OPM GROUP

Stratified medicine: a public dialogue
Final report

Report to Innovate UK
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Innovate UK is the new name for the Technology Strategy Board

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Executive Summary

CHAPTER SUMMARY

Even the best therapies are not equally effective in all patients: stratified medicine aims to deliver the right treatment to the right patient, at the right time. The Technology Strategy Board, with Sciencewise, asked OPM Group to run a public dialogue programme which gave people the chance to have their say on these new techniques. This is a summary of our findings; and you can watch the dialogue in action in this video:

Video produced by CloseUp Research.

About the dialogue

The Technology Strategy Board sees stratified medicine as a leading area of healthcare research with the potential to provide significant benefits to patients and effect strategic shifts in the way healthcare is delivered. Understanding these shifts is vital to ensure that new techniques are used in the best interests of all involved. As the project brief set out:

> "This project is not so much about the possible parameters of these changes in treatment as about identifying the human issues that are raised by stratified medicine and what these will mean for how it is delivered, for the individuals who will benefit from it, for their families, and for those for whom there will not be immediate benefits."

The Technology Strategy Board/ Sciencewise[1]

To find out how people understand these issues the OPM Group designed and ran 19 deliberative workshops involving around 180 participants, including members of the public with no specific knowledge of stratified medicine, young people, patients and medical students.[2] We used a range of tools to explore the science, the social issues and the implications for patient care. These tools included animation, video testimonies, hypothetical scenarios and discussion activities - you can see these materials on the project website http://stratifiedmedicine.wordpress.com.

The final event in this project was a workshop for stakeholders involved in the development of stratified medicine, designed to consider the implications of our findings for the development of stratified medicine. This report presents our findings as well as the future challenges we identified for stratified medicine under four main themes:

- DEFINITION AND COMMUNICATION
- IMPLICATIONS FOR PATIENTS AND CARE
- SOCIAL ISSUES AND CONSEQUENCES
- RESEARCH, TESTING AND DATA SHARING

[1] "The Sciencewise Expert Resource Centre (Sciencewise-ERC) is funded by the Department for Business, Innovation and Skills (BIS). Sciencewise-ERC aims to improve policy making involving science and technology across Government by increasing the effectiveness with which public dialogue is used, and encouraging its wider use where appropriate to ensure public views are considered as part of the evidence base. www.sciencewise-erc.org.uk

[2] We reserve the term 'participants' for those people involved in the 19 workshops. The term 'stakeholder' refers only to people with a direct professional interest in the development of stratified medicine.

Our findings

Definition and communication: challenges

- Having a clear, consistent definition of stratified medicine
- Presenting a realistic picture of stratified medicine, its pros and cons
- Continuing to engage the public and patients

1. The first challenge to developing a more stratified healthcare system is **having a clear, consistent definition** to communicate with patients and the public about changes that are taking place. Participants in the dialogue often felt that the terminology being used was inaccessible and had negative connotations:

> "I don't like the term 'stratified medicine', it makes one think of strata in society and I think there is a danger of it being viewed as elitist..."

Dialogue participant, London public group

By presenting and illustrating it clearly in the dialogue, the concept of stratified medicine was easy enough for participants to grasp and was seen in a broadly positive light. When talking to stakeholders, however, we found them using a range of different definitions of stratified medicine and related concepts such as personalised and precision medicine. This could cause confusion and misunderstandings when the public and stakeholders talk to each other about the development of stratified healthcare.

2. Participants and stakeholders emphasized the importance of **presenting a realistic picture of stratified medicine**, including its pros and cons. To avoid raising unrealistic hopes or fears for patients, they felt that information about stratified medicine should be balanced and not over- or under-promise. Accurate information about the pros and cons of stratified medicine would provide the public with a counter-balance to simplistic or sensationalist media coverage.

> "If one patient did not get treatment because they weren't suitable, the media would just present the story as 'patient refused treatment'."

Dialogue participant, London public group

Participants also identified the importance of healthcare information being communicated through trusted channels, with GPs identified as a particular group to whom the public turn for impartial advice.

3. Many participants felt that **continuing to engage with the public** was as important as accurate and accessible information for patients. Participants were keen to be involved in the development of new healthcare models as citizens: they did not want to be merely passive recipients of information communicated via the media. This conflicted with the views of some medics who felt the priority should be explaining individual treatment options to patients.

"Stratified medicine is not what is needed to communicate to people, they don't need to know why they are getting the drug, but just feel confident about the drug they are getting."

Stakeholder, London stakeholder workshop

Implications for patients and care: challenges

- Support patients to make sound treatment decisions
- Support patients for whom there is no current treatment
- Provide the right facilities and training to healthcare professionals

1. Participants identified **supporting patients to make sound treatment decisions** as a challenge for stratified medicine. Many believed that more stratified approaches would increase the amount of information with which clinicians and patients need to deal.

"Some patients will really struggle with choice – having to take hard decisions could be very stressful."

Dialogue participant, patient group

Participants had many different views about the level of information they would want, particularly when testing might give results in terms of probabilities. They wanted to ensure that more straitfied approaches don't detract from the shared responsibility for decision making which they believe most patients want in healthcare.

2. Participants highlighted the importance of support for **patients for whom tests would show no current treatment**; they felt it was likely that increased testing for likely treatment success would identify more of these cases. Participants saw two main challenges: first, that doctors could be constrained by test protocols from **making all efforts** to find effective treatments, including treatments more commonly used for other conditions.

"Individual doctors should have the freedom to make independent decisions – it would be worrying

> if SM meant more rules and proscribed pathways that didn't allow doctors to use their intuition and professional judgement."

Dialogue participant, patient group

The second challenge was ensuring that sufficient attention and resource is given to areas such as **counselling and palliative care** rather than focusing exclusively on new treatments.

3. Participants felt that healthcare professionals would need appropriate resources and training if they were to support patients effectively. There were concerns that if **investment in facilities and training is limited**, change would not filter into practice and patients would not benefit from developments in stratified medicine. Participants identified training healthcare staff to deal with new testing and treatment protocols as important. They felt that GPs in particular needed support as they play a vital role in a system where more specialised treatments might be available in secondary care and GPs are the gatekeepers to access.

> "It is pretty significant if you are treated by a GP who is unaware that superior treatments exist."

Dialogue participant, Glasgow public group

Social issues and consequences: challenges

- Understand and mitigate any implications for equality
- Define the role of the private sector in developing stratified medicine
- Develop understanding of the costs/benefits of stratified medicine

1. Equality of access was one of the most prominent themes of the dialogue. Participants emphasised the importance of **understanding and mitigating any implications that stratified medicine might have for equality**. They based their discussions primarily on the principle of universal access to healthcare. For some participants the concept of 'stratifying' patients seemed akin to restricting treatment. They were concerned that factors other than medical need might determine access to treatment, including age, ethnicity, geographical location or financial situation. Some of the most pressing concerns were about the possible exacerbation of existing health inequalities based on ethnicity.

> "What if there are more black people in category C, the category that don't benefit from a particular

medicine, does this mean other ethnicities get better medication? I would be bothered about that."

Dialogue participant, young patient group

As well as inequality in treatment, participants were concerned that research might focus on particular demographic groups, or simply the most tractable medical problems, and thus exclude some people in the long term.

2. Participants felt it was important to **define the role of the private sector** in changes to the healthcare system resulting from stratified medicine. Many participants felt that healthcare and medical research should not be driven by profit-making. They felt that the profit motive conflicted with the principle of universal healthcare as a public good, which informed many people's views. Participants worried that the development of new treatments by the private sector would provide an opportunity for commercial companies to move into new areas of the healthcare system. Participants were also concerned about the private sector profiting from research at the expense of improving outcomes for all.

"It would be concerning if the pharmacy companies financing this then get to monopolise the market and drive the prices up for the system as a whole."

Dialogue participant, Glasgow public group

3. Participants felt it was important for the public to develop an **understanding of the costs and benefits** of stratified medicine to the UK healthcare system. For some participants this was the one factor that they felt would most affect their support of stratified medicine as a whole, given the current constraints on NHS resources. Stakeholders' discussions made it clear that determining the balance of costs and benefits is not straightforward even among experts.

Research, testing and data sharing: challenges

- Give research participants a choice about how and who uses their data
- Reconcile the role and perception of the medical research industry
- Engage the public in regulation on data sharing

1. Participants in this dialogue were broadly positive about contributing data to medical research, provided that research participants have a **choice about how their data is accessed and shared and by whom**. They were most positive about contributing to research carried out by the public or third sector, where data was anonymised and held securely.

> "I see this – my reaction is – yes I want to give my data, how can I help future generations?"
>
> **Dialogue participant, London public group**

The fundamental caveat for participants was trust: they felt they would be most likely to contribute to medical research where they could be confident about the uses to which the data would be put in advance of giving consent. Participants saw a need to give actively informed consent, not necessarily at the time of diagnosis or treatment when patients are most vulnerable.

2. Reconciling the **role of the private sector in research** with public perceptions was another challenge. Some participants felt that where they contributed to research with the intention of benefiting others, that contribution should not be used to generate profits for private companies such as insurance and pharmaceuticals. This was accompanied by a lack of trust where the private sector was concerned:

> "Pharmaceutical companies' using it [data] is less trustworthy, they will use it because there is a profit to be made, they will compromise it."
>
> **Dialogue participant, young patient group**

3. There are particular challenges associated with **engaging the public on the regulation of data sharing**; concerns for some were exacerbated by lack of knowledge of existing regulatory structures. However it was clear that participants are keen to be involved, both in research and in developing policy which reflects their hopes and concerns.

About the dialogue

CHAPTER SUMMARY

During this project we met with more than 200 people at 19 workshops, from 5 patients coming together for an evening in November, to 50 stakeholders at a whole day summit in January. This chapter explains our approach to the stratified medicine dialogue; you can see it in action via this video:

Video produced by CloseUp Research.

The Technology Strategy Board sees stratified medicine as a leading area of healthcare research with the potential to provide significant benefits to patients and affect strategic shifts in the way healthcare is delivered. Understanding these shifts is vital to ensure that new techniques are used in the best interests of all involved. As the project brief set out:

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The final event in this project was a workshop for stakeholders involved in the development of stratified medicine, designed to consider the implications of our findings for the development of stratified medicine. This report presents our findings as well as the future challenges we identified for stratified medicine under four main themes:

- DEFINITION & COMMUNICATION
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- RESEARCH, TESTING & DATA SHARING

In reading this report it is important to note that the process undertaken was designed to explore a wide range of views. The participants were recruited to this end and were not statistically representative of the UK population. You can read more about our process in the **Methodology** section of this report.

[3] "The Sciencewise Expert Resource Centre (Sciencewise-ERC) is funded by the Department for Business, Innovation and Skills (BIS). Sciencewise-ERC aims to improve policy making involving science and technology across Government by increasing the effectiveness with which public dialogue is used, and encouraging its wider use where appropriate to ensure public views are considered as part of the evidence base. www.sciencewise-erc.org.uk

[4] We reserve the term 'participants' for those people involved in the 19 workshops. The term 'stakeholder' refers only to people with a direct professional interest in the development of stratified medicine.

Our findings

The findings of the dialogue are presented below, following the four themes identified:

- Definition and communication

- Implications for patients and care

- Social issues and consequences

- Research, testing and data sharing

Definition and communication

CHAPTER SUMMARY

If stratified medicine is to become a part of everyday healthcare practice, patients, healthcare professionals and the public then good communication is essential to enable patients to take an active part in treatment decisions. We found that the public were more than capable of getting to grips with the complex concepts involved, but it was important to them to understand how they applied in practice. In a world where healthcare frequently makes the front pages, people are alert to exaggeration - being honest about the pros and cons was seen as crucial.

1
Definition & communication

What did we ask?

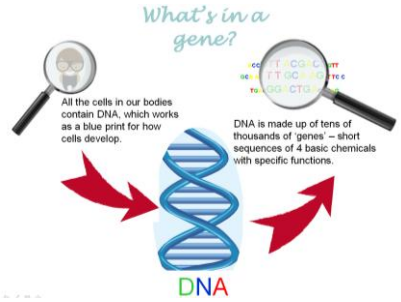
The activities under this theme were designed to answer the question "how should we talk about stratified medicine?" We used a range of techniques to identify not just what people understood by the term but how they came to that understanding. We explored the information participants found helpful or confusing and their preferences for different terms, analogies and types of information.

What do people understand by stratified medicine when they first hear the term?

We produced a two-minute animation that explained the basic concepts of stratified medicine and showed this to all participants to prompt initial discussion. You can watch this video online here.

What information do people need to understand stratified medicine?

Based on the scoping and pilot process we designed a discovery process through which participants explored basic concepts such as genetics and disease risk. We wanted all participants to develop a basic understanding of the building blocks of stratified medicine.



When is stratified medicine going to happen?

One of the main findings of our initial research was that stratified medicine is developing at different rates in different areas of healthcare. To help explain this we created a medical history timeline to give participants a sense of perspective about the speed of medical developments from the Ancient Greeks through to the near future.

What terms should we use to minimise confusion?

Each time we met them we asked participants how they would explain stratified medicine to a stranger on a bus. We used this question to track participants' understanding of the concept of stratified medicine, to see how and if it changed as they were exposed to different perspectives. It also helped us to identify the language with which they felt most comfortable.

All images Damn Fine Media

1
Definition & communication

What did we find?

- First impressions
- Defining and naming: the Stratified Medicine message
- Communicating to the public: the right channels
- Information: how much is too much?

First impressions

"I knew nothing about stratified medicine, looked it up on the internet... absolutely useless. Today I think I understand what it is and I understand what it could become in the future."

Dialogue participant, London public group

Discovery session, London workshop

Most participants came to the public dialogue with little if any knowledge about stratified medicine. The term itself made many people doubt whether they would be able to engage with it at all, but as the process went on all participants became increasingly comfortable with the topic. They were broadly supportive of stratified medicine at the start and most did not change their views over the course of the two workshops. However, as they viewed and discussed more information, participants developed a more detailed, nuanced and balanced understanding of stratified medicine, including its negative and positive implications.

Defining and naming: the Stratified Medicine message

An early session of each dialogue workshop focussed on how participants understood the term 'stratified'. Initial reactions to the terminology were typically negative, with participants feeling that the term was inaccessible and unclear. Through the introductory animation and subsequent learning exercises participants quickly came to understand the basic premise: that stratified medicine is a medical strategy according to which treatment is prescribed based on testing methods that identify the likely success of particular treatment options for different groups of patients. The more participants understood about the topic the more they felt that 'stratified' was an accurate term. However, there was general consensus at the public workshops that while it may be accurate the term would be inaccessible to ordinary people. Some related this to concerns about inequality in the relationship between medical professionals and patients, arguing that use of jargon could make patients feel less able to take an active part in decision making:

> "It sounds like gobbledegook, which doctors use anyway. If a doctor tells you something you just agree. You don't disagree."

Dialogue participant, Glasgow public group

Participants suggested alternatives to 'stratified' such as 'personalised' or 'bespoke'. However many options were criticised for giving the misleading impression that stratified medicine would be based on individual rather than group characteristics. Other suggestions raised by the general public included 'targeted medicine' or 'focussed testing', which they felt would avoid the negative connotations of the term stratified:

> "I don't like the term 'stratified medicine', it makes one think of strata in society and I think there is a danger of it being viewed as elitist. … [BBC presenter] Michael Mosely was calling it 'personalised medicine' [in a recent show] but I think that raises expectations because it's not aimed at the individual but groups of people."

Dialogue participant, London public group

For others the term 'medicine' was the source of some confusion, with participants assuming that the dialogue was about specific drug treatments, rather than medicine in the broader sense, i.e. the practice of medicine.

Overall, public participants felt that using non-technical language and plain English to explain stratified techniques was vital. For example, one participant from the self-facilitated groups argued that "warmer, more friendly terms and language" should be

used, with healthcare professionals trying "to avoid using jargon or terms only those in the medical industry are likely to understand". In contrast, some participants and some stakeholders at the workshop emphasised that the public is not best served by over-simplified messages that fail to address the nuances behind stratified approaches:

> "We need to be able to unpack the complexity and nuance of stratified medicine and the range of activities encompassed by the term stratified medicine – avoiding simplistic labelling of it to patients"
>
> **Stakeholder, London stakeholder workshop**

> "Do not be afraid to treat the public as adults and engage them in a dialogue even though the learning process will be lengthy"
>
> **Dialogue participant, London public group**

Our experience in this dialogue suggests there is a fine line to be negotiated between intimidating patients and the public with over-technical language, and helping them to develop a sufficiently detailed understanding of the concept. Picking up this theme at the workshop, one stakeholder argued that communicating stratified medicine should be done incrementally over a medium to long period, building up awareness and understanding over time. This stakeholder described this process as a "progression of diminishing simplifications". This is broadly the approach we took in the dialogue. The process began with the familiar situation of a GP appointment and an explanation of the trial and error approach often used in current treatment. We moved on to look at the application of stratified medicine to more complex conditions where outcomes might be more nuanced.

Public participants felt that case studies were especially useful for explaining stratified medicine. Many public participants commented too that the video in which a patient with chronic myeloid leukaemia explained his own experience of stratified medicine brought the complex concept to life and helped them to understand what it could mean in practice. They recommended more of these practical examples to aid understanding.

A caveat to this approach is found in feedback from stakeholders attending the workshop, who were shown the initial dialogue findings alongside the materials we used in the dialogue. A few stakeholders felt that the picture presented in the dialogue was more positive than was warranted by the current state of research in their field. As we note later in this report, over-promising is a real risk in communicating early in the development of a new technology and attempts to clarify should not over-simplify at the expense of important but more complex messages.

The 'newness' of the approach was also a point of some contention. At the scoping stage of the dialogue we identified a debate about whether stratified medicine really represented a new approach or was simply a repackaging of the type of incremental improvement which happens all the time in medicine. Some participants felt that by describing stratified medicine as new, innovative or revolutionary it implied a level of improvement in treatment outcomes which might not be warranted. Participants felt it was more useful to describe it as an evolution in practice, a point with which stakeholders at the workshop widely agreed.

Communicating to the public: the right channels

Many participants thought it was important that awareness-raising about stratified medicine goes beyond those in need of treatment and encompasses the broader public. They suggested using public education campaigns to raise awareness amongst the wider public. Since stratified medicine may change the experiences people have of the healthcare system, participants felt it was important that the public understand the reasons behind these changes. In this vein, one participant in the self-facilitated groups suggests that bodies such as the Technology Strategy Board[5] should target a broader audience in their communications:

> "The [Technology Strategy] board should also think about who they want to communicate with. As things stand the first time you may come across the concept of stratified medicine is when you are ill and need treatment. It is worth thinking about communicating with the public at large, not just those who are ill and need medical treatment."

Dialogue participant, self-facilitated group

Participants made a variety of recommendations about the media that could be used to increase awareness and public understanding of stratified medicine, including TV and newspaper ads or social media. Some participants mentioned examples from other sectors that they felt were successful such as episodes of science programme Horizon that they had enjoyed, or popular science presenters like Patrick Moore or Brian Cox. Others suggested that more events where the public and patients could interact with researchers would be beneficial, often citing their experience in the dialogue as an example. Among public participants, many suggested that GPs would have an important role in communicating new approaches to patients, although there was some concern about the cost implications if training was required.

