



Enhancing the use of scientific evidence to judge the potential benefits and harms of medicines

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Executive summary

Recent high-profile media debates about the use of statins to prevent cardiovascular disease, of Tamiflu to treat flu and of the HPV vaccine to prevent cervical cancer have opened up public debate about medical and scientific claims. These debates have queried whether the underpinning evidence for the use of licensed medicines is robust, relevant to the patient population and trustworthy, or has been communicated accurately in an accessible and usable way.

Poor-quality evidence about medicines, or misrepresentation or misperception of evidence, may present risks to health, for example by leading to under- or over-medication, and prevent the full realisation of the health gains from medical innovation. The work summarised in this report was triggered by these concerns, and aims to improve the use of scientific evidence to judge the potential benefits and harms of medicines.

The Academy of Medical Sciences believes that scientific evidence should be at the heart of decision-making about the use of medicines. We define good scientific evidence as data or information derived from research that uses robust and reliable scientific methodologies, and seeks as far as possible to eliminate or minimise biases. Scientific evidence is subject to check and challenge and the evidence base for any medicine may evolve with the generation of further research data. New findings may reinforce or alter assessments of the benefits and harms of a medicine as applied to different populations and/or individuals. This evolution is inherent in the scientific process. Those who make decisions about medicines, whether regulators, healthcare organisations or healthcare professionals, must have access to robust and reliable scientific evidence and make the best use of such evidence. Patients too should be able to access reliable evidence, and this should be presented in an intelligible form that allows them to use it in their own decision-making.

Decisions about medicines are made by many bodies and many individuals. Some are public bodies, such as the National Institute for Health and Care Excellence (NICE) and the Medicines and Healthcare products Regulatory Agency (MHRA), which provide guidelines and recommendations about the safety, efficacy and cost-effectiveness of medicines. Others are healthcare providers, as well as individual healthcare professionals, patients and carers. This report is primarily focused on the use of scientific evidence by those at the latter end of the spectrum, where most concern has been expressed.

Many factors may influence an individual's decision to take or refuse a medicine, including media exposure, prior experience, and beliefs about health, illness and treatments. Our surveys showed that only about one-third (37%) of the public said they trusted evidence derived from medical research, but around two-thirds (65%) trusted the experiences of friends and family. This report explores how the generation, trustworthiness and communication of scientific evidence can be improved to strengthen its vital role in decisions by patients, carers, healthcare professionals and others about the benefits and harms of medicines. The report has been prepared by an Oversight Group with a diverse range of expertise, underpinned by engagement with citizens, patients and healthcare professionals.

Do we have relevant and robust scientific evidence?

If we are to enhance the vital role of scientific evidence in informing decisions about medicines, we must ensure that the evidence is robust, reliable and relevant to the people it intends to inform. Past research on medicines has not always addressed all of the issues and outcomes that matter most to patients. There is now a widespread acknowledgement that involving patients, carers and frontline clinical staff in

the design, delivery and dissemination of research is essential to ensure its relevance and effectiveness. We recommend a number of actions that should be taken by funding bodies, universities, research institutions, medical research charities and the pharmaceutical industry to increasingly involve patients, carers and members of the public more closely in the way research is done, and encourage patients to seek and request opportunities to take part in the co-production of evidence.

The research community has honed highly effective methods for determining the benefits and harms of medicines. These methods include:

- Randomised controlled trials (RCTs), which are usually the best way of generating robust evidence about the benefits and harms that are directly caused by an intervention. It can, however, be challenging to generalise results from RCTs to wider patient populations and to know the potential impact of use of that intervention in routine clinical practice.
- Epidemiological or observational studies, which can provide useful information on the generalisability of results to wider patient populations, although their interpretation can be limited by the lack of control for bias and confounding factors.
- Syntheses of evidence, including systematic reviews and meta-analyses of RCTs, which provide an important mechanism of combining and appraising the available evidence on a given treatment, and for identifying the extent to which the evidence is consistent and generalisable across populations.

A key consideration in the critical appraisal of evidence is whether the method employed to generate the evidence was appropriate for the research question under investigation. Such a judgement is central to the evaluation of the benefits and harms of medicines and is crucial in ascertaining whether the evidence presented is fit for purpose.

We call for a much better understanding within the research and healthcare communities of the strengths and weaknesses of different methods of generating evidence, and a readiness to consider and test new approaches. This is needed in part because the digital revolution has changed the landscape of knowledge and information. Increasing availability of clinically relevant data collected outside the controlled conditions of a clinical trial presents new opportunities to enhance our understanding of treatments across a variety of populations and settings. Although these additional data are subject to biases, which limit their usefulness in making treatment comparisons or evaluating the effectiveness of medicines, they can provide valuable additional information. More work is needed to realise the potential of these data. This would need to address infrastructure and skills; policies for data standardisation, access and linkage; and the critical study of the research methodologies used to derive evidence from such data.

Is scientific evidence trustworthy?

Even if care has been taken to address the questions that are relevant to patients, and appropriate methods have been used to address the research question at hand, judging the trustworthiness of the evidence is still demanding. It will depend on the integrity of the process used to derive the data and the robustness of the findings. Communicating data in a way that enables others, including patients, to assess them is also important for those who need to judge whether data are trustworthy.

The majority of evidence about medicines published in reputable journals is of good quality and trustworthy. Recent concerns about a lack of reproducibility of some preclinical scientific studies have, however, raised questions about the quality of the evidence. If these questions are not resolved, uncertainty can arise and trust can be undermined. The Academy, along with the Wellcome Trust, the Biotechnology and Biological Sciences Research Council (BBSRC) and the Medical Research Council (MRC), has previously considered issues around research reproducibility. In this report we emphasise the important role of universities and institutes in creating environments that uphold the highest standards of research integrity and facilitate robust, high-quality research, incentivised through the effective use of the Research Excellence Framework assessment process. Concerns about selective publication of evidence can make it hard to judge trustworthiness. We conclude that researchers, whether in academia or in industry, and journal editors must commit to publishing rigorous research regardless of results, and must use accessible formats where appropriate.

Academics, industry, public research funders (including medical research charities), the media, publishers, patients and healthcare professionals all have interests in the outcomes and use of scientific research. These interests sometimes lead to actual or perceived conflicts. Judgements on the trustworthiness of scientific evidence can be made only if information is available on the interests of the individuals and organisations who have been involved in producing, interpreting and communicating this evidence. We support a commitment to ‘intelligent openness’, whereby this information is disclosed in a manner that is accessible, assessable and usable by the intended audience, while respecting privacy and reasonable commercial concerns.

The pharmaceutical industry and those funded by it are particularly mistrusted. In our surveys, four out of five (82%) general practitioners (GPs) and two out of three (67%) British adults agreed with the statement that clinical trials funded by the industry were often biased to produce a positive outcome. Similar views were expressed in our deliberative public dialogue activities and in the Wellcome Trust’s regular survey of public attitudes to science. We believe that recent industry-led initiatives justify greater trust in the evidence produced by the commercial sector, though more needs to be done. Ongoing efforts include sharing data from clinical trials, disclosing funding received by healthcare professionals, adhering to voluntary codes of practice and enhanced regulatory oversight. More generally, the scientific community must do more to communicate the benefits of collaboration between academia and industry in the development of new medicines, while upholding the highest standards of research integrity.

We recommend the establishment of frameworks for identifying and declaring interests (including in publicly accessible registers) and, when relevant, managing competing or conflicting interests. Given concerns about the trustworthiness of clinical trials conducted by academia and funded by industry, we have developed high-level principles to govern research funding, study design, trial registration, publication of contracts, data holding, access and analysis, and publication of findings. We recommend that funding bodies, academia and industry implement these principles and, in particular, that they develop clear guidance on how they should be implemented.

Finally, we emphasise that the existence of competing interests does not necessarily mean that evidence is biased, or lacks rigour or credibility. Journalists and other commentators should not focus on the existence of such interests, but on whether they are appropriately managed so that their impact on the impartiality and objectivity of the evidence is minimised.

Is scientific evidence communicated effectively?

We should all expect to receive accurate, accessible and usable information about the potential benefits and harms of medicines. This information should be available to guide decisions, and healthcare professionals have a responsibility to impart it when informing patients about treatment options. Information that fulfils these criteria is not always available, and many medical information sources are not suitable for the general public. In particular, patient information leaflets included in medicine packaging often fail to fulfil the criteria we would expect for effective communication. We recommend that they should be revised in consultation with patients and carers to present a clearer, more simplified and balanced appraisal of the benefits and potential harms of the medicine. NHS Choices is already a trusted source of information for citizens, patients and healthcare professionals, and we recommend ways in which it can be improved to deliver a high-quality information service on the potential benefits and harms of medicines.

Healthcare professionals have an important role to play in communicating evidence, risk and uncertainty, and in discussing these in the context of the patient’s understanding of their illness and treatment. We encourage efforts to equip healthcare professionals to engage in shared decision-making with their patients, and have developed a series of questions to support both patients and healthcare professionals in conversations about the use of medicines.

We make detailed recommendations, targeted at all those involved in the generation and communication of research relevant to medicines development, to assist responsible, accurate and balanced reporting in the media. This includes developing a ‘traffic light’ system for press releases; guidelines to promote best practice for journalists, press officers and researchers; and workshops for news editors, sub-editors and non-specialist journalists to enhance their understanding and reporting of scientific processes.

Practical implications and future challenges

In the report, we make a series of recommendations aimed at strengthening the use of scientific evidence by the public, patients and professionals when judging the potential benefits and harms of medicines. Implementation of our recommendations will require a concerted effort by all those involved in the generation and use of evidence. Representative bodies such as the Medical Royal Colleges and industry trade bodies have a key role. The REF can galvanise a culture shift in universities and research institutions. We recommend that its next iteration recognises an institution's reproducibility efforts, 'intelligent openness' initiatives, and the robustness of the approaches taken to ensure accurate portrayal of their research in the media.

In formulating this report, we were conscious of the increasing numbers of people with more than one long-term condition ('multimorbidity'), for whom treatment decisions may be multiple and complex. As the Academy has previously outlined, this enhances the need for effective strategies that embrace public health measures to prevent common chronic diseases. These must give attention to the social determinants of health as well as considering the preventive potential of personalised or 'precision' medicines.

We acknowledge that some of our recommendations require renewed efforts by all healthcare professionals and that this will be challenging given the current pressures in the NHS. Additional resources will be needed to accommodate some of our recommendations – for instance in relation to the time needed to communicate evidence and facilitate shared decision-making. In particular, healthcare professionals would benefit from aids that can be used to inform decisions involving the large number of patients with multimorbidity. New methods of machine learning and artificial intelligence hold promise for developing decision-making tools in the face of this complexity. Alongside decision aids, we support a care planning approach that ensures that time is available to address the concerns of people with complex needs and engages them fully in shared decision-making. We endorse 'goal-orientated medicine' in which the focus of the consultation is guided by issues that matter most to patients.

Ultimately, the decision to use a medicine that is offered lies with the patient or carer. In this report, we make recommendations that seek to strengthen what we believe should be a central role for scientific evidence in this decision-making process. Nevertheless, we recognise the need for a much deeper understanding of the other factors, behaviours, beliefs and sources of information that influence these decisions.

The attitudes of all stakeholders and the scientific evidence available to them will continue to evolve, particularly if the prospect of personalised (precision), pre-emptive medicine is realised. There must be a commitment to an ongoing dialogue focused on understanding the attitudes and perspectives of patients, the public and healthcare professionals; addressing their concerns; and supporting their involvement in the generation and communication of evidence about medicines. Organisations involved in evidence-based health and social care must remain committed to optimising the generation and communication of evidence if the full benefit of scientific advance is to be realised. The Academy stands ready to play its part.

Recommendations

Recommendation 1: Involving patients, carers and the public in research

Building on existing good practice, **funding bodies, universities, research institutions, medical research charities** and the **pharmaceutical industry** should increasingly seek to involve patients, carers and the public in the design, delivery and dissemination of research, and consider it a key part of how research excellence is characterised across the system as appropriate. Processes and practices for involving patients, carers and the public in research should be systematically evaluated to inform the evidence base and enhance future practice. Specifically, we recommend that:

- a. **Research funders**, including **medical research charities** and **industry**, require applicants to detail in their grant applications their plans for involving and engaging patients and the public in their research as a condition of funding. Funders should evaluate whether involvement and engagement initiatives have been carried out and request that these are described in the end-of-grant report or in other reporting systems such as Researchfish.
- b. **Universities, research institutions** and **industry** tackle the barriers to patient, carer and public involvement and engagement, paying particular attention to training and support for researchers and the public.
- c. **Research funders** from across the sector, including **medical research charities** and **industry**, come together to develop a mechanism of monitoring the development of relevant and appropriate activities for involving and engaging patients and the public in research. They should identify best practice and ensure it is disseminated to researchers and the public. An initial meeting on this topic could be led by **INVOLVE**, part of the National Institute for Health Research (NIHR).

Recommendation 2: Addressing gaps in training in research methods and statistics

We recommend that those involved in the conduct of clinical research, including **universities, research institutions** and **industry**, should provide training in research methods and the use of statistics in evaluating the benefits and harms of medicines for staff across all career stages, from early career researchers to established researchers, as part of their continuing professional development (CPD). Similar courses should be provided for healthcare professionals by **universities** and **Medical Royal Colleges** as part of their training or CPD programmes. Existing courses should be reviewed and, where necessary, new courses established to accommodate the full range of evidence-generating approaches for assessing the benefits and harms of medicines. These should assess the relative value, strengths and

limitations of different approaches, including new and emerging methods, and the questions they are best suited to address. These bodies should also instil an ethical research framework within which they expect staff to work, as outlined in the ‘Universal ethical code for scientists’, and promote high standards of research conduct.¹ The Health Education England (HEE)/NIHR Masters in Clinical Research degree is an example of how training in research methods could be delivered for researchers.²

Recommendation 3: Enhancing the recognition of robust research findings

We recommend that in the next Research Excellence Framework (REF) process, the **Higher Education Funding Council for England** (HEFCE, relevant functions expected to be assumed by Research England in the future) and its **counterparts in the devolved nations** should incorporate Lord Stern’s recommendation for a new, institutional-level environment assessment. We propose that such environment assessments record measures taken to increase the robustness and reliability of research, including work to ensure adherence to ethical codes of research practice, data-sharing policies, and recognition and reward for efforts to enhance reproducibility.

Recommendation 4: Ensuring best use is made of new sources of evidence

To complement current initiatives to improve data sharing and linkage, we recommend that:

- a. **Funding bodies** invest in research into understanding how to view and interpret the totality of outcomes from different study designs, including randomised controlled trials (RCTs), observational studies and novel approaches. We also recommend that they prioritise research into improving methodologies for analysing data from new sources of evidence, such as ‘real world data’, that take account of bias and confounding. This work should include investment in capacity building for skills in managing and analysing large data sets, as well as developing appropriate environments for greater data sharing and linkage, and quality-assured platforms for health research and real-time monitoring of outcomes. These platforms must provide appropriate safeguards to ensure data subjects’ privacy and confidentiality.
- b. The **global research community** works together to develop internationally agreed data standards, best practice guidelines and robust methods for collecting, analysing and using ‘real world evidence’ to inform the use of medicines.

Recommendation 5: Publication of research findings

We support ongoing initiatives to enhance the dissemination of and access to research findings, including greater publication of rigorous results regardless of outcome, reporting of findings in more accessible formats, trial registration, and infrastructure funding for data archiving and curation. To complement these efforts, we recommend that:

- a. **Universities, research institutions** (led by Universities UK) and **industry** (led by the Association of the British Pharmaceutical Industry, ABPI, and the BioIndustry Association, BIA) support their staff in academia and industry in their efforts towards increased openness by providing appropriate incentives, rewards and recognition, and systems to enable this, such as those outlined in the Academy's report, 'Improving recognition of team science contributions in biomedical research careers'.³ These organisations should recognise clear and accurate communication of research findings as an explicit criterion for career progression, promotion and reward.
- b. The **Higher Education Funding Council for England** (HEFCE, relevant functions expected to be assumed by Research England in the future) and its **counterparts in the devolved nations** galvanise change by requiring that institutional 'intelligent openness' initiatives are reflected in REF environment statements in the next REF process, in addition to the reproducibility efforts described in **Recommendation 3**.
- c. **Those who fund research**, including **industry**, incentivise the communication of results for the projects that they support by requiring in applications an effective plan for the communication and 'intelligent openness' of results. Researchers would need to demonstrate that they had adhered to these as a condition of future funding.

Recommendation 6: Developing frameworks for declaring and managing interests

To facilitate greater declaration and management of interests, we recommend that:

- a. **Research Councils** and **Universities UK** (for academic research), **trade bodies** (for commercial research), and the **media regulators** (including the Independent Press Standards Organisation, IPSO, and the Independent Monitor for the Press, IMPRESS) develop frameworks for declaring and managing financial and non-financial, direct and indirect interests that fit the needs of staff in their sectors. Where these are already in place, they should be reviewed in light of the principles we outline in **Online annex F**.⁴ These frameworks should provide a protective environment, where interests can freely be declared and discussed to ensure that appropriate safeguards can be put in place should a competing or conflict of interest be identified.
- b. The **International Committee of Medical Journal Editors'** (ICMJE) declaration of interests is adopted as a standard format for declaring interests across the sector.⁵ In the spirit of 'intelligent openness', organisations should use this standardised declaration to establish publicly accessible registers of interests (for example on organisational websites).

