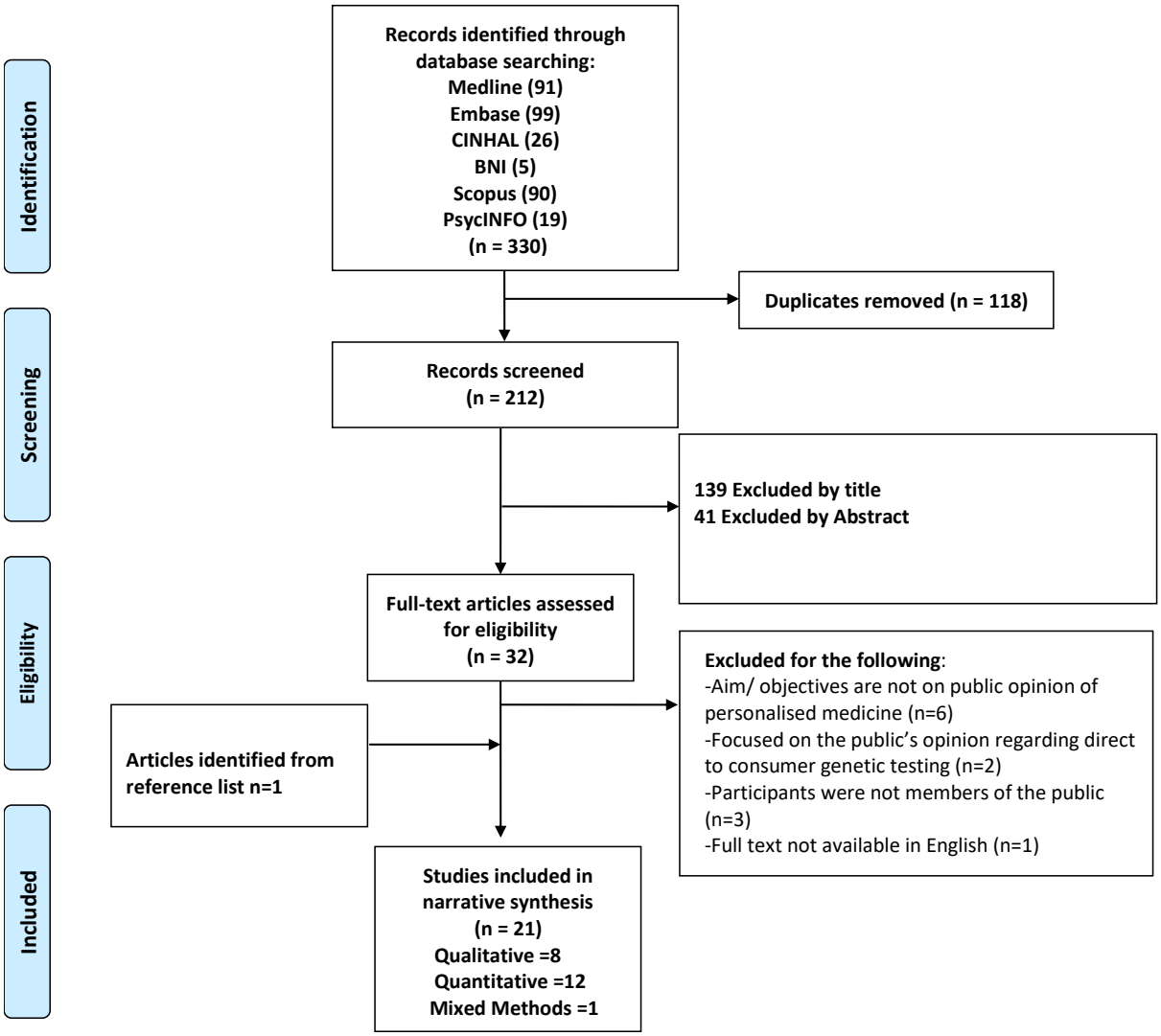

Figure 1. Prisma diagram for the inclusion of studies reporting public opinion of PM.