[5] Participants across all strands, but most commonly the self-facilitated groups, sometimes struggled to understand the role of the Technology Strategy Board as a facilitator of medical development rather than a delivery body.

Young people and stratified medicine

As part of the dialogue we convened three groups of young adults aged from 18 to 25 years old. One group was facilitated by our team and two were facilitated by the young people themselves. In this box we take a brief look at their views and how these differ from those of the wider public. Most notable is the extent to which groups were similar. On the important social issues and potentially controversial areas such as data sharing, there were more similarities than differences between the groups.

Defining Stratified Medicine

Young people were not comfortable with the word 'stratified'. Like participants in other groups, they argued that it was too technical and intimidating for ordinary citizens. Their suggestions for alternative names were also similar to those made in other groups and included "customized" or "personalised" treatment.

Young people were particularly concerned about the possibility of genetic stratification being seen as prejudicial towards some groups. This concern was raised by other groups too, but they tended to focus more broadly on other aspects of stratified medicine such as its position within the evolution of medicine and the need to manage expectations. Young people seemed particularly concerned about the possible racial and ethical implications that they felt could arise from genetic stratification (see **Equality of access**).

Method and Format of Communication

Young people raised a number of points about communicating stratified medicine, many of which echoed points made by the public and stakeholders. These included the concern that the media might misrepresent the issues. Young people talked extensively about social media, although this was also discussed by other groups suggesting that the divide between the two was not as large as might be assumed. They also had greater expectations that 'people' should be involved in decision making. For example one suggested:

"Media could act like a web connecting it all together, the public voice. Use social media like Facebook and Twitter, collect and collate people's feedback, then the people in power should listen to it."

Dialogue participant, young people group

Some young participants favoured using documentaries and information leaflets to educate people about stratified medicine. One suggestion was for GPs to be obliged to explain stratified medicine to their patients, as is currently the case with sexually transmitted diseases.

The public generally felt that honesty and realism were crucial to get the message across effectively, with many highlighting the importance of presenting stratified medicine in a balanced way. Participants felt it was essential to include the advantages of stratified medicine and the risks involved, its successes and failures, so as not to generate false expectations and hope, or unwarranted fear and scepticism.

Public participants thought it was inevitable that much of the information the public receive about stratified medicine will come from the news media. Reflecting this, many participants saw a need to actively involve the mass media in public awareness raising and increasing understanding.

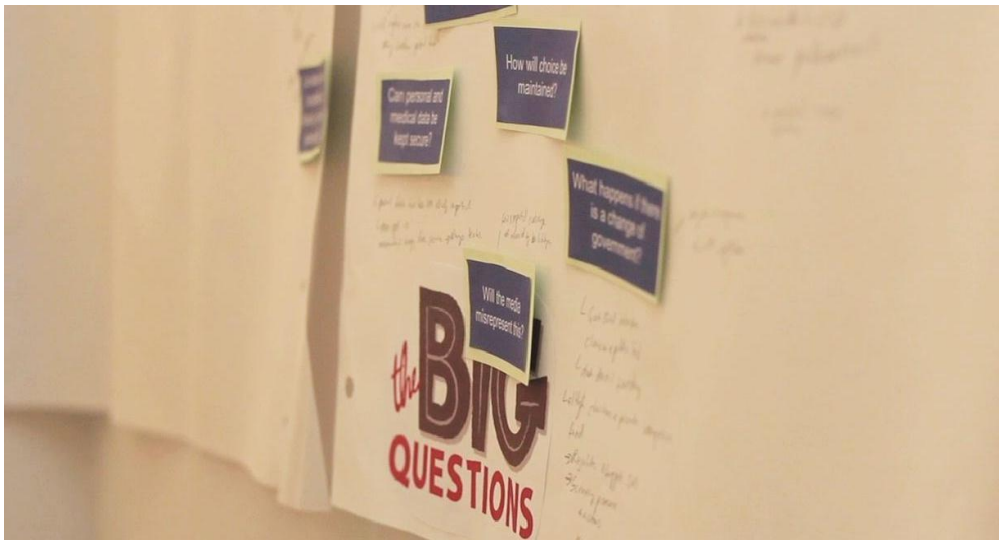
> "[The media should] tell people about SM honestly, fairly and responsibly, a lot of the information will come through the media."

Dialogue participant, young patient group

Alongside their desire to involve the media, participants were concerned about sensationalist coverage, which might distort the public's understanding of stratified medicine, for example by focussing on headline-grabbing cases. They saw this as a significant risk because coverage is often based on individual examples, or particular aspects of a story, and might not reflect the overall picture. Even though participants in the workshops expressed a lack of trust in the media because of the tendency to sensationalise stories they still felt that the wider public (and by extension themselves without the benefit of the knowledge they had acquired) could be misled by this type of coverage.

> "If one patient did not get treatment because they weren't suitable, the media would just present the story as 'patient refused treatment'."

Dialogue participant, London public group



Social issues discussion notes, public workshop London

This theme of trust recurs throughout the findings; in relation to the doctor-patient relationship, and where stratified medicine research relies upon patients contributing data. As with data sharing, when it came to information giving, public participants tended to perceive medical professionals, particularly in the NHS, and charities as more credible than the private sector or media. Trust was also discussed in some depth at the stakeholder workshop, where stakeholders agreed that it was important to identify trusted channels to communicate with the public. Stakeholders were split as to whether communications seen as issuing from government would be trusted. Some stakeholders felt that the public might regard these with mistrust, while others disagreed and supported the use of public information campaigns.

Information: how much is too much?

The public dialogue project was designed to give participants the information and understanding they needed to engage with stratified medicine as an approach to medical treatment and research in depth and from a range of perspectives. The extent to which this type of understanding was necessary for patients and the public was an area of some disagreement. In the public workshops there tended to be strong support for increased public understanding and awareness raising activities. However others, including some at the stakeholder workshop and the medical students who took part, felt it was more important that patients understand their own treatment options, and that this could be done without explaining the 'theory behind them'.

> "Stratified Medicine is not what is needed to communicate to people, they don't need to know why they are getting the drug, but just feel confident about the drug they are getting."

Stakeholder, London stakeholder workshop

Others disagreed, arguing that providing as much information as possible is necessary for patients to properly exercise choice. For example:

> "If there is a body of research behind what's happening in a consultation, some people will Google it anyway so they will know. I think people have a right to at least some information about the decisions that lie behind their healthcare."

Stakeholder, London stakeholder workshop

What next?

At the stakeholder workshop held after the main dialogue we asked a group of 50 stakeholders to review the initial findings and tell us what they thought they could mean for the development of stratified medicine. We refined these suggestions with the help of the project oversight group and the Technology Strategy Board to identify the main challenges for stratified medicine arising from the dialogue.

Developing a coherent message
Communication about stratified medicine has to be based on a single, cohesive description that is used consistently in public and among researchers and funders. Stratified medicine might not be the right term for this task.

Being realistic about what can be done and when
Managing expectations is vital; communicating about stratified medicine must not raise hopes which cannot be met. This means not presenting the approach as a radical new method, but as evolving practice, with different rates of progress in different diseases. Giving the pros and cons is necessary to avoid perceptions of bias.

Finding trusted channels to communicate
Trust is crucial when communicating with people about healthcare - people are more likely to trust information given to them by their GPs and other healthcare professionals, patient groups and charities. Other bodies such as industry are less trusted, but there is scope to improve this. A caveat: people are astute about messaging - if information isn't balanced then it won't be trusted regardless of who delivers it.

The need for publicity on 'stratified medicine' versus specific stratified treatments
While public participants were often keen to see widespread publicity about stratified medicine stakeholders tended to think that it was more important to inform people about specific treatments or about the workings of the medical research industry more generally as background before they could engage with the concepts of stratified medicine.

Continuing to engage with the public and patients
This dialogue highlighted a number of areas where the public and patients are cautious about the development of stratified medicine, and where further dialogue is needed to understand those concerns. This project was a starting point in a much longer conversation with the public and patients.

Implications for patients and care

CHAPTER SUMMARY

Changes to the healthcare system mean changes to the experience of individual patients. Understanding just how individual those patients are was a strong theme in the findings. Not everyone wants the same amount of involvement in decision making about their care and some were afraid that a stratified approach based on rigorous testing would be impersonal. The consequences for those who would not benefit initially were also a concern – no one wants to see patients left without options.

2
Implications for patients & care

What did we ask?

In this second topic we wanted to look at the individual perspective: what could stratified medicine be like for patients, their families and healthcare professionals? We particularly wanted to understand how participants felt about situations where some people benefitted more than others. We asked them to think about the issues and to consider potential solutions. We discussed these issues at the stakeholder workshop at the end of the project as well.

What are the implications for those who benefit?

We showed participants video testimony of a patient with chronic myeloid leukaemia who had been successfully treated with a stratified approach for a number of years, to help them understand the potential benefits and risks. We encouraged discussion on the risks of side effects and the amount of information they would need to make treatment decisions for themselves. You can see this video online here.

(Image: Close Up Research)

What are the implications when some patients benefit and others don't?

We used the hypothetical scenario of sisters with different types of breast cancer to explore the implications of stratification where treatments are not available for all groups of patients.

What should happen next?

We asked participants to give us recommendations about the role of different stakeholders in developing stratified medicine, including the public and patients, healthcare professionals, the government, industry and the media.

2
Implications for patients & care

What did we find?

- First impressions
- Knowledge, choice and patient information needs
- Implications of greater knowledge and choice on patient wellbeing
- Other patient support needs
- Patients with no suitable treatment option
- Patients' relationships with the healthcare system and professionals
- Implications for healthcare professionals

First impressions

Participants in the dialogue saw more effective care as the primary benefit of stratified medicine. They saw that, in theory, a stratified approach would enable doctors to identify the right treatment for a patient sooner. It would also minimise the need for a trial and error approach which often entails significant side effects, delays and stress. Many participants had personal experiences of the negative side effects of medication.

> "Stratified medicine sounds like a good idea if treatment is more specific to you and you don't have to bounce between pills as frequently and suffer the side effects."

Dialogue participant, young patient group

Knowledge, choice and patient information needs

Many groups discussed patient choice and whether or not stratified medicine would entail more or less patient choice. Most participants thought that it was important to protect patient choice, as either a choice between different treatment options, or as a choice between a stratified and a traditional approach. However they felt that not all patients would want to use this choice, as we discuss further below.

Participants argued that patients would need a range of information in order to exercise choice. This includes clear, objective information and advice on the treatment options available, the practicalities of the treatments, potential side effects and the likelihood of success. Information should be available from a variety of sources, including GPs, high-quality internet resources, patient groups and charities, and patients should be able and encouraged to ask questions. Both dialogue participants and stakeholders noted the particular difficulties of communicating risk information, which often comes as a percentage, and which different patients can interpret very differently.

"It is important that whoever tells the patients what stratified medicine is about, they do so objectively and are on hand to explain it further."

Dialogue participant, young patient group

Implications of greater knowledge and choice on patient wellbeing

Participants felt that patients would react in varied ways to the greater knowledge and choice associated with higher levels of diagnostic testing in stratified medicine. Some participants were concerned that the potential need to choose a treatment, or even to know more about their condition, could cause patients additional stress and impact on their mental health and wellbeing. On the other hand, many participants thought that they themselves would like to have more knowledge of their condition so that they could be fully involved in making treatment decisions. Participants were more likely to talk about 'patients' and in particular older patients being overwhelmed by information, but see themselves as capable of being involved in decision making. It may be that participants were overestimating their own capability and the projected concern for 'patients' more accurately reflects their views.

"Some patients will really struggle with choice – having to take hard decisions could be very stressful."

Dialogue participant, patient group

Participants had extensive discussions about the implications of patients being told about incidental findings of conditions they had or were at risk of having. [6] Some participants thought the likelihood of incidental conditions being identified would increase as more tests are carried out per patient, and their views were mixed about whether or not they would want to be told about these. Many participants said they would want to know in order to 'nip it in the bud' or make changes in their lifestyle or environment that could mitigate the condition. Others felt that 'ignorance is bliss', and thought the worry this information would cause them would outweigh any benefits of knowing. Some participants said they would only want to be told about these findings if there was anything that could be done.

"If you are at high risk it might mean for the rest of your life you do everything in your power not to get it, making all sorts of lifestyle changes in the efforts to compensate – it could feel like a life sentence for

[6] Incidental findings are previously undiagnosed conditions identified during testing or treatment for unrelated conditions.

some, while others might be more proactive and positive in the face of increased risk."

Dialogue participant, London public group

Overall, the general consensus was that personal characteristics and particular conditions would play a role in how much information patients would want. Participants felt it was important that doctors develop a clear understanding of how much different individuals wish to know before carrying out tests, particularly with genetic testing.

"Some would only want to know if the risk is high as it might affect life choices i.e. might prevent me from doing certain things such as high intensity sports, or completely alter career choices unnecessarily."

Dialogue participant, Self-facilitated group

Healthcare professionals at the stakeholder workshop and in the medical student group discussed other positive implications for patient wellbeing of greater patient knowledge and choice. These include the benefits of more accurate diagnosis and treatment in cases where patients contest professionals' decisions for good reason – as doctors are not always right, and tests can give incorrect results. Medical students noted that patients who feel they have made the choice themselves are more likely to comply with the treatment regimen.

Other patient support needs

Many participants felt that patients would need additional forms of support when undergoing treatment in a stratified system. A variety of suggestions were made, including counselling and patient peer-support groups, as well as a buddy-system based on support from ex-patients or those going through the same treatment. Charitable organisations such as Macmillan were seen as important providers of the kind of secondary support needed to help patients make decisions, cope with bad news, and overcome negative side effects or impacts upon well-being.

"Patient support groups are important because information is not just about fact sharing, it will support people and make them feel as though they are better able to cope."

Dialogue participant, London public group

Public participants and patients in particular were concerned that increased specialisation would lead to services being available only in specialised centres spread

across the country. Many were worried that this could increase difficulties of access for patients, who might have to travel further to access the right treatments.

Patients with no suitable treatment option

One of the scenarios used in the dialogue explored the idea that new diagnostic tests would identify patients for whom no treatment was suitable, where a non-stratified approach would have been to try a range of treatments. Participants were concerned about this possibility, and worried that people in this situation might feel “left in the wilderness” and lose hope. To help these patients, measures to improve quality of life, high quality palliative care, and other forms of support were seen as vital.

Medical students had similar concerns, emphasising the importance for the patient-doctor relationship of being seen to do everything possible. Participants emphasised the importance of doctors communicating the news that there was no treatment option in a sensitive manner, and some suggested it is important to explain to these patients how this decision was made and why the normal treatment options are unsuitable.

Plenary session, London workshop

Some stakeholders at the workshop noted that decisions in stratified medicine about whether a treatment is suitable for a patient are very rarely certain and are normally based on percentage likelihood of success and risk of side effects. They commented that doctors need to be very sure they are correct if they are going to deny someone treatment, and questioned what level of certainty is appropriate for this. Participants in the dialogue mirrored these concerns, saying they would want to know what the level of certainty was and asking what would happen in borderline cases.

A variation on this issue was discussed by participants in the adult patient group, all of whom had experience of treatment by specialists for a life-threatening condition. These participants were concerned that stratification would lead to greater rigidity in the treatments available to healthcare professionals. These participants cited examples

where specialists had prescribed courses of treatment 'off label' on the basis of their personal experience, which had been successful where other healthcare professionals had anticipated failure. Patients wanted to be sure that this type of innovative and potentially life-saving practice would not be curtailed by stricter testing regimes and licensing.

> "Individual doctors should have the freedom to make independent decisions – it would be worrying if SM meant more rules and proscribed pathways that didn't allow doctors to use their intuition and professional judgement."

Dialogue participant, patient group

Another concern raised by a few stakeholders at the workshop is that stratified medicine could lead to an increase in patients identified as suffering from 'syndromes without a name' (SWAN). They suggested that by setting clearer definitions for conditions (for example biomarker tests) some patients currently treated under one condition might be ruled out. The stakeholders felt that support for SWAN patients was highly variable across the healthcare services and saw it was vital that training be improved to ensure that patients 'reclassified' as suffering SWAN continued to receive high quality care.

Patients' relationships with the healthcare system and professionals

Participants explored some of the resourcing implications of stratified medicine and how these would affect patients. Many expected that the new services and increased resources needed to implement stratified medicine would be very costly, and were concerned that the NHS would not be able to fund this. They thought that stratified medicine was likely to increase doctors' workloads and so might reduce the quality of attention and care provided to individual patients. This concern was compounded by the fear of some participants that stratified techniques themselves might lead to less personal care. Participants worried that doctors would focus on screening and testing to place patients in treatment groups, with decisions based on statistics and impersonal datasets rather than a holistic assessment of the individual based on face-to-face interaction and knowledge of their situation. Some associated stratified medicine with increased testing and thus with greater mechanisation or even automation if testing took place in a lab, rather than the more common clinical tests used currently. They were concerned that patients' emotional needs must to be taken into account alongside their medical needs.

> "Rather than looking at the whole person you could end up looking at patients on the basis of a load of stats."

Dialogue participant, London public group

In contrast, some participants felt that improved testing would free up doctors to spend more time with the patient, and that additional information would help patients take a more active role in their treatment. Another view was that patients would be passed between many different healthcare professionals who would not know them personally: this was a particular concern for patients with chronic conditions, as discussed in the box below. The possibility that the role of GP might change was also suggested by stakeholders in the workshop.

> "Stratified medicine will require a greater role for specialists in the NHS – GPs may become more about signposting and referring to regional centres."
>
> **Stakeholder, London stakeholder workshop**

Stratified medicine and chronic conditions

A number of the participants involved in the dialogue were patients with chronic conditions – including both adult and young patient groups. Overall, these participants were positive about the idea of stratified medicine, in particular because it offered the possibility of reduced incidence and severity of side effects and the need to find an appropriate treatment.

"There were two of us there who had tried every single drug ever invented for rheumatoid arthritis and failed to respond to 70% of them, and when we did find something it had the most amazing consequences, so it would have been nice not to go through that for 15 years, that concept is very easy to sell to people."

Facilitator/participant, self-facilitated group

Participants with chronic conditions did have significant concerns about the implementation of stratified medicine however, often based on their own negative experiences of the healthcare system. They stressed the importance of investing sufficiently in training of clinicians and providing adequate capacity.

Participants with chronic conditions commented on the importance of investing in research into chronic conditions – and not just focusing on high profile conditions such as cancer.

Many were concerned about patient-doctor relationships in a stratified system. They were worried that they would get passed around between different clinicians, who would not know their circumstances well. Some participants said that in their experience patients with a better relationship with their doctor end up getting more consistent and higher quality treatment. To address this issue some suggested that patients with chronic conditions should have a central doctor responsible for coordinating their care.