Recommendation 7: Developing best practice guidelines for academia–industry relationships

Informed by, but not reliant on, the development of the frameworks described in **Recommendation 6**, we recommend that **funding bodies, academia** (led by Universities UK) and **industry** (led by the ABPI and the BIA) work together to develop clear guidelines that define best practice in terms of the relationship between academia and industry and the management of competing interests that might arise. In developing these guidelines, these organisations should consider how the following key principles are implemented when evidence related to the use of medicines is developed in academic clinical trials funded by a commercial partner (full details in **Online annex F**):

- **Research funding:** All funding from commercial partners should be disclosed and governed by the institution’s policies for such funding, which should be informed by the best practice guidelines we recommend are developed. Academic researchers should be aware that other personal payments such as consultancy fees, and payments for speaking at meetings or sitting on advisory panels could raise potential concerns that their research is biased and untrustworthy. There should be greater openness about how the research funding is distributed within the institution (e.g. the NHS Trust or research department).
- **Study design:** Academic and commercial partners should work together to design studies in a way that minimises biases as far as practically possible. All protocols should be made publicly available on completion of the research to allow for independent analysis of the design and methods, and researchers should be transparent in publications about how the study was designed. Consideration should be given as to whether study designs could benefit from public or patient involvement and external peer-review.
- **Trial registration:** All clinical trials should be registered on a recognised, open and searchable trials register with a summary of the trial protocol, before the first participant is recruited. We strongly encourage the registration of observational epidemiological studies that explore the effects of treatments.
- **Contracts:** All contracts between academia and industry should be made publicly available (with personal and commercially sensitive information redacted) and should provide clarity on specific items, including data access and holding, details of funding and to whom it is paid, and conditions for data analysis and publication. All contracts should also include a requirement to disclose competing interests.
- **Data holding and access:** Data should be managed responsibly, in a way that protects confidentiality for justifiable commercial, privacy, safety and security reasons. Contracts should clearly specify who holds the data, what the data can be used for, who they can be used by and with whose agreement, and who can access the data and by what means, providing justification for any limits to data access.
- **Data analysis:** Academic and commercial partners should work together to ensure that data analysis is conducted in a way that minimises biases as far as is practically possible. They should also be transparent about the analytical process in their publications. Data analysis should be undertaken by statisticians independently from the study teams, monitored by an independent Data Monitoring Committee (DMC) and auditable.⁷
- **Publication of findings:** Neither partner should restrict the publication of findings, which should be published in full regardless of the outcome. A summary of results should be made publicly available on the database where the trial is registered within one year of completion of the trial, or within the timelines agreed if a deferral has been granted. Where applicable, the full Clinical Study Report, or its equivalent in non-commercial settings, should also be made publicly available. Where appropriate consent has been provided, de-identified individual patient-level data should be made available to researchers on request, with a commitment that no reasonable request would be refused.

Recommendation 8: Improving the content of patient information leaflets

We recommend that the **European Commission** and the **European Medicines Agency (EMA)** work with **the national regulatory authorities in EU Member States, pharmaceutical companies** and **patients, carers and the public** to improve the comprehension and readability of patient information leaflets in line with the current legislation. We recommend that such work is prioritised and ensures that a balanced appraisal of the medicine's potential benefits and risks is made accessible in these documents. In doing so, they should draw on the experiences of initiatives to enhance the accessibility of information about the potential benefits and harms, such as the Drug Facts Box initiative in the United States (US). We applaud the efforts of the Medicines and Healthcare products Regulatory Agency (MHRA) to date to improve the content and accessibility of patient information leaflets and encourage the regulator to continue its work in this area.

Recommendation 9: NHS Choices as a central repository of information on the benefits and harms of medicines

To enhance the availability and accessibility of contemporary information on medicines, we recommend that **NHS Choices** and its **equivalents in the devolved nations** develop clear information on the benefits and harms of medicines, and act as a central repository for use by patients and healthcare professionals. This online source of information should make direct reference to the underlying evidence; be updated as further evidence emerges; and detail relevant, robust and evidence-based decision aids that can be used by patients and healthcare professionals. In developing material, NHS Choices and its equivalents should continue to work with patient groups and medical research charities, increasingly consulting pharmaceutical companies as they move towards providing information on new drugs, and should coordinate with the MHRA to increase the availability, accessibility and reliability of information about the benefits and harms of medicines. NHS Choices and its equivalents, and the valuable information provided by **medical research charities**, should meet NHS England's Information Standard and the Plain English Campaign's Crystal Mark.^{8,9}

Recommendation 10: Improving the reporting of scientific evidence in the media

To complement current initiatives to improve the reporting of scientific evidence in the media, we recommend that:

- a. The **Science Media Centre** works to develop criteria for and implement a ‘traffic light’ system for press releases of medical research that grade both the relevance of the research to clinical application and the robustness of the study. We also recommend that the **Science Media Centre** develops a series of workshops for news editors, sub-editors and non-specialist journalists to enhance their understanding and reporting of the scientific process.
- b. **Stempra** develops a code of practice for press officers to encourage best practice. Organisations that become a signatory to these principles could be authorised to use a hallmark to provide a clear signal that best practice guidelines for accuracy are promoted within the organisation, thereby increasing the credibility of the press release.
- c. **Funders** develop a code of practice for their grant awardees around how to describe the science that they fund in the media. This approach received support from the Chief Executive of the Medical Research Council (MRC). We therefore recommend that MRC leads on coordinating the development of this code of practice with the other major UK funders.
- d. **Universities** and **research institutions** play a greater role in ensuring that the research they host is portrayed accurately in the media. The **Higher Education Funding Council for England** (HEFCE, relevant functions expected to be assumed by Research England in the future) and **its counterparts in the devolved nations** should incentivise them to do so by requiring that the robustness of the approaches they adopted forms part of the institutional environment statement submitted to the REF, in addition to the reproducibility and ‘intelligent openness’ efforts described in **Recommendations 3** and **5** respectively.

Recommendation 11: Supporting joint decision-making between healthcare professionals and patients

To support joint decision-making between healthcare professionals and patients, we recommend that:

- a. **General practices** ensure that enough time is available through care planning and that adequate resourcing is provided by commissioners of primary care services to address patients' priorities and concerns regarding medication decisions. As proposed in **Recommendation 9**, the evidence provided by NHS Choices should assist in informing patients alongside their discussions with healthcare professionals.
- b. The **National Institute for Health and Care Excellence (NICE)**, in discussion with **NHS Choices** (or its equivalents in the devolved nations), coordinates the development of decision aids based on robust evidence, the source of which is open to scrutiny. These aids should be used to inform the decision-making process, helping patients and healthcare professionals decide on the most suitable course of action, including optimising treatment strategies and supporting the discussion of non-drug alternatives, such as lifestyle changes. The effectiveness of different forms of decision aids, including the use of machine learning and artificial intelligence, and their relative utility, should be subject to research evaluation and supported by funders, including the **National Institute for Health Research (NIHR)**.

Recommendation 12: Continuing dialogue and engagement with patients and the public

To ensure the health system remains responsive to evolving public attitudes towards health, the use of medicines and the role played by scientific evidence in decisions about their use, we recommend that:

- a. **Health-related organisations** continue their dialogue and engagement with the public to ensure that they are responsive to evolving public attitudes and patient needs, and that they are engaging communities in enhancing the use of evidence as part of the decision-making process.
- b. **The Wellcome Trust** incorporates questions into its regular survey of public attitudes to science to monitor the impact of the recommendations made in this report on the use of evidence within the healthcare sector and in decision-making.¹⁰

References and notes

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4. <http://www.acmedsci.ac.uk/evidence/annexes/F>
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7. The Research Ethics Service (now part of the Health Research Authority) defines a DMC as 'a group of people that reviews accumulating data in a clinical trial and advises the sponsor (directly or indirectly) on the future management of the trial. It mainly reviews safety and efficacy data but may also see quality and compliance data. The DMC is usually privy to interim comparisons by arm and sees data in a format that is not normally widely shared beyond the core statistical team.' National Research Ethics Service, National Patient Safety Agency (2010). *Data monitoring committees in clinical trials: Guidance for research ethics committees*. <http://www.hra.nhs.uk/documents/2013/10/data-monitoring-committees-in-clinical-trials.pdf>
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This report identifies how scientific evidence can be better generated and communicated to play a greater role in decisions about medicines.



1. Introduction

This report was catalysed by recent high-profile controversies over the use of statins to prevent cardiovascular disease. Although generating much media attention and sowing confusion in the minds of many healthcare professionals¹¹ and patients, many of the contentious issues involved are by no means confined to statins.^{12,13}

Box 1 illustrates other case studies – including Tamiflu to treat flu, unjustified concerns about links between the measles, mumps and rubella (MMR) vaccine and autism, the human papilloma virus (HPV) vaccine to prevent cervical cancer, and hormone replacement therapy (HRT) to treat the symptoms of the menopause. These case studies collectively draw attention to the importance of improving the quality, trustworthiness and communication of scientific evidence to enable us all to make better-informed decisions on the use of medicines, particularly in relation to their potential benefits and harms. The level of concern generated by the statins case and others culminated in a letter from the Chief Medical Officer for England to the Academy of Medical Sciences, asking us to explore the underlying issues and make recommendations to address this challenge. This report is our response to that letter, as well as to concerns expressed by a wide range of stakeholders.

Box 1. Case studies to illustrate the challenges addressed in this report¹⁴

Statins (see **Online annex A** for a detailed account)¹⁵

Statin treatment reduces the risk of cardiovascular disease. In 2014, the National Institute for Health and Care Excellence (NICE) recommended a lowering of the threshold for offering statin therapy for the primary prevention of cardiovascular disease.¹⁶ The threshold change reignited debate about the medicalisation of healthy people, the trustworthiness of evidence in view of ties with industry, the relative merits of different types of scientific evidence, misleading reporting by the mainstream media, the lack of availability of data for wider scrutiny and the applicability of the evidence to different groups of people.¹⁷ Healthcare professionals were left confused about whether they should offer statins, and patients were not sure about whether they should take them.^{18,19}

Tamiflu

Tamiflu is an antiviral produced by Roche for the treatment and short-term prophylaxis of flu. A Cochrane systematic review of the effectiveness of Tamiflu, based on an analysis of clinical trial data, concluded the drug gave a modest reduction in flu symptoms but found no evidence that it reduced hospitalisation, pneumonia or virus transmission.^{20,21} In conducting this analysis, the Cochrane Collaboration initially had difficulty accessing the relevant data from Roche.²² Widely reported in the national media, the review's conclusions were met with claims that the government had wasted £500–600 million stockpiling Tamiflu.^{23,24} A subsequent study of observational data from the 2009 flu pandemic showed that deaths in hospitalised patients had been reduced when Tamiflu had been used.²⁵ Although some argue that these observational data are more relevant than the clinical trial data, as the observational data relate to pandemic rather than seasonal flu, others argue that they should not be used to inform policy as observational data are more susceptible to biases and confounding. The fact that the study was funded by Roche (albeit through an unrestricted educational grant) has also caused some to dismiss the findings in view of perceived conflicts of interests. The Academy of Medical Sciences and the Wellcome Trust have recently published a review of the evidence for the treatment and prophylaxis of flu, which supports the use of neuraminidase inhibitors such as Tamiflu within 48 hours of the onset of symptoms in patients that need hospitalisation (including pregnant women), but recognises the lack of evidence to guide treatment decisions for other high-risk groups and children.²⁶ The debate highlights the difficulties faced by the government and healthcare professionals when different types of evidence are available; some with perceived conflicts of interest. This case study also emphasises the need for openness in decision-making processes to allow wider society to judge whether decisions are made based on sufficiently robust and relevant evidence.

Measles mumps and rubella vaccine

In 1998, Dr Andrew Wakefield published a case series (an early report investigating a consecutive series of 12 children) suggesting, but not proving, that there might be an association between the onset of autism and bowel disease and the receipt of the combined measles, mumps and rubella (MMR) vaccine.²⁷ Despite multiple studies failing to confirm that the vaccine was a risk factor for autism,^{28,29,30,31,32} Wakefield continued to advocate discontinued use of the combined MMR vaccination in favour of single measles, mumps and rubella vaccinations, which he believed would be a safer alternative to the combined vaccine and could potentially decrease the risk of an adverse event occurring.^{33,34,35,36} The controversy received widespread coverage in the mainstream media, causing public concern and affecting parents' immunisation decisions.^{37,38,39} Confidence in the vaccine fell among parents and healthcare professionals, and national MMR vaccine coverage fell from over 90% in 1994 to around 80% in 2003–2004, corresponding with a significant increase in the incidence of measles.⁴⁰ Twelve years after its publication, Wakefield's 1998 paper was fully retracted by *The Lancet* and Wakefield was struck off the UK medical register, but the controversy has had a lasting impact on perceptions of vaccines.^{41,42,43,44,45,46,47} The General Medical Council concluded that Wakefield had failed to disclose his potential conflicts of interest when applying to undertake and when publishing his research: he had failed to report to the ethics committee and to the editor of *The Lancet* his involvement in litigation against the manufacturers of the MMR vaccine and his receipt of funding from the Legal Aid Board, and he failed to disclose to the editor of *The Lancet* his involvement as the inventor behind a patent relating to a new vaccine for the elimination of the measles virus.⁴⁸ Concerns have also been raised that Wakefield's 1998 paper contained fraudulent data.^{49,50,51} Crucially, this example emphasises the importance of robust evidence on causality between treatment and outcome, of balanced media coverage that accurately reflects risk, benefit and uncertainty, and of appropriately declaring and managing interests.

Hormone replacement therapy

Hormone replacement therapy (HRT) is used to treat the symptoms of the menopause. Evidence consistently indicates that HRT is beneficial in reducing menopausal symptoms, including hot flushes, and in preventing and treating osteoporosis, leading to an improved quality of life.^{52,53,54} Initial observational studies suggested that HRT might reduce the risk of heart disease in addition to its beneficial effects on alleviating menopausal symptoms,^{55,56,57,58,59,60} but subsequent results from randomised trials refuted these claims and reported that HRT instead increased the risk of coronary heart disease and breast cancer.^{61,62,63,64} The resulting confusion and significant reduction in the number of women using HRT illustrates the difficulties people face in balancing risks and benefits in the face of competing evidence. More recent evidence consistently shows decreased heart disease and mortality when HRT is initiated shortly after the onset of the menopause in younger healthy women.⁶⁵ However, the use of HRT has been associated with a potentially increased risk of developing breast, endometrial or ovarian cancer, and venous thromboembolism (blood clots).^{66,67,68,69} In 2007, the Medicines and Healthcare products Regulatory Agency (MHRA) published a safety update for the use of HRT concluding that the overall risk of heart disease and other adverse events is very low in healthy younger women who use HRT, but that older HRT users have a much greater overall risk of these events.⁷⁰ It also highlighted that the risk of breast cancer, ovarian cancer and endometrial cancer due to HRT increases with the duration of use. As the balance of benefits and harms of HRT will differ for every woman depending on the age at which HRT is started, the duration of use and the type of HRT, it is recommended that the lowest effective dose should be used for the shortest time possible for all women, and its use should be reviewed regularly, at least once a year. This example catalysed debate about the relative strengths and limitations of different study designs and about the reliability of evidence that has been obtained by or produced in partnership with industry, with some claiming that these studies emphasised the potential benefits over the likely harms.⁷¹ This example highlights the importance of responsible, accurate and balanced media reporting of research findings by all parties involved in the generation and communication of research.

Human papilloma virus vaccine

The human papilloma virus (HPV) vaccine protects against the strains of HPV most likely to cause cervical cancer and in 2008 was introduced into the UK routine immunisation programme for 12- to 13-year-old girls.⁷² There has been adverse media coverage about whether the potential benefits outweigh the potential harms, which has restricted uptake of the vaccine.⁷³ Indeed, allegations about the safety of the HPV vaccines have been reported, in particular in reports of girls developing postural orthostatic tachycardia syndrome (POTS) or chronic fatigue syndrome after HPV vaccination.^{74,75} However, a large study found no link between HPV vaccines and chronic fatigue syndrome.⁷⁶ Further, the European Medicines Agency recently carried out a review of the evidence surrounding reports of POTS and another syndrome, complex regional pain syndrome (CRPS), in young women given HPV vaccines.⁷⁷ The agency concluded that the overall occurrence of CRPS and POTS in vaccinated girls was no higher than would be expected in the general population and that there was no evidence that HPV vaccines could cause these syndromes. Although some data have also suggested a potential link between the vaccine and thrombosis, the weight of the evidence does not support this association.⁷⁸ Overall, studies continue to suggest the benefits of HPV vaccines outweigh the known side effects, with minimal documented adverse effects.^{79,80} Over 80 million girls and women worldwide have received these vaccines, which are expected to prevent many cases of cervical cancer and other HPV-related cancers and conditions.⁸¹ This case study highlights the need for balanced media coverage.

1.1 How we make decisions about medicines: the role of scientific evidence

Before considering those issues that relate to the generation and communication of scientific evidence, it is crucial to appreciate that decisions about medicines taken by patients and carers are shaped by a complex array of influences, such as cultural factors, past experiences, beliefs, trust, cognitive biases and the presence or absence of symptomatic disease. An analysis of this field is beyond the scope of this review, but those seeking a broader appreciation are referred to an accompanying paper about decision-making on the Academy's website.⁸²

Instead, in this report we focus on the role of scientific evidence about the potential benefits and harms of medicines in informing decisions regarding their use. As illustrated by the case studies, such evidence can be the source of much contention, yet also has the greatest potential for providing robust and reliable information about the potential benefits and harms of medicines. Scientific evidence is the only type of evidence that can be subject to systematic check and challenge. The purpose of this report is therefore to identify how this evidence can be better generated and communicated so that it plays a greater role in decisions about medicines, while respecting the other factors that influence the choices of patients, carers and citizens.

There are few studies into whether providing patients and carers with the scientific evidence about the potential benefits and harms of medicines influences decision-making about medicines.⁸³ Nevertheless, we believe such evidence should be available for those who do wish to use it to inform their healthcare decisions. Further, scientific evidence should be a key consideration in healthcare professionals' decisions about prescribing or recommending treatment approaches.

At the start of our work, there were perceived concerns around the following issues related to scientific evidence: the trustworthiness, accessibility, assessability and usability of scientific evidence that may be used to inform decisions about medicines; campaigning viewpoints and media representation of scientific findings that may not sufficiently reflect the complexity or nuance of the evidence and its implications; and the increasing use of medicines to tackle ill-health, manifesting itself in debates about medicalisation and over- or under-medication. To put these perceptions on a more robust footing and rationalise what issues we should seek to address in a highly complex area, we undertook extensive public engagement and deliberative dialogue.⁸⁴ Our surveys of public and general practitioner (GP) attitudes to medicines, and the scientific evidence underpinning their use, reinforced the sense of a rising tide of concern.⁸⁵ About two-thirds (67%) of British adults and four-fifths (82%) of GPs believed that clinical trial research funded by the pharmaceutical industry was often biased to produce a positive outcome. About half (47%) of British adults agreed that, where possible, doctors should prescribe preventive treatments even if these had moderate side effects, while only about one-third (34%) of GPs said the same. Finally, the use of medical evidence was less trusted than the experiences of family and friends, with about two-thirds (65%) of British adults stating that the experiences of their friends and family were a trustworthy source of information, but only about one-third (37%) trusting evidence from medical trials.