Assessment of study quality

The mixed methods appraisal tool (MMAT) 2011 version [10] was applied to each study by the authors to give an assessment of the methodological quality. The MMAT was chosen as it was designed for the appraisal stage of a complex systematic review that includes quantitative, qualitative and mixed methods studies. The MMAT comprises of 2 screening questions and 4 criteria assessing the methodology that are specific to the study design. A score can be derived of 0% (no criteria met) to 100% (all 4 criteria met).

Summary measures and data synthesis

A qualitative thematic synthesis of results was performed. A minimum of two authors reviewed each paper.

Results

Table 1. Characteristics of studies included in the review (presented in chronological order)							
Author & (publication year), study location	**Study population**	**Selected sample characteristic (age, gender, ethnicity, education level)**	**Sample size**	**Study design**	**Recruitment method**	**Results**	**MMAT score**
Rogausch et al. (2006) Germany [22]	Adult members of the public (with a respiratory condition) and General Physicians (GPs)	Mean age 57.6 Public: 55% female. GPs: female 25%	302	Quantitative, telephone survey	Convenience sampling	95.9% of patients would accept pharmacogenomic testing prior to receiving a prescription for asthma medication. 94.4% felt it would be advantageous to know their genetic disposition. Younger patients were generally more likely to be hopeful about the usefulness of pharmacogenetic testing (OR = 2.12; CI = 1.01–4.46).	50
Nielsen & Modrup (2007) Denmark [17]	Adult members of the public	50.5% Female. Further education 55.3%	3000	Quantitative Internet-based survey	Purposive sampling	Increased knowledge of pharmacogenetics among participants who have experienced lack of effect and side effects of medicines and have had medical investigations. 79.1% of participants think that society needs pharmacogenetics, while 3.7% do not think so,	75
Nielsen & Modrup (2007) Denmark [23]	Adult members of the public	50.5% Female. Further education 55.3%	3000	Quantitative Internet-based survey	Purposive sampling	14.1% of participants had heard of pharmacogenomics. 89% indicated willingness to receive pharmacogenetic treatment in future. 81% would choose to use a pharmacogenomics-directed drug rather than an 'ordinary drug'. Generally positive attitude towards pharmacogenomics. No significant results showing that experiencing side effects is connected to the respondents' general attitude to the use of pharmacogenetics in medicinal treatment.	50
Barr et al. (2008) UK, Poland, Germany & Denmark [16]	Public and mental health service users	Not documented.	96	Qualitative, focus groups	Purposive sampling	Broad support for genome-based therapies for depression. Public groups felt pharmacogenomics was generally a good idea and felt positive towards it. The public focus group from Poland were particularly positive. Service users had concerns whether genetic testing was applicable to depression.	50
Issa et al. (2009) USA [21]	Adult members of the public	53% male. 66% Caucasian, African American 20.7%. University degree or higher 66%,	32	Qualitative, focus groups	Convenience sampling	Participants in all 4 focus groups demonstrated a limited understanding of the genetic basis of PM. Majority of participants indicated a preference for the use of pharmacogenomics testing for the purpose of improving drug prescribing. Participants were concerned with issues surrounding privacy and confidentiality of genetic test results, particularly with respect to access of information by insurers or employers.	50
Haddy et al. (2010) Australia [14]	Public with a chronic health conditions or family member with chronic health condition	Age range 18->60 years. 74% female.	35	Qualitative, focus groups	Purposive sampling	Majority of participants unfamiliar with the genetic basis of PM. Pharmacogenetic testing viewed as being potentially positive. Concerns regarding storage and privacy of genetic information and the costs involved.	75
De Marco et al. (2010) USA [24]	Adult members of the public	Female 77.1%. 70% African American, 30% Caucasian. Secondary school	48	Qualitative, focus groups	Convenience sampling	All focus groups shared generally positive views on PM with the view it has the potential for medication with fewer side effects and less 'trial and error prescribing'. African American group more concerned regarding cost of personalised medicine	75