"I would be a bit concerned – if you have a long-term chronic condition you want someone who knows you."

Dialogue participant, young patient group

Implications for healthcare professionals

Dialogue participants felt that the primary implication of stratified medicine for healthcare professionals would be the need to learn new approaches and to update their knowledge on an ongoing basis. The identified learnings included new methods and pathways of testing and diagnosis involved in stratified medicine as well as the new stratified treatments which will continue to be developed over time. Some participants expressed concern that financial constraints and capacity issues within the NHS could

mean that the necessary training and learning would not take place, or not be done to a high enough standard. They felt this would be detrimental to patient care.

> "It is pretty significant if you are treated by a GP who is unaware that superior treatments exist."

Dialogue participant, Glasgow public group

Many participants and some stakeholders at the workshop emphasised the importance of training healthcare professionals, particularly GPs, in how to communicate complex and sometimes upsetting information to patients, and how then to help and support them to make decisions if there are choices involved. The communication skills of clinicians were thought to be particularly important in cases where patients are unsuitable for particular treatments that others are able to receive.

> "It requires patient management – she [the hypothetical patient] will be really disappointed and expecting to be eligible like her sister. These findings need to be presented with the utmost sensitivity."

Dialogue participant, London public group – referring to the scenario where Angela is found not to benefit from treatment used for her sister Susie

Discussing the implications for healthcare professionals at the workshop, some stakeholders suggested that increased patient choice under stratified medicine will impact on the role of healthcare professionals beyond their increasing role as information providers. Increased choice for patients necessarily means a decrease in the decision-making power of clinicians – and some felt this would mean allowing patients to make decisions clinicians disagree with. Some stakeholders suggested that this would be a difficult thing for some clinicians to do – particularly those from the older generations who were trained under a more paternalistic healthcare model.

> "If you're going to give people a choice, you've got to accept that they might make the wrong one."

Stakeholder, London stakeholder workshop

What next?

At the stakeholder workshop held after the main dialogue, we asked a group of 50 stakeholders to review the initial findings and tell us what they thought they could mean for the development of stratified medicine. We refined these suggestions with the help of the project oversight group and the Technology Strategy Board to identify the main challenges for stratified medicine arising from the dialogue.

Supporting patients who don't benefit
Where stratification identifies that current treatments won't be effective, participants believed that patients and their families need extra support. This might be palliative care or counselling services. Doctors noted this challenge too; they saw a responsibility to demonstrate to their patients that they have explored the full range of options.

Improving provision of information to patients
If patients are to make informed decisions in the face of more complex probabilistic information it is vital that the information is delivered in an accessible way. Thinking about this in the broader context of educating the public about healthcare is important.

Challenges in delivering testing
There are many barriers to implementing new testing regimes, ranging from consistency of laboratory facilities to knowledge of primary physicians. Thought needs to be given to what happens after a treatment or diagnostic test is licensed to make sure it is available to clinicians to use; it must be both practical and cost-effective.

Involving GPs
General practitioners are the face of healthcare to the majority of the population – they need enough information to reassure an increasingly well-informed public. As more specialised and complex services develop there's a need for consistency in signposting patients to the right services in order to avoid perceptions of a postcode lottery.

Training for healthcare professionals
The public felt that healthcare professionals would require additional training to understand and effectively implement stratified medicine. Stakeholders saw a particular need for communication training for frontline staff while medical students (who were based in secondary care centres) were less concerned about specific training, seeing developments in clinical practice as the norm. It will be important to identify specific training needs as techniques come into practice.

Social issues and consequences

CHAPTER SUMMARY

Equality of access was the dominant concern of dialogue participants; stratified medicine is about the right treatment for the right patient but that shouldn't mean only for the patient who happens to be in the right place at the right time. The role of the private sector was a related concern. Participants trust the NHS, despite the challenges of limited resources, and are cautious about the private sector stepping into the breach without effective regulation by government and others.

3
Social issues & consequences

What did we ask?

Where the previous topic focused on the experience of the individual, at this stage we wanted to explore with participants what stratified medicine means for the healthcare system. The scoping review identified a number of issues, but we also made space for people to tell us what they thought the issues were. This topic had fewer set piece activities, and many of the findings emerged from discussions that started under another topic and grew organically.

What are the human issues participants identify for themselves?

At the end of the first of the reconvened sessions we asked participants to write down the issues they thought we should discuss in the reconvened session. We gave a few examples as prompts, but wanted as far as possible to capture the issues that emerged spontaneously from the first day of dialogue.

What priority do people give to the different social issues?

We took the social issues participants suggested in the two public workshops in London and Glasgow, and combined them with the findings of the scoping review to come up with a list of 16 questions. In the second session we asked participants to prioritise the issues, ranking them from least to most concerning. While the ranking itself was a useful exercise, the most important output of this session was hearing the debates participants had as they weighed up the issues.

What are the implications of stratified medicine for the healthcare system?

Towards the end of the dialogue events we asked participants to tell us what they imagined would change in a healthcare system where stratified approaches were commonplace. We asked them to work through the patient pathway; from diagnosis to treatment and survivorship, thinking about the information and services they would want.

Testing ⇨ Diagnosis ⇨ Treatment

What did we find?

- EQUALITY OF ACCESS
- RESOURCE REQUIREMENTS FOR STRATIFIED MEDICINE
- THE ROLE OF THE PRIVATE SECTOR
- POLITICAL ISSUES - GOVERNANCE AND REGULATION

Equality of access

Equality of access to stratified treatments was one of the most common concerns expressed by participants in the dialogue, whether in terms of socio-economics, age, ethnicity or geographical location. Public participants, young people and many stakeholders at the workshop all advocated strongly for the maintenance of universal access to the most up-to-date treatments through the NHS. Participants were often concerned that the development and implementation of stratified medicine would be so expensive as to prevent treatments being available on the NHS. They felt this might mean treatments were only available privately, and this would increase health inequalities on socio-economic lines.

> There was a lot of mistrust that this was not being developed to benefit the population as a whole under the NHS, most felt it would be something available a long way down the line and would only be for those who could afford it.

Facilitator note, self-facilitated group

Some stakeholders at the workshop also discussed the way in which NICE licenses new treatments, suggesting that cost might prohibit their availability on the NHS.

> "Private healthcare providers are likely to offer treatments and therapies which NICE does not approve"

Stakeholder, London stakeholder workshop

Many participants were also greatly concerned about inequalities of access across ethnic divisions; with many stressing that ethnicity should not be a factor in determining access to treatment. As noted below, some young people in particular perceived a connection between 'stratification' into treatment groups and racial profiling – careful thought must be given to how this perception can be avoided.

> "We have come so far as a community to be together, now we are going back to being segregated i.e. black wards, white wards, coloured wards."

Dialogue participant, self-facilitated group

Other participants expressed concern about the possibility of discrimination based on age, suggesting that more expensive treatments were 'rationed' and only available to the young on the basis of cost versus impact calculations. Concerns about a 'post-code lottery' in service provision were also prevalent among public participants.

> "Things change very quickly in some fields of medical research, like breast cancer. How will developments be shared and incorporated systematically across organisations in different parts of the country? Will the best treatments only be available in London?"

Dialogue participant, adult patient group

Many participants believed that stratified medicine would lead to a higher degree of specialisation and expertise being concentrated in a small number of health centres spread across the country. To mitigate this, both public participants and stakeholders at the workshop supported nation-wide planning and programmes to transfer knowledge and expertise across medical centres in the UK. While seeing the logic in central planning some stakeholders did question whether this conflicted with what they saw as a trend towards more localised management of public health services.

These concerns about equal access to treatment related in many cases to fears about the practical development of stratified approaches, such as resource availability. However, participants did recognise that poor information or communication could exacerbate public concerns about access. An example given at the stakeholder workshop was that of two patients with apparently the same condition being prescribed different treatments, based on relevant clinical criteria. Where there is some other (unrelated) difference between the two patients - for example which health authority they live in, or their ethnicity - it would be easy for that difference to be perceived as the basis for the different treatments. Participants in public workshops, who were briefed on examples, were particularly aware that in cases where genetic testing is involved there could be interplay of ethnicity and treatment group, causing further concern about inequality.

Stratified Medicine and Ethnicity

As mentioned above, one of the distinctive features of a small number of groups, particularly young people and some self-facilitated groups, was a discussion about the potential for stratified medicine to prompt racial discrimination. In this box we explore these perceived implications of stratified medicine upon issues of race and exclusion.

For some groups, such as young people, concerns were focussed on the use of genetic testing. Some participants thought that if the different treatment groups were based on different genetic profiles they might coincide with ethnic differences. They were particularly concerned by situations like the hypothetical patient scenario we used, where testing identifies that there are no successful treatments available. The group questioned whether it was more likely that ethnic minorities would face this scenario, or if testing could be used to legitimise existing health inequality.

"What if there are more black people in category C, the category that don't benefit from a particular medicine, does this mean other ethnicities get better medication? I would be bothered about that."

Dialogue participant, young patient group

In other groups, particularly one community group which was self-facilitated, concerns were less specific to stratified medicine and more on the perception that medical research and development was institutionally racist.

"Using people as guinea pigs... Drugs have been based all along on Caucasians and their makeup...Why did they use the word "Groups" and not "Race"... Basically this is research on people; we think it's on black people."

Participant facilitator, self-facilitated group

Although it was most clearly articulated in these two groups there was a very strong general consensus in the dialogue that limitations on access to treatment based on racial factors would be unjustifiable. It is possible that these issues were less prominent in the public workshops where our sampling approach meant participants were very mixed demographically – in contrast the self-selecting, self-facilitated groups were drawn from existing groups which tended towards greater demographic homogeneity.

Clearly, genetic stratification for clinical reasons is not equivalent to racial prejudice, but what these concerns do highlight is that interpretations of medical developments can be influenced by worldviews based on inequalities and prejudices that do exist. Participants were in many cases acutely aware of health inequalities, and the potential for developments which could exacerbate these. The fact that these concerns were most prevalent in the self-facilitated groups emphasises the importance of clear and accurate communication. Racial prejudice was not mentioned in the materials provided leaving a vacuum into which underlying perceptions were applied.

Resource requirements for stratified medicine

As described above access concerns on ethnicity, social status and location were common and a belief in universal provision is prevalent in the dialogue. However, participants were also concerned that the public health system might lack the necessary resources to develop and deliver stratified medicine treatments universally:

> "Is it cost that is stopping it happening now? … If we don't have enough money will people not get treated?"

Dialogue participant, Glasgow public group

Some participants felt that the role of private healthcare providers could increase if stratified treatments were available privately and not on the NHS, which many considered a negative development. Others felt the private healthcare system in the UK is not big enough for this to be a major concern.

Apart from investment in new drugs and treatments, participants thought that stratified medicine would require investment in developing testing centres as well as staff training and more patient advice and support. Some public participants expressed concerns that the NHS staff were already over-extended and questioned where extra capacity might come from.

> "How is this going to work when we are saying this will require more staff and training yet the government are cutting the number of staff in the NHS and the training they receive?!"

Dialogue participant, Glasgow public group

Others, however, envisaged the possibility for long-term savings through more accurate diagnosis and appropriate treatments. Stratified medicine was seen by these participants as a wise investment, a change in direction which might involve large upfront costs but deliver longer term savings. Not everyone was convinced by potential cost savings however. Some felt that new conditions and treatments would always evolve in tandem so no overall savings could be made. Discussing this issue at the workshop some stakeholders felt it was more realistic to expect efficiency gains rather than financial savings.

> "I don't think we'll save money because new diseases come up and need new treatments. What we can do is get better value – reduce wastage."

Stakeholder, London stakeholder workshop

Regardless of the prospects for efficiency savings, participants felt that the development of stratified medicine will result in difficult decisions about the eligibility criteria for treatments in the face of limited resources. Where more expensive treatments could be beneficial it will be necessary to decide what likelihood of success merits treatment, as one stakeholder at the workshop put it:

> "Rheumatoid arthritis £900 per year per treatment. Who gets it? Only those that have 100% chance of success? Or those with 10% as well?"

Stakeholder, London stakeholder workshop

This notion of the likelihood of success was also discussed by public participants on a larger scale; some debated the merits of investing in the development of new treatments if the benefits were small in scale or limited to a few patients.

> "If costs of SM are so high that they have to increase taxes this might be more concerning; if it's impacting people drastically for little gain we're not sure people would support it! But if it benefits people in a positive way and people can see and demonstrate the benefits you can't argue. Evidence of this is important."

Dialogue participant, Glasgow public group

Some participants extended this discussion to debate the alternatives of investing in stratified medicine versus large-scale, low-cost interventions. This may be a useful area for further research as participants in this dialogue did not discuss this extensively. What participants more often referred to was the range of other priorities they saw for the NHS, which included prevention of common diseases, encouraging healthy living and alternative therapies.

The Role of the Private Sector

Most participants thought that the private sector has an important role in the development of stratified medicine, in funding research and resourcing the development of bio-banks as well as new drugs and treatments. However, as discussed above there were concerns about the involvement of private companies – for example, the extent to which they could be trusted with personal data. Participants such as medical students, who had more knowledge of the medical research field tended to be most positive about the involvement of the private sector:

> "If Pharma[ceutical] companies are accessing your data in order to make new medicines and therefore make money – so what? They're developing treatments – that's a positive."

Dialogue participant, medical student group

Public participants tended to raise concerns about the extensive involvement of the private sector in the healthcare system. Most participants were worried about the influence of profit incentive and the potential for large pharmaceutical corporations to monopolise markets in certain products. Other participants were concerned about the development of patented drugs that are too expensive to use for much of the population.

> "It would be concerning if the pharmacy companies financing this then get to monopolise the market and drive the prices up for the system as a whole."

Dialogue participant, Glasgow public group

This was a particular concern for young patients, with one participant giving their perspective on current HIV treatments as an example:

> "At the moment the big pharma companies have a monopoly over certain drugs. In HIV this has been a big problem and they are responsible for many deaths as they won't release the patent – how will stratified medicine help change that?"

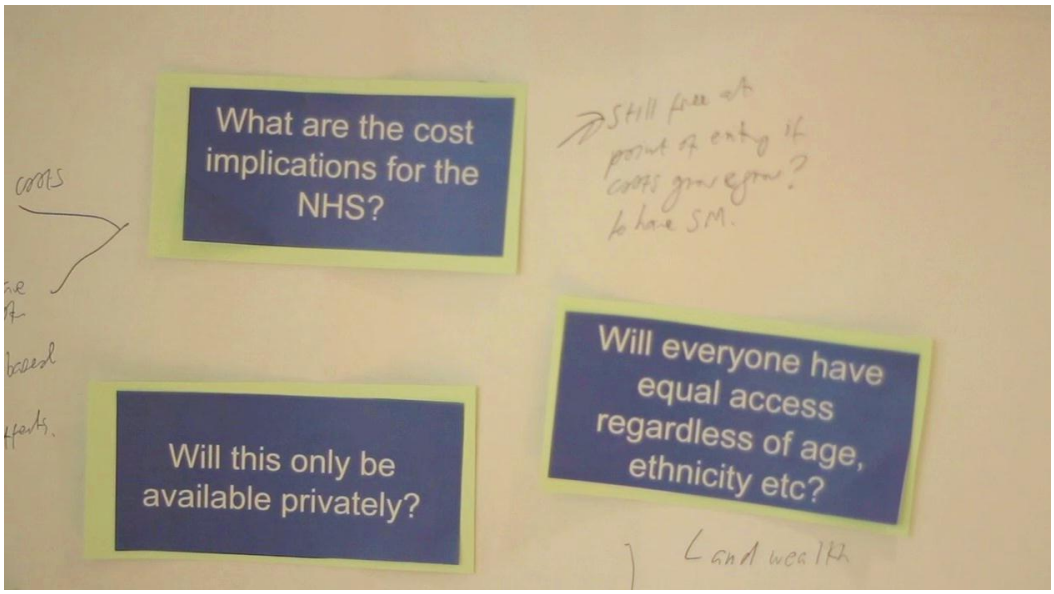
Dialogue participant, young patient group

Many public participants said that regulation of private sector companies operating in this area should be tight. Regulation should include measures to ensure the anonymisation of data as well as banning the sale of personal data between different kinds of private companies. Indeed, access to data by insurance companies, banks, or employers, for example, was perhaps the major concern that participants had regarding the development of stratified medicine, and many were adamant that these organisations should be prevented from accessing people's medical data (see Who has access? Who benefits?).

Apart from concerns about profit motives and data security, some participants worried that private sector involvement in the implementation of stratified medicine would herald greater levels of privatisation within the NHS as a whole:

"Who will fund it? If it's privately funded what implications does that have? Does stratified medicine open the door to more privatised health services, if getting stratified medicine becomes so costly would you have to self-fund?"

Dialogue participant, London public group



Social issues discussion notes from public workshop in London

A related concern for participants in the public groups, and some of the self-facilitated groups in particular, was the role of the private sector in determining the direction and focus of medical research. Participants were worried that stratified medicine would enable companies to focus their research on treatments likely to be effective for the largest number of patients. If research showed that 90% of patients with a particular condition had common treatment responses, and 10% did not, participants thought industry were most likely to focus on treatments for the 90% as the potential 'customer base' would be larger. Concerns that this could leave out people with rarer medical conditions were common amongst participants across workshops:

"As the groups become smaller and smaller as stratified medicine progresses and develops, there will be people left in groups that no-one has any financial incentive to focus on because they are too small. When we are part of a large generic group, the numbers involved create enough of a financial

incentive for researchers and the pharmaceutical industry to find treatments for us."

Dialogue participant, self-facilitated group

Participants in some groups felt that this was already happening, referring to 'sexy diseases' which capture the majority of charity funding. For some participants, the perception that financial incentives might skew the research agenda linked to the issue of equality of access, and concerns about the implications for those who cannot currently be treated. Some participants felt there was a role for government to subsidise research into less common treatments, or those which could be seen as less lucrative for industry.

Political Issues - Governance and Regulation

Participants across the different strands often discussed the role of government and other institutions in regulating stratified medicine in response to concerns outlined above. In many cases participants were not familiar with the current governance arrangements for medical research. Rather than dedicating time to explaining these arrangements we aimed to capture the principles behind people's statements.

Regulation: Testing and Data Sharing

Regarding testing and data sharing (see Regulation and security), participants' main concern was ensuring anonymity and confidentiality and enforcing regulations put in place to this end:

"Government role - ensure data is safe and have a deterrent to make sure."

Dialogue participant, Glasgow public group

Related to this was the notion that since people would be sharing data voluntarily, the data collected should be used solely for research purposes and not for profit-making endeavours. Many participants felt that it was unethical for profits to be made from data donated for broadly humanitarian reasons; and some participants suggested that if profits are made, companies should be required to pay something back to the healthcare system or even to the donors themselves.

"[Donated data should be] only for research, not for sale – we've given the data as goodwill so unethical use or someone profiting from it is therefore not right."