Other concerns were raised by our deliberative dialogue activities; for example, a paucity of support structures and decision aids to help patients and healthcare professionals make decisions in the face of increasingly complex illnesses; a culture in which patients, healthcare professionals and governments often resort to medicines rather than lifestyle changes; and an expectation for the medical profession to provide decisive advice in situations characterised by uncertainty and conflicting pressures. These and other factors may ultimately result in confusion, where healthcare professionals, such as GPs, clinicians and prescribing nurses and pharmacists, are unsure whether to prescribe medicines, and patients and citizens more widely are unsure what advice to follow.

1.2 Conduct and scope of the project

To address the issues identified, we drew on the deliberations of three parallel work streams, which were underpinned by extensive public engagement (summarised in **Box 2**). Full details of the conduct of the project can be seen in an online supplement.⁸⁶ Through workshops, public dialogue and surveys, we explored three main topics:

- The value and limitations of different ways of generating scientific evidence.
- The factors that may influence the trustworthiness of that evidence, particularly the role of competing interests and their management.
- How to communicate scientific evidence better about medicines' potential benefits and harms.

Our public engagement activities provided us with invaluable insights into how scientific evidence is currently used by healthcare professionals and the general public, and some of the key barriers to its more widespread use. This information, as well as validating the concerns that had catalysed the report, helped to shape our conclusions and recommendations. These in turn were tested with key stakeholders from across the biomedical community (including funding bodies, patient groups, trade bodies, journals and medical research charities). The project was overseen by an Oversight Group (detailed in **Annex I**), assembled to reflect relevant constituencies and disciplinary perspectives. The report was reviewed by an external panel appointed by the Council of the Academy of Medical Sciences and was approved by the Academy's Council.

We confined our deliberations to medicines to make this project manageable and did not consider devices, procedures or diagnostics. We did not attempt, nor did we have the capacity, to replicate the work of NICE or the MHRA and comment authoritatively on the scientific evidence on the use of a range of specific medicines. We recognise that there are other forms of evidence that can be used to influence decisions about medicines, such as clinical audit data. We also recognise that in any health system with a finite budget, clinical effectiveness and cost-effectiveness are closely intertwined considerations. In this report, however, we have confined our analysis to scientific evidence obtained in biomedical research on the safety, efficacy and clinical effectiveness of medicines. We do not consider the costs or cost-effectiveness of medicines. Although they are by no means the only cause for concern, given the prominence of statins as a catalyst for this report, we explore in **Online annex A**⁸⁷ the extent to which our recommendations, had they been in place, might have averted the damaging controversy around their use, which resulted in many people at high risk of cardiovascular disease stopping their treatment.⁸⁸

Box 2. Contributory elements to the project

The programme of work comprised four contributory elements that all fed into this final report of the Oversight Group as follows (see online supplement for further detail):⁸⁹

- A Working Group study exploring the ‘Sources of evidence for assessing the safety, efficacy and effectiveness of medicines’, to evaluate the strengths and limitations of evidence from different sources.⁹⁰ The study was informed by a workshop on ‘Evaluating evidence in health’ held in 2015.⁹¹
- A workshop to explore issues pertaining to ‘conflicts of interest’, including how interests (such as the source or model of funding) might impact on the validity (or perception of the validity) of evidence, and how to effectively manage conflicts of interest.⁹²
- Two workshops to consider how to effectively communicate evidence about medicines, including one specifically focused on the media.⁹³
- Surveys of GPs and the public and a programme of deliberative public dialogue that engaged the public, patients and healthcare professionals and explored how individuals perceive and interpret medical scientific evidence. This dialogue underpinned the whole programme of work and helped to ensure that the views of wider society were appropriately taken into consideration in our deliberations.^{94,95}

1.3 Audience and structure of the report

This report was informed by deliberative public dialogue, but is aimed principally at those most able to implement recommendations, including policymakers, regulators, healthcare professionals, active patient groups, funding bodies, research institutions, pharmaceutical companies, academic journals, mainstream media outlets, professional bodies and individual researchers. We have also produced animations and a summary of the report for a more general audience.^{96,97}

The first step in enabling greater use of scientific evidence in judging medicines’ potential benefits and harms is ensuring that we generate robust and relevant evidence, which we consider in **Chapter 2**. We then explore how to enhance both actual and perceived trustworthiness of this evidence (**Chapter 3**), before considering how it can be communicated better to inform decision-making (**Chapter 4**). Finally, we present our conclusions and the implications of this report to enable greater use of scientific evidence to judge the potential benefits and harms of medicines (**Chapter 5**).

To increase the readability of the report, we use the term ‘the public’ throughout. This should be considered to represent the many different people, publics and perspectives within society, with acknowledgement that there is always a diversity of views and attitudes within society.

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Scientific evidence about medicines needs to be robust and relevant to inform decisions.



2. Do we have robust and relevant scientific evidence?

Overview



- Sound evidence-based decision-making relies on robust and relevant evidence. Effective methods exist to assess the potential benefits and harms of medicines. New methods are emerging as data collection and synthesis advance, and their development and evaluation should be supported.
- Involving patients and the public in research enhances its quality, relevance and effectiveness by ensuring that it is informed by and addresses patients' priorities and needs. Funding bodies, universities and research institutions should increase efforts to involve patients, carers and the public in the design, delivery and dissemination of research.
- When rigorously conducted, syntheses of evidence (i.e. systematic reviews and meta-analyses of randomised controlled trials, RCTs) can provide a robust approach to combining and appraising the available evidence on a given treatment, and are crucial to informing clinical practice.
- Usually, a fully-randomised, well-blinded, large-population RCT will be necessary to reliably determine the benefits and harms of medicines that are directly caused by the intervention under investigation. However, high-quality observational studies can be informative where RCTs have not yet been conducted or are unlikely to be, for example in rare diseases research.
- Researchers and healthcare professionals involved in the conduct of research should receive training in research methods and the use of statistics in testing medicinal products so that they can accommodate different evidence-generating approaches in their work and better understand, utilise and communicate research findings. Further, all healthcare professionals should have an improved appreciation of research methods and statistics so that they can better judge the value of the results in informing their advice.
- All those involved in the research process should continue to act together to identify and deliver ways to improve the reproducibility and reliability of research at an international level. To galvanise a culture change within universities and research institutions, the Research Excellence Framework (REF) should require that measures to increase the robustness and reliability of research are reflected in the institutional-level environment statement.
- The increasing availability of clinically relevant data collected outside the controlled conditions of conventional RCTs (so-called 'real world data') presents new opportunities to investigate the use of medicines in settings that better reflect the reality of healthcare. Funding should be allocated to: research into improving methodologies for analysing data from these new evidence sources; capacity building for managing and analysing large datasets; and secure platforms for data sharing and linkage as well as real-time monitoring of health outcomes.
- These emerging sources of evidence are growing in stature and should be developed and evaluated so that their potential contribution is fully realised. These data are, however, subject to biases, which limit their ability to make treatment comparisons or evaluations of the effectiveness of medicines.

Perspectives we heard in our dialogue with citizens, patients and healthcare professionals



- Concerns that the evidence base does not always contain answers to questions that matter most to patient needs, and that research is not always conducted on populations that represent the groups for whom medicines are being recommended.
- Views among the public and patients that patients should receive care, rather than taking an active role in learning about the nature of that care or asking their healthcare professionals questions.
- Patient and public lack of familiarity with the process of generating scientific evidence, leading some to perceive personal experiences as more reliable than scientific evidence.
- Low awareness among patients and the public of different types of study designs and their purposes, and that evidence continues to be generated once a medicine is available on the market.
- Limited appreciation among patients and the public of the uncertainty inherent in research findings and the applicability of results to different groups of patients. Overall, medicines that are available on the market were viewed as safe and effective for all.
- The tendency for specialist healthcare professionals to engage more with primary studies of medicines (e.g. RCTs), whereas generalist healthcare professionals rely more on syntheses of evidence (e.g. systematic reviews or meta-analyses) or guidelines.
- The challenge for some healthcare professionals in assessing the quality of the evidence and its relevance to their own practice. There were also concerns from some healthcare professionals that they might not always consider the totality of the evidence on a medicine, which could skew decision-making.

As we heard during our deliberative dialogue, we believe that scientific evidence about the potential benefits and harms of medicines needs to be both robust (i.e. rigorous and repeatable) and relevant (i.e. addresses questions that matter most to those patients that will ultimately use the medicine) if it is to have greater prominence in informing their use by patients and healthcare professionals in clinical practice. In this chapter, we explore how the relevance and robustness of evidence can be enhanced, and how emerging sources of evidence might be used to further our knowledge about the potential benefits and harms of medicines.

2.1 Scientific evidence needs to be relevant: public, carer and patient involvement in research

To improve patient health and develop medicines of clinical value, it is critical to understand the needs and priorities of patients. It has been estimated that between 30% and 50% of patients taking medicines for chronic conditions do not take their medicines as prescribed.^{98,99,100} If research is more relevant to patients, it may well result in better uptake of and adherence to medicines.

We heard repeatedly throughout our evidence-gathering efforts that patient needs are poorly considered in the design, analysis and evaluation of clinical studies. Effective patient, carer and public involvement (PPI) in research can help here (see **Box 3** for an example). Indeed, by taking into account users' perspectives, and ensuring that research is informed by patients' preferences and needs, the quality, relevance and effectiveness of research can be enhanced.^{101,102,103,104} PPI can also be used to improve how research is prioritised, communicated and utilised; identify new avenues for research, potential ethical concerns and outcomes that matter to patients; and influence funding decisions.¹⁰⁵ Further, patients and patient groups can help in mobilising patients and carers to engage in clinical research and even contribute to new and innovative ways of supporting or analysing research (see **Boxes 4** and **5**). PPI can be a mutually beneficial relationship. For example, PPI can benefit patients by facilitating communication between patients and healthcare providers, improving their comprehension of medical information and the understanding of their disease, and providing a more individualised approach to healthcare.¹⁰⁶

Many funders, including the National Institute of Health Research (NIHR), the Medical Research Council (MRC) and medical research charities, have adopted PPI practices with great effect – from setting research priorities that meet patient priorities and determining outcomes that matter to patients and carers, to using their insights and experience to present evidence in a more accessible and useful way.^{107,108,109,110} Organisations across the biomedical research sector, such as the National Institute for Health and Care Excellence (NICE) and the Royal College of Physicians, are also increasingly seeking to involve patients and the public in their work.^{111,112} However, much scientific research is still undertaken without meaningful PPI, with researchers seen as reluctant to share the control of the research process with the public and patients.^{113,114,115}

Box 3. Incorporation of fatigue as a standard outcome in rheumatoid arthritis clinical trials

When designing a core set of outcomes to be used as an international standard in rheumatoid arthritis clinical trials, health professionals and methodologists failed to incorporate several outcomes that mattered to patients. One of these was fatigue, which is reported by almost every patient. Fatigue was subsequently added to the core set following a decade of research into this symptom.^{116,117,118,119}

Box 4. Patient involvement in cystic fibrosis research

Cystic fibrosis is a progressive genetic disease that causes persistent lung infections and limits the ability to breathe.¹²⁰ To accelerate the development of medicines for this disease, the Cystic Fibrosis Foundation founded the largest clinical trials network in the world, the Cystic Fibrosis Therapeutics Development Network, and pioneered an innovative venture philanthropy model of drug development, providing early stage funding to biotechnology and pharmaceutical companies for research into new medicines for this disease.^{121,122,123} These efforts resulted in the development of a revolutionary new drug, ivafactor (trade name: Kalydeco), in a disease with a high unmet medical need.

A recent survey has shown that although there has been a positive shift in researchers' understanding and attitudes to public engagement over the last decade, a number of barriers remain, including issues of competing time pressures, support, funding, training and recognition.¹²⁸ Two further limitations to PPI include the fact that involvement is often sought from a select group of interested patients, which may not be representative of the wider patient population, and the approach is designed around the research process (e.g. meetings and committees) rather than around the needs of patients and the public. Establishing environments where patients are not just active participants in their care but also advocates for (properly-designed) research, actively requesting opportunities to take part in trials, would aid the generation of reliable research. This would require a shift in the public's view of research from something that is done to them, to something that they could promote themselves and be involved in its co-production (see **Box 6**).

Box 5. Citizen science: involving the public in the generation of evidence

Propelled by new technology, the past decade has seen a rise in citizen science, where members of the public contribute to the generation of evidence often under the direction of, or in collaboration with, professional scientists or institutions.¹²⁴ Recent examples include Cell Slider, where images of cancer cells were analysed by volunteers, and Fold.it, where members of the public played games to resolve how proteins fold into three-dimensional structures.^{125,126} Moreover, there are growing numbers of examples where social media is playing a significant role in enabling and empowering patients, carers and the public to be involved in and contribute to research important to their condition. One such example is the 'Cloudy with a chance of pain' project, which is using patient data collected via a smartphone app to examine whether the weather affects pain in patients with arthritis or chronic pain.¹²⁷

The Academy of Medical Sciences' 'Improving the health of the public by 2040' report has noted the vital role of public involvement and co-production in ensuring health research meets future challenges.¹³⁴ We applaud the efforts of the National Coordinating Centre for Public Engagement, NIHR's INVOLVE and the James Lind Alliance, which provide support to researchers and universities in engaging with the public, and bring patients, carers and frontline clinical staff together to prioritise research needs.^{135,136,137}

Box 6. Evidence co-production

Evidence 'co-production' is a growing aspiration for healthcare researchers and research funders. This reflects the increasing recognition of the benefits of ensuring evidence generation is a joint venture between patients and the public, researchers and healthcare professionals (see **section 2.1**). The concept of 'co-production' broadly describes the establishment of an equal and reciprocal relationship between professionals, the people using their services and the wider community during a project.¹²⁹ Nesta has identified six principles that underpin this concept:¹³⁰

- **Assets:** transforming the perception of people from passive recipients to equal partners.
- **Capacity:** building on what people can do and supporting them to put this to work.
- **Mutuality:** reciprocal relationships with mutual responsibilities and expectations.
- **Networks:** engaging a range of networks inside and outside of 'services', including peer networks, to transfer knowledge.
- **Blur roles:** removing tightly defined boundaries between professionals and recipients to enable shared responsibility and control.
- **Catalysts:** shifting from 'delivering' services to supporting this to happen and catalysing other action.

There is a lack of consensus on the application of this concept to healthcare research. 'Evidence co-production' has been wrongly used as a label for effective PPI; instead, the term describes a fundamentally different research design and delivery strategy that positions patients and the public as equal partners with researchers and health professionals at every stage in the process of evidence generation.¹³¹ To date, the co-production model has largely been applied to health services rather than health research; however, it is now gaining popularity with health researchers and research funders. Indeed, the NIHR lists the six principles of co-production as a starting point for their broad vision of achieving '*a population actively involved in research to improve health and wellbeing for themselves, their family and communities*'.¹³² To this end, INVOLVE is currently leading a project on behalf of the NIHR to develop some principles for co-production in a health research context that will support the more widespread adoption of co-production methodology and approaches.¹³³

Recommendation 1: Involving patients, carers and the public in research



Building on existing good practice, **funding bodies, universities, research institutions, medical research charities** and the **pharmaceutical industry** should increasingly seek to involve patients, carers and the public in the design, delivery and dissemination of research, and consider it a key part of how research excellence is characterised across the system as appropriate. Processes and practices for involving patients, carers and the public in research should be systematically evaluated to inform the evidence base and enhance future practice. Specifically, we recommend that:

- a. **Research funders**, including **medical research charities** and **industry**, require applicants to detail in their grant applications their plans for involving and engaging patients and the public in their research as a condition of funding. Funders should evaluate whether involvement and engagement initiatives have been carried out and request that these are described in the end-of-grant report or in other reporting systems such as Researchfish.
- b. **Universities, research institutions** and **industry** tackle the barriers to patient, carer and public involvement and engagement, paying particular attention to training and support for researchers and the public.
- c. **Research funders** from across the sector, including **medical research charities** and **industry**, come together to develop a mechanism of monitoring the development of relevant and appropriate activities for involving and engaging patients and the public in research. They should identify best practice and ensure it is disseminated to researchers and the public. An initial meeting on this topic could be led by **INVOLVE**, part of the National Institute for Health Research (NIHR).

As an important aspect of research excellence, patient, carer and public involvement in research could be reflected in the next REF process.

2.2 Scientific evidence should be robust

2.2.1 Strengths and limitations of current methods of assessing the potential benefits and harms of medicines

There is a range of effective designs to assess the potential benefits and harms of medicines, and new methods are emerging. All approaches to the evaluation of evidence have strengths and limitations, which we summarise below. Please see the 'Sources of evidence for assessing the safety, efficacy and effectiveness of medicines' report for a more in-depth discussion of alternative trial methods that have been developed to address some of the limitations of conventional trial designs, and of areas where new strategies are required (summarised in **Box 7**).¹³⁸ We focus particularly on the quantitative measures used to address questions about the potential benefits and harms of medicines.