		education level 79.2%,				and they were less likely to trust their health professional and therefore accept recommendation of PM.	
Butrick M et al. (2011) USA [28]	Adult members of the public	Mean age 47 years. Female gender 67%. 46% Caucasian, 47% African American.	387	Quantitative, Vignette based survey	Convenience sampling	Overall participants found genetically personalised medicine as 'comparably effective' as conventional medicine but were reluctant to take up personalised medicine. Participants from an ethnic minority background (who were predominantly African American) reported lower adherence intention to genetically personalised medicine compared to non-minorities.	25
Tercyak et al. (2011) USA [31]	Public who are parents of children <17 years of age	Mean age 35 years. 44% Caucasian, 54% Black African American or Caribbean. 24% university level education.	219	Quantitative, survey	Purposive sampling, online	51% of participants would agree for their child to undergo a genetic test if offered. Factors increasing the willingness for their child to undergo genetic testing were: being the child's mother, perceiving the child to have greater disease risk and valuing knowing about gene health links	75
Gordon et al (2012) USA [30]	Adult members of the public	40% male and 60% female. 68% Caucasian. 60% college education.	60	Qualitative, Individual semi structured interviews	Purposive sampling	Approximately 66% planned to act on their genomic risk assessment results by making or planning lifestyle or behavioural changes. 25% were concerned regarding the confidentiality of genetic information.	75
Haga et al. (2012) USA [13]	Adult members of the public	Female 52%. Caucasian 78%, Black African American 16%, Asian 4%. University degree 42%.	1139	Quantitative, telephone survey	Stratified random sampling	After initially being told of the risks of pharmacogenomic (PGX) testing 65% of respondents were extremely/somewhat likely to agree to a PGX test. However, once informed of the benefits of PGX testing this increased to 82% of respondents showing interest. Experiencing a drug side-effect was significantly associated with likelihood of testing OR 1.56 p=0.042.	75
Gollust et al. (2012) USA [18]	Public who had received personalised medicine	Female 64%. 87.9% Caucasian, 5% African American. University degree 31.9%.	369	Quantitative, Internet-based survey	Convenience sampling	Awareness of 'personal genomics' was high, 78% of those had heard of the term before (22.1% had never heard of personal genomics, 58.9% had heard a little, 18.9% had heard a lot). 18.9% were concerned that results of PM could cause denial of insurance.	25
Green et al. (2013) UK [29]	Adult members of the public	Mean age 21.5. 78% female. 70% Caucasian.	158	Quantitative, Scenario-based questionnaire	Convenience sampling	Participants were less willing to use a personalised medicine over a pharmaceutical medicine. Personalised medicine was not considered less harmful or more beneficial than conventional pharmaceutical medicines.	50
Bombard et al. (2013) Canada [25]	Adult members of the public	Age: 43% 18-39, 29% 40-54, 14% 55-70 years. 50% Caucasian	14	Qualitative, focus group	Purposive sampling	Majority felt that personalised medicine increases care. Concern that PM could lead to stratification of patients appropriate for certain treatments and therefore result in the 'rationing of care'. Concern regarding discrimination from employment and insurance sectors. Concern of cost of PM and whether it is "value for money". Concern health care systems and providers unprepared to implement PM.	75
Chan et al. (2014) Singapore [27]	Public and patients receiving warfarin	Public: mean age 52.5, male gender 27.3%. higher education: 41.7% Patients: mean age 57.3, male gender 73.7%, higher education: 28.4%	381	Quantitative, survey	Convenience sampling	38% of patients and 60% of participants from general public sample were either 'somewhat wiling' or 'very willing' to undergo warfarin PGX testing. Participants in the general public sample without a history of an ADR tended to be more willing to undergo warfarin PGX testing than those who had experienced an ADR.	50
Zhang et al. (2014)	Public and medical students	No details provided	567	Quantitative, Explorato	Convenience samplin	36% of lay respondents misidentified what was meant by personalised medicine. Proper explanation before PGX testing	50