Dialogue participant, Glasgow public group

Although participants commonly saw a role for the government to put in place measures to ensure data is used properly, there was some debate as to the extent to which the

government itself could be trusted to identify and serve the public interest in this respect. Some participants argued that, in the words of one participant at the young people's workshop, "government can't be trusted". Some participants saw it as essential that the regulating agency should be neutral and independent, free from both financial (typically the pharmaceutical industry) and political (primarily government) interests in the development of stratified medicine. Participants made a range of suggestions about who could regulate testing and data sharing, including existing bodies such as NICE and the BMA; while a popular suggestion was for the formation of some kind of independent panel. Although there was a range of views on the appropriate make up of such a body, there was general agreement that it should include experts in medical ethics, who were unattached to political or financial interests, as well as public and patient representatives, and potentially representatives from the healthcare system and research. On the basis that data is likely to be shared internationally, some participants suggested that a global regulatory body or data sharing agreement is needed.

Ensuring Equal Access – regulation, policy and delivery

Given the concerns outlined above many participants argued it was important for the government to take an active role in ensuring equality of access to stratified medicine treatments:

> "[It should be a government role] to ensure that stratified medicine is available to all equally and minimize discrepancies between rich and poor."
>
> **Dialogue participant, Glasgow public group**

Participants envisaged responsibility for ensuring equal provision and universal access to treatments to take place at both the abstract institutional level and the more relational level of the relationship between health practitioners and patients (for more on the latter aspect see section 'Patients' relationships with the healthcare system and professionals'). The main focus of the dialogue regarding regulation was the institutional and legislative level. Public participants had many and varied ideas about particular legislation and policy, but generally agreed that the basic role for the state was to use its powers to ensure equal access. In many cases participants were unclear on the existing frameworks to control medical developments and so were not able to make specific suggestions although they did suggest general principles.

One principle participants noted was the importance of drawing upon the expertise of clinical experts as well as the experience of patients and citizens when forming policy by involving them in policy making processes. It is, however, noteworthy that some public participants expressed doubts as to the extent to which 'top-down' or state-led efforts could be expected to influence practice on issues such as equality. They pointed out that legislation and policy often fails to translate into practice, and can be delivered ineffectively. Another principle participants supported was working collaboratively in order to draw upon the resources and expertise of different partners when delivering services. Some participants highlighted third sector and private organisations, arguing

that any attempt to implement stratified medicine would have to take clear account of their role.

In contrast, the quite general points made by the public stakeholders at the workshop suggested some specific measures to regulate access issues, for example refining the process by which NICE licenses new treatments.

Participants often had more specific comments about access issues in policy and practice at the level of doctor-patient interaction (as discussed in Patients' relationships with the healthcare system and professionals). Participants recognised that cultures and practices vary across the NHS, but suggested specific cases where they felt a need for change to accommodate stratified medicine. Most importantly in this regard was the notion that in the current model of healthcare provision GPs are seen as 'gatekeepers' to more specialised treatment. Some participants were concerned that rather than directing patients to more specialist services, GPs are incentivised to protect access. Some participants felt that the introduction of more stratified medicine would mean treatments delivered by more specialist staff in a larger number of specialist centres. As less care is delivered by generalists such as GPs, their role in linking patients to specialist treatment becomes more prominent. GPs are essentially the first link in this chain and participants were concerned that they could block patients from entering appropriate treatment pathways.

Regulating Markets

Participants' discussions on market regulation focused primarily on the role of government as a 'background' actor investing in research in strategic areas and stimulating markets, rather than as a direct provider of research and services. Market regulation was seen as one of government's main responsibilities. Some participants were especially concerned that private companies would make large profits from stratified medicine, and called for government regulation to curtail this:

> "Don't think that profit should be allowed to be made in health systems. Government should regulate (inc. how much profit can be made, how much can be charged etc.)"
>
> **Dialogue participant, young patient groups**

As already noted, participants from the young experts group argued that private sector involvement is to be welcomed for the funding and resource it provides to develop new drugs and treatments. However, the general attitude towards the involvement of the private sector amongst public participants was a sceptical one, for example with many participants raising concerns about the potential for the privatisation of the healthcare system. It is perhaps for this reason that the state, (meaning both government and healthcare bodies such as the NHS) was understood by public participants to have a role in such areas as generating and enforcing anti-monopoly laws and licensing frameworks, as well as in stimulating the market by providing subsidies for 'risky' research and supporting small enterprises set up in this area.

3
Social issues & consequences

What next?

At the stakeholder workshop held after the main dialogue we asked a group of 50 stakeholders to review the initial findings and tell us what they thought the findings could mean for the development of stratified medicine. We refined these suggestions with the help of the project oversight group and the Technology Strategy Board to identify the main challenges the dialogue identified for stratified medicine.

Analysing the costs and potential savings
In a constrained financial situation people want to understand the long and short term costs and benefits of a new approach. Demonstrating the case for new approaches in particular disease areas is vital to ensure support for stratified medicine. Public and stakeholders weren't in agreement about whether it would result in increased or reduced costs, suggesting a need for further research into the economics of stratified approaches before claims can be made about cost savings.

Coordinating development
There is a clear need for centralisation in some aspects of stratified medicine, e.g. data sharing, but people are wary of losing the benefits of local access and control.

Differential possibilities for disease groups
Participants felt that stratification could amplify the existing tendency for research to focus on some conditions at the expense of others. For example if it was possible to identify two variants of a disease affecting 90% and 10% of patients respectively, research would focus on that majority, disadvantaging the minority. Some people suggested that funding should be structured to prevent this and support research which doesn't focus on the most common or lucrative treatments.

Providing sufficient resources
Public participants were concerned that the potential of stratified medicine would not be realised if sufficient resources weren't made available for training and delivery once new techniques are developed.

Thinking about regulation and implementation together
Stakeholders are concerned that approaches to regulation and licensing might not keep pace with developments, particularly for diagnostics, which don't follow the traditional clinical trials route.

Understanding and addressing potential effects on equality of access
One of the biggest fears for some participants was that stratification could lead to discrimination, and could be used to legitimise existing health inequalities, be they ethnic, regional or demographic. There is a need to ensure participants understand to what extent racial characteristics are relevant to stratified medicine, but participants also felt there was a need for government to ensure equality of access but not on the mechanism for this.

Understanding of regulation

Participants often had limited knowledge of the existing systems which regulate the development of new treatments. Helping the public to understand this system, including its strengths and weaknesses would allow them to engage more easily with the question of how it will respond to new approaches like stratified medicine.

Research, testing and data sharing

CHAPTER SUMMARY

Participants recognise that data sharing is crucial to the development of stratified medicine and are happy for their data to be used in research that could help others. There were a number of caveats to their contribution: data security, limits on who has access, and concerns about the profit motive for research. Getting the consent process right is central to public acceptance of data sharing; consent must be genuinely informed and there are no shortcuts to this.

4
Research, testing & data sharing

What did we ask?

Developing stratified medicine depends on the availability of large clinical and genetic data sets, which in turn depends on patients and the public consenting to their data being shared between researchers. We explored a number of scenarios and real life cases of testing and data sharing, focusing on those areas that the scoping work suggested could be contentious: who has access to data, what type of testing is involved and what information participants need to make an informed choice.

How do people see current practice?

Cancer Research UK has been collecting samples from surgical patients at centres across the UK as part of a project to compile a database of genetic information about tumour types. We filmed an interview with one of the staff involved in this project. She explained to participants how the current process of consent works, and this prompted discussion about the ethics of donation. You can see this video online here.

How do people respond to testing in different clinical settings and for different disease types?

To investigate whether the type of test would affect people's attitudes to sharing samples and data for research we gave participants a list of four scenarios to explore. These included both mental and physical health conditions, and a range of clinical settings and testing protocols:

1) Patient with early stage arthritis visiting their GP for a routine blood test	3) Patient with schizophrenia at their clinical psychiatrist taking part in an MRI scan and psychological interview
2) Patient having a diagnostic HIV blood/saliva test at their GPs	4) Person taking part in NHS Bowel Cancer Screening Programme – taking the screening test at home

What did we find?

What kind of tests?

One aspect of stratified medicine which the dialogue explored was the willingness of different groups of people to accept novel diagnostic tests, either for treatment or research purposes. When it comes to testing in order to prescribe treatments participants across the board identified strongly with the view that reducing trial and error would improve the experience of patients, and that generally speaking additional testing to avoid side effects and delays would be welcomed.

To explore whether participants' acceptance of novel diagnostic tests was affected by the type of condition or test protocol involved, we asked participants to explore a range of scenarios (see previous page). On the whole, participants were happy to undergo simple tests such as blood and urine tests, which were familiar and could be delivered in the familiar setting of a GP surgery. However while most participants were supportive of more 'invasive' tests such as biopsies or MRI scans where these could improve treatment outcomes, some had reservations, in particular for methods seen as more intrusive, such as lifestyle questionnaires. This finding is echoed in recent work on perceptions of mental health service users by Kings College London (see page 56). Other participants felt that the context in which testing happened would affect their willingness.

> "The way you answer questions depends on who is asking you for the information; if I was going to my specialist I would be OK to answer anything, if it was someone new I'm not sure."

Dialogue participant, young patient groups

When discussing testing with medical students and stakeholders they often identified potential problems with the implementation of novel testing processes. They were concerned that without significant investment current systems won't deliver consistent quality testing quickly enough. They saw this as a potential barrier to the introduction of stratified approaches into practice.

In the patient groups participants raised concerns about the potential harms of testing, identifying these as physical harms resulting from test protocols such as biopsies, or

indirect harms arising from inaccurate test results and incidental findings.[7] We can hypothesise that this reflected their greater experiences with the healthcare system and perceptions of the fallibility of testing which the public groups did not pick up on so frequently.

Where the public did talk about the incidental findings of a test, much of the discussion centred on whether or not participants would want to know if they were at risk of developing a particular condition. Participants' views on this issue were highly diverse. Some argued for a right to blissful ignorance and others insisted that doctors should have the responsibility for informing their patients fully in all circumstances. Often discussions led to the conclusion that this type of decision can only be made on an individual basis, and if stratified medicine does result in more testing and thus more incidental findings (as participants suspected) healthcare professionals should support patients to understand what incidental findings could occur and respect their preferences. Similar concerns were expressed by participants who followed a line of reasoning that higher prevalence of testing for disease risk (rather than simply incidence) coupled with developments in genetics would lead to other consequences such as genetic testing of children.

> "Could you use genetic tests to look at the likelihood of illnesses in children? Could newborns be tested for future illnesses?"
>
> **Dialogue participant, Glasgow public group**

[7] Incidental findings are previously undiagnosed conditions identified during testing or treatment for unrelated conditions.

Stratified medicine in mental health

To help participants consider the acceptability of testing in different settings we presented scenarios including that of a patient diagnosed with schizophrenia who is asked to take a range of psychological tests and an MRI scan as part of research towards stratification. In our initial pilot session with members of the public, a subset of participants expressed the view that they would be less likely to take part in research into mental health conditions than physical equivalents. This pattern was repeated in the public dialogue where the majority of participants felt they would be willing to take part in research on mental health with some distinctive concerns. There was strong support for research in this area from those who had some experience with mental health, primarily as carers or family members; because they thought more accurate prescription would reduce the incidence of side effects they experienced.

Participants felt uncertain about the extent to which those with acute mental health conditions could adequately consent to take part in clinical research, suggesting that additional steps would need to be taken:

"A lot more care needs to be taken over consent – you might have to repeat the process on different days, make sure they know exactly what they are signing up to and how their consent will be used."

Dialogue participant, Glasgow public group

Others felt that there could be issues with the types of test, for example participants felt that physically demanding procedures such as MRIs could be distressing for patients. Participants were also cautious about the use of psychiatric tests such as interviewing; some distinguished between the 'personal' data collected and other 'physical' test data:

"[Interview data is] more subjective and might not be true on any other data day"

Dialogue participant, London public group

As well as these more practical concerns participants in public groups in particular had less well-defined concerns about how stratified approaches could be applied to mental health. They reflected that this could be related to the continued stigma attached to mental health which they felt strongly ought to be overcome. Some groups, notably in the Glasgow workshop, were explicit that mental and physical health should not be considered differently. The medical students also had a positive view, suggesting that mental health was a fertile area for research because 'people who have been successfully treated are often eager to contribute'.

The dialogue project did not sample mental health patients or carers; however recent research by Diana Rose at Kings College London with patients and carers echoes some of these themes. There was recognition of the particularly severe side effects experienced by many mental health patients, and optimism that stratified approaches could reduce this problem. There was also concern about different testing procedures, both physically demanding processes such as MRI scans and more personally challenging protocols such as cognitive testing. This issue is explored in more detail in a forthcoming issue of Mental Health Today (forthcoming).

Data for research: an altruistic response

In the public workshops, and especially those with young people, participants often had limited knowledge about the process of medical research and who was involved. Few participants had experience of research, with the exception of patient groups who were more familiar. We used the example of a bio-bank project involving a partnership between pharmaceutical companies, NHS and a medical research charity to help participants understand what stratified medicine research could look like.

Expert participant at public workshop, London

Participants were generally positive about the idea of donating samples for medical research and about bio-banks, particularly if the sample was gathered as part of ongoing treatment. A number of participants expressed surprise that samples removed for medical tests were not already used for research, as a matter of course.

When asked about their response to testing for research in the context of different disease areas, participants tended to feel that they would contribute in all the scenarios we presented. However, dialogue participants often felt they would require different reassurances about confidentiality and anonymity in cases such as mental health and sexually transmitted diseases where they believed there might be negative consequences of the results being revealed to employers, for example. As one participant said:

> “What about data that could count against you, this is the data that really matters”

Dialogue participant, London public group

Across the dialogue strands participants were positive about the principle of contributing to medical research which could benefit others; there was a clear sense of responsibility to others.

> "I see this – my reaction is – yes I want to give my data, how can I help future generations?"
>
> **Dialogue participant, London public group**

There was relatively widespread recognition among participants that, generally speaking, medical research was necessary to develop new treatments and improve care. However most participants had limited knowledge of the medical research process and few had experience of it, other than those in the patient groups. Alongside this overall support for contributing to research, both the public and patients identified important boundaries that they felt should be respected by the medical research community. Where there was more opposition to research, in one of the self-facilitated groups for example, this stemmed from a conception of research as making people into 'guinea pigs' and was related to a lack of trust in the institutions who might carry out research, particularly the private sector.

Who has access? Who benefits?

A frequent concern about the more widespread use of medical tests was who would be able to access the resultant data. Participants in all groups tended to express greater trust in the NHS, charities and academia than in pharmaceutical companies. Young patients in particular were sceptical about the role of private enterprise:

> "Pharmaceutical companies' using it [data] is less trustworthy, they will use it because there is a profit to be made, they will compromise it."
>
> **Dialogue participant, young patient group**

The notion of trust was, as might be expected, strongly related to feelings about who should have access to data. The same group of young patients argued that in a situation where the same research could be carried out either by a private pharmaceutical company or by a not-for-profit body, they would prefer their data be shared with the not-for-profit. Participants were not wholly unsympathetic to the idea of medical research as an industry; however they were more cautious when discussing examples where they felt that public good or benefit was not the primary motivation. Some participants seemed to regard voluntarily contributing their data as an act of altruism; they were uncomfortable with the idea of it being used by industry for financial gain. Some participants, for example in the Glasgow group, argued that where data obtained from the NHS led to profits for industry they should be returned to the NHS.

> "If any pharma company is going to make a profit from stratified medicine there has to be something

in place that says they will put something back into the NHS."

Dialogue participant, Glasgow public group

In other cases participants referred more generally to negative media coverage of the pharmaceutical industry explicitly, or made more oblique references:

"There is something dark that niggles in my mind about pharmaceutical companies."

Dialogue participant, London public group

Discussions about who should have access to data were linked with discussions about the use to which data would be put. There were strong feelings from many participants across the dialogue that insurance companies should not have access to individual or population level medical data which they could use to limit access to insurance or increase premiums. This was one of the most commonly raised issues in the data sharing discussion. These concerns were often linked to fears about the potential for genetic testing to identify disease risk; in particular participants felt that probabilistic information about risk could be misused and disadvantage people who may never go on to develop a condition. In workshops where it was discussed, participants felt that genetic discrimination should be actively regulated against; responding positively to the example of legislation in the US to prohibit such discrimination in relation to insurance, employment and social interactions.

"This is the big downside of stratified medicine for me. I am happy with all the medicine etc. but it seems risky to get these tests done as then you might not qualify for insurance."

Dialogue participant, Glasgow public group

Concerns about data access were not limited to the private sector. A number of participants expressed concern about the government and police having access to medical, and particularly genetic, data. These concerns proved prescient, with media coverage of the NHS Care Data Scheme highlighting this issue during the production of this report.[8] As with the insurance case, participants felt that where data was contributed for the purpose of medical research the spirit of that contribution should be respected and participants should not have to fear indirect consequences. For a few groups, noticeably in Glasgow where there was more focus on potential cross-border issues in relation to England/Scotland, there were some concerns about sharing data

[8]"Police will have 'backdoor' access to health records despite opt-out, says MP". Published online 6 February 2014 www.theguardian.com/society/2014/feb/06/police-backdoor-access-nhs-health-records

internationally. Participants felt that data should remain within a familiar regulatory system.

Considering these concerns, some public participants suggested that those donating data should have the option to specify who should be allowed access to it, for example ruling out private companies but allowing access to universities and healthcare trusts.

Regulation and security

Most participants were not familiar with the existing systems that regulate medical research. For example, participants in public workshops talked about the need for oversight of medical researchers to ensure that trials met ethical criteria. This is currently the role of ethics boards.

The more participants learnt about the anonymisation of data the more confidently they expressed their willingness to take part in medical research. Participants were less confident about contributing data which was only psuedonymised; they feared that even with strict security if it was made available widely enough it could be de-anonymised. Participants were also more concerned that access to pseudo-anonymised data should be more limited, for example it should not be available to those with an interest in identifying individuals, including insurance companies.

Data security was discussed in most groups, prompted by its inclusion in the social issues exercise where the card asked “Can data be shared accurately and efficiently, can the IT systems cope?” In many groups the immediate response to this was an immediate ‘no’, based on their perception of the NHS and government generally as ineffective providers of IT services. Participants referred to their own experiences of poor data sharing in the healthcare services they use, or to reports in the media of security breaches in other sectors. They saw these as particularly harmful in terms of loss of confidence in a service.

> “Whilst the group didn’t foresee major issues with security occurring on any regular basis, they recognised it is certainly possible that data security could be breached, and should this happen it would be very damaging to the medical industry and of great concern to the public.”
>
> **Facilitator note, self-facilitated workshop**

Concerns were often focused on the physical systems rather than the regulatory ones, as one participant noted:

"Government computer systems don't have a good reputation"

Dialogue participant, Glasgow public group

The process of consent

Participants felt that the consent giving process should cover the issues discussed above such as who can access data, the reasons for wanting access and the security and governance arrangements in place. Aside from their practical concerns there was a feeling among many participants that consent giving also had value in recognising and respecting the active contribution of research participants.

"This has to be an informed choice; they have to have the respect to ask."