Box 7. Areas where new strategies to evaluate the safety, efficacy and effectiveness of novel treatments are required

As described in detail in the 'Sources of evidence for assessing the safety, efficacy and effectiveness of medicines' report, new strategies to evaluate these features for novel treatments are required in:¹³⁹

- **Rare diseases**, where small numbers of geographically scattered patients make large RCTs impracticable.
- **Emergency situations**, where the spread of the disease, geographical dispersion and mortality rates can pose practical, ethical and methodological problems. New ethical strategies might be required in rare diseases and emergency research.¹⁴⁰
- **Stratified, personalised or precision medicine**, where the stratification of disease may, in the future, limit the ability to conduct large RCTs.
- **Patients with multiple illnesses** (also known as multimorbidity), where co-occurring conditions might influence the response to treatment.¹⁴¹

2.2.1.1 Randomised controlled trials

Well-designed RCTs are usually the best way of generating robust evidence about the effects of treatments.¹⁴² Their main strengths are their ability to minimise the effect of biases and confounding owing to their use of randomisation to different treatment groups, control groups and blinding techniques. They are ordinarily the only method that can detect, in an unbiased manner, moderate but clinically important effects that are directly caused by the treatment under investigation. However, when strict participant eligibility criteria are used in an RCT it can be a challenge to generalise results to wider patient populations and to know the potential impact on routine clinical practice. For example, many efficacy studies designed for regulatory purposes are undertaken under strictly-controlled settings with narrowly-defined patient populations; therefore, when considered in isolation, they have limited ability to inform wider clinical practice compared to effectiveness studies, such as pragmatic trials.¹⁴³ Individual RCTs also generally have limited ability to detect rare or long-latency harms.

2.2.1.2 Observational studies

High-quality observational studies can be informative where RCTs have not yet been conducted or are unlikely to be (for example in rare diseases research). With careful interpretation of the results, they can provide an important source of evidence about the potential benefits and harms of medicines.¹⁴⁴ Notably, observational studies can provide valuable information about large effects or rare outcomes, which are too infrequent for their reliable assessment in RCTs.¹⁴⁵ Well-designed observational studies may also provide important information on the safety, and sometimes the effectiveness, of medicines, and on the generalisability of results to different groups and the wider population. However, because participants are not randomly assigned to treatments, there is a danger that conclusions will be influenced by bias; for example if those who receive the treatment differ in some systematic way from those who do not.

2.2.1.3 Syntheses of evidence

One of the concerns expressed about evidence of benefits and harms is that the participants in clinical trials are not representative of the patients that will be treated (i.e. concerns about the generalisability of results to wider populations). Syntheses of evidence (systematic reviews or meta-analyses of RCTs)¹⁴⁶ are important mechanisms for combining relevant high-quality evidence about a medicine from a range of individual studies focused on a particular clinical indication. Crucially, meta-analyses of data from RCTs with differing

eligibility that include large numbers of patients can allow the findings obtained from narrowly-defined patient populations to be more widely generalisable, addressing in large part the concern expressed by both healthcare professionals and patients that the evidence on a drug may not be relevant to their particular circumstance. Meta-analyses can either synthesise aggregate (trial-level) data or individual patient data (IPD). Properly-conducted IPD meta-analyses provide the potential to address specific questions more reliably and completely, as the underlying raw data are re-analysed together as if in one large trial. Such studies are able to provide synthesised analyses of patient-level data from all of the relevant RCTs of the effects of treatment in particular types of patient (e.g. low or high risk, men or women, older or younger people) and on particular types of outcome. This approach has been used to assess the safety and efficacy of statin therapy in various populations.^{147,148,149}

Rigorous syntheses of evidence represent a robust, high-quality approach to combining and appraising the available evidence on a given treatment, and are crucial to informing clinical practice. However, syntheses of evidence do have limitations and have recently faced criticism for being redundant, misleading and conflicted.^{150,151} For example, they cannot correct for biases from selective publication (i.e. publication of positive findings at the expense of 'negative', null, or inconclusive data) and are only as reliable as the primary studies included in the analysis. Well-conducted evidence syntheses attempt as far as is practically possible to reduce the effect of such biases, as summarised in the Cochrane 'Handbook for Systematic Reviews of Interventions'^{152,153} and in **Chapter 3** we explore initiatives that aim to increase the publication of rigorous results regardless of whether they are positive, 'negative' or inconclusive.

2.2.1.4 Critical appraisal of the evidence

'Hierarchies of evidence' (see **Table 1** for an example) provide a crude ranking of specific study designs in terms of producing robust results. The majority place large RCTs, or meta-analyses of RCTs, at the top of the classification. However, it would be dangerous to assume that observational data are invariably of less use than data from RCTs.¹⁵⁴ While hierarchies can be useful 'rules of thumb', they should not be used prescriptively, nor as a substitute for good judgment in the critical appraisal of the evidence, the rigour of the study and appropriateness of the methodology from which the evidence has been generated.¹⁵⁵

This judgement is central to the evaluation of the benefits and harms of medicines and is crucial in ascertaining whether the evidence presented is 'fit for purpose'.^{156,157} Key considerations include whether the size of the effect is large enough to have been reliably detected in the study design that was used, whether the findings are plausible (based on sound biological principles), whether they extend to the treatment populations of interest (i.e. are generalisable) and whether they reliably demonstrate a causal link between the treatment and the outcome. Those evaluating the evidence also need to consider whether the evidence generated from population-based trials is relevant and therefore usable to inform individual-level decisions. Indeed, as discussed in **Chapter 4**, even with the most robust evidence, there will always be some uncertainty regarding the application of the evidence of benefits and harms to a specific individual, the potential outcomes and the likelihood of these outcomes.

Some researchers have strongly held views on the relative merits of different study designs, which polarise debates about the benefits and harms of medicines. The type of evidence, and methods needed to analyse that evidence, will depend on the research question being asked.¹⁵⁸ For example, in certain circumstances (e.g. when exploring patient and healthcare professional experiences and perceptions), robust qualitative studies use more appropriate methods than conventional quantitative studies. What is important is that users of the evidence are aware of the trade-offs being made so that they can use it appropriately. **Online annex B** summarises the most appropriate approaches for the evaluation of treatment effects in specific research scenarios.¹⁵⁹ **Online annexes C** and **D** outline some principles for the academic/evidence community or consumers of evidence respectively to consider when evaluating evidence.^{160,161}

Table 1. An example of a hierarchy of evidence^{162,163}

Level	Criteria
1++	High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias.
1+	Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias.
1-	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias.
2++	High-quality systematic reviews of case-control studies or cohort studies, or high-quality case-control or cohort studies with a very low risk of confounding, bias or chance.
2+	Well conducted case-control or cohort studies with a low risk of confounding, bias or chance.
2-	Case-control or cohort studies with a high risk of confounding, bias or chance.
3	Non-analytic studies (e.g. case report, case studies).
4	Expert opinion.

Hierarchies of evidence crudely rank specific study designs by their ability to produce robust and reliable results. While they can be useful 'rules of thumb', they should not be used prescriptively. Good judgment in the critical appraisal of the evidence is still necessary, particularly about the rigour of the study and appropriateness of the methodology from which the evidence has been generated. For example, it should not be assumed that observational data are invariably less useful than data from RCTs.

2.2.1.5 Training needs for researchers and healthcare professionals

We heard that there is still a gap in training in research methods and statistics for researchers and healthcare professionals alike. We therefore encourage funding bodies to continue to provide support for career development opportunities. Exemplars include the NIHR Research Methods Programme and the MRC Skills Development Fellowships.^{164,165} Such training should enable researchers who are involved in the assessment of benefits and harms of medicines to better understand (and communicate) the strengths and limitations of different study designs, and accommodate different evidence-generating approaches as part of their research. Training should extend to information governance, privacy, confidentiality and data sharing (see **section 2.4**). The biomedical community should also be receptive to different methods of generating knowledge, for example those generated in disciplines outside the biomedical sphere such as in the social sciences.¹⁶⁶ We note that the Royal Pharmaceutical Society has launched a toolkit for pharmacists to identify, recognise and further develop their research skills and help them engage in activities that generate evidence.¹⁶⁷

Recommendation 2: Addressing gaps in training in research methods and statistics



We recommend that those involved in the conduct of clinical research, including **universities, research institutions** and **industry**, should provide training in research methods and the use of statistics in evaluating the benefits and harms of medicines for staff across all career stages, from early career researchers to established researchers, as part of their continuing professional development (CPD). Similar courses should be provided for healthcare professionals by **universities** and **Medical Royal Colleges** as part of their training or CPD programmes. Existing courses should be reviewed and, where necessary, new courses established to accommodate the full range of evidence-generating approaches for assessing the benefits and harms of medicines. These should assess the relative value, strengths and limitations of different approaches, including new and emerging methods, and the questions they are best suited to address. These bodies should also instil an ethical research framework within which they expect staff to work, as outlined in the 'Universal ethical code for scientists', and promote high standards of research conduct.¹⁶⁸ The Health Education England (HEE)/NIHR Masters in Clinical Research degree is an example of how training in research methods could be delivered for researchers.¹⁶⁹

2.2.2 The robustness of scientific evidence: the importance of research reproducibility

Replication is key to the scientific process, allowing research findings and scientific theories to be tested and either confirmed, refined or corrected. Due to the nature of the biomedical research, including the natural variability in biological systems, it is accepted that a proportion of research findings will not be reproduced and will ultimately be corrected through the scientific process.¹⁷⁰

There has, however, been growing concern about the number of findings in the literature that cannot be reproduced, with reports both in the general and scientific media about failures to replicate findings.^{171,172,173} A number of activities have highlighted the issues and suggested how improvements can be made to increase the reliability of scientific evidence.^{174,175,176} The Academy held a symposium jointly with the major UK funders of biomedical research to identify the potential causes of irreproducibility and ways in which they might be addressed;¹⁷⁷ a later statement has identified actions that have been taken since the meeting.¹⁷⁸

We welcome these initiatives, which demonstrate that it is a shared responsibility of all those involved in the research process to promote the robustness of scientific findings, including ensuring high standards of research integrity (both methodological and ethical integrity), as described in the 'Universal Ethical Code for Scientists'.¹⁷⁹ We support ongoing efforts across the biomedical community and urge all those involved in the research process to continue to act together to identify and deliver proportionate measures to improve the reproducibility and reliability of research, including the following:

- Higher education institutions and industry should encourage and reward behaviours that are conducive to good research practice (e.g. sound application and interpretation of statistical analyses, data sharing, protocol publication, team work and peer-review, among others) that should inform professional opportunities and career progression. We commend and support Universities UK's 'Concordat to support research integrity' and the All European Academies' 'European Code of Conduct for Research Integrity'.^{180,181} Reflecting the requirements of the EU Clinical Trials Regulation (EU No 536/2014), higher education institutions and industry should mandate best practice in terms of clinical trial registration, publication and data sharing (see **Online annex F**).^{182,183}

- Journals and publishers should ensure that work submitted for publication receives adequate methodological scrutiny, including of statistical approaches where appropriate. They should mandate that sufficient information is available in the final publication to allow studies to be independently repeated and that authors adhere to internationally agreed publication guidelines such as CONSORT, STROBE, PRISMA and ARRIVE, among others.^{184,185,186,187}
- Those that fund research, including funding bodies and industry, should develop or review existing guidelines for their grant awardees around how to implement their data access policies – requiring that data are made available to the scientific community with as few restrictions as possible in a timely and responsible manner – so that the policies are more consistently and appropriately applied in practice.^{188,189,190,191} They should continue to fund studies that are of sufficient size to reliably detect the outcome of interest and those that aim to investigate the robustness of findings. They should recognise the value of replication studies and foster collaborative work where needed.

A culture change within universities and research institutions will be necessary to further enhance attention paid to the reproducibility and reliability of research. The Higher Education Funding Council for England (HEFCE, relevant functions expected to be assumed by Research England in the future) and its devolved counterparts should catalyse these improvements in the next REF process, expected in 2020–2021. We welcome Lord Stern’s recommendation for a new, institutional-level environment assessment, which should include a statement of how institutions support high-quality research.¹⁹² HEFCE and its equivalents in the devolved nations should incorporate this recommendation as they set out proposals for conducting the next REF, and require that environment statements encourage reproducibility efforts and institutional support for good practice in the next REF process. The ‘score’ related to the environment statement needs to have adequate weighting to incentivise the right culture and behaviours.

Recommendation 3: Enhancing the recognition of robust research findings



We recommend that in the next Research Excellence Framework (REF) process, the **Higher Education Funding Council for England** (HEFCE, relevant functions expected to be assumed by Research England in the future) and its **counterparts in the devolved nations** should incorporate Lord Stern’s recommendation for a new, institutional-level environment assessment. We propose that such environment assessments record measures taken to increase the robustness and reliability of research, including work to ensure adherence to ethical codes of research practice, data-sharing policies, and recognition and reward for efforts to enhance reproducibility.

2.3 New sources of evidence

The digital revolution has created new ways of acquiring, storing, manipulating and transmitting large volumes of data.¹⁹³ Greater sharing and linking of healthcare and other data provide opportunities to conduct further research to improve patient outcomes and to inform and enhance health.¹⁹⁴ For example, evidence generated from new data sources, such as so-called ‘real world data’, can provide valuable information on a medicine, including its safety, the generalisability of findings about the medicine obtained in RCTs to wider patient groups, and longer-term outcomes once the medicine has been licensed and is used in clinical settings that better reflect the reality of healthcare.¹⁹⁵ Despite these benefits, data sharing among researchers remains relatively uncommon and healthcare and other data are not readily accessible.^{196,197,198}

2.3.1 What is meant by the terms ‘real world data’ and ‘real world evidence’?

In this report, we define ‘real world data’ as clinically relevant data collected outside the context of conventional RCTs. Such data can stem from a diversity of sources, including but not limited to primary and

secondary care data, routine administration (e.g. welfare, tax, educational records), registries, population health surveys and social media.^{199,200} 'Real world evidence' is the information (evidence) generated from the analysis of 'real world data' using robust and reliable scientific methodologies.

These terms lack universal definitions and some professionals reject them, as they could lead to the perception that data collected in experimental studies (like RCTs) are not representative of real life situations. However, these terms are increasingly accepted and frequently used in industry, regulatory bodies and common parlance. For example, the European Medicines Agency's (EMA's) adaptive pathways scheme requires the use of 'real world data' to complement evidence from RCTs (see **Box 9**).²⁰¹ Clear and internationally agreed definitions are therefore needed, such as those we provide above. **Box 8** describes some common misunderstandings of these terms.

Box 8. Common misconceptions about 'real world data' and 'real world evidence'

- 'Real world evidence' does not specify a research design. Despite this, 'real world evidence' is frequently contrasted with research designs such as RCTs, which is unhelpful and inaccurate.
- Although 'real world data' typically arise from electronic health records or administrative data (or combinations thereof), they may also originate from research studies, provided they are representative of the population, contemporary, report key outcome measures or have other useful characteristics. The key is to make best use of all data resources to best address the research question under investigation, whatever their provenance.
- 'Real world evidence' can be used to inform various stages across the lifecycle of a medicine. Indeed, its use is not limited to the regulatory approval of a medicine and post-approval research, and it can also be utilised in drug discovery, target validation and drug repurposing research programmes.

2.3.2 Opportunities of 'real world data'

'Real world data' provide an opportunity to investigate the use of medicines in clinical practice or in settings that better reflect the reality of healthcare (e.g. prescribing patterns, clinical outcomes, patient safety data associated with the use of medicines or follow-up of individuals participating in RCTs more efficiently and for longer periods).^{202,203} 'Real world evidence' generated from these data, including that generated through PPI, has the potential to complement evidence collected in RCTs. For example it can be used to provide further knowledge about the safety of a medicine once it has been licensed or about the generalisability of results from RCTs to wider populations of interest.²⁰⁴ 'Real world data' could be particularly useful for studies with large effect sizes, small patient populations or in complex settings such as remote geographical locations.

'Real word data' also provide an opportunity to capture patient experiences or patient-reported outcomes in clinical practice in a more systematic way to inform the evidence base about medicines and help scientific evidence evolve, for example through identifying where further RCTs could usefully be applied to establish a previously unappreciated causal link (see **section 2.2**). They can also be used to improve our understanding of care quality and outcomes,²⁰⁵ for example by estimating unmet medical need or the potential benefits and harms of medicines in wider groups of patients;^{206,207} personalising treatment decisions;^{208,209} and, although not considered in detail in this report, evaluating costs, health outcomes and cost-effectiveness of treatments.²¹⁰ In the future, it is conceivable that 'real word evidence' could inform the evaluation of efficacy

and effectiveness of medicines, the licensing of medicines, and the expansion and refinement indications for existing medicines.²¹¹ Adaptive pathways, launched in 2014 by the EMA, represent an area where ‘real world data’ will be increasingly used to help assess the efficacy and effectiveness of new medicines (see **Box 9**).²¹² However, there is a paucity of good practice examples of how such data can be used effectively. Methodologically sound strategies for collecting and analysing ‘real world data’ to support the assessment of efficacy and effectiveness need to be identified. Further oversight and collaboration is needed in this area.

Various initiatives have considered, or are currently underway to explore, the use of new data sources – these are described in detail in the Academy’s ‘Sources of evidence for assessing the safety, efficacy and effectiveness of medicines’ report.²¹³

Box 9. Adaptive pathways

Adaptive pathways were introduced by the EMA in 2014 as an iterative approach to bringing medicines to the market, where the development of a medicine is initially targeted at a well-defined group of patients likely to benefit the most from treatment, followed by prospectively planned phases of evidence gathering to expand its use to wider patient population, if appropriate.²¹⁴ Such pathways aim to balance timely access to new medicines for patients with an unmet medical need with the requirement for adequate information on the benefits and harms of medicines. In these settings, ‘real world data’ are crucial for the monitoring of medicines, complementing and enhancing evidence collected in RCTs.

In the future, increasingly prevalent sources of information, such as social media, internet searches, mobile devices, health apps and wearable technologies, will provide further opportunities to enhance our understanding of the potential benefits and harms of medicines, including how these impact on individuals’ behaviour. The Academy’s ‘Improving the health of the public by 2040’ report explores in more detail the challenges of making sense of these data.²¹⁵

2.3.3 Challenges to the use of ‘real world data’

There is wide-ranging diversity in the robustness of ‘real world data’, which can range from data collected in rigorously-conducted pragmatic trials, through administrative data collected in the NHS and data collected in disease-specific registries, to data posted on social media websites. The robustness of the data will need to be carefully considered in any analysis using data from these various sources. ‘Real world data’ are subject to biases and confounding, as described in **section 2.2.1.2**. Therefore, while they have potential for providing additional information on a medicine, there are challenges in using ‘real world data’ for treatment comparisons and the reliable assessment of treatment effects, unless the effects are large and relate to rare outcomes.^{216,217,218} ‘Real world data’ are already being used for pharmaco-vigilance purposes – via the Medicines and Healthcare products Regulatory Agency’s (MHRA’s) Yellow Card Scheme²¹⁹ or in the EMA’s adaptive pathways (**Box 9**) for example – but further research is needed before all forms of ‘real world data’ can be reliably used to evaluate the effectiveness of medicines. Standards and best practice guidance on the methodologies to assess the benefits and harms of medicines are needed. A culture shift and training are also required so that researchers are better equipped and prepared to consider new approaches to best answer the research question under investigation. The use of ‘real word evidence’ is also limited by constraints on accessibility to data and the lack of infrastructure to support linkage of data from these different resources.