Canada [20]				ry survey	g	appeared to be the most important issue to the respondents. Respondents who were more knowledgeable about PGXx were also more comfortable with PGXx testing.	
Eastman et al. (2014) USA [19]	Adult members of the public	Gender male: female 1:1 ratio	1024	Qualitative, telephone survey	Not noted in the paper.	16% of respondents were informed about what personalised medicine is. 69% of respondents interested in learning more about PM. 77% willing to have PM if physician recommends it. Main concern access and affordability.	25
Lachance et al. (2015) Canada [26]	Members of the public and patients with chronic health conditions	Mean age public 32.6 years. Patient group 1 mean age 56.8, patient group 2 mean age 72.5. Education: greater than secondary school in public 88%.	450	Quantitative, Cross-sectional survey	Purposive sampling	90% of participants were willing to undergo pharmacogenomics testing if it showed whether a particular medicine would work for them. Healthy individuals were more concerned than the two patient groups regarding employment and health insurance discrimination and confidentiality. If pharmacogenomic test revealed that drug would be ineffective or cause severe side-effects, less than half of participants would adhere with test advice.	75
Garfield et al. (2015) USA [15]	Adult members of the public	Mean age 52 years. 48% male. 31% university degree.	602	Quantitative, national survey	Probability proportional to size (PPS) weighted sampling approach	Low familiarity with the term personalised medicine (73% had never heard of the term before). Once PM explained 63% of participants thought personalised medicine would have a positive impact. At significant levels ($p < 0.05\%$) respondents who rated their health as very good to excellent report having a higher knowledge of personalized medicine and perceive it more positively.	100
Kichko et al (2016) USA and Germany [11]	Public and physicians	Public: 48% male and 52% female. Physicians: 58% male, 42% female.	602	Mixed methods	Purposive, community based	45% of public aware of personalised medicine in USA and 33% public in Germany. 69% of public in USA and 54% German public thought PM potential to deliver better medical care and to become a medicine of the future. Age, gender, health insurance availability and insurance coverage had no influence on PM acceptance by the public ($p > 0.05$). 60% of public (both USA and German group) shared opinion that personalized drugs are more effective than standard drugs. Opinion that PM causes fewer side effects: public 38% in USA and 50% Germany. Strong concerns raised about genetic data privacy protection.	50
Lee et al (2017) USA [12]	Members of the public and public who had received personalised medicine	Mean age 59.5 years. 50% male, 50% female. 55% Caucasian, 45% African American. 51% higher education level.	22	Qualitative, semi structured interviews	Purposive sampling	Both groups agreed pharmacogenomics could inform prescribing. Concerns over insurance coverage and employment discrimination. Both groups wanted physicians to engage participants and to utilize shared decision-making when considering pharmacogenomic-based prescribing.	100

Table 1. Characteristics of studies included in the review (presented in chronological order)

Results

Studies identified

In total 21 papers were included in the review. The total number of participants from the studies included was 9507. The number of participants in each study varied significantly, with a mean average of 453 participants per study and a participant range of 14- 3000 (table 1.) Of the 21 studies, 13 included solely members of the public as participants.

Data synthesis

A qualitative synthesis of the public opinion on the barriers and facilitators to implementation of PM are presented as three key themes (table 2)

Familiarity and willingness to use personalized medicine
A barrier that was a common finding was that participants were unfamiliar with what PM is and what it involves [11-20]. Eastman et al. reported that only 16% of their participants from the public were familiar with the concept of PM ([19]. Issa et al. found during focus groups with participants, who had been recruited from outpatient clinics, that most had an awareness of the term PM but had a limited understanding of its genetic basis [21]. The public often had a different perception of what PM involved, such as thinking that it was gene therapy or would give the patients their disease risk for all diseases [18].