Dialogue participant, Glasgow public group

Participants wanted clear information about the way in which information collected would be stored, including who would have access to it and for what purpose before they gave consent. They identified the point of diagnosis as a difficult time to ask for consent; many felt that patients might not consider the issues properly in the midst of the more immediately pressing issue of the diagnosis. Some had suggestions about how healthcare professionals could ensure that patients understood fully what was being asked of them.

"It is important for this information to be explained face to face, as well as on paper, as when you are in hospital there is a tendency to sign all paperwork without reading it through."

Dialogue participant, London public group

This view was reinforced in discussion at the stakeholder workshop where some clinicians reported their feelings that patients were given consent forms as part of a whole range of mandatory paperwork, which made it much less likely that they would read the consent form carefully. Some stakeholders discussed the Care.Data programme, which was introduced shortly before the workshop. While supportive of the goals there were some stakeholders who felt the introduction of opt-out consent had been poorly managed. They felt it was important people were encouraged to fully consider the consequences of consent decisions:

"It [the Care.Data leaflet] came through my letter box like a pizza menu. The kind of distribution used

for questionnaires means the sheets are posted with junk-mail, people ignore it."

Stakeholder, London stakeholder workshop

Another suggestion made by participants in different groups was that participation could be enhanced if people were more informed about the outcomes of taking part. They suggested that reports back to participants in studies where findings lead on to new treatments would be welcomed as a way of confirming that their trust and altruism had been warranted.

Optimism in conclusion

Publics and patients raised many concerns about data sharing. However, most participants were, in principle, very happy to contribute to research. Even generic consent which gives permission for data to be used in as yet unspecific studies was not considered unacceptable; rather participants felt that they would need an appropriate degree of information about access and purpose which they could trust before taking part. The findings seem to bear out the following stakeholder comment:

"The assumption that people's default position is not to want to share data is not true. People do want data shared it is just that they feel that the appropriate infrastructure for safe data sharing is not in place."

Stakeholder, London stakeholder workshop

What next?

At the stakeholder workshop held after the main dialogue we asked a group of 50 stakeholders to review the initial findings and tell us what they thought they could mean for the development of stratified medicine. We refined these suggestions with the help of the project oversight group and the Technology Strategy Board to identify the main challenges for stratified medicine arising from the dialogue.

Being upfront about what data will be used for
People are sensitive to the potential for their data to be used in ways which they did not envisage when they gave consent. Participants often made assumptions about how medical research works, for example underestimating the role of industry, and so were suspicious about those uses. By making information about the purpose of data collection and data security as clear as possible, the uncertainty would be reduced and people reassured about sharing their data.

Asking for consent at the right time
The point of diagnosis is a stressful time for patients and not necessarily the best time to give informed consent for medical data to be shared. Participants were cautious about processes where patients don't consider the issues fully, either because they are opt-out, or because information is not accessible. They also felt there was a need for clinicians and researchers to be sensitive to individual patient needs.

Quality of data and analysis
Large data sets are only useful if they contain high quality data; stakeholders identified lack of clinical data as a significant barrier to research. Others felt that statistical analysis and validation of markers was another area for development.

Involving patients in research
The public dialogue demonstrated the extent to which the public are keen to be involved in developments in healthcare from the policy stage to individual research projects. By giving them a more active voice patients feel more connected and in control and are thus more likely to want to get involved.

Explaining the role of data
Data collection and sharing is essential to the development of stratified approaches, but the links between research and treatment are not always well understood and this can raise suspicion. Demonstrating the value of contributing data by talking about outcomes would help participants understand why they are being asked to contribute in new ways.

Methodology

CHAPTER SUMMARY

This chapter describes the process by which we carried out the dialogue over a nine month period in 2013/2014. It explains how the project came about, who we met with and what we discussed, as well as how we drew the conclusions you see presented in this report.

Background to the project

The UK Stratified Medicine Roadmap: The Nine Themes

1. Incentivising adoption
2. Increasing awareness
3. Patient recruitment – consents and ethics
4. Clinical trials
5. Data – collection, management and use
6. Regulation and standards
7. Intellectual property
8. Bio-banks and biomarkers
9. Increasing the impact of R&D investment

The roadmap is a plan of action agreed by the investors in the Stratified Medicine Innovation Platform and their stakeholders in 2011.

Healthcare is currently the most highly funded priority area for the Technology Strategy Board, which is the UK innovation agency working to stimulate innovation and economic growth in the UK. Part of that funding is being used to promote the development and uptake of stratified medicine, which is the science of identifying the right treatment for the right patient at the right time. The Technology Strategy Board is working with partners including the National Institute for Health and Care Excellence (NICE), the Medical Research Council, Arthritis Research UK, Cancer Research UK, the Department of Health and the Scottish Government Health and Social Care Directorate to invest a combined total of £200 million over 5 years via the Stratified Medicine Innovation Platform ('the Platform').

In 2011 the Platform put together a roadmap highlighting nine areas they saw as vital to support uptake of stratified medicine. In many of these areas such as increasing awareness, patient recruitment and data collection, management and use, there were clear questions to be answered about how the public, patients and healthcare professionals would receive the proposed changes. In light of these knowledge gaps the Technology Strategy Board began to discuss the possibility of a public engagement project with Sciencewise experts in dialogue involving science and technology.

The Technology Strategy Board and Sciencewise decided that the right way to explore these questions was through a process of dialogue, rather than research. Dialogue differs from research in a number of important ways, which influenced the eventual design of the project. It treats those involved as citizens rather than research subjects, working with them to understand their views. It is a deliberative process - it happens over an extended period of time, with the way in which people's views form, change and evolve a main output. Dialogue brings together experts such as scientists with the public and policy makers to debate directly, on an equal footing, to share their views and knowledge. It is also important that dialogue happens at the right stage in the development of a policy, so that the findings can influence the direction this takes. Sciencewise guiding principles sum it up as:

> "Public dialogue is a process during which members of the public interact with scientists, stakeholders (for example, research funders, businesses and pressure groups) and policy makers to deliberate on issues relevant to future policy decisions."
>
> **Sciencewise Guiding Principles 2013**

The first step towards the dialogue was to set up an oversight group for the project; a group of people with specialist knowledge and expertise who could ensure the process was fairly, objectively and sensitively conducted. This group included experts from

Stratified Medicine Dialogue Oversight Group

Andrew Acland, Sciencewise

Simon Denegri, Involve

Alastair Kent, Genetic Alliance

Louise Leong, Association of the British Pharmaceutical Industry

Nikolas Rose, Kings College London

Joyce Tait, University of Edinburgh

Naho Yamazaki, Academy of Medical Sciences

medical research and bio-ethics, alongside representation from medical charities, patient groups and the pharmaceutical industry. The oversight group was charged primarily with ensuring good governance of the project throughout, from commissioning to final reporting. The group reviewed the dialogue process, advised on content and expert involvement and attended dialogue events.

OPM Group and creative partners DFM [9]and Close-Up Research[10] were commissioned by the Technology Strategy Board in summer 2013, with co-funding and mentoring from Sciencewise,[11] to deliver a programme of public and stakeholder dialogue events over a period of nine months. The initial idea of the project had been developed into four distinct purposes, which underlie all the work that has taken place since:

Purpose 1: To discover the diversity of public opinion about stratified medicine and, in the process, also to discover how best to explain what it involves, and which terms are least likely to cause confusion, misinterpretation or misunderstanding, so that stratified medicine and the issues it raises can be discussed effectively with patients, their families, and members of the public generally.

Purpose 2: To explore the possibilities of stratified medicine through a process that enables patients and members of the public to identify advantages and disadvantages that developers and healthcare providers may be overlooking, and to think creatively about ways to amplify the former and mitigate the latter.

Purpose 3: To identify what steps practitioners and other healthcare providers will have to take to communicate the complex information that patients and their families will need about the testing processes that stratified medicine requires, and the support that different strata of patients will require before, during and after treatment.

Purpose 4: To establish what sort of ethical framework and practical approaches to consent are needed for trials that will build patient and public confidence to support the sharing of the personal data necessary to ensure the effectiveness of stratified medicine.

Emerging throughout the project was the need to find a clear mechanism to ensure the findings of the dialogue were understood and acted upon by the relevant stakeholders, something our methodology took into account.

[9] Close-Up research how people live, and make films in the process, to help find solutions to real-life problems. See their work at: www.closeupresearch.com

[10] Damn Fine Media (DFM) create factual videos and animations which make information memorable. See their work online at: www.damnfinemedia.co.uk

[11] [11] Sciencewise is funded by the Department for Business, Innovation and Skills (BIS). Sciencewise aims to improve policy making involving science and technology across Government by increasing the effectiveness with which public dialogue is used, and encouraging its wider use where appropriate to ensure public views are considered as part of the evidence base. www.sciencewise-erc.org.uk

Our approach

Stratified medicine is a complex and technical topic which is not widely understood by the public yet – this presented particular challenges for the dialogue. We worked with two creative partners to create materials which communicated both the topic and the potential implications clearly, accurately and in an engaging manner. Our aim was to create materials that not only worked for the dialogue but could have a life beyond it. All materials are freely available online at stratifiedmedicine.wordpress.com.

To inform the dialogue materials and processes, we carried out a scoping exercise in which we interviewed six people working in and around stratified medicine, as well as reviewing significant recent literature on the topic. This review (included in Appendix D) helped us to agree what the dialogue should focus on with the project oversight group. For example, we agreed to focus primarily on physical health conditions and stratification largely on biological factors to allow participants to focus on a few specific examples. We also agreed that there is clearly a spectrum of approaches ranging from stratification (which operates at the level of groups of patients) to personalisation (where treatments are tailored to the individual); we were explicit about this with participants, rather than creating an artificial distinction.

Once we had developed a suite of materials, we went out to gather a diversity of views on the topic. This report provides a summary of the findings of 19 workshops with over 200 people, over a four month period – you can see a full list in Appendix A. Our approach involved four strands of events, each seeking a different perspective on the issues, using a different method, but covering the same topics and using the same materials, to enable us to compare and contrast the findings. Throughout the report you will find references to the differences in views emerging from particular strands or groups. The four strands are described here, and you can see the process plan which guided each session in Appendix B:

Public workshops: (October 2013)

- **Diverse participants**: The aim of these workshops was to engage a diverse group of members of the public who we did not expect to have any prior knowledge of the topic. The participants were recruited by a professional agency to meet a quota broadly representative of the UK population. Participants were given a small financial 'thank-you' to recognise the time and energy they had given to the process. This helps to recruit participants with no prior interest in the topic. We held workshops in London and Glasgow, with around 30 participants each.
    - **Highly structured process**: We staffed each of these workshops with a full team of experienced facilitators and expert participants. The participants worked through a schedule of activities covering all the topics we identified at scoping. Views were recorded in a number of different ways at different points in the process.
    - **Full days, reconvened**: The public workshops were the longest in the programme, with participants spending two full days with us. We met on

Saturdays, with two weeks between each event to allow people time to consider, discuss and re-evaluate their views.

Targeted workshops: (October and November 2013)

- **Those with an interest**: For this strand we wanted to understand the views of groups who would be most affected by the development of stratified medicine: adult and young patients, young people and future healthcare professionals (medical students). Each group had between four and ten people.

- **Flexible process**: We provided an experienced facilitator to each group, but allowed more flexibility in which topics groups covered, choosing from the full set used in the public workshops. This enabled us to focus on those areas which participants had most to say about: for example patient groups were able to provide much greater detail on care implications than the public.

- **Evening sessions, reconvened**: As with the public workshops we invited each of our targeted groups to meet twice, with time in-between to consider the issues we had discussed. These groups met for around two and a half hours each time. The exception was the medical students whose schedule only allowed for one session of around four hours.

Self-facilitated groups: (November and December 2013)

- **Expanding the scope**: For these workshops we chose groups which had not been represented in large numbers in the other strands, including people with chronic health conditions and minority ethnic groups. Seven workshops were held, with an average of eight participants at each session.

- **Real world process**: The self-facilitated groups were provided with the same materials as the other groups but one group member was asked to facilitate the discussion after a briefing with one of our team. We wanted to explore how people interpreted stratified medicine outside of the more managed process of the main dialogue, as they might encounter it in the real world.

- **Single sessions, individual follow up**: The self-facilitated groups had the shortest discussions, just one session of around 2 hours. This reflected both the more limited nature of debate which might naturally occur in an everyday setting. We followed up each session with a telephone interview with the group's facilitator, to ensure we captured as much data as possible. For more on the challenges and success of these groups see overleaf.

Self-facilitated workshops

One of the primary aims of this dialogue was to understand how best to communicate stratified medicine to the public. The process the public and patient workshops went through gave participants time to learn about the subject, to reflect on the issues and explore them with each other and experts. However when the public hear about stratified medicine for the first time it will not be in the context of a managed workshop with experts present, which is why we also ran self-facilitated workshops. In these sessions participants were recruited from pre-existing community groups, so all participants including the facilitator were peers. The sessions were shorter, lasting around two hours, and while all the materials were made available to participants they did not have the benefit of experts to expand on them. In this way we hoped to test what happened 'in the real world' when people learn about stratified medicine for the first time.

This strand of workshops was distinct from the more managed groups and raised particular challenges, on which our learning is reflected below. Overall we feel this approach added to the breadth and richness of the data from which we could draw for this report, and in some cases identified new issues and interpretations that we would not otherwise have seen. For example, as described in **Equality of access**, some of the self-facilitated groups focused strongly on the possibility that stratification could be along ethnic or racial lines – something that was much less clearly articulated in other strands. Part of this difference may be explained by demographics – the self-facilitated groups involved existing community organisations and thus a higher level of demographic consistency of participants than the more managed groups where diversity was deliberately sampled for. It is also possible that the absence of a member of the project team in the 'researcher' role made participants less likely to adapt their responses to what they perceive as the desired outcome, and thus free to express more negative interpretations.

In practice we found that:

The amount of time spent briefing the facilitator pays off: one of the most successful groups was run by a participant who had initially attended one of the managed groups, where facilitators gave less time we found they ran into questions they couldn't answer in the session. Briefing can help to reduce the variability in the level of detail groups cover, which was much higher than in the managed groups.

Learning and reflection interviews improve data: the difficulty of accurate note taking should not be underestimated; the practice of interviewing the facilitators soon after the session added a great deal of valuable data.

Identifying groups with an interest: where the topic was more closely aligned with the interests of the group, participants were more likely to engage fully with the process. This also affected the extent to which incentives (which we offered to groups rather than individuals) were important to their participation.

Communicating stratified medicine: recruiting groups to take part was an excellent experiment in communicating the topic. We found that the animation and a simple information sheet were useful tools to engage people in the topic, but in our initial approach we avoided the term stratified medicine as facilitators found it off-putting.

Stakeholder workshop (January 2014)

To support stakeholders in taking forward our findings we brought together participants from across the dialogue to meet with the Technology Strategy Board, the project oversight group and around 40 stakeholders representing industry, academia, government and the third sector. At this final full day workshop we asked stakeholders and dialogue participants to review the findings of the dialogue project and explore the implications for the future development of stratified medicine. The outputs of that workshop are incorporated into this report in the form of recommendations at the end of each chapter.

Stakeholder workshop

The table below summarises the participation in each of the four strands. More details on who attended each of the individual workshops can be found in **Appendix A:**

Public workshops	Targeted workshops	Self-facilitated workshops	Stakeholder workshop
30 participants per session	5-12 participants per session	5-12 participants per session	50 participants
Quota sampled	Recruited via intermediary groups	Pre-existing groups	Invited stakeholders identified by the Technology Strategy Board
Two full day sessions, two weeks apart	Two evenings, two weeks apart	One session, around two hours	Full day workshop
Total of 60 participants	Total of 40 participants	Total of 80 participants	Total of 50 participants

From data to findings

Data collection

The 19 workshops in the dialogue programme produced a wide range of data, summarised below.

- **Digital recordings**: At all of the public, targeted and stakeholder workshops our facilitators used digital audio records to keep a record of the discussion. These were used to aid the facilitators in transcribing their notes.
- **Facilitator notes**: As well as recording the conversations, facilitators at all events kept notes of the discussion using pro forma which were later transcribed and analysed. The same pro forma were used by the leaders of the self-facilitated workshops, who posted back their notes for transcription.
- **Participant outputs**: In several of the activities, such as the social issues ranking, we asked participants to create their own record of the discussion. These were also transcribed and analysed.
- **Learning and reflection interviews**: to supplement the notes they kept of the workshops we conducted a telephone interview with the lead of each self-facilitated group to help us understand more about the course of the discussion and the dynamics of the group. The notes of these interviews were also transcribed and analysed.

Analysis

All of the data, once transcribed, were analysed by the analysis team to produce the findings presented in this report. All the data described above was entered into a qualitative analysis system which allowed us to code and interrogate it. Each set of workshop data was categorised according to the specific workshop and strand to enable comparisons to be made. In this way, we could compare the views expressed across the different samples, for example groups of young people and groups of patients. It also allowed us to look across the different methodologies, the self-facilitated groups versus the more managed public workshops.

While this categorising did allow us to compare the different groups we did not attempt to identify individuals, for example we did not record demographic data about each participant. This reflects the fact that all the dialogue events were based on group discussions, so it would not be possible to separate the views of individual participants.

As well as categorising the data according to its sources we applied thematic analysis, grouping all comments under common themes. We started with the four broad themes under which this report is organised:

- Definition and communication
- Implications for patients and care
- Social issues and consequences
- Research, testing and data sharing

We refined this analysis further using more specific themes as we found them in the data, for example grouping together all suggestions of alternative terms for stratified medicine, or views on who should have access to medical data. This analysis underlies the findings reported here, with participant views on particular issues grouped together and indications given where views were more or less common to specific groups.

It is important to note that while we engaged with a wide range of participants through the dialogue it cannot be said to be representative of the population as a whole. The findings represent the views expressed by particular people in a particular setting, responding to the particular information presented to them. Reflecting this throughout the sections of this report which document our findings we will regularly refer back to the materials, activities and discussion prompts used in the dialogue. The materials we presented went through a rigorous process of review by the oversight group and the Technology Strategy Board to ensure they were balanced, accurate and accessible. You can see many of them online at http://stratifiedmedicine.wordpress.com and we hope that they will be useful to others who want to discuss these issues with the public and stakeholders.

Review

Initial findings were presented to stakeholders at the workshop in January 2014 and valuable feedback was incorporated into this final document. This report itself has been internally reviewed by our project director, Diane Beddoes, and externally reviewed by the project oversight group before publication. The project as a whole was independently evaluated and the findings of that evaluation are available on the Sciencewise project website www.sciencewise-erc.org.uk/cms/developing-stratified-medicine/.

What next?

At the stakeholder workshop held after the three strands of the main dialogue we asked a group of 50 stakeholders to review the initial findings and tell us what they thought these mean for the development of stratified medicine. Working with the project oversight group and the Technology Strategy Board we grouped stakeholders' input to identify challenges which must be overcome to develop stratified medicine in ways which take account of the human issues identified.