We welcome the major investment in infrastructure for research into data sharing and linkage in the UK, such as the Farr Institute of Health Informatics Research and the Administrative Data Research Network,^{220,221,222} and policies from research funders to encourage standardisation of data, open access and

greater data sharing.^{223,224,225,226} Further quality-assured data platforms that allow researchers to undertake randomised non-experimental studies and enable real-time monitoring of outcomes should be developed. Data sharing and linkage must go along with protecting patients' privacy and confidentiality. A recent report from Dame Fiona Caldicott outlines data security standards for handling health and social care information to support data sharing.²²⁷ This is an area where ethical issues and public views require examination, and we support proposals to establish a Council for Data Science Ethics.²²⁸

In tackling the issues listed above, consideration needs to be given to the resource implications and wider opportunity cost of data sharing, and ensuring that the UK has the capacity and skills to manage and analyse large datasets.^{229,230,231} These concerns are not unique to healthcare research and a number of initiatives to address them are underway.^{232,233} The research community will also need to work internationally to identify best practice, learning from and building on successful initiatives across the globe.²³⁴ Working internationally will be particularly important for setting international data standards, data models, algorithms and methods of analysis, and establishing a clearer understanding of situations where 'real world data' analyses may or may not provide useful, reliable additional evidence.

One of the priorities we endorse, identified by our 'Sources of evidence for assessing the safety, efficacy and effectiveness of medicines' study, is for research funders to support research into new methodologies for understanding how to view and interpret the totality of outcomes from different study designs (e.g. RCTs, observational studies and novel approaches), and for improving methodologies for analysing data from new data sources, such as 'real world data'.

Recommendation 4: Ensuring best use is made of new sources of evidence



To complement current initiatives to improve data sharing and linkage, we recommend that:

- a. **Funding bodies** invest in research into understanding how to view and interpret the totality of outcomes from different study designs, including randomised controlled trials (RCTs), observational studies and novel approaches. We also recommend that they prioritise research into improving methodologies for analysing data from new sources of evidence, such as 'real world data', that take account of bias and confounding. This work should include investment in capacity building for skills in managing and analysing large data sets, as well as developing appropriate environments for greater data sharing and linkage, and quality-assured platforms for health research and real-time monitoring of outcomes. These platforms must provide appropriate safeguards to ensure data subjects' privacy and confidentiality.
- b. The **global research community** works together to develop internationally agreed data standards, best practice guidelines and robust methods for collecting, analysing and using 'real world evidence' to inform the use of medicines.

2.4 Conclusions

If greater account is to be taken of scientific evidence when decisions are made about the prescription and use of medicines, it is essential that the evidence is relevant both to the condition and patient to be treated and is as sound as possible. Relevance can be better assured through engaging the public, patients, carers and frontline clinical staff in the research process – particularly the identification of the health needs that a treatment for a particular condition should address – but more evidence is needed on the best methods for involving patients, carers and the public effectively in such processes. Our recommendation for appropriate involvement of patients, carers and the public in research (**Recommendation 1**) should prevent situations

such as that described in **Box 3**, where research fails to address outcomes that matter most to patients. Research outputs would therefore be of increased quality, relevance and effectiveness.

Robust and reliable research is dependent on the highest standards of research integrity (both methodological and ethical integrity), good research design (including the use of the most appropriate methodology to address the question), appropriate statistical analysis and attention to those factors that optimise research reproducibility. The importance of research reproducibility is reflected in several of our case studies, such as the case study on the measles, mumps and rubella (MMR) vaccine, where a single irreproducible study fuelled significant controversy over the potential harms of the vaccine (**Box 1**). Enhancing the recognition of robust research findings, as we recommend in **Recommendation 3**, should increase people's confidence about the potential benefits and harms of medicines, meaning such controversies are less likely to occur. Universities, as hosts of most academic research, have a responsibility to cultivate a culture that promotes the generation of the highest-quality scientific evidence. We believe the new REF institutional environment statement can do much to capture and incentivise measures to advance this agenda.

Although there are currently appropriate methods to assess the potential benefits and harms of medicines, new methods are emerging – and should continue to be developed and evaluated – to address the challenges posed by complex research areas (such as research in rare diseases, emergency situations and multimorbidity); new ways of identifying and treating disease (for example, stratified medicines); and new data sources (including large datasets, social media, wearable technology and health apps, among others). There are many examples of the challenges associated with weighing up the outcomes from different study designs, as seen for instance in our case studies on statins and Tamiflu. In both of these examples, controversy was sparked by differing interpretations of the evidence in view of the relative strengths and limitations of different study designs. Our recommendation for research into new study designs and methodologies (**Recommendation 4**) aims to prevent such controversy and ultimately aid governments, healthcare professionals, patients and citizens in decision-making about medicines.

The increasing availability of clinically relevant data collected outside the controlled conditions of conventional RCTs presents new opportunities to explore the benefits and harms of medicines in settings that may better reflect the reality of healthcare. These should be supported and encouraged so that they can be exploited to their full potential for patient and societal benefit. This will require addressing a number of current barriers – not least around data sharing and linkage – and a research culture shift towards a broader appreciation of the relative value and limitations of various methods of generating and evaluating evidence, and willingness to consider and evaluate new approaches. Our research training recommendations seek to address this need. A significant component of the controversy relating to statin prescription and usage related to a lack of appreciation of the strengths and limitations of various methodologies, sowing confusion in the minds of healthcare professionals and patients alike. Ensuring healthcare professionals and researchers are trained to interpret different types of scientific evidence would help patients and healthcare professionals better weigh up the potential benefits and harms of medicines when discussing treatment options, and reduce the likelihood of similar research controversies occurring in the future (**Recommendation 2**).

Further, even though a substantial amount of research is conducted before medicines are approved for widespread use, it is important to recognise that knowledge about medicines evolves post-licensing, once they are used in much larger and heterogeneous populations. This further evidence should be used in more systematic and detailed ways to further define the circumstances under which a medicine is effective.

Ultimately, the availability and use of medicines must balance the need for high-quality evidence to make an informed decision with timely access to medicines for patient and societal benefit. Some decisions about the use of medicines will inevitably have to be made in the face of incomplete evidence and competing priorities. A recent example was the decision by government to stockpile the antiviral Tamiflu as a precautionary response to the threat of a highly virulent H5N1 flu pandemic. This decision was based on a range of considerations, including economic, public health, political and ethical factors, as well as the scientific evidence.²³⁵ Nevertheless, decisions on the use of medicine should be re-appraised as new evidence on the benefits and harms of medicines emerges. Openness about the decision-making processes is needed to allow wider society to judge whether decisions are made based on robust and relevant enough evidence.

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223. <http://www.dcc.ac.uk/resources/policy-and-legal/overview-funders-data-policies>
224. <http://www.rcuk.ac.uk/research/datapolicy/>
225. <http://www.wellcome.ac.uk/About-us/Policy/Spotlight-issues/Data-sharing/>
226. <http://www.cancerresearchuk.org/funding-for-researchers/applying-for-funding/policies-that-affect-your-grant/submission-of-a-data-sharing-and-preservation-strategy/data-sharing-guidelines>
227. National Data Guardian for Health and Care (2016). *Review of data security, consent and opt-outs*. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/535024/data-security-review.PDF
228. <https://www.parliament.uk/business/committees/committees-a-z/commons-select/science-and-technology-committee/news-parliament-2015/big-data-dilemma-government-response-15-16/>
229. Academy of Medical Sciences & Wellcome Trust (2016). *Summary of a joint workshop to explore the ICMJE proposal on ‘Sharing clinical trial data’*. <http://www.acmedsci.ac.uk/viewFile/58206ac524230.pdf>
230. Horton R (2016). *Offline: Data sharing—why editors may have got it wrong*. *Lancet* **388(10050)**, 1143.
231. SAS & Tech Partnership (2014). *Big data analytics: assessment of demand for labour and skills 2013-2020*. https://www.thetechpartnership.com/globalassets/pdfs/research-2014/bigdata_report_nov14.pdf
232. <http://www.rcuk.ac.uk/research/infrastructure/big-data/>

233. National Data Guardian (2016). *Review of data security, consent and opt-outs*. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/535024/data-security-review.PDF
234. Current examples of successful initiatives exploring the use of 'real world data' include:
- The US Food and Drug Administration (FDA) Sentinel and Mini-Sentinel initiatives in the United States, which allow researchers to monitor the safety of FDA-regulated medical products (<http://www.fda.gov/Safety/FDAsSentinelInitiative/ucm2007250.htm>).
 - The Clinical Practice Research Datalink in the UK that provides anonymised primary care records for public health research (<https://www.cprd.com/intro.asp>).
 - The use of unique patient identifiers – known as the Community Health Index (CHI) number – for data linkage in Scotland (<http://www.scot-ship.ac.uk/overview.html>).
 - UK Biobank, which provides anonymised data and samples from 500,000 volunteers for health research. These data have been linked to national death and cancer registries, and national hospital data electronic record systems for all its participants. UK Biobank is also increasingly linking its data to the primary care records of its participants in England, Wales and Scotland (<http://www.ukbiobank.ac.uk/general-practice/>).
 - International efforts to use administrative health data to inform optimal use of treatments in light of uncertainties in assessment. See Schneeweiss S, et al. (2011). *Assessing the comparative effectiveness of newly marketed medications: methodological challenges and implications for drug development*. *Clinical Pharmacology & Therapeutics* **90(6)**, 777–790.
235. Academy of Medical Sciences & Wellcome Trust (2015). *Use of neuraminidase inhibitors in influenza*. <http://www.acmedsci.ac.uk/viewFile/561595082cd83.pdf>

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Scientific evidence is undermined if it is not trusted by those it hopes to inform.



3. Is scientific evidence trustworthy?

Overview



- Multiple factors contribute to the trustworthiness or perception of the trustworthiness of data, including: the integrity of the process used to derive data; the robustness of the results; the manner in which data are disclosed, communicated and promoted; and perceptions of the individuals or organisations generating the evidence.
- Academics, industry, public research funders, communication outlets, patients and healthcare professionals all have interests in the outcome and use of scientific research, which sometimes lead to actual or perceived conflicts of interest. Interests can be financial (e.g. source of funding) or non-financial (e.g. strong belief in a scientific theory, eagerness for career progression), and both direct or indirect (e.g. a close association with an individual who has a relevant interest). All researchers and research institutions have interests; they are not confined to commercially-funded research and researchers.
- Judgements about the trustworthiness of scientific evidence require information to be available about interests of the individuals and host organisations involved in producing, interpreting and communicating it.
- There should be a clear commitment across the biomedical sector, both in academic and commercial settings, to 'intelligent openness', whereby this information is disclosed in a manner that is accessible, assessable and usable by the intended audience, while respecting privacy and reasonable commercial concerns. Transparency is often not enough for this purpose, particularly when it consists merely of placing information in the public domain without ensuring that it can be accessed or understood by those for whom it may be relevant.
- Competing interests cannot always be avoided, but they can often be managed in ways that give confidence in the results that are generated or scientific advice that is given.
- Sustaining the United Kingdom's (UK's) outstanding performance in biomedical research requires close partnership between academia, industry, the NHS and the regulatory sector. Academic cooperation with commercial partners will be increasingly required for the development of new medicines. We welcome current initiatives by the pharmaceutical industry, publishing sector and biomedical community to encourage best practice and increase openness around trials and collaborations with academia.
- We do not believe that findings from academic research funded by commercial partners, such as the pharmaceutical industry, are compromised when safeguards are in place to ensure the integrity of the research and to check that outcomes are trustworthy and are perceived as such.

Perspectives we heard in our dialogue with citizens, patients and healthcare professionals



- Limited awareness of the range of organisations involved in generating medical evidence, such as academic researchers and regulators.
- A negative view of the pharmaceutical industry as a sector that puts profits before public interest. There was widespread distrust in pharmaceutical companies' capacity to carry out independent research. Their profit motive was also perceived as 'corrupting' academic research conducted in partnership with industry.
- Limited recognition of the time and resources needed to bring a medicine to market, including the impact of failure rates.
- Increased trust in research undertaken in the absence of the profit motive (e.g. by publicly funded research institutes), which was viewed as more rigorous and independent.
- Some scepticism of the involvement of pharmaceutical companies in the generation of medical evidence and limited awareness of regulation that governs the work of these organisations.
- Fears about the lack of transparency that were linked to past instances of pharmaceutical companies concealing information.

The utility of scientific evidence is lessened or undermined if it is not trusted by those it intends to inform. A lack of trust in health research, which is perceived by others as being compromised by ties with industry, was highlighted as a major concern by the Chief Medical Officer for England in her letter to the Academy in which she asked us to consider developing this report. Multiple factors contribute to the trustworthiness or perception of the trustworthiness of data, including the:

- Integrity of the process used to derive data: data will be more trustworthy where they have been generated using the most appropriate methods, obtained ethically and produced in a rigorous research environment (see **section 2.2.1**).
- Reproducibility (robustness) of the results: findings will be more trustworthy when they stand the test of replication and are shown to be reproducible by an independent party (see **section 2.2.2**).
- Manner in which data are disclosed, communicated and promoted by researchers, institutions and funders: results will be more trustworthy when they are reported in a balanced and responsible fashion, when claims about the potential benefits and harms of medicines are not distorted or exaggerated, and when they are presented in the context of previous findings with the necessary research caveats (see **Chapter 4**).
- Perceptions of the individuals or organisations generating the evidence, including motive and the prospect of profit: the trustworthiness of research findings will be undermined if those generating the evidence are not perceived as trustworthy (see **sections 3.1 to 3.4**).

In recent years, there have been efforts, in part driven by government, to increase transparency, openness and accountability across sectors.²³⁶ While such efforts are commendable, there needs to be a move towards 'intelligent openness', where data are not simply disclosed but are accessible, assessable and usable by the relevant audiences.²³⁷ 'Intelligent openness' about the factors described above is needed to enable informed judgements to be made about the trustworthiness of scientific evidence, which is essential if it is to achieve greater prominence. In this chapter, we consider in turn the implications of 'intelligent openness' for the publication of research, and for the declaration and management of interests.

3.1 Implications of ‘intelligent openness’ for the publication of research

There should be a clear commitment within the biomedical community to ‘intelligent openness’ of research and data, as far as is compatible with privacy and reasonable (declared) commercial interests (e.g. a short period of confidentiality to allow a patent to be filed or information related to a manufacturing process or other non-clinical information relevant to competitors). This should not be taken to allow clinical data to be withheld. The Academy supports the principles of the AllTrials campaign, which calls for all clinical trials, whether conducted by academia or commercial partners, to be registered and their full methods and summary results reported.^{238,239} We welcome the requirement by some journals that trials are registered as a condition of publication, and urge all journals to adopt such a policy.

A culture shift toward ‘intelligent openness’ will require concerted efforts from across the biomedical community. We welcome ongoing efforts across the sector and encourage stakeholders to make further progress, including:

- Researchers in academia and industry, and journals committing to publishing rigorous research whether or not results are positive, ‘negative’, null or inconclusive,²⁴⁰ and considering providing lay summaries or patient perspectives (e.g. the BMJ initiative²⁴¹) so that the results are more widely accessible and intelligible. It is unacceptable for any investigator to deliberately withhold data, particularly adverse event data, as this could result in harm to patients (see **Box 10**). Similarly, it is also unacceptable for accusations of malpractice to be made or implied without supporting evidence.
- Those that fund research, including industry, contributing to the funding of infrastructure for data archiving and curation to support ‘intelligent openness’ efforts. In developing these, funders should look to good practice examples.^{242,243}
- Universities and research institutions supporting staff in their ‘intelligent openness’ efforts. The Higher Education Funding Council for England (HEFCE, relevant functions expected to be assumed by Research England in the future), and its counterparts in the devolved nations, can perform an important role in galvanising change by requiring that institutional ‘intelligent openness’ initiatives are reflected in Research Excellence Framework (REF) environment statements in the next REF process (see also **Recommendation 3**). In light of the Higher Education Research Bill, we anticipate the establishment of UK Research and Innovation (UKRI) as an umbrella body to coordinate research funding.²⁴⁴ Once in place, UKRI should play a key role in stimulating change and coordinating many of our recommendations aimed at Research Councils.

Recommendation 5: Publication of research findings



We support ongoing initiatives to enhance the dissemination of and access to research findings, including greater publication of rigorous results regardless of outcome, reporting of findings in more accessible formats, trial registration, and infrastructure funding for data archiving and curation. To complement these efforts, we recommend that:

- Universities, research institutions** (led by Universities UK) and **industry** (led by the Association of the British Pharmaceutical Industry, ABPI, and the BioIndustry Association, BIA) support their staff in academia and industry in their efforts towards increased openness by providing appropriate incentives, rewards and recognition, and systems to enable this, such as those outlined in the Academy’s report, ‘Improving recognition of team science contributions in biomedical research careers’.²⁴⁵ These organisations should recognise clear and accurate communication of research findings as an explicit criterion for career progression, promotion and reward.

- b. The **Higher Education Funding Council for England** (HEFCE, relevant functions expected to be assumed by Research England in the future) and its **counterparts in the devolved nations** galvanise change by requiring that institutional ‘intelligent openness’ initiatives are reflected in REF environment statements in the next REF process, in addition to the reproducibility efforts described in **Recommendation 3**.
- c. **Those who fund research**, including **industry**, incentivise the communication of results for the projects that they support by requiring in applications an effective plan for the communication and ‘intelligent openness’ of results. Researchers would need to demonstrate that they had adhered to these as a condition of future funding.