Thirteen of the papers reviewed found that participants were willing to use PM after the concept had been explained by the researcher [12-13, 15-17, 19, 21-26]. There was variability between studies on how willing participants were to accept the use of PM and facilitator and barriers have been identified that contribute to this. Willingness to use PM was as high as 96% in a paper involving patients with asthma and COPD [22] and as low as 38% of patients in a study evaluating willingness to undergo warfarin pharmacogenetic testing [27]. A facilitator identified in four studies found that people were more willing to use PM if their health professional offered PM as part of a shared decision-making process through use of good communication skills [12, 14, 19, 28]. Participants who had previously experienced an adverse drug event (ADR) was found to be a facilitator in a study by Haga et al. [13], but Chan et al. [27] found participants without a history of an ADR were more willing to accept PM than those who had experienced an ADR.

Sociodemographic factors that were facilitators towards the willingness to use of PM were identified as being a young adult [13, 22] and having a higher level of education [13, 27]. Individuals who described themselves as having good health were more likely to consider using PM [13, 15]. A barrier that was identified is that people from ethnic minority backgrounds were less likely to accept PM and had more concerns with its use [13, 24, 28].

Perceived benefits of PM
An important facilitator identified by eight studies found that the public, once informed about PM, thought that the use of PM would provide better health care and health benefits for patients [11, 15-16, 18, 21-22, 25, 29]. Garfield et al. found that 95% of their participants expected PM to have a positive impact [15]. A further facilitator is that participants thought that PM has the potential to improve efficacy of prescribed medication for patients [11-12, 17, 21-22, 26]. Five studies found that the public expected PM to lead to fewer ADR's than standard medicine [11, 17, 22, 24, 26]. Participants had an impression that PM would result in less trial and error prescribing, with one participant describing it as 'it's not as time consuming as it is if you keep going back and forth to the doctor trying to figure out what's gonna work' [24]. A further perceived benefit of PM was that it could be an economic advantage to society with the potential for improved health, treatment efficacy and fewer ADRs [11, 17].

Perceived risks of PM
In all 21 studies, the participants raised concerns regarding the use of PM. An important barrier to the use of PM, raised in 11 studies, was the concern that results from genetics

tests used for PM could lead to patients experiencing health insurance discrimination [12, 14, 17, 21-22, 24-25, 27-28]. Participants were concerned in particular that their health insurance cost could increase with the use of PM and that it may not be covered by their insurance [12, 14, 17, 21-22, 24-25, 27-28]. Concerns regarding health insurance and PM varied depending on the study country and was not raised in studies in the UK, where health care provision is largely universal [16, 29]. The potential for employment discrimination was identified as another barrier for the use of PM and Lachance et al. found that this was of greater concern to healthy individuals than those with chronic health problems [12, 15 22, 25-26]. A further important barrier that was raised in eight studies was a concern that individuals' genetic information may not be stored confidentially and securely [14, 16, 22, 25-26, 28, 30].

A healthcare concern with the use of PM was that its use may limit patients' access to certain treatments if they were not genetically suitable for them [17, 22-23, 25]. A barrier identified in two studies carried out in the USA and Canada was that participants were concerned that the health care systems and health care providers were currently unprepared to implement PM [25, 30]. Bombard et al. found that participants were concerned health systems were unprepared particularly in the areas of laboratory genetic testing and health care provider's knowledge in interpreting genetic test results [25].

Themes of facilitator and barriers to public use of Personalized Medicine	
Facilitators **References**	**Barriers** **References**
Familiarity and willingness to use personalized medicine Relationship and interpersonal skills of HP [12, 14, 19, 28]. Self-rated good health [13, 15]. Previous experience of an adverse drug reaction [13]. Sociodemographic factors: young adult, higher level of education [13, 17, 22, 27].	**Familiarity and willingness to use personalized medicine** Participants unfamiliar of what PM is and what PM involves [11-20] Previous experience of an adverse drug reaction [27]. Sociodemographic factors: less willing to use PM if from an ethnic minority background [13, 24, 28].
Perceived benefits of PM Better health care and treatment efficacy: [11-12, 15-19, 21-22, 25-26]. Fewer side effects/ adverse drug related events than standard medicine [11, 17, 22, 24, 26]. Increased knowledge about the individual patient to help decision making [12, 24]. Economic advantage to society [11, 17].	**Perceived benefits of PM**
Perceived risks of PM	**Perceived risks of PM** Risk of Discrimination (employment and insurance) [12, 14-15, 17, 21-22, 24, 25-28]. Potential to limit access to certain treatments [17, 22-23, 25]. Confidentiality and safe storage of PM data [14, 16, 22, 25-26, 28, 30]. Concern health care systems and providers unprepared to implement PM [25, 30]