Resource list

Materials used in the dialogue
Available on the project website: http://stratifiedmedicine.wordpress.com
Reports on stratified medicine
European Science Foundation, 2012. *Personalised Medicine for the European Citizen: Towards a more precise medicine for the diagnosis, treatment and prevention of disease (iPM)*, Strasbourg: European Science Foundation. Available online
Ketner, S. L. ed., 2012. *Personalised Medicine: Status Quo and Challenges*, Brussels: EuropaBio. Available online
National Research Council of the National Academies, 2011. *Towards Precision Medicine: Building a Knowledge Network for Biomedical Research and a New Taxonomy of Disease*, Washington DC: The National Academies Pres. Available online
Nuffield Council on Bioethics, 2003. *Pharmacogenetics: ethical issues*, London: Nuffield Council on Bioethics. Available online
Nuffield Council on Bioethics, 2010. *Medical profiling and online medicine: the ethics of 'personalised healthcare' in a consumer age*, London: Nuffield Press. Available online
Technology Strategy Board, 2011. *Stratified Medicine in the UK: Vision and Roadmap*, Swindon: Technology Strategy Board. Available online
The Academy of Medical Sciences, 2013. *Realising the potential of stratified medicine*, London: Academy of Medical Sciences. Available online
Current stratified medicine research
Cancer Research UK's Stratified Medicine Programme see website
Projects sponsored by the Medical Research Council's Stratified Medicine Initiative see website
Case studies of stratified medicine compiled by the Academy of Medical Sciences see website
Research and policy on data sharing
Caldicott review 2013: an independent review of information sharing in health and social care Available online

Appendices

The four sections of the appendices are:

- Appendix A: a list of each dialogue event and details of who attended

- Appendix B: a process plan detailing how each public, targeted and self-facilitated event was run

- Appendix C: a process plan detailing how the stakeholder workshop was run

- Appendix D: the scoping review prepared at the start of the project to describe the current state and scope of stratified medicine

Appendix A: Dialogue events

Participant group	Location	Format	Participants
Public workshops (October 2013)			
Public	London	Two full day sessions, two weeks apart	- 24 members of the public, quota sampled by a professional recruitment agency to broadly represent UK demographics - Session 1 attended by 2 experts: Dr Desmond Walsh, Medical Research Council and Dr Eddie Blair, Integrated Medicines - Session 2 attended by 1 expert: Loic Lhuillier, the Technology Strategy Board
Public	Glasgow	Two full day sessions, two weeks apart	- 27 members of the public, quota sampled by a professional recruitment agency to broadly represent UK demographics - Session 1 attended by 2 experts: Prof Anna Dominiczak, Glasgow University and Prof Andrew Biankin, Glasgow University - Session 2 attended by 2 experts: Prof Joyce Tait, Edinburgh University and Prof John Gordon, Glasgow University
Targeted workshops (November 2013			
Adult patients	London	Two evening sessions, ~2 hours, two weeks apart	- 5 adult patients, recruited via a disease specific support group
Young patients	London	Two evening sessions, ~2 hours, two weeks apart	- 15 young patients (18 – 25), recruited via a disease specific support group

Young people	London	Two evening sessions, ~2 hours, two weeks apart	- 9 young people (18-25), recruited via a youth organisation
Medical students	Glasgow	One morning session, ~4 hours	- 9 medical students undertaking foundation training at the University of Glasgow, recruited via teaching staff at the University
Self-facilitated workshops (December 2013)			
Other (BME)	Huddersfield	One session of around two hours	- 5 adult women recruited via a community group
Patients	York	One session of around two hours	- 8 adult patients recruited via a disease specific support group for a common chronic condition
Patients	London	One session of around two hours	- 8 adult patients recruited via a disease specific support group for a common chronic condition
Young people	London	Two sessions, 2 hours and 1 hour	- 25 young people (18-25), recruited via a youth organisation
Young people (BME)	London	One session of around two hours	- 5 BME young people (18-25), recruited via a youth organisation
Other (BME)	Manchester	One session of around two hours	- 7 BME adults recruited via a community group
Other (parents)	Manchester	One session of around two hours	- 5 adult parents recruited via a community group
Stakeholder workshop (January 2014)			

Stakeholders	London	One full day	Approx. 50 participants comprising: - Around 5 participants from self-facilitated workshops - Around 5 members of the project oversight group and Technology Strategy Board staff - Around 40 participants invited by the Technology Strategy Board representing: the pharmaceutical and diagnostic industry; research institutions, both hospital and university based; medical research charities; practicing healthcare professionals; and healthcare policy makers.

Appendix B: Process plan: public, targeted & self-facilitated workshops

The table below shows the suite of activities and discussion topics developed for the main part of the dialogue – not all groups covered each item, given the different timetables for each strand. We have indicated which groups covered each discussion in the table; please note that times given are for the public groups, the strand workshops were shorter and so sessions were often covered more quickly.

Session	Description	Materials	Length	Groups
Definition and communication				
Video animation	SESSION AIM: to understand participants' initial responses to stratified medicine SESSION OUTPUT: insight into participants initial understanding and responses to stratified medicine Participants watch video animation introducing stratified medicine and discuss initial reactions in small groups.	Animation (video)	20 minutes	Public Adult patients Young patients Young people Medical students Self-facilitated groups
Stratified medicine timeline	SESSION AIM: to develop participants understanding of timeframe for development of stratified medicine SESSION OUTPUT: n/a Participants are presented with a timeline showing how the development of stratified medicine fits into the history of medicine. Participants are encouraged to explore the timeline.	Stratified medicine timeline (Online)	15 minutes	Public Adult patients Young patients Young people

Discovery process	SESSION AIM: to introduce basic scientific concepts SESSION OUTPUT: insight into initial understanding and responses to stratified medicine and related concepts Participants are asked to compile a list of risk factors and relevant medical tests for four categories of disease risk: environmental, genetic, physical characteristics and infectious. Examples are given on posters and participants are also encouraged to expand on these based on their own knowledge of medicine/healthcare.	Answer sheet (pdf) Information sheets: Environmental factors (pdf) Genetic factors (pdf) Physical factors (pdf) Infection factors (pdf)	60 minutes	Public Adult patients Young people
Stratified medicine on a bus	SESSION AIM: to map participants changing definitions of stratified medicine SESSION OUTPUT: participants own definitions of stratified medicine at different points in the dialogue Participants were asked how they would describe stratified medicine to someone they met on a bus. The question was asked at the end of each session to map change.	n/a		Public Adult patients Young people Medical students
Implications for patients and care				

Patient perspective	SESSION AIM: to understand participants' responses to the implications of stratified medicine from a patient perspective and their information needs SESSION OUTPUT: insight into participants' views on the implications of stratified medicine from a patient perspective and their insight on information needs from a patient perspective Participants watch video featuring testimony of adult patient treated successfully with Imatinib, a stratified treatment for chronic myeloid leukaemia.	Patient perspective (video)	45 minutes	Public Adult patients Young patients Young people Medical students Self-facilitated groups
Angela and Suzie	SESSION AIM: to understand participants' responses to the different implications of stratified medicine for different groups of patients SESSION OUTPUT: Identification of opinions and initial acceptability of the differential impacts of stratified medicine Participants read and discuss hypothetical scenario in which sisters Angela and Suzie are both diagnosed with breast cancer. Suzie is in the treatment group for an effective targeted therapy; Angela is in the treatment group for which only basic therapies are available.	Angela and Suzie (pdf)	45 minutes	Public Adult patients Young patients Young people Medical students

Patient pathways	SESSION AIM: to explore with participants the implications of stratified medicine for care in the future and understand their responses to these changes and identify their information and support needs. SESSION OUTPUT: insight into the implications for care pathways in the future from patient experience perspective Facilitator asks participants to suggest what changes to facilities/capacity or information/support will be needed in the healthcare system to make stratified medicine commonplace. Participants asked to think about different points on the patient pathway; testing, diagnosis, treatment, and about patients benefitting and not benefitting from stratified medicine.	n/a	45 minutes	Public Medical students
Social issues and consequences				
Social issues generation	SESSION AIM: for participants to identify possible wider social implications of stratified medicine and to explore how participants understand the topic at the end of workshop 1 SESSION OUTPUT: Identification and opinions on social and wider implications of stratified medicine, including cost and participants own working definitions at the end of workshop 1. Participants are asked to work in small groups to list the social issues they are concerned about regarding stratified medicine. Facilitators prompted only if participants were stuck.	n/a	45 minutes	Public

Social issues ranking	SESSION AIM: to understand participants' views on the social issues and wider implications, and pros and cons of stratified medicine following workshop 1 and their thinking time in between workshop 1 and 2 SESSION OUTPUT: understanding of participants understanding at the start of workshop 2 Participants are asked to prioritise social issues associated with stratified medicine (issues based on the outcomes of the social issues generation exercise). Facilitators capture rationale as well as prioritisation.	Social issues (pdf)	45 minutes	Public Adult patients Young patients Young people Medical students Self-facilitated groups
Making stratified medicine happen	SESSION AIM: to generate participants' different insights into: how to make stratified medicine work SESSION OUTPUT: insight into individual participants' recommendations for different stakeholder groups Participants asked what role they see for different groups in making stratified medicine happen in line with their views and concerns about it. Participants are asked about: the public and patients; doctors and healthcare professionals; the government; research scientists; industry (pharmaceutical and diagnostics); and the media.	n/a	30 minutes	Public Adult patients Young patients Young people
Research, testing and data sharing				

Research perspective	SESSION AIM: understand participants' responses to the data requirements of stratified medicine SESSION OUTPUT: insight into participants' opinions and attitudes toward participation in clinical trials and patients' data being routinely gathered in wider clinical settings Participants watch video featuring manager of a bio-bank describing the process of patients contributing tissue samples for the Cancer Research UK stratified medicine programme. Facilitators lead discussion on whether participants would donate, what information they would want to decide, views on data collection, storage and sharing.	Research perspective (video)	60 minutes	Public Adult patients Young patients Young people
Testing and data sharing scenarios	SESSION AIM: understand participants responses to the data requirements of STRATIFIED MEDICINE SESSION OUTPUT: insight into participants' opinions and attitudes toward patients data being routinely gathered in wider clinical settings Participants read and discuss four different scenarios where they might be asked to take a diagnostic test and subsequently allow the results to be included in research programmes.	Consent scenarios (pdf)	50 minutes	Public Young people Medical students
Other				

Overall attitude	SESSION AIM: to capture people's overall view on stratified medicine, to capture the most pressing issues for participants SESSION OUTPUTS: insight into the issues most pertinent to whether participants were positive or negative about the development of stratified medicine At the end of the second workshop participants were asked to indicate on a simple chart how they felt about stratified medicine (positive/ negative) and identify the main pros and cons they saw.	n/a	5 minutes	Public Adult patients Young patients Young people Medical students Self-facilitated groups

Appendix C: Process plan: stakeholder workshop

The stakeholder workshop followed a different process to the other workshops as its aims were to:

1. Build awareness and understanding of the results of the stratified medicine public dialogue, in the context of stratified medicine advancing in future

2. Identify the implications of the results of the public dialogue for the advancement of stratified medicine

3. Where possible, identify first steps for key players to adopt when moving forward with stratified approaches

Session	Description	Materials	Length	Groups
Definition and communication				
Stakeholder views	SESSION AIM: to understand stakeholder views on some of the questions we asked in the scoping review and the dialogue events as well as their initial perceptions of public views SESSION OUTPUTS: Sense of main issues for stakeholders prior to hearing the dialogue findings, will be integrated into reporting Participants gave their initial views on the human issues of stratified medicine in the context of their involvement	n/a	60 minutes	Participants mixed by facilitators into 4 groups of around 12 participants
Exploring the dialogue	SESSION AIM: to present the dialogue process and findings SESSION OUTPUTS: participants have an understanding of the dialogue process, a sense of its value to different people involved, highlights of findings, opportunity to ask questions	Dialogue findings presentation (online)	75 minutes	All participants

	The OPM Group project manager presented the initial findings of the dialogue, with an opportunity for questions.			
Implications of the findings	SESSION AIM: Participants to explore the findings further, compare them with their own experience; consider them in the light of their practice/expectations for future practice SESSION OUTPUTS: insights into the findings in the context of stakeholder views Participants were able to choose from one of the four themes of the dialogue findings: definition and communication; implications for patients and care; social issues and consequences; and research, testing and data sharing. In small groups participants were encouraged to explore where the findings were surprising, challenging or fit with their own experiences, and what they might mean for practice.	n/a	60 minutes	Participants self-selected one of four groups based on themes of findings
Identifying next steps	SESSION AIMS: 1) Participants identify implications of findings for the development of stratified medicine; 2) Participants work on the recommendations identified to brainstorm ideas for taking them forward SESSION OUTPUTS: List of potential recommendations/challenges. Plan for action on each recommendation. Participants were asked to think about the challenges/recommendations they saw in implementing stratified medicine in light of the findings. All suggestions were recorded but participants were asked to select one or two which they felt most strongly about and develop these ideas in more practical terms.	n/a	60 minutes	Participants self-selected one of four groups based on themes of findings

Appendix D: Scoping review August 2013

Objectives

This short report summarises the findings of the scoping review carried out as the first stage of the design of this dialogue project on stratified medicine. The purpose of the scoping review is to inform the design of the dialogue process, by exploring relevant literature and stakeholder perspectives to:

- Develop a deeper understanding of the issues surrounding the introduction of stratified medicine to clinical practice
- Identify the language, analogies and comparisons which are currently used to describe stratified medicine
- Identify organisations and networks from which participants may be recruited, particularly in the patient strand.

Methodology

The scoping review combines two components; a rapid review of key documents, and semi-structured interviews with a range of stakeholders involved in stratified medicine. The outputs are summarised in this report under the topic areas identified with the Technology Strategy Board as foci for the dialogue, shown below, and one additional section on language and analogies:

Dialogue topics
1: Explore the definition & communication of stratified medicine, including information needs of different groups
2: Identify potential social issues & consequences, explore the pros and cons - consider how to amplify & mitigate
3: Consider differential implications for patients - and possible safeguards for this
4: Explore how stratified medicine may contribute to better care and identify opportunities for innovation (including data sharing/testing)
5: Identify attitudes to testing/data sharing, discuss an ethical framework and potential safeguards
6: Consider how to reconcile patient desires/needs and healthcare costs

Rapid document review: A great deal of scientific research, social and medical, has been carried out into stratified medicine. To gain an overview of this research we summarised major review and position papers from science organisations. A bibliography is included at the end of this document.

Stakeholder interviews: Working from an initial list developed at the inception meeting with the TSB we selected six individuals to interview, aiming to gain a range of perspectives on stratified medicine. Each interview was carried out by telephone and lasted around one hour. Interviewees

were guided through a series of questions based on the topic list, as well as being asked to share their own understandings of and questions about stratified medicine. Their input is summarised alongside the literature findings below, with attribution by sector only, as per the table below.

Interviewee	Sector
1	Regulatory body
2	Social scientist
3	Patient voice organisation
4	Patient support group (disease specific)
5	Research charity (Disease group)
6	Pharmaceutical industry

A working definition of stratified medicine

The scoping review identified a number of areas where a range of views exist on how stratified medicine is defined, with different interpretations having different implications for the content of the dialogue project. We have identified a small number of questions which we would like to discuss with the oversight group, to help us refine the working definition of stratified medicine which we will take forward into the dialogue materials and events. Our questions are:

- **Can 'stratification' include any personal characteristic, or just biological?** Should we discuss the use of lifestyle, behaviours, social and environmental factors? (Only one of the reviewed documents and one stakeholder frequently mentioned lifestyle and environmental factors as considered alongside biological factors).
- **Should it include both high & low-tech tests/solutions?** Much of the literature, and the interviews, focused on 'high tech' techniques such as genetic testing, however approaches such as stratification according to observational data were also mentioned.
- **When will the diagnostics be used?** Should our working definition of stratified medicine include a preventative/diagnostic approach based on identifying risk (i.e. screening everyone), or be about quantifying risks which are already identified (i.e. once a disease occurs).
- **When does stratification become personalisation?** Our conclusion from the scoping review is that personalised and stratified approaches exist on a spectrum, with poorly defined boundaries between the two. Agreeing a definition for the dialogue will help us to focus the materials and discussions.
- **Is there a long-term vision?** Some of the literature, and stakeholders felt that personalised medicine was a development of stratified medicine, envisioning a system where: ‘one would be able to access a comprehensive, contextualised dataset for each citizen and use the information to identify those measures that will best support the health and wellbeing of that person'. We would like to test whether this is seen by the oversight group as an inevitable, desirable, or contingent consequence of introducing more stratified approaches.

Summary of the review

1. Explore definition and communication of stratified medicine, including information needs of different groups

Much of the literature reviewed is not limited to a narrow definition of stratified medicine, but rather uses similar and overlapping terms including personalised medicine/ healthcare, precision medicine, pharmacogenetics, and genomic medicine. The term stratified medicine itself is variably defined, and the main aspects of this are discussed below.

Both the literature and stakeholders emphasise the need to communicate clearly the nature and impacts of stratified medicine for different groups. Frontline healthcare staff is seen to play an important role in this communication, and some of the literature argues for extra training and other resources to be provided to increase their understanding and capacity to communicate stratified medicine to patients. The most frequently mentioned issues arising in the literature include how much information to give to patients, and how to communicate risk to patients.

DEFINING STRATIFIED MEDICINE

One of the most striking features of the review was the range of definitions offered for stratified medicine. While there are clearly some features which occur in all definitions, there are other aspects which are less clear.

- The Academy of Medical Science report observes a definition of stratified medicine as *"the grouping of patients based on risk of disease or response to therapy by using diagnostic tests or techniques"* – these diagnostic tests will identify the status of particular 'biomarkers', which have been shown to be related to treatment response or disease risk – and will allow patients to be provided with the treatment most likely to work well for them. This forms the basis of our working definition.
- Stratified medicine is commonly seen in the literature as changing the way we classify diseases from one based on treatment to one based on underlying mechanisms and causes at a molecular level. This may mean that two people presenting very similar symptoms may be treated in very different ways and could be said to have different diseases.
    - However in many cases diagnoses (at least in the short to medium term) will still rely on symptoms, as we are very unlikely to find the mechanisms behind and biomarkers for all diseases.
- Stakeholders and literature agree that stratified medicine defines a narrower range of approaches than personalised medicine. The latter "integrate[s] data on the entire dynamic biological makeup of each individual as well as the environmental and lifestyle factors that interface with this makeup to generate a complex, individual phenotype. Using this information, models can be generated to identify the most appropriate healthcare choices from treatment to prevention, in individual citizens." *(ESF Look Forward*). In contrast, stratified medicine retains an element of aggregation and is not so closely targeted.
    - One stakeholder talked about the 'level of granularity' as a useful difference between stratified and personalised medicine (Regulatory body), and most agreed that stratified and personalised medicine are on a spectrum rather than being distinctly different approaches.
    - Other suggestions from stakeholders are that personalised medicine includes broader types of characteristics, morphological features, environmental exposures or lifestyle data (as stratum), and incorporate both low and high tech treatments and diagnostic techniques. (Social scientist)

Evolution or step change? Most stakeholders felt that introducing stratified medicine into practice was more of a gradual change than a revolution

- "*Stratified medicine is an evolution, we've always done it, but previously we used age, sex and symptoms to stratify; now we are increasingly using imaging and molecular level markers.*" (Social scientist)
- "*The key difference from current medicine is that SM is a more detailed diagnosis than 'the average patient'. In the current system you treat a range of people using the best available treatment, in a SM scenario you identify a much smaller group of people, and then still treat them using the best available treatment.*" (Regulatory body)
- Another suggested it be defined negatively: *"It's about not using a treatment that wouldn't be expected to work in a particular patient*." (Pharmaceutical industry)

The role of genetics: The extent to which stratified medicine is primarily or even exclusively composed of genetic tests and treatments is a subject of some debate in the literature; however it is clear that genetic medicine plays a major part in the shift to a more stratified approach.