Box 10. Rofecoxib and increased cardiovascular risk²⁴⁶

Rofecoxib (trade name: Vioxx) was developed by Merck for the relief of signs and symptoms of osteoarthritis, the management of acute pain and the treatment of menstrual pain.²⁴⁷ It was introduced in 1999 as a safer alternative to other pain-relieving drugs, such as the nonsteroidal anti-inflammatory drug naproxen. In 2000, Merck published results of the Vioxx Gastrointestinal Outcomes Research (VIGOR) study, which showed rofecoxib-treated patients had fewer gastrointestinal side effects than naproxen but a four- to five-fold increased risk of myocardial infarction (heart attack).²⁴⁸ The authors of the study claimed that this apparent increased risk was due to the cardio-protective effects of naproxen rather than a harmful effect of rofecoxib, although further research was needed. In 2004, Merck voluntarily withdrew rofecoxib from the market following its Adenomatous Polyp PRevention On Vioxx (APPROVe) study, which showed an increased risk of myocardial infarction and stroke in rofecoxib-treated patients compared to placebo.²⁴⁹ Before its withdrawal in 2004, over 80 million patients had taken rofecoxib and sales had reached US\$2.5 billion in 2003.²⁵⁰ It was used by about 400,000 people in the UK, with over 2.1 million prescriptions for rofecoxib dispensed in England at its peak in 2003.^{251,252}

Concerns were raised about the integrity of the data on adverse cardiovascular events published in the VIGOR study,^{253,254} although the authors of the study defended their analysis.²⁵⁵ Merck was also criticised more widely for the way it dealt with assessing the potential cardiovascular risk of rofecoxib,^{256,257} for example:

- Not designing trials to specifically assess cardiovascular risk, despite the potential cardiovascular risks being noted in a study it sponsored published in 1999;²⁵⁸ the US Food and Drug Administration (FDA) was also criticised for not compelling Merck to undertake these studies.^{259,260}
- Reporting that the increased cardiovascular risk only became apparent after 18 months of rofecoxib use in the APPROVe study,²⁶¹ a statement that was later withdrawn after Merck admitted the statistical approach used was incorrect.²⁶²

Meta-analyses have suggested that evidence that rofecoxib increased the risk of heart disease was available as early as 2000 and the drug should have been withdrawn from the market earlier,^{263,264} although Merck has disputed some of these findings.²⁶⁵

3.2 'Intelligent openness' in declaring and managing interests

Commitment to the generation and use of reliable evidence to improve people's health is a matter of common, rather than differing, interest across the healthcare sector.^{266,267,268,269} However, the interests of those involved in research are not uniform. They may diverge and sometimes conflict (see **Box 11**). The management of interests is an area that has come under increased scrutiny and – as our workshop on 'Conflicts of interest', public dialogue, and surveys of general practitioners (GPs) and the general public attest – remains a key concern for many stakeholders.^{270,271,272}

Box 11. Examples of potential conflicting interests of those involved in research across the healthcare sector

- Patients have interests in receiving care and their desire for access to novel, effective treatments may be in conflict with the need to gather information on a large enough scale to produce reliable results (similar interests might also exist in academia and industry).
- Clinicians may seek to try innovations before the evidence has been fully assessed and without the monitoring that will be needed to ascertain whether they are successful.
- Researchers may have staked their reputations on the validity of a hypothesis and be reluctant to accept that it is disproved or not substantiated.
- Research institutions have reputations to protect and may be reluctant to accept that some projects failed or were inconclusive.
- Research funders, whether or not they invest for profit, seek to ensure that their investments represent good value and may be reluctant to accept that promising lines of inquiry have failed or proved inconclusive.
- The media and publishers (including specialist publications such as journals) seek to increase readership and sell copies of their publications, and may publish – and in some cases hype – findings that are not sufficiently robust or reliable.
- Commercial partners, such as the pharmaceutical industry, need to ensure a return on investment in new treatments. We heard in our dialogue activities that interests relating to links with commercial partners are of particular concern and we therefore explore them further in **section 3.3**.²⁷³

In alignment with NHS England's recent description, we define conflicts of interest as:²⁷⁴

'A set of circumstances by which a reasonable person would consider that an individual's ability to apply judgement or act, in the context of [his/her work] is, or could be, impaired or influenced by another [competing] interest they hold.'

While an interest (see **Box 12**) in itself does not inherently present a conflict or a competing interest (as these will be context-dependent), 'intelligent openness' about interests is needed to inform judgements about the trustworthiness of evidence. **Online annex E** provides further information on competing/conflicting interests.²⁷⁵

Box 12. Definition of 'interests'

As described by NHS England, 'interests' can arise in a number of different circumstances:

*'A material interest is one which a reasonable person would take into account when making a decision [...] because the interest has relevance to that decision.'*²⁷⁶

Interests can be:

- **Financial:** where an individual may get direct financial benefit²⁷⁷ from the consequences of a decision they are involved in making. There are different types of financial interests, such as funding for independent research and personal payments (e.g. consultancy fees, payments for speaking at meetings or sitting on advisory panels), among others.
- **Non-financial:** where an individual may obtain a non-financial benefit (either professionally or personally) from the consequences of a decision they are involved in making, such as increasing their professional reputation or promoting their professional career.
- **Indirect:** where an individual has a close association²⁷⁸ with another individual who has a financial or non-financial interest and would stand to benefit from a decision they are involved in making.

Competing interests cannot always be avoided, but they can be managed in ways that can enhance confidence in the results that are generated. For instance, robust research design helps minimise the risk that competing interests undermine the reliability of evidence. A good example of this is the use of 'blinding' techniques, which ensure that participants and researchers in clinical trials cannot tell who is receiving which treatment, thereby reducing the risk that prior expectations influence the results.

All those involved in the research process have a duty to recognise, publicise and manage interests, thereby ensuring the integrity of the research process. This includes researchers in academia and industry, journalists and journal editors, and funders. Organisations involved in the research process should develop frameworks for declaring and managing interests.

We believe that the overarching principles for managing and declaring interests are that all those involved in research and its communication should:

- a. **Identify** interests, particularly those that may present real or potential conflicts in a given context, and so may undermine the confidence in the evidence on which patients, clinicians and policymakers need to be able to rely when taking decisions.
- b. Take steps to **mitigate** the risks that these interests may impair the quality or undermine the credibility of the evidence being generated or relied upon, for example by minimising avoidable conflicts.
- c. **Be open** about the interests and any mitigating steps taken so that those who use the evidence can assess whether it can be trusted. Potential competing interests that are effectively managed should not undermine the credibility and trustworthiness of the research.

Recommendation 6: Developing frameworks for declaring and managing interests



To facilitate greater declaration and management of interests, we recommend that:

- a. **Research Councils** and **Universities UK** (for academic research), **trade bodies** (for commercial research), and the **media regulators** (including the Independent Press Standards Organisation, IPSO, and the Independent Monitor for the Press, IMPRESS) develop frameworks for declaring and managing financial and non-financial, direct and indirect interests that fit the needs of staff in their sectors. Where these are already in place, they should be reviewed in light of the principles we outline in **Online annex F**.²⁷⁹ These frameworks should provide a protective environment, where interests can freely be declared and discussed to ensure that appropriate safeguards can be put in place should a competing or conflict of interest be identified.
- b. The **International Committee of Medical Journal Editors'** (ICMJE) declaration of interests is adopted as a standard format for declaring interests across the sector.²⁸⁰ In the spirit of 'intelligent openness', organisations should use this standardised declaration to establish publicly accessible registers of interests (for example on organisational websites).

3.3 Commercial partners: involvement in the development of evidence about medicines and partnerships with academia

3.3.1 *Is the widespread mistrust in commercial involvement in the development of evidence about medicines justified?*

As highlighted in our public dialogue and surveys, there is widespread distrust of commercial involvement in the development of evidence about medicines.^{281,282,283,284} It should be noted that there is evidence to suggest that patient groups tolerate commercial involvement more highly than healthy groups,^{285,286,287} and that it is the prospect of excess profit (as opposed to simply the prospect of profit) that causes public concern.²⁸⁸ Commercial pressures have the potential to influence what research is carried out, how it is carried out, whether and how it is disseminated, and the analysis of evidence in decision-making. With increasing collaborations between academia and industry, there are concerns that these pressures may also influence those working within the academic sector. These concerns are not exclusive to biomedical research; similar anxieties have been voiced in other sectors, for example the involvement of industry in research about obesity,^{289,290,291} genetically modified crops²⁹² and climate change.^{293,294}

We recognise that there have been some serious cases of poor practice in the past, where commercial considerations have led to the promotion of harmful medicines, or of medicines that were more expensive but not more effective than the standard treatment.²⁹⁵ However, the solution is not to treat all industry-linked research as flawed, which would damage drug development. Rather, steps should be taken to prevent such cases from occurring in the future.

There is evidence that published clinical trials are statistically more likely to report a favourable result if they are sponsored (i.e. funded and managed) by industry or if they are undertaken by researchers that have a declared interest linking them with industry.^{296,297,298,299,300,301,302,303} This association between favourable results and industry sponsorship may represent poor practice by the researchers and organisations involved as a result of actual and unconscious bias, or it may be an artefact. For example, Flacco *et al.* (2015) provide an explanation based on pharmaceutical practice.³⁰⁴ Pharmaceutical companies invest in preliminary trials (e.g. Phase I and Phase II studies) and might carefully decide to fund only those Phase III trials that are more likely to yield a positive outcome. With insight from clinicians, patients and other experts, they might decide

to abandon trials that are less likely to succeed in terms of patient recruitment and retention. They might also choose more cautiously the outcomes, comparators and other design features, resulting in more favourable outcomes, or choose not to invest resources in publishing trials with less positive outcomes, as resources are redirected towards developing other promising targets if medicines fail in trials. Understanding whether associations between clinical trials sponsored by industry and the publication of favourable results represent bias or have a justifiable rationale can only be achieved if there is adequate 'intelligent openness' in the research process.

We agree with the Association of the British Pharmaceutical Industry (ABPI) that progress can nevertheless be made to prevent poor industry practice that has occurred in the past.³⁰⁵ Although we focus on research in this report, it is important to note that poor practice in company departments that are not concerned with research (e.g. pricing and marketing) can also tarnish the reputation of industry research and collaborations, and the reputation of the industry more widely.³⁰⁶ We also acknowledge that perverse incentives in academia – such as rushing to finish and publish research, self-promotion and tough competition for funding and publication in prestigious journals – can lead and sometimes have led to poor-quality research practices.^{307,308,309} Further, failure to publish clinical trials is also an issue in academia.³¹⁰ Indeed, researchers who have worked in academia and industry have argued that checks and balances on methodological integrity are generally more rigorous in industry than across academia, largely because of the strict regulatory environment.^{311,312,313}

3.3.2 What mechanisms have been established to improve research standards in industry?

The majority of studies into the effect of sponsorship by, or links with, industry in the findings cited above encompass research that was undertaken before recent initiatives to support enhanced openness around clinical trials were implemented. We welcome current initiatives aimed at ameliorating the situation by increasing openness around trials and collaborations with academia, including actions taken by the pharmaceutical industry to:

- Establish databases providing access to de-identified patient-level data, where feasible.^{314,315}
- Assure better openness of clinical trial results by developing best practice guidelines for sharing clinical trial data.^{316,317,318,319,320}
- Increase openness around funding of research undertaken by healthcare professionals or healthcare organisations via the ABPI 'Disclosure UK' database, which details 'transfers of value' (payments made to professionals for activities such as consultancy and advisory boards, speaker fees and sponsorship to attend meetings) from the pharmaceutical industry to healthcare professionals and healthcare organisations.³²¹ We understand that due to data protection regulation, healthcare professionals and organisations cannot be mandated to disclose their transfers of value on the 'Disclosure UK' database. However, we encourage healthcare professionals and healthcare organisations, including non-governmental organisations, charities and patient groups, to agree to their transfers of value being disclosed on this database. We note some pharmaceutical companies have chosen not to fund healthcare professionals and healthcare organisations that do not agree to their funding being disclosed. We also commend those GPs who have voluntarily declared their interests on the 'Who pays this doctor?' website.³²²

Registration of clinical trials and publication of summary reports on recognised, open and searchable databases also make the process more transparent.^{323,324} Recent initiatives aimed at tracking data-sharing efforts on clinical trial websites and transparency about outcomes in clinical trials demonstrate the desire for external scrutiny.^{325,326} Funding bodies and research organisations are increasingly requiring trial registration, which is a legal requirement for trials on some medicinal products in the European Union (EU), United States (US) and five other countries.^{327,328} The Health Research Authority in England expects all clinical trials to be registered as a fundamental best practice standard and has made this a condition of ethics approval for trials since September 2013.³²⁹ The publishing sector has supported trial registration, with the International Committee of Medical Journal Editors (ICMJE) requiring trial registration as a condition of consideration for publication since 2004,³³⁰ and has developed best practice guidelines to enhance the reporting of clinical trials.^{331,332} As mentioned previously, we support the policy whereby journals publish findings only from trials that have been appropriately registered, and believe that all journals should adopt such a policy. There is, however, evidence that this policy is not being enforced, even within ICMJE member journals; there therefore needs to be continued focus on compliance with these requirements.^{333,334,335,336}

Independent governance structures exist to further assure the integrity of clinical trials. This structure includes peer-review, independent ethical review and regulatory overview, including Good Clinical Practice inspections

conducted by the Medicines and Healthcare products Regulatory Agency (MHRA) in the UK.³³⁷ Many pharmaceutical companies also adhere to a voluntary code of practice put in place to ensure high standards across the sector.³³⁸ In the UK, this is regulated by the Prescription Medicines Code of Practice Authority.³³⁹

The full effect of these efforts has yet to permeate the research system and further research will be required to assess the impact of these initiatives in the future, including areas where further progress is still needed. As discussed in **section 3.3.5**, it is also important that these efforts are better publicised to allay undue concern.

3.3.3 The benefits of collaboration between academia, industry and other sectors across the biomedical sciences

The UK has an outstanding record in biomedical research, which supports the development and evaluation of new and existing medicines. Key to sustaining this performance is close partnership working between academia, industry, the NHS and the regulatory sector. The charitable sector also collaborates with industry to ensure that new medicines and interventions are fit for purpose and deliver maximum benefit to patients and wider society.³⁴⁰ Each sector plays a vital role in the research landscape and brings unique but complementary strengths to the diverse partnerships.

Partnerships between academia and commercial partners are particularly important in preclinical drug discovery, where different perspectives, skills and technologies in academia and industry complement each other to facilitate the conversion of science into innovative products (see **Box 13**). Recent years have seen a move towards open innovation and industry externalisation of research and development. Such collaborative research models now involve genuine partnerships, for example involving industry providing access to data (e.g. biomarkers, compounds) or state-of-the-art technologies to academics and other experts.³⁴¹ Two examples include 'Open Targets', a public-private initiative to generate evidence on the validity of therapeutic targets, and the 'Tres Cantos Open Lab', where industry provides access to expertise and resource to support research into treatments for the developing world.^{342,343} Such collaborations will be increasingly required for the development of new medicines, not least because research and development in healthcare is expensive and costs can often be met only by industry, whose resources far exceed the money available from charities and governments.³⁴⁴

Box 13. The development of a new medicine achieved through industry/academic collaboration

The case studies below demonstrate some of the synergies between academia and industry, with academia capable of pursuing innovative and potentially risky new research avenues, and industry providing expertise and funding to successfully take forward promising new products through clinical trials to market.

The development of abiraterone as a novel treatment for prostate cancer

Prostate cancer is stimulated by the production of testosterone. In the 1990s, castration (removal of testicles) and hormone therapy were commonly used to stop testosterone production but often failed to eradicate the tumour. Scientists at the Institute of Cancer Research (ICR) devised a chemical – abiraterone – which specifically and irreversibly inhibited the enzyme CYP17, important in testosterone synthesis in the different locations in the body where it is produced.^{345,346}

Through subsequent collaborations with Boehringer Ingelheim, Cougar Biotechnology and Johnson & Johnson (which acquired Cougar Biotechnology), abiraterone was shown to be safe and to cause tumour shrinkage and a decline in prostate-specific antigen levels in treated participants.^{347,348} Abiraterone was approved for use by the FDA in 2010, followed by the European Medicine Agency (EMA) in 2011. Abiraterone is now used in the treatment of patients with advanced prostate cancer who have stopped responding to other types of hormone therapy. Worldwide sales of abiraterone amounted to US\$2.75 billion in 2011–2012.³⁴⁹ The drug was approved for metastatic castration-resistant prostate cancer before chemotherapy by the National Institute for Health and Care Excellence (NICE) in 2016.³⁵⁰

Tomudex for chemotherapy in advanced colorectal cancer

Scientists at the ICR developed thymidylate synthase (TS) inhibitors for the treatment of colorectal cancer in the late 1970s. The team discovered a highly specific inhibitor, CB3717, which had substantial clinical activity but gave rise to serious side effects.³⁵¹ The ICR collaborated with ICI Pharmaceuticals (which later became Zeneca Pharmaceuticals) leading to the discovery of ZD1694 (trade name: Tomudex) a specific inhibitor of TS. Tomudex was launched in 1998, manufactured by AstraZeneca and records more than US\$100 million in annual sales.³⁵²

Carboplatin: chemotherapy treatment for multiple cancers

Researchers at Michigan State University discovered cisplatin, a chemotherapy agent used to treat a wide range of cancers, including lung and ovarian, in 1972. However, cisplatin is associated with a number of unpleasant side effects.³⁵³ A second-generation drug, carboplatin, was discovered by the Michigan State team.³⁵⁴ Carboplatin was then developed at the ICR in London, and the pharmaceutical company Bristol-Myers Squibb gained FDA approval for carboplatin under the brand name Paraplatin in March 1989. It became the gold standard treatment for ovarian cancer, as well as being used to treat many other cancers.³⁵⁵

Temodar/Temodal: chemotherapy treatment for brain tumours

A research team at Aston University in Birmingham discovered the chemotherapy agent temozolomide, effective in the treatment of brain tumours, building on work dating from the 1970s. Phase I and Phase II trials were managed by Cancer Research UK's Drug Development Office.^{356,357} The charity's commercial and development arm, Cancer Research Technology, licensed the drug to the pharmaceutical company, Schering-Plough. Phase III studies found that temozolomide in combination with radiotherapy resulted in a significant increase in survival with minimal side effects.³⁵⁸ The drug, marketed as Temodar in the US and Temodal in Europe, was approved by the FDA and EMA in 1999. In 2008, the medicine made US\$1.02 billion for Schering-Plough (now Merck), achieving blockbuster drug status.³⁵⁹

There are a number of reasons why we believe it remains essential that industry plays a central role in clinical trials:

- There is valuable knowledge and expertise in industry research teams, both in conducting clinical trials and in knowledge of the medicine under investigation, accrued from many years of development. In the interests of patients, this should be exploited.
- As for all applicants, when applying for marketing authorisation, regulators expect industry to have complete knowledge of all trial data submitted as part of their portfolio – from design through to analysis and reporting. This means that industry has to have intimate knowledge of all design and analysis features of the research they are submitting, limiting the extent to which clinical trials can be undertaken independently from industry.
- Many clinical trials, especially Phase III trials, are multi-national, multi-centre studies, the coordination of which can be achieved more easily/effectively by industry with international reach.
- Due to the resources involved, the vast majority of licensed medicines are developed by, or in association with, the pharmaceutical industry.³⁶⁰ Without industry trials, it is likely that the number of medicines that are licensed will decrease, to the detriment of patient health.