Table 2. Themes of facilitator and barriers to public use of Personalized Medicine

Discussion

Summary

The need to embed personalized medicine into day-to-day health care is well-established [4, 5]. This systematic review of 21 studies demonstrates an overall keen interest in a substantial proportion of more than 9000 members of the public, including patients, from North America, UK and continental Europe, to engage in a wider discussion on this important subject. The introduction of personalized medicine represents a “revolution” within healthcare systems [32], and the public as key stake-holders, will play a critically important role in its implementation. The study shows that, despite a limited understanding of the underlying principles, the public is generally enthusiastic about the introduction of personalized medicine. The study also defines areas where progress can be made to enhance this understanding and address legitimate concerns. Crucially, the review fails to identify evidence of a systematic exploration of the public’s views on personalized medicine in Africa, South America and Asia, where personalized medicine-related treatment approaches will inevitably influence the management of common diseases over the next decade.

An important purpose of this systematic review is to understand the public’s views regarding personalized medicine in the context of key recent pronouncements of public policy in this area. To appreciate the level of commitment to personalized medicine expressed recently at the highest level, it may be relevant to reflect on a few recent statements of public policy in this regard. The following are excerpts from ex-President Obama remarks “personalized medicine -- gives us one of the greatest opportunities for new medical breakthroughs that we have ever seen -- and that’s the promise of precision medicine -- delivering the right treatments, at the right time, every time to the right person -- and for a small but growing number of patients, that future is already here [33]. Simon Stevens, chief executive of NHS England wants the health service to move “from mostly one-size-fits-all treatment to genuinely personalised care -- The NHS should be at the forefront of this global medical revolution” [4, 34]. This systematic review shows (table 1) that this commitment towards PM is broadly matched by reciprocal enthusiasm and interest for PM among most of the participants from North America, the UK and Continental Europe.

Several important concerns and recommendations identified worldwide could help focus the development of PM and public engagement strategies in this regard. Firstly, the public prefers a holistic approach to medical practice that is maintained in tandem with the development of PM [14]. Thus, for example, much of the disease burden in an individual with asthma and allergy may result from sensitisation to particular allergens and differences in response to medication, and this pattern could vary greatly between individuals. The correct approach thus requires a wider interpretation and practice of PM, exploring disease heterogeneity in individuals within the context of their genetic traits, to develop personalized strategies for management that are underpinned by information from careful history-taking and appropriate investigations [35]. There is also public concern regarding costs, insurance and employment-related discrimination resulting from the introduction of PM into mainstream healthcare [12, 14-15, 17, 21-22, 24, 25-28]. Despite clear intentions at the highest levels to introduce PM for the benefit of society and to engage the public, there is little or no evidence of organisations such as the FDA or the NHS facilitating dialogue with the public to manage these concerns. Indeed, concern regarding discrimination at insurance and employment levels could represent a major barrier for recruiting people to a future national genome

database to facilitate day-to-day care, unless specific data management rules can be developed through effective public consultation.

Importantly, our search strategy failed to identify relevant studies from Africa or South America and only 1 study in Asia. Yet, any significant shift in clinical practice in North America and Europe is likely to influence treatment options in these continents. Public opinion regarding PM is also likely to be influenced by cultural influences that can vary between different nations. This systematic review thus points towards the need for exploratory studies in these continents to assess the views of the public regarding PM. Initially, it may be necessary to work on increasing awareness regarding PM among different communities and providing access to the relevant information. Subsequently, we will need to explore perceived benefits and concerns, which may differ across cultures.