- Genetics is relevant to stratified medicine in several different ways: people's genetic make-up can affect their susceptibility to certain diseases; their reaction to medicines (and therefore the relative effectiveness of these); and the genetics of diseased cells (which can differ from a person's healthy cells, particularly in cancers) can affect which treatment they are best targeted with.
- Gene/medicine/disease interactions are very complex. Relatively few conditions are monogenetic, but most genetic conditions are multifactorial with genes playing a role in addition to a person's environment, lifestyle etc.
    - Whether or not a patient will get a condition is therefore uncertain, and genetic tests can only give risk predictions (e.g. having a biomarker for cancer risk does not mean an individual will get cancer)
- Most stakeholders were keen to point out the breadth of stratified medicine, noting that it is not limited to applications involving genetics or cancer:
    - Molecular research is at the forefront of research in stratified medicine at the moment, but it is just as important in the wider context of improving healthcare outcomes. (Research charity)
    - Increasing the precision of diagnosis might have implications for better management of conditions as well as treatment - thinking about the 'lived disease experience.' (Patient voice organisation)
- The literature also flagged up that genetic data is not the only relevant information and it is not always the most useful or predictive. E.g. blood tests, cholesterol tests, and HIV tests can all give highly predictive, reliable information without genetic analysis. Non genetic tests can also give indirect genetic information.

COMMUNICATION AND INFORMATION NEEDS

The literature and stakeholders were in agreement that there will be different information and communication needs in stratified medicine scenarios relative to the current situation; and that patients don't just need information, they need to understand it and its significance. The relationship between information provision, healthcare literacy and the implications of more stratified approaches for shared decision making recurred frequently through the stakeholder interviews and this review.

- Some of the literature suggested that to facilitate the uptake of SM, frontline healthcare staff such as GPs need to be aware of the clinical utility and benefits of SM.
- The speed of change of understanding and evidence in this field was felt to make communication to non-experts (particularly the general public) difficult.
- Healthcare professionals will need to judge how much information to give patients, and at what stage to give this. This is especially problematic for complicated fields such as cancer.
    - A common question in the literature was how much information patients need when a diagnosis is being made using a stratified approach: do they need to know all variables involved, just the final decision, or the whole context?
- Several stakeholders discussed the extent of "health literacy", with some noting that there can be a generational disparity, with older people less comfortable with, and eager for, medical information and decision making to be shared with them. (Regulatory body) This theme recurs through several topics.
- Some literature identified a risk of oversimplification – they felt that the public need to understand the complexity of gene/medicine interactions.

Communicating risk: As with many topics identified in the scoping, communication of risk is not new to stratified medicine; however it is clear that more complex information is likely to be given to patients in a stratified medicine world. The dialogue materials will need to reflect this fact, and the scoping review provides a number of insights into the consequences of stratified medicine in this area.

- Patients need to be given risk information in a way which empowers them to make decisions.
- In practice, much information given to patients will come as probabilities – patients and healthcare professionals need to understand this. (The latter will likely require training to understand and communicate effectively.)
- Healthcare professionals also need to recognise that individuals have very different baselines for risk acceptability.
- Patients need to understand that biomarkers and biomarker tests are not always 100% accurate, and that there are still risks. There may also be contra-indications to a treatment, even if the biomarker is correct. (Regulatory body)

2. Identify social issues & consequences, explore pros and cons – amplify & mitigate

The scoping review identifies a wide range of potential social issues and consequences relating to stratified medicine. The primary benefit of stratified medicine is seen as improved health outcomes for patients who will have more appropriate treatment in a timelier manner. Stratified medicine is also considered beneficial by some as it may increase patient choice and control, improve public health literacy and behaviours, reduce costs for the NHS, and stimulate economic growth and skilled job creation. Some of these benefits are thought to rely on investments in the education of patients, the public and healthcare professionals around stratified medicine.

Potential drawbacks identified in the literature include the impact on patients of finding out they are unsuited to many/any treatments, the possibility of incorrect or misleading test results, issues relating to an increasingly medicalised society and the individualisation of healthcare, and the likely increase in direct-to-consumer diagnostic tests.

Many of the potential benefits of stratified medicine incorporate both medical outcomes and associated social benefits: these are considered under topic 4: opportunities for better care.

CHOICE AND CONTROL

Views differ on whether patient choice and control over their healthcare will increase or be limited by stratified medicine, both in real terms, and in their perception of choice.

- The literature identifies that more information and greater involvement in decision making may increase individual's choice and capacity to exercise choice.
    - However if greater diagnostic accuracy rules out some treatments or drugs which have previously been prescribed for a particular treatment patients could perceive this as reducing choice.
- In the interview with a regulatory body representative, a situation was described in which there are 8 treatment options for disease X in the unstratified situation, versus 2 treatment options for the particular strata of disease. The patient might have previously thought they had 8 'chances' to find a treatment that works, now they only see 2. (Regulatory body)

HEALTH LITERACY AND INFORMATION

Patients will (need to) become more involved in decisions about their healthcare, particularly regarding the diagnostic tests and therapeutic options available. This will necessitate greater patient knowledge and understanding (health literacy), which in turn will have consequences.

- Some of the literature envisions a changed relationship between healthcare professionals and patients. Healthcare professionals will need to be able to communicate effectively with patients to explain the process, options and implications, allowing the patient to come to an informed decision.
    - Healthcare professionals will require training, tools and education materials to help them accomplish this, as well as needing more time with patients.
- Patients and professionals will need access to high-quality, clinically approved information – particularly on the internet, but also in other forms for patients who cannot or do not want to access the internet. Due to the prevalence of low quality, misleading, or incorrect information on the internet, some sources suggest developing an official accreditation scheme for online medical information websites.
    - Some literature suggests a link to the debate about making more clinical trial data available to patients.
- Several stakeholders talked about shared decision making as a relevant corollary to stratified medicine - which presents both challenges as more complex information becomes relevant, and opportunities to engage patients better in decision making. (Patient voice organisation, Regulatory body)
- Increased health literacy and patient involvement in decisions were felt in the literature to have additional overall benefits – for example via increased understanding of preventative measures leading to patients adopting healthier lifestyles.

UNWELCOME RESULTS

Many of the social issues identified in the scoping relate to the consequences of more detailed diagnosis where patients receive information that would not currently be available.

- The literature identifies a question about who should be 'responsible' for handling risk? The patient, the medical professional, or the state?
    - Not all patients will want to know the same amount of information about risk or their conditions.

    - Testing one individual can also alert relatives to important genetic conditions – however this is additionally a potential ethical problem, as it is only the individual who made the original decision to know, not the relatives.

- Some patients might find out there are no medicines that can be prescribed to treat their condition, or that there is no treatment at all, with a need identified in the literature to consider the psychological implications of this, as well as the potential for discrimination (as discussed under topic 3).
- The possibility of information leading to stigma or information abuse (e.g. blackmail) is raised, with the review noting that information cannot be unknown once it is known.
- The possibility of false negative, false positives and misleading results must be considered, with the literature raising the possibility that test results may 'create needless confusion or anxiety, [and] lead to unnecessary invasive procedures that carry additional risks.'
    - In particular genetic tests will not always accurately predict someone's response to a treatment; other factors affect responses including age, gender, interaction with other medicines, and diet.
- Possible delays in treatment while waiting for test results to come back was a concern for some, with a question raised about whether it would be appropriate to prescribe treatment without administering a test if there is one, or without waiting for the results.

Home tests: The literature suggests that there will probably be a rise in home tests available direct-to-consumer. Whilst these give patients more choice about their care, they also involve risks as they are easy to misinterpret and can in some cases be unclear, unreliable or inaccurate. There is potential adverse health outcomes, unnecessary worry or inappropriate reassurance, and could lead patients to self-prescribing (as many medicines are now available online).

- Some sources recommend increased governmental regulation in this area (including limiting which tests are allowed to be sold directly), as well as communication to the public of the risks of self-diagnosis, and training for healthcare professionals about how to communicate with patients about these issues and interpret the test results.
- Direct-to-consumer testing may also increase costs to the NHS if it leads to unnecessary follow-up testing, according to one document.

CHANGING PERCEPTIONS OF MEDICINE

Medicalisation: Some literature and stakeholders argued that stratified medicine might contribute to changes in the understanding and perception of health and illness through the medicalisation of ordinary variation, including for children – particularly where tests are predictive.

- One stakeholder raised the issue, but suggested that it may be adding to an existing trend: "as more and more things are becoming 'medically relevant' there's a convergence between lifestyle and health." They gave examples such as remote monitoring tools which share information with doctors. (Social scientist)
- Another stakeholder talked about the potential for increased capacity to diagnose risk to create pre-patients/patients in waiting. This already exists (e.g. we know obesity relates to diabetes), but will become a more common issue with SM, and with technology which confronts people with more risk information. (Regulatory body)

Individualisation: Some items of literature raise the possible risks that SM will further individualise understanding of health, to the detriment of understanding the structural and contextual influences on it (e.g. social and environmental influences).

- An increased emphasis on individual responsibility is seen as potentially leading to victim blaming – there is a need to consider the risk of marginalising groups by labelling them as 'irresponsible' when they fail to follow advice on exercise, diet, etc. and a need to bear in mind the social factors that influence those choices.

Consequences for patient groups/charities: Several stakeholders discussed the implications of stratified medicine for patient groups, the majority of which are currently structured around disease groups. Representatives of these groups are the mechanism by which patients are involved in healthcare policy currently, so there may be a question of whether this representation will continue to make sense in a stratified situation.

- Currently the model of involving patients and the public in healthcare is based on representatives – but will it still be possible to have representatives if everyone is different? (Patient support organisation)
- One gave the example of breast cancer. Currently there are thousands of patients with one disease, forming a community, but in a stratified world there could be hundreds of different types, would this change the feeling of solidarity? (Patient voice organisation)
- However the patient support group representative interviewed felt that this was likely to be offset by an existing trend for more specific patient groups, facilitated by the internet as a tool to help disparate groups to connect with common features. (Patient support group)

CLINICAL TRIALS

The review suggested that as stratified medicine develops more patients will be involved in clinical trials (either directly or through their data/samples being used for this). Public understanding of these needs to improve and potential participants need to be given all the information and support necessary to make an informed decision about whether to do so.

- However stakeholders also noted that individual trials might include fewer individuals, as they selected more relevant subjects. (Regulatory body, pharmaceutical industry)
- There were concerns from stakeholders that an approach based on smaller-scale, more targeted trials would be incompatible with the current system for regulating drugs. They worried that regulators expecting to see large-scale trials would be unlikely to approve on the basis of smaller ones, as there is no consensus on what best practice looks like here. (Patient support group, Pharmaceutical industry)
- *For more on clinical trials see topic 4.*

WIDER BENEFITS

- The literature suggests in various places that there may be benefits to the economy and jobs: including the pharmaceutical industry, diagnostics industry, infrastructure, IT, statistics which all have opportunities for growth.
    - As one stakeholder pointed out, stratified medicine has already been identified as a priority by the Technology Strategy Board, indicating support for stratified medicine as an economic driver.

3. Consider differential implications for patients – and safeguards

The literature identifies a range of possible differential implications for patients which need to be addressed or monitored to ensure an ethical and effective implementation of stratified medicine. In particular, it is felt to be important to consider the needs of patients who are identified as unsuitable for any available treatment; patients with diseases which become 'rarer' due to stratification; people

less or not able to engage with their healthcare decisions; and areas which have poorer health infrastructure and/or lower test usage. Additionally, some of the literature discusses the possibility and potential impacts of stratification along ethnic or racial groups which may arise. There are some links to discussions about healthcare costs, mostly around geographical availability of particular treatments or diagnostics.

AVAILABILITY OF TREATMENTS

The most prominent concern around availability was the potential for situations to arise where stratified medicine identified that there were no potential treatments available for a particular patient. As with many of the ethical issues associated with stratified medicine, this is not a novel risk. There are already situations where no treatment is available, a point the dialogue will bear in mind, while exploring the issue in the new context.

- The literature suggested that stratified medicine in some cases will rule out patients for whom the available medicine will likely not be effective or suitable – what happens if there are no alternatives? Should the person still receive the medicine? Even if it is likely to cause side effects or adverse reactions? Should they have to fund this themselves?
    - Stakeholders pointed out the converse of this as some patients may benefit more from SM than others – e.g. being 'fast tracked' if you have the right biomarkers. (Social scientist)
- The concern was not shared by the pharmaceutical industry representative interviewed. They felt that it was unlikely that diagnostics would be developed for which there were no treatments, given the structure of drug/diagnostic development. (Pharmaceutical industry)
- A related point raised in the literature was whether patients could (or should) be prescribed a medicine even if they do not wish to take an associated test? If a medicine was only licensed on the basis of a test then would it still be allowed to be given without the test? Currently off-label prescribing does occur, and it is not clear how stratified medicine would affect this.

RARE DISEASES

The scoping identified a concern that as diseases become redefined and some are shown to be rarer, it may be difficult to get pharmaceutical companies and others to fund research and development into treatments.

- Rare disease campaigners argue that findings from rare disease research are very often applicable more widely – if stratification makes more conditions 'rare' then this becomes increasingly important – research has to look at applicability beyond the specific condition.
- Some suggest incentives might be necessary to encourage research into rare diseases/patient groups. 'One possibility would be to apply existing legislation which encourages the development of medicines for 'orphan diseases', by offering tax credits, incentives for research and extended patent protection.'
- Another potential implications mentioned by a stakeholder was unintended consequences of SM for 'odd ones out' where the marker is not quite right – e.g. subtly different genetics. Would these patients fall between the cracks in a system where treatment is targeted? (Social scientist)

HEALTHCARE LITERACY

Different people will be differently able to engage with stratified medicine and participate in their healthcare decisions – it needs to be ensured that people who are unable or unwilling to do so do not receive worse care because of this.

- The literature points out the obvious fact that there are wide healthcare literacy differences (linked to education, interest, time, access to information, etc.)
    - Some sources suggest governmental support and funding will be required to increase medical literacy in the population.
    - Others identify a need to cater to those who are unable/unwilling to access information on the internet (commonly older people – who are often the heaviest users of healthcare).
- Not all patients will want to participate in decisions made about their care, especially if this involves processing a lot of information which they may not have the time, prior knowledge or inclination to do.
    - Should people be able to choose to delegate responsibility for making choices back to medical professionals?
- Not all patients have the capacity to participate in decisions about their care (e.g. the very young or elderly), there are questions about who responsibility is delegated to in the more complex decision making of stratified medicine.
- The literature identifies a need to ensure that race, culture, socioeconomic context and gender are adequately represented in datasets to ensure that stratified medicine develops for the benefit of all.

GEOGRAPHICAL DISPARITY

Both literature and stakeholders emphasise the importance of ensuring that high quality tests and treatments are equally accessible to all patients in all locations at the right time. There was a feeling that infrastructure is not equally distributed and test usage is inconsistent.

- To improve this the literature suggests a need for increased clinical acceptance of the value of genetic testing, increased knowledge among clinicians of how to apply tests and interpret results, increased NHS informatics capacity, and may need national commissioning.
- There may need to be new facilities for testing to be created – allowing results to be quickly and efficiently obtained (e.g. at GP surgeries, hospitals, specialised testing facilities).
- Ensuring equal access is also important at the research stage as efficacy data needs to come from the widest possible population.
- Some stakeholders mentioned the potential for different healthcare commissioners to make different decisions about which treatments should be funded or not. (Research charity) With the literature suggesting that the localisation agenda may have a detrimental impact on this.
- If SM leads to an increase in private testing, the literature raised the concern that this may undermine equal access to healthcare.

STRATIFICATION AND DISCRIMINATION

The literature identified the possibility of some racial or ethnic stratification of treatment response as some genetic variants are more common in certain groups than others. This may lead to perceptions of discrimination if different treatment options are deemed more appropriate in different cases.

- The literature identifies implications for the design of clinical trials which need to ensure that medicines are validated in the populations they are intended to be used on (this has implications for trials being conducted in other countries).

  - But it is important to emphasise that there is considerable variation within ethnic groups as well as between them and genetic testing may be a more accurate way of predicting response than relying on racial or ethnic classification.
  - Regulatory bodies should 'exercise careful scrutiny over claims as to racial specificity in the marketing of pharmacogenetic tests and medicines'.
  - It is important that people involved in research are 'sensitive to the potential for misunderstanding and prejudice arising from racial stereotyping'.
- It is possible that stratification may lead to members of some ethnic groups being denied access to medicines that people from other ethnic groups suffering from the same condition are allowed. This would be especially problematic if the former group is already socially and medically disadvantaged. The literature suggests that it is not possible to predict how likely this problem is, but it should be monitored.
- One stakeholder suggested that there is potential for stratified medicine to create new kinds of discrimination, extending across more biological markers (not just genetic discrimination) giving the example of some countries which already limit access to IVF based on biological marker of age rather than physical age. (Social scientist)

4. Explore how it may contribute to better care, identify opportunities for innovation (incl. data sharing/testing)

The literature identifies a number of ways in which stratified medicine may contribute to better care for patients. Most apparent are the potential health benefits, as stratified medicine is expected to improve patient safety and treatment efficacy with the treatments already on offer, and also contribute to improvements in the development and licensing of pharmaceuticals and diagnostics not currently on the market. Additionally, much discussion in the literature focuses on anticipated changes to the functioning of clinical trials and the issues raised by this. Stakeholders highlighted a number of areas, such as management of chronic and degenerative conditions, which were not discussed extensively in the literature.

BENEFITS FOR PATIENTS

The literature, and stakeholders, described many situations where it was felt stratified approaches could benefit patients. The main points related to improving safety (fewer adverse reactions and side effects), adjusting dosage, enhancing efficacy (not giving medicines to people who won't respond to them).

Side effects: One of the most commonly raised advantages was a reduction in the incidence of adverse effects of treatments as stratification identifies those likely to respond best to a given treatment.