Given the concerns around the role of commercial partners in clinical research, we focus in **Online annex F** on how the overarching principles for identification, mitigation and management, and openness of interests should be applied to the development of evidence related to the use of medicines in academic clinical trials funded by a commercial partner.³⁶¹ These high-level guidelines are designed to foster more trustworthy collaborations between academia and industry. The biomedical research community, including universities, research institutions, commercial partners and funding bodies, will need to work together to develop clear guidance on how these principles should be implemented in practice. We welcome NHS England's recent guidance on 'Managing conflicts of interest in the NHS' and the ABPI 'Disclosure UK' database, described above.^{362,363,364}

3.3.4 Academic expertise on advisory committees

Another area of concern is academic experts with industry links providing guidance about medicines on advisory committees.³⁶⁵ Researchers who have engaged with companies or patient groups may be regarded as having competing interests (regardless of the nature of the engagement), but they will also be those with the greatest expertise in a medical condition or particular treatment. Automatically excluding these experts from providing advice on the potential benefits and harms of medicines will have a negative impact on evidence-based policymaking. We recommend that attempts to manage such interests should be sought as a first recourse. Expertise should be excluded only where competing interests cannot be managed in a way that maintains the objectivity of the decision-making process. In certain circumstances, it might be appropriate to incorporate expertise in an advisory rather than a decision-making capacity. In others it might be appropriate for members to have no industry links. For example, members of the Commission on Human Medicines (CHM) provide advice directly to the Licensing Authority for medicines and for this reason they are not permitted to hold any current personal interests in the pharmaceutical industry.^{366,367} The CHM abides by a detailed code of practice and is transparent about members' interests in its annual report.³⁶⁸

3.3.5 Portrayal of industry links in the media

Academic researchers' links with industry have been used, particularly in the media, as a proxy for bias or as a means to question their credibility or that of their research.³⁶⁹ We believe that the fact that academic research is sometimes funded by industry should not be taken to show that it is automatically compromised, and that safeguards – such as those described in **Online annex F**³⁷⁰ – can be put in place to ensure the integrity of the research and thereby the trustworthiness of the outcomes.

We urge journalists to evaluate research in terms of how far it meets the best practice guidelines outlined in **Recommendation 7**, rather than assuming that research with industry funding is inevitably compromised. They should also be aware that accusations of conflict of interest are routinely made against industry-funded research by those who have their own competing interests (e.g. making a career as a commentator on research, or promoting an alternative treatment approach). We encourage more effective engagement with citizens and healthcare professionals on the value of industry–academia collaborations and the regulatory systems that govern the development of medicines (that all parties must abide by, including industry) to allay concerns and rectify any misconceptions.

Recommendation 7: Developing best practice guidelines for academia–industry relationships



Informed by, but not reliant on, the development of the frameworks described in **Recommendation 6**, we recommend that **funding bodies, academia** (led by Universities UK) and **industry** (led by the ABPI and the BioIndustry Association, BIA) work together to develop clear guidelines that define best practice in terms of the relationship between academia and industry and the management of competing interests that might arise. In developing these guidelines, these organisations should consider how the following key principles are implemented when evidence related to the use of medicines is developed in academic clinical trials funded by a commercial partner (full details in **Online annex F³⁷¹**):

- **Research funding:** All funding from commercial partners should be disclosed and governed by the institution's policies for such funding, which should be informed by the best practice guidelines we recommend are developed. Academic researchers should be aware that other personal payments such as consultancy fees, and payments for speaking at meetings or sitting on advisory panels could raise potential concerns that their research is biased and untrustworthy. There should be greater openness about how the research funding is distributed within the institution (e.g. the NHS Trust or research department).
- **Study design:** Academic and commercial partners should work together to design studies in a way that minimises biases as far as practically possible. All protocols should be made publicly available on completion of the research to allow for independent analysis of the design and methods, and researchers should be transparent in publications about how the study was designed. Consideration should be given as to whether study designs could benefit from public or patient involvement and external peer-review.
- **Trial registration:** All clinical trials should be registered on a recognised, open and searchable trials register with a summary of the trial protocol, before the first participant is recruited. We strongly encourage the registration of observational epidemiological studies that explore the effects of treatments.
- **Contracts:** All contracts between academia and industry should be made publicly available (with personal and commercially sensitive information redacted) and should provide clarity on specific items, including data access and holding, details of funding and to whom it is paid, and conditions for data analysis and publication. All contracts should also include a requirement to disclose competing interests.
- **Data holding and access:** Data should be managed responsibly, in a way that protects confidentiality for justifiable commercial, privacy, safety and security reasons. Contracts should clearly specify who holds the data, what the data can be used for, who they can be used by and with whose agreement, and who can access the data and by what means, providing justification for any limits to data access.
- **Data analysis:** Academic and commercial partners should work together to ensure that data analysis is conducted in a way that minimises biases as far as is practically possible. They should also be transparent about the analytical process in their publications. Data analysis should be undertaken by statisticians independently from the study teams, monitored by an independent Data Monitoring Committee (DMC) and auditable.³⁷²
- **Publication of findings:** Neither partner should restrict the publication of findings, which should be published in full regardless of the outcome. A summary of results should be made publicly available on the database where the trial is registered within one year of completion of the trial, or within the timelines agreed if a deferral has been granted. Where applicable, the full Clinical Study Report, or its equivalent in non-commercial settings, should also be made publicly available. Where appropriate consent has been provided, de-identified individual patient-level data should be made available to researchers on request, with a commitment that no reasonable request would be refused.

3.4 Conclusions

'Intelligent openness' about the robustness and reliability of results (see **sections 2.2.1** and **2.2.2**), the way in which research findings are disclosed and communicated, and the interests of the individuals or organisations that generate the evidence, is required if those that intend to use the evidence are to make informed judgements about its trustworthiness. Increased openness has the potential to engender trust in those generating scientific evidence and could be monitored by dialogue and surveys such as those we conducted at the outset of our project. Concerns about selective publication of evidence in the case of Tamiflu undermined trustworthiness in the body of evidence on which decisions about the stockpiling of this drug were made. If implemented, our recommendation about publication of research findings (**Recommendation 5**) could prevent similar situations occurring in the future.

We recommend that the biomedical community as a whole commits to 'intelligent openness', of both research findings and interests. This will require a significant culture shift, which has long been called for but is now more than ever vital to instil. Exercises such as the REF and industry taking the lead on driving an open culture can galvanise change, but it will ultimately only be realised with concerted effort across the sector, from researchers recognising the need for greater openness to organisations establishing the relevant structures to support them in their efforts.

It became clear during our evidence-gathering efforts that the management of interests, especially those related to commercial partners, remains of key concern for many stakeholders, not least patients and the public. Yet collaboration between academia and industry will increasingly be needed to maintain the UK's outstanding record in biomedical research, which contributes to the development and evaluation of new medicines, making it essential to address this issue.

To allay concerns, we recommend that frameworks for declaring and managing interests are established as well as guidelines to define best practice in terms of the relationship between academia and commercial partners. Our case studies outline several instances where consideration of the potential benefits and harms of medicines has been influenced by complex issues surrounding the trustworthiness of those conducting the research. Examples include our case studies on hormone replacement therapy, Tamiflu and statins. The steps towards greater declaration and management of interests outlined in our recommendations (**Recommendations 6** and **7**) would help mitigate such issues in the future.

Informing the public's perceptions of the relationship between academia and commercial partners is critical. We encourage more effective engagement with patients, the public and healthcare professionals about the regulation of medicine development and of the value of academia–industry research. Together with a commitment to greater openness, there is the prospect of influencing the perception of industry in a positive manner. If effected, this would have done much to alleviate many of the concerns related to statins and Tamiflu for example, as illustrated in our case studies. Without such appreciation, there is a risk that the availability of new and use of existing medicines may be unnecessarily compromised.

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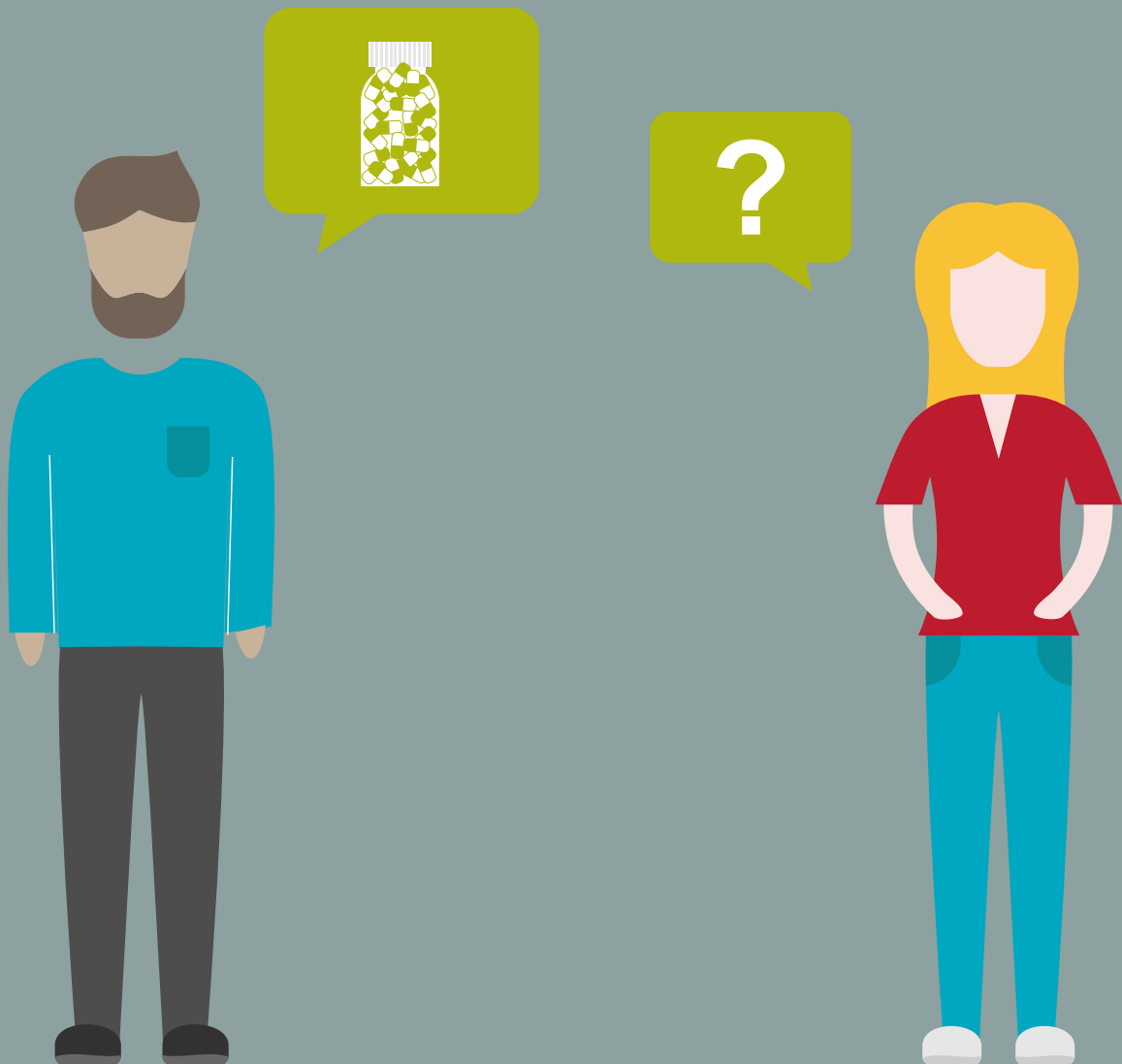
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Communication should not be to persuade or coerce, but to help inform decisions.



4. How can we most effectively communicate scientific evidence?

Overview



- Scientific evidence about the potential benefits and harms of medicines must be presented in a clear, accessible and usable way so that people can make sense of it. Currently, much evidence is widely regarded as falling short of these requirements and consequently initiatives are underway to address this.³⁷³
- The content and readability of patient information leaflets should be improved. They should include a balanced appraisal of the benefits and harms of medicines.
- NHS Choices, which is already trusted and used by many patients and healthcare professionals, should be established as a central repository of clear, accurate, up-to-date and evidence-based information on the potential benefits and harms of medicines.
- Healthcare professionals should effectively communicate the evidence around the benefits and harms of medicines, risk and uncertainty. They should be supported by decision aids, algorithms and other tools that facilitate conversations around treatment approaches. The development of such tools should be prioritised and informed by robust evidence, the source of which is open to scrutiny.
- All parties involved in the generation and communication of evidence, including researchers, press officers, journalists and other communication experts, have a shared responsibility to ensure the information conveyed to the public is accessible, accurate and balanced, but not oversimplified. To that end, a 'traffic light' system grading the relevance of research to clinical application and the robustness of the study should be developed, as well as codes of practice for press officers and researchers.
- Literacy and numeracy levels in many medical information sources are inappropriate for the general public. In parallel with ensuring communications are as accessible and intelligible as possible, we need to ensure patients and the public are better equipped to make full use of medical information sources.
- We support shared decision-making as a model of good practice for evidence-based decision-making during consultations.

Perspectives we heard in our dialogue with citizens, patients and healthcare professionals



- Concerns from patients and the public that they are not taught, nor are they equipped, to question advice from healthcare professionals and the underpinning evidence on which treatments are prescribed.
- Poor understanding of statistics by patients and the public (but also by some healthcare professionals).
- The lack of relevance of statistical evidence on populations to patients' individual decisions.
- The paucity and poor communication of information about the regulatory process, the research ecosystem and the role that medical evidence plays within that system, which ultimately undermines trust in the drug development system and in the safety and efficacy of drugs.
- Time pressures on healthcare professionals to communicate evidence during a consultation. The need to encourage, support and give the necessary tools to healthcare professionals to tailor medical evidence to the different contexts they encounter.
- The need for balanced reporting of the consensus on the best interpretation of the evidence, rather than presenting the extremes of disagreement.
- The role of healthcare professionals as 'filters' and 'translators' of complex information. Most of the public participants suggested they would not be confident enough to assess this information themselves and rely on a trusted healthcare professional to communicate this to them.
- Requirement for better access to medical evidence that can be understood by the lay person, and better signposting to reliable information sources. The need to put pressure on the media and websites promoting non-evidence-based treatment approaches.
- Poor drug information leaflets, which were heavily criticised for being impenetrable and in some cases unreadable.
- The concern from both patients and healthcare professionals about the plethora of information available and the challenge of making sense of it.

Individuals – including patients, citizens and healthcare professionals – have a right to reliable and accurate information on the potential benefits and harms of medicines to make informed healthcare decisions.³⁷⁴ This information needs to be trusted (we consider the trustworthiness of evidence in **Chapter 3**) and relevant.

The vast majority of the evidence that is produced about a medicine presents an aggregate effect (i.e. an average effect across a group of individuals). Even with the most robust evidence, there will always be a degree of uncertainty as to how the evidence of benefits and harms might apply to a specific individual, what the outcomes might be, and how likely these outcomes might be. Where there is uncertainty, it is particularly inappropriate to ignore the patient's perspective, as patients will vary in their willingness to accept uncertainty or risk. Further, we heard that there was a widespread assumption that medicines either worked or did not, and that healthcare professionals should be able to tell patients with certitude whether a treatment will work for them. However, scientific evidence does not always provide clear answers, and healthcare professionals can, at best, only give a probability based on the evidence and the patient's particular circumstances. There should be more openness in our communication with the public about

the uncertainty of scientific evidence, with a move to a shared recognition with the patient that individual outcomes are hard to predict and therefore that a period of 'trial and error' and monitoring of drug use should be expected. This thinking forms the basis of the New Medicines Service run by pharmacies in England, whereby patients that are prescribed new medicines to treat certain long-term conditions are eligible to receive additional help and advice about their medicine from their pharmacist.³⁷⁵

Accurate reporting of scientific evidence in the media was highlighted as one of the most important challenges during our evidence gathering. Sensationalist reporting that emphasised conflicts without weighing up the evidence did much to fuel the statins controversy, for example. We first address how to enhance the communication of scientific evidence about medicines more broadly before focussing on its reporting in the media.

4.1 Providing clear and accurate information to patients

Our 'Communicating evidence about medicines' workshop highlighted the importance of openness, honesty and clarity as a basis for communicating evidence about medicines to support informed choice. It also indicated the need for effective communication to embrace what might happen and how likely it is to happen.³⁷⁶ The aim of effective communication should not be to persuade or coerce individuals, but to enable them to come to an informed decision. Good communication techniques and initiatives exploring how to effectively present information on the benefits and harms of medicines that were discussed at the workshop are presented in **Boxes 14** and **15**.

Box 14. Good communication techniques identified throughout our project³⁷⁷

- Users, including patients and the public, should be involved in co-designing information products to identify needs and preferences, and provide feedback.
- Absolute risk figures should be presented and appropriately contextualised so that users can make sense of the numbers presented.
- Tables and graphics should be used, while vague qualitative terms (e.g. 'low risk') should be avoided.
- Layering of information (summaries followed by increasingly detailed accounts) can help to guide audiences through complex issues.
- Breaking information into smaller clearly differentiated sections, the use of subheadings, font choice and the use of colour to emphasise key points, can enhance understanding and readability.
- Web and digital tools offer compelling interactive ways of presenting information; they should be explored to provide more personalised communication without becoming unnecessarily complex.
- Communication of information should be based on a distillation of all relevant information. That based on incomplete information risks misinforming patients and the public.
- Information on baseline risk of the individual (if possible) compared to population averages should be available to enable correct framing of any risk reduction or treatment benefit.
- The potential benefits and harms of medicines should be considered together, rather than in isolation.

- Absolute risk reduction, generally expressed in terms of natural (or expected) frequencies, should be presented where possible, as these are best understood by patients and the public. ‘Numbers needed to treat’ can be confusing to individuals but can be effective at conveying the limited proportion of people who benefit from most treatments. Relative risk reduction tends to exaggerate benefits and harms, but is more generalisable as it does not depend on a specific time frame and baseline risk (e.g. ‘medicine x reduces risk by one-third’). Relative risks should not be used on their own, but only to show the basis for an individual’s absolute change in risk.
- Both positive and negative framing should be used. For example, when stating that 99 in 100 people will not suffer from a disease, the opposite framing of 1 person in 100 will, should also be highlighted.

Box 15. Initiatives and examples exploring improvements to available information on the benefits and harms of medicines

- The European Union (EU) Innovative Medicines Initiative PROTECT project aims to improve monitoring of benefits and harms of medicines and early detection of adverse drug reactions in Europe using different data sources.³⁷⁸ The project is also exploring effective visual representations of quantitative information on benefits and harms to support more effective decision-making.³⁷⁹
- The EU DECIDE project aims to improve the dissemination of evidence-based recommendations.³⁸⁰ As part of this project, digital tools have been developed to provide new ways to present information, including interactive summaries of findings that present key information on the benefits and harms of treatments and ‘interactive evidence to decision’ frameworks that facilitate the incorporation of evidence into healthcare decisions.^{381,382}
- The European Medicines Agency (EMA) European Public Assessment Reports are generated for each medicine the EMA regulates, summaries of which are published on the EMA website and include a lay summary aimed at the general public.³⁸³
- As discussed in **section 4.1.1**, Drug Facts Boxes were developed in the United States (US) and draw on publicly available regulatory documents submitted to the US Food and Drug Administration (FDA) to present evidence on the potential benefits and harms of medicines in a simple table, inspired by nutritional information boxes on US cereal boxes.³⁸⁴
- The NHS breast cancer screening leaflet is regarded as an exemplar for providing a balanced summary of the potential benefits and harms, without promoting a specific course of action.³⁸⁵

4.1.1 Patient information leaflets

Patient information leaflets, the package inserts that are included with the medicines, might in some instances be the only source of information that an individual will access for a medicine. However, they are particularly poor at outlining the potential benefits of treatments for a number of reasons, including the fact that current legislation does not require benefits to be described in patient information leaflets and some might view the description of benefits as direct to consumer advertising, which is in contravention with the European Federation of Pharmaceutical Industries and Associations' (EFPIA's) Code of Practice on Relationships between the Pharmaceutical Industry and Patient Organisations,³⁸⁶ and the UK's Association of the British Pharmaceutical Industry (ABPI) Code of Practice for the Pharmaceutical Industry.³⁸⁷

Patient information leaflets are highly regulated by the EU Directive 2001/83/EC.³⁸⁸ In 2015, the European Commission published a review of the shortcomings of patient information leaflets and made a series of recommendations to enhance their comprehension and readability; these included the increased involvement of patients, better guidelines and sharing of best practice.³⁸⁹ It is unclear what progress has been made in implementing these recommendations.

We welcome the work that is being done by the Medicines and Healthcare products Regulatory Agency (MHRA) in the United Kingdom (UK) to promote best practice and encourage improvements to be made within the current legislative framework. Nevertheless, we recognise that there are limitations to what the MHRA can achieve without legislative support and therefore recommend that the European Commission and the EMA work with the national regulatory authorities in EU Member States, pharmaceutical companies and patients to progress these recommendations as quickly as possible. In doing so, they should draw on experiences of initiatives aimed at enhancing the accessibility of the potential benefits and harms, such as the Drug Facts Box initiative in the US (see **Box 15**).³⁹⁰ Drug Facts Boxes were considered in our public dialogue and 'Communicating evidence about medicines' workshop,^{391,392} and have been shown in experimental studies to enable individuals to make improved judgements about medicines.^{393,394,395,396}

We recognise that the UK leaving the EU might present opportunities for improving patient information leaflets in the UK; however, considering the size of the UK market and the pressures on industry in a global market, it is likely that the UK would still benefit from adhering to harmonised criteria for patient information leaflets across the EU, which makes continued engagement with the European Commission a priority.

Recommendation 8: Improving the content of patient information leaflets



We recommend that the **European Commission** and the **European Medicines Agency** (EMA) work with **the national regulatory authorities in EU Member States, pharmaceutical companies and patients, carers and the public** to improve the comprehension and readability of patient information leaflets in line with the current legislation. We recommend that such work is prioritised and ensures that a balanced appraisal of the medicine's potential benefits and risks is made accessible in these documents. In doing so, they should draw on the experiences of initiatives to enhance the accessibility of information about the potential benefits and harms, such as the Drug Facts Box initiative in the United States (US). We applaud the efforts of the Medicines and Healthcare products Regulatory Agency (MHRA) to date to improve the content and accessibility of patient information leaflets and encourage the regulator to continue its work in this area.

4.1.2 NHS Choices as a central repository of reliable evidence on the potential benefits and harms of medicines

In addition to those listed above, patient information leaflets have two other significant limitations: the information is received too late to inform decisions regarding initiation of treatment during consultations with healthcare professionals; and, as printed documents, there are logistical issues in keeping the information up-to-date as new evidence emerges. We therefore advocate that a trustworthy, online source of information about the potential benefits and harms should be established. We believe that NHS Choices could fulfil this role by acting as a central repository for relevant, accessible, assessable, usable and trustworthy summaries of the evidence on the benefits and harms of medicines, which can remain contemporary as new evidence becomes available.³⁹⁷ We heard that many healthcare professionals already use this website during consultations. Such a central repository could therefore be used by patients and healthcare professionals alike. It could support discussions between them by providing links to robust, evidence-based decision aids and other tools, such as those produced by the National Institute for Health and Care Excellence (NICE) and other organisations.^{398,399,400} We are pleased that NHS Choices is already working to update their platform in line with our thinking.

In developing its material, NHS Choices should continue to work with patient groups and medical research charities, increasingly consulting with pharmaceutical companies as they move towards providing information on new drugs, and coordinate with the MHRA. NHS Choices should also consider how to structure the information they provide to allow a clear appraisal of the potential benefits and harms of alternative options, as is done in Drug Facts Boxes and Option Grids.^{401,402} It should make full use of infographics to communicate numeric information, and cross-reference to the high-quality information produced by patient and medical research charities.

Initiatives exist to signpost to clear, accurate and trustworthy information, including NHS England's Information Standard that demonstrates an organisation's commitment to trustworthy health and care information, and the Plain English Campaign's Crystal Mark that denotes clarity.^{403,404} We recommend that these standards are met in information provided by NHS Choices and others, such as patient and medical research charities.

Recommendation 9: NHS Choices as a central repository of information on the benefits and harms of medicines



To enhance the availability and accessibility of contemporary information on medicines, we recommend that **NHS Choices** and its **equivalents in the devolved nations** develop clear information on the benefits and harms of medicines, and act as a central repository for use by patients and healthcare professionals. This online source of information should make direct reference to the underlying evidence; be updated as further evidence emerges; and detail relevant, robust and evidence-based decision aids that can be used by patients and healthcare professionals. In developing material, NHS Choices and its equivalents should continue to work with patient groups and medical research charities, increasingly consulting pharmaceutical companies as they move towards providing information on new drugs, and should coordinate with the MHRA to increase the availability, accessibility and reliability of information about the benefits and harms of medicines. NHS Choices and its equivalents, and the valuable information provided by **medical research charities**, should meet NHS England's Information Standard and the Plain English Campaign's Crystal Mark.^{405,406}

4.1.3 The role of healthcare professionals

Many patients want to make decisions about their healthcare in discussion with their healthcare professional (in a process called ‘shared decision-making’ – see **section 4.3.2**).^{407,408} However, others may want, and trust, their healthcare professional to make decisions for them that are in the best interest of their health.⁴⁰⁹ Accuracy of, and trust in, healthcare professionals’ decision-making therefore becomes critical. In turn, healthcare professionals need to be fully informed and in a position to communicate the rationale behind their decision (including risk and uncertainty) so that patients fully understand and are able to commit to the proposed approach. Since patients may perceive evidence, risk and value differently, and numeracy and literacy levels vary,⁴¹⁰ information and support should be tailored as far as possible. The interpretation of a recent legal judgement puts increased focus on tailoring information on potential benefits and harms of medicines to individual circumstances.⁴¹¹ A recent report highlighted the need to communicate relevant and understandable information to patients, with evidence that this could lead to improved health outcomes and, ultimately, to cost savings for the NHS.⁴¹² Concerns have been raised about the challenges faced when making decisions about medicines when patient have multiple co-occurring conditions or long-term conditions.^{413,414} We discuss these in further detail in **Chapter 5**.

We support the activities of higher education institutions, Medical Royal Colleges and other professional bodies to ensure that communication training for healthcare professionals places due emphasis on communicating evidence on the benefits and harms of medicines, risk and uncertainty to patients in their curricula. They should involve patients and the public in the design and delivery of such training.

4.1.4 Patient involvement in their own healthcare

We believe that patients and citizens have a right, desire and responsibility to inform themselves about their medical condition and treatment options. As discussed above, patient information leaflets, NHS Choices, healthcare professionals and health-related charities are important sources of information and can also direct patients and the public towards reliable information online.

There is evidence to suggest that patients asking questions about their treatment options, the possible benefits and harms of those options, and the likelihood of the benefits and harms happening to them, can also lead to improved provision of information by healthcare professionals.^{415,416} We have developed a series of questions for patients and healthcare professionals to support them in this process (**Online annex G**).⁴¹⁷ Using such questions could drive evidence-based practice, strengthen communication between patients and their healthcare professional and, ultimately, improve safety and quality.^{418,419}

4.2 Evidence reporting in the media

The mass media (television, radio, and printed and online news) are an important conduit for obtaining health information. People find out about science most regularly from traditional media, with three-fifths (59%) of the surveyed public using television as one of their regular sources of information on science, and a quarter (23%) using newspapers as one of their regular sources.⁴²⁰

Health information presented via these channels needs to be balanced and accurate to avoid both undue concern and unfounded hype about research findings. All parties involved in the science and health communication pathway – from researchers, to university and medical/patient charity press offices, to journalists – have a responsibility to promote accuracy and balance. All constituencies might experience pressures to maximise their exposure. However, the short-term gains of increased media coverage are likely to be offset by long-term reputational damage when, under public scrutiny, shortcomings are identified.⁴²¹ Although it can give reliable information, health information presented on social media and blogs represents another challenge: it has considerable potential to influence health behaviours, but its accuracy is difficult to assure and such channels can aid the dissemination of inaccurate, sensationalised or unbalanced material.

4.2.1 Roles and responsibilities of researchers, press offices and journalists

All those involved in the generation and communication of research have responsibilities for accurate and balanced reporting in the media. We outline individual responsibilities below.

4.2.1.1 Researchers

Researchers should recognise the importance of communicating their work and engaging with the media to ensure that research findings are accurately reflected, but also to correct any misrepresentations that might occur. We endorse the values and responsibilities of scientists set out in the 'Universal Ethical Code for Scientists' – rigour, respect and responsibility – values that should permeate the entire communication pathway.⁴²² Researchers should be supported by their organisation's press offices, which should facilitate conversations between journalists and researchers. Funders should develop a code of practice for their grant awardees outlining how to describe the research that they fund in the media. To enhance journalists' (and healthcare professionals') understanding of study findings, researchers should highlight the uncertainties of their research and the remaining gaps in evidence; this is particularly important in syntheses of evidence (systematic reviews and meta-analyses), which are crucial in informing clinical practice.

4.2.1.2 Press offices

Press offices, as key intermediaries between researchers and journalists, have a number of important roles to play. They should:

- Ensure that press releases are balanced, include research caveats, present novel findings in the context of previous research, explain what more needs to be done to secure clinical impact, and not exaggerate, distort or change the main research conclusions (see **section 4.2.2.1** for further information).
- Provide access to the complete research paper alongside the press release, which should be clearly labelled (e.g. editorial opinion piece, original research, conference abstract, etc.).
- Support researchers in navigating the media process, for example by providing media training for researchers, clearly communicating the processes and timelines under which journalists work and supporting researchers when engaging with the media.
- Encourage researchers to respond to the media should their research be misrepresented.

Press offices in medical research charities have a particularly important role in providing expert input to journalists and acting as a 'moderating voice' should research findings be over- or under-sold. To enhance standards across the sector, the British Science Association provides training and support for press officers, and an increasing number of university science communication courses are being established.⁴²³

4.2.1.3 Journalists

Journalists have a duty to accurately portray research findings, signpost to study limitations, and not unduly alarm or overhype claims. To verify the validity of their reporting, they should seek independent expertise from academia, industry and medical research charities, among others.

In addition, they should place findings in the context of previous research (prior evidence). There is a tendency for news organisations to report claims and counterclaims about medicines in successive pieces, with little willingness to summarise the state of the argument in one article (except, potentially, in a longer, more detailed 'news feature').⁴²⁴ This makes it difficult for the public to assess news about treatments, especially when the emphasis is on the latest element of a controversy. However, there is considerable public interest in providing a complete picture on the potential benefits and harms of medicines to responsibly inform healthcare decisions.

Journalists should adhere to the Science Media Centre's '10 best practice guidelines for reporting science & health stories' commissioned by Lord Leveson in the wake of his inquiry, which provide clear practical guidance towards improving the accuracy of reporting of research.⁴²⁵ We recommend that regulators like the Independent Press Standards Organisation (IPSO) and the Independent Monitor for the Press (IMPRESS) should adopt these principles as their standards for use in the newsrooms and should work jointly with the scientific community on enforcing these standards in the news.^{426,427} To encourage best practice, the Science Media Centre should also establish a series of workshops for news editors, sub-editors and non-specialist journalists to enhance their understanding and reporting of scientific processes.

We heard how science and health specialist journalists play an important role in ensuring responsible reporting of research findings. They should be championed by the research community, which should better engage with them on medical research that appears in the press. Their expertise should also be better utilised by non-specialist journalists.

Journalists that follow these principles should be rewarded for their good practice, for example by an award such as the Society of Editors' Science and Health Journalist of the Year award;⁴²⁸ those that do not should be publicly held to account via organisations such as Full Fact or programmes such as More or Less.^{429,430} Such outlets should receive constructive help in this task from professionals willing to monitor their own discipline, if it is to be discharged effectively. A recent report from the House of Commons Science and Technology Committee recommended that the Government should ensure that '*a robust redress mechanism is provided for when science is misreported*'.⁴³¹

4.2.2 Improving current practice

To enhance the communication and dissemination of clear, accurate and balanced information about the potential benefits and harms of medicines, we explore below possible ways to improve press releases of research, the accuracy and balance of reporting, and the availability of reliable sources of information.

4.2.2.1 Press releases

Journalists are often criticised for irresponsible reporting.^{432,433} However, a recent study found that many exaggerated claims can be traced back to the press release, further emphasising the key role of press offices (see **section 4.2.1.2**) and scientists in ensuring these are accurate and balanced.⁴³⁴ Our workshop on 'Communicating evidence in the media' challenged the commonly held assumption that press releases are less likely to be covered by journalists if research caveats are included. To the contrary, journalists welcomed and encouraged caveats in press releases, which they found helpful for interpreting the research, providing confidence that they were given a complete picture.⁴³⁵

Of key concern are unsubstantiated claims about the potential of early stage research on future treatments or on the practice of medicine. Early stage research can, and should, be reported, but claims about its potential should not be exaggerated. **Box 16** provides good practice techniques for press releases. Further practical next steps are discussed in the 'Communicating evidence in the media' workshop report (see Box 1 of the report).⁴³⁶

Box 16. Good practice for press releases identified throughout our project

Press releases should:

- Include research caveats and clear descriptions of context, including the previous evidence.
- Be clear about whether the press release is peer-reviewed evidence or opinion – to that effect they should be clearly labelled (e.g. editorial opinion piece).
- Provide a link to the original study (as should the news article).
- Be clear on the purpose of the press release (e.g. need to share critical safety information, the desire to 'inform' or educate, or about self-promotion).
- Be diligently checked by the original researcher to ensure accuracy.
- Include, where available, absolute risk as well as relative risk.
- Avoid statistical concepts that are hard to interpret, such as odd ratios.
- Be clear about whether the reported finding is a correlation or causation.
- Be developed with the target audience in mind to ensure that they are relevant. This may mean developing different press releases for different news outlets.

We recommend that a ‘traffic light’ system for press releases of medical research should be developed by the Science Media Centre for press offices to use before publication to rate their release according to:

1. **The relevance of the research to clinical application:** e.g. red, early stage research in test tubes or cells; amber, science whose translation into humans still needs to be demonstrated; and green, studies for which the relevance to humans is clear. A dimension of this includes the length of time to clinical application.
2. **The robustness of the study:** e.g. red, preliminary findings; amber, larger peer-reviewed studies but whose findings still need to be independently confirmed; and green, large rigorous studies that have been independently confirmed.

Such a system would help various audiences assess the stage and reliability of the research, including journalists. It would be important to carefully explain how such a system would work to avoid the misconception that research marked as red or amber is irrelevant, unnecessary, unimportant or likely to fail to progress any further. If implemented, we encourage the system to be initially piloted with a small number of university press offices.

We support the broad principles outlined in the guide to being a media officer developed by Stempra, a network for science public relations and communications professionals.⁴³⁷ However, it does not address in sufficient detail the concerns we raise about the presentation of scientific evidence. We therefore recommend that Stempra develops a code of practice for press officers to encourage best practice. Hallmarks