Strength and limitations

A key strength is this is the first systematic review of the public perception of PM since 2006 and the facilitators and barriers identified can be used by health professionals and researchers to engage the public and patients in PM.

A limitation is the studies included are heterogeneous and variability in the methodology makes it challenging to compare the findings from each study included in this review. The heterogeneous nature of the studies prevented a robust statistical analysis to be carried out. Use of the MMAT tool allowed the authors to assess the quality of qualitative, quantitative and mixed methods studies, although the tool does have limitations. The MMAT tool relies on good quality of reporting and a lack of a methodological criterion being described in the paper does not necessarily mean that the criterion was not met [36] The MMAT tool questions to assess the qualitative papers are noted by the authors to be less precise than the quantitative questions.

A further limitation within this area of research and therefore the papers within this review is the need to first explain the term PM to participants. There is a risk of bias at the study level as the facilitators will have their own fixed definition and this will be affected by their own personal beliefs and interests in PM.

Future perspective

The field of personalised medicine over the next 10 years is expected to continue to expand and be increasingly used as part of mainstream healthcare once there is an increase in public engagement activities in this field that are based on an up-to-date understanding of public opinion. It is predicted that exploratory studies will be carried out in Africa, South America and Asia to assess the views of the public regarding PM.

Executive Summary

- The review shows that, despite a limited familiarity of the underlying principles, the public is generally enthusiastic about the introduction of PM.
- Important barriers toward the implementation of PM are the public concern regarding costs, insurance and employment-related discrimination. Progress can be made to enhance this understanding and address legitimate concerns through public engagement.
- The review fails to identify evidence of a systematic exploration of the public’s views on personalized medicine in Africa, South America and Asia, where personalized

medicine-related treatment approaches will inevitably influence the management of common diseases over the next decade.

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The authors have highlighted a small number of references that are of particular significance to the subject as **"* of interest"** and provide a brief synopsis can be read in table 1.

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Appendices

Appendix 1) search strategy

Date range used (5 years, 10 years): 2006 onwards

limits used (gender, article/study type, etc.): none

search terms and notes (full search strategy for database searches below):

Relevant natural language and controlled vocabulary terms were identified, selected and combined. Initial search strategy reviewed and agreed upon by search requester. The following terms were included in the literature search: personali#ed medicine, personalized medicine, individuali#ed medicine, pharmacogenomics and nutrigenomics. This was combined with terms for public opinion/support or understand or perception or acceptance or awareness.

Search strategies were adapted to the search facilities of the medical information resources used. Medline (Ovid Medline(r) epub ahead of print, in-process & other non-indexed citations, Ovid Medline(r) daily and Ovid Medline(r) 1946 to present) and Embase (Embase 1974 to 2018 week 07) searched via Ovid, Cinhal, bni, Psycinfo searched via hdas, Scopus searched via its native interface. Final result sets were de-duplicated in endnote.

Appendix 2) inclusion and exclusion criteria

Inclusion criteria	**Exclusion criteria**
Published 2006 to current	Published prior 2006
Aim/objective of the paper was public's opinion of PM/ pharmacogenetics and the outcomes/ results reflects this.	Focused on the public's opinion regarding biobanks
Included secondary data	Focused on the public's opinion regarding direct to consumer genetic testing
Included paper with opinions of 2 groups of people (once one group were members of the public)	Focused on the public's opinion regarding PM for research purposes only
Written in English	Written in a language other than English (as there was not sufficient funds or time to invest in translating articles)
Study design can be quantitative or qualitative	Opinion of healthcare professionals/researcher/ geneticist only
	Focus of article is on genomic risk profiling only
	Focus of article is on stem cell research
	Focus of article is on the ethics of PM
	Excluded editorials, conference abstract, reviews and commentaries
	No full article published (i.e. abstract only).