- The literature suggested that patients will be more comfortable taking medicines if they know they are not in a group likely to experience particular side effects. They will also be better able to plan ahead to prepare themselves for any side effects which are deemed likely.
  - The pharmaceutical industry representative picked up on the issue of side-effects, arguing that more targeted treatments might be expected to have less side effects as they impact on fewer physical processes than current treatments. (Pharmaceutical industry)

Management of conditions: Some stakeholders emphasised that it is important to consider how SM can help the management as well as the treatment of conditions

- Patients often ask about what good research will do for them because the treatments won't be available during their lifetime – so it is important to think about quality of life as well as 'lived disease experience'. (Patient voice organisation)
- The interviewee gave the example of how more accurate diagnosis could enable better management e.g. vascular dementia and Alzheimer's disease have different disease pathways – a better diagnosis could empower people to make better arrangements for their own ongoing care.

Adherence to treatment regimens: Two stakeholders talked about adherence, suggesting that stratified approaches could help to improve rates.

- One stakeholder suggested that this is a major challenge in the current system and one likely to persist in a stratified context, with even more complex information to give to patients, and potentially much more expensive treatments. (Patient support group)
- However there was also some optimism, with one stakeholder suggesting that stratified medicines might be expected to increase adherence if patients were seeing demonstrable benefits from treatments with the first prescription, avoiding drop-off. (Pharmaceutical industry)

Availability of testing: A major challenge to these changes identified by several stakeholders was the availability of the necessary facilities in primary care settings - currently most complex testing takes place in a centralised context which is both expensive and time-consuming. A key innovation area will be changes which make testing easier and cheaper, and incorporating the correct expertise to interpret test results accurately. (Pharmaceutical industry & research charity)

IMPROVEMENTS IN PHARMACEUTICAL R&D

There was a general sense in the literature, and among stakeholders, that stratified medicine could provide opportunities for treatment research and development to proceed in new directions. One of the most commonly cited arguments was that targeted trials would be more economical to run, as well as potentially improving the success rate of potential treatments.

Development of treatments: Stakeholders and literature identified both potential advances in R&D, and areas where regulation may need to evolve to keep pace with developments.

- Some drugs that are not currently approved by the regulator might only be suited to a particular subgroup (so efficacy was masked in the original trial) – SM will help with this (particularly if retrospective analysis can be done on trial data).
- SM could be used to improve existing medicines as well as develop new ones (as the former might not be profitable to pharmaceutical companies this may need to be incentivised).
- Two stakeholders discussed the need for research and development to consider the potential for very specifically targeted treatments to have wider applications - this has been shown to be the case in some rare disease work (see topic 6 for discussion of particular examples). (Pharmaceutical industry & Patient voice organisation)

Lab developed tests: There is currently different regulation for manufactured diagnostic products and lab developed tests (the latter is not regulated). With the increase of testing it is necessary to ensure the efficacy of all tests, as studies show that some in use currently are much worse than others at identifying the same biomarker.

- Some suggest there should be a legal requirement to use the companion diagnostic test approved in the clinical trial. This will also increase the financial incentive for companies to develop an effective test.

- Others suggest accreditation of laboratories that develop and use 'in house' tests.

CLINICAL TRIALS

The scoping identified optimism that clinical trials may be radically different as it may no longer be necessary or useful to recruit thousands of people to any given trial if more relevant patient populations can be recruited (although still with high enough numbers to demonstrate significance of effects).

- Testing will be done on people with a specific biomarker – reducing the likelihood of adverse reactions.
    - However recruiting patients from particular strata to clinical trials may be difficult. Some suggest a need to run education and public awareness campaigns about the benefits to the community of participation in research.
- One stakeholder suggested that initially recruitment may be based on treatment to date (and its success or failure) as a proxy measure. (Regulatory body)
- The research charity representative emphasised the importance of a shift to locally delivered trials (i.e. in which patients do not have to travel) as important given the need to recruit from a smaller population. (Research charity)

Alternative models: Some of the literature discussed ways in which citizen collaboration/citizen led research has already been used effectively, and could help people play an active role in their own and others healthcare and wellbeing.

- One interviewee talked about the potential for 'real life' research - as genomic data becomes more easily available and digital technologies develop it may be possible to recruit widely across a much larger geographical area than was previously possible. (Patient support organisation)

New requirements for researchers: In a few places stakeholders and literature made suggestions about new requirements for research in the stratified context.

- The literature identified a need for clarification about whether researchers have a 'duty to inform' participants of clinically relevant results given the potential for research to take place at some remove from the original patient involved via tissue banks etc.
- One stakeholder questioned whether it should become a requirement for clinical research in stratified medicine to include consideration of how a treatment/diagnostic would be put into practice. (Patient voice organisation)

5. Identify attitudes to testing/data sharing, discuss an ethical framework and potential safeguards

There is extensive discussion in the literature of issues around the collection and use of patient data and samples for research and testing purposes. It is generally argued that the more patient data is available to researchers the better for the advancement of stratified medicine; however important questions are posed regarding the practicalities and ethics of this. Related to these questions, the literature also discusses various possible systems for the regulation and governance of data and sample collection and use, as well as the ethical issues relating to this. Additionally, issues relating to the need for informed consent from patients in a variety of circumstances are discussed. Stakeholders also discussed issues of data sharing, with more mixed views on how much of a concern this was likely to be for patients.

THE NEED FOR MORE DATA

The literature depicts a widely recognised need for large scale datasets in SM to facilitate research, development, regulation, assessment, valuation, and the stratification of treatment. Some regard this as one of the fundamental requirements for the developed of stratified approaches.

- However, one stakeholder questioned whether more data is always good – SM needs wide data, but this must be balance against the fact that some data collection can be harmful (e.g. screening programmes which have a net societal cost). Cost/benefit needs to be considered on an individual and societal level when thinking about this. (Social scientist)

TYPES OF DATA

Within this data collection there were a number of different perspectives on what types of data would be most relevant - relating to the discussion in topic 1 about the definition of stratified medicine, some literature/stakeholders took a more narrow view and focused on molecular data, while others suggested a much broader range including lifestyle data.

- The literature agrees that data for stratified medicine should include that generated in clinical trials and also (in an ideal situation for researchers) patient data gathered in normal clinical settings.
    - Such data could include: genomic, phenotypic/clinical, environmental, lifestyles, behaviour, outcome data, longitudinal data, etc. (although not all sources suggest all of this is necessary, particularly if taking a narrower definition of stratified medicine).
- Some literature suggests that SM research would particularly benefit from (and some say require) access to NHS data/medical records – which is comprehensive and longitudinal – and also allows for long term follow-up.
    - There is also the suggestion of using lifestyle, behaviour and health data collected through smartphones, credit cards etc. in research, with some stakeholders thinking this is particularly important, and should be longitudinal.

DATA SYSTEMS

Both literature and stakeholders agree that large quantities of data are not sufficient to enable more stratified research and treatment; there is also a need for increased interconnectivity and sharing of data. This has a number of ethical implications (discussed below) as well as some practical challenges.

- Currently the NHS has excellent data, but this exists in ‘silos across the UK healthcare system’, and in a range of formats and databases – for maximum impact it needs to be joined up.
    - But there are questions about how this will be dealt with – a need is identified for IT solutions for capturing, communicating, storing and analysing data?
- One document suggests the development of national and international databanks/bio-banks, in order to facilitate this it is argued there is a need to develop and agree standardised protocols for data collection.
- Another document suggests that legislation could be changed to allow the creation of ‘independent health record banks’ which could be the sole keepers/custodians of an individual’s health records, objectively serving all stakeholders authorised to access the records.
- A more radical solution proposed in some literature is for individuals themselves to keep their health records and other relevant information through a technological interface. This gives them

more control over their data and information, but would need to 'ensure the right to manage one's own data does not turn into the duty to do so for those who do not have adequate resources (economic or time resources; health or computer literacy skills).'

STORING, OWNING, TRANSFERRING AND SHARING DATA: ETHICAL ISSUES

A wide range of issues were raised in relation to data needs of stratified medicine - however both literature and stakeholders pointed out that these issues are often common to many areas of medicine, rather than being unique to the stratified medicine question. The dialogue materials will seek to draw out those areas which are distinct in the stratified scenario, in order to add to, rather than recreate, existing research in public/patient views on data.

Access to data for research: The main theme here was about increasing/simplifying access for researchers to the kind of large-scale datasets which facilitate stratified medicine development.

- One document recommends the approach of the Economic & Social Research Council (ESRC) which mandates that all funded research is placed in a publicly available archive.
- The literature identified a need to balance patient privacy against effective research access, with suggestions such as 'data-transfer agreements that forbid researchers who receive de-identified data from trying to re-identify patients or donors'.
- Discussing data security and privacy with stakeholders revealed a range of views, with most feeling that this was **not a major concern for most patients**:
    - One interviewee (social scientist) suggests that while there is still some fear about data being illicitly accessed it is more likely your online banking details will be stolen than your sequenced genome;
    - Others suggest that concerns about patient data are more prominent in clinicians and researchers than among patients, who are often less worried than experts anticipate (patient voice organisation).

Commercial access: Some stakeholders suggested that the division between 'commercial' research and 'public' or even 'university' research might be an important one for patients providing data. (Research charity)

- The literature identified similar concerns, noting that personal health data is commercially valuable and wider collection/sharing may have financial implications.
- There were also practical concerns about giving data to commercial institutions: for example if you shared your data with one company, what happens if it changes hands? (Especially if that means it is relocated to another country with different protection.)

Insurance companies and employers: concerns about the potential for data collected for stratified medicine research or treatment to be shared with insurance companies and employers were raised predominantly by stakeholders. As with many other aspects of data issues these are not exclusive to stratified medicine, but are pertinent to the increased availability of predictive or risk data more generally.

- Questions included whether there would be a difference between predictive data and diagnostic data? Predictive/risk data has the potential to have a much longer-term financial impact.
- For health insurance the literature considered whether test results could/would/should be used to determine eligibility for treatment paid for by health insurance, or in the NHS.
- There were questions about the implications of stratified diagnostics to life insurance: there is currently a voluntary moratorium on genetic testing being taken into account for almost all insurance. Currently the only case in which this is allowed is Huntington's disease for life insurance policies over £500,000.

- Stakeholders mentioned both health and life insurance in relation to fears about data sharing. One argued that equally problematic was data being passed to employers - with failure by employers to understand the nature of long term managed conditions a particular concern. (Patient support group)

CONSENT ISSUES

One of the most frequently discussed issues in the context of data was patient consent. The literature, and stakeholders, tended to agree that the existing system of providing consent would be limiting to stratified medicine, while emphasising the need to maintain the same levels of rigour and trust for patients in any new system.

- The literature identified that professionals have a responsibility to make sure patients are fully informed (and understand) in order to give their informed consent. This is especially important when individuals with high stakes conditions (e.g. cancer) are involved in clinical trials.
- Ideally (for researchers) consent would be given to unlimited future use of data – as there are practical difficulties in going back to the patient for each use of their data, but could possibly offer people different levels of consent if they would not want it used for particular types of research or by particular people.
    - Mechanisms need to be developed for obtaining broad and enduring consent (generic consent forms). Some hospitals already run generic consent for patient samples.
- Several suggest the need for a streamlined process for trial consent, while one document proposes that consent models could be based on (identifiable) information only being shared by professionals for the public good.
- Stakeholders interviewed questioned whether positive results in the context of cancer (e.g. Cancer Research Stratified Medicine pilot programme) would apply more widely - there may be particular circumstances under which patients are happy to consent to data use, while other cases might not be suitable. (Research charity)

6. Reconcile patient desires/needs and healthcare costs

There is a small amount of discussion in the literature reviewed on how the introduction of stratified medicine may affect healthcare costs, with mixed views on whether it will result in cost savings for the NGS. Stratified medicine may result in less wastage of treatments and more knowledge of cost effectiveness, which should save money, but it is also likely to increase the cost of individual treatments as pharmaceutical companies will want to increase the pricing to account for smaller patient groups. Additionally the cost of diagnostic testing needs to be factored in.

There is also a small amount of discussion about how patient needs and desires may be reconciled with healthcare costs, largely focusing on equity and access issues (relating closely to topic 3). Some stakeholders felt it was likely that questions would be raised in the dialogue about costs in the context of healthcare funding generally, while others suggested that treatment costs are not generally raised as a concern by patients.

COSTS IN THE HEALTHCARE DELIVERY SYSTEM

Both in the literature and interviews there were differing views about the consequences of stratified approaches for healthcare delivery costs, with a number of factors to be considered.

Costs of diagnosis: Stakeholders and literature were divided as to whether the increased costs of more complex testing and treatment would be offset by increased accuracy of treatment.

- Some of the literature identified that the proportion of tested patients identified as suitable for a given treatment would have an impact on overall costs, as would the difference in treatment outcomes.
- Stakeholders highlighted the need to factor in the cost of diagnostic tests for those who test 'negative', recognising that there could be increased costs for those who are not candidates for stratified treatments as well as those who are. (Regulatory body)
- In contrast one interviewee thinks there may be a misconception that the testing process will be where additional costs lie – they felt that actually the expensive part would be interpreting the data, which requires appropriately trained medical staff. (Social scientist)
- One stakeholder was concerned that policy-makers may see this as an opportunity to introduce fees: e.g. people having to pay for the more advance diagnostic tests which enable a more precise diagnosis – e.g. you can be diagnosed with 'dementia' for free, but if you want to know what kind you'll have to pay for a brain scan. (Patient voice organisation)

Costs of treatment: Discussion of treatment costs in literature and interviews primarily focused on the costs of drugs, with some debate about the role of government and industry in establishing pricing mechanisms under a new model.

- The literature raised the argument that new drugs are sometimes only marginally better than standard care, but much more expensive, raising issues around the value of marginally improved patient outcomes.
- Some stakeholders discussing this issue felt that pharmaceutical companies might see treatments which are targeted at a smaller pool as 'big ticket' items and price them accordingly. (Regulatory body)
- The most common argument for cost savings in the literature was that stratified medicine would provide the information needed to assess the cost-effectiveness of treating different groups of people – if they are less likely to respond, or more likely to have an adverse reaction for example.
    - However it was felt that there was a need to keep in mind justice and equity, as discussed in topic 3– 'sometimes it will be right to allocate resources to treatments of conditions that might otherwise not be considered cost-effective, in order to ensure a fairer distribution of healthcare'. (Nuffield Council on Bio-ethics)

The healthcare market: The literature in some places suggested that SM may change the NHS market and necessitate changing to pricing structures because you have smaller and smaller response groups.

- The Academy of Medical Sciences report recommends 'introduction of pricing and reimbursements system that enables prices to be adjusted over time to reflect changes in value' and separates the value of stratification between the therapeutic and diagnostic components of the SM product.

COSTS OF DEVELOPING NEW TREATMENTS

As in topics 2 and 3, the role of stratified medicine in changing the clinical trials model was discussed by several stakeholders and frequently mentioned in the literature. Cost issues focused on two points; the extent to which stratified medicine would change the market conditions and thus the treatments researched, and the costs of trials themselves (covered in topic 3).

Which treatments are developed: Some of the literature reviewed suggested that stratified approaches would disincentivise R&D due to the smaller patient populations and required investment in developing a diagnostic. They argued that as in treatment, the smaller the patient population the less economical the process– some felt that incentivising the financing system would be necessary to address this.

- Interestingly the pharmaceutical industry representative interviewed felt this was not a concern. They argued that pharmaceutical companies are motivated by 'unmet clinical need' within a clearly defined population, which represents the best profile to develop a treatment which is very effective in the right patients, and has the potential to be useful in other conditions. (Pharmaceutical industry)
- Gleevec[12] was an example mentioned by two stakeholders who referred to it as an example of a pharmaceutical company developing a treatment which seemed only to treat a very small population, which has since been shown to have applications in a much wider range of conditions. (Pharmaceutical industry & patient support group)

Costs of trials: Both the literature and stakeholders (including pharmaceutical industry and patient support group representatives) suggested that a shift away from large-scale clinical trials to more targeted models might reduce the costs of bringing new treatments to market.

PATIENT PERCEPTIONS

There was more limited discussion in the literature on patient perceptions of cost implications of stratified medicine – suggesting this may be a useful area to address in the dialogue.

- One review and some stakeholders suggested that 'some patients may see stratification as a method of rationing'.
- The perception of some interviewees was that the 'average patient doesn't tend to think about the costs of their treatment'. (Regulatory body)

Identify the language, analogies and comparisons which are currently used to describe stratified medicine

The purpose of this section is to inform the detailed design of the dialogue materials by exploring the ways in which stratified medicine is, and should, be talked about. In general stakeholders emphasised how important it is to get the terminology and communication right, as one said 'this determines how well it is accepted in the clinical setting – regardless of the strength of the science.' (Patient voice organisation) Many of the issues raised relate to topic 1, definitions and communication, so this section aims to pull out what is different rather than repeating.

Naming the dialogue: The scoping clearly identified debate about the appropriate terminology to be used, with 'stratified' by no means an uncontroversial choice.

- Stakeholders and literature emphasised the need to be careful about language with negative connotations e.g. 'profiling' or 'personalised' relating to personal budgets. Several interviewees dislike the term 'stratified', feeling it was not a sufficiently commonly understood term and one suggested 'targeted medicine' instead.

[12] Gleevec was a drug developed by Novartis pharmaceuticals in the late 90's initially to treat chronic myeloid leukaemia, which has since been shown to be effective in multiple other cancers where the same enzyme is involved.

Public perception: How stratified medicine will be perceived by dialogue participants is an important consideration in designing materials.

- Several stakeholders discussed the risk of either presenting an overly rosy picture, or raising unnecessary fears, in the dialogue. As one stakeholder said: “There is some pressure to be evangelical about SM, some people want it to be ‘sold’ to the public, and expect the public to understand care straight away. Medics can be too focussed on the new and innovative.” (Patient voice organisation)
- Others emphasised the need to present a patient-oriented story about SM, and the importance of this debate taking place 'in the clinics rather than in the newspapers'. (Patient voice organisation)

Starting from scratch: As discussed under topic one, stakeholders often suggested a need to be clear that stratification does already happen in current medical practice – presenting the topic as completely novel may be confusing.

- One stakeholder suggested that it could be useful to start with particular examples of stratification that we already do: age, gender, etc. – which people will be comfortable/familiar with but don’t think of as stratified. (Social scientist)
- In a similar vein some thought it was important to understand that the public don’t always have a good understanding of the caveats associated with the current medical system – they don’t recognise that there are always risks and so might interpret the risks associated with stratified medicine as greater than currently faced. (Regulatory body)
- The literature discussed examples of risk stratification for prevention (e.g. scoring risk and acting appropriately) which may be useful to communicate how stratified medicine is already being used effectively in some cases.

Examples of stratified approaches: It is clear from the scoping that it is important not to only talk about cancers – although it is in many ways a classical example of stratification, and an area of considerable research potential. (Pharmaceutical industry, research charity)

- Several stakeholders mentioned **Herceptin** as an example people may be familiar with. (Social scientist)
- Another stakeholder talked about **warfarin** as a drug where dosage is already based on companion diagnostics and about **statins** as a key example of an ‘un-stratified’ approach. (Pharmaceutical industry)
- Another felt it would be better to use examples which are hypothetical, because it allows you to talk about the numbers without involving the emotions of a real disease.(Regulatory body)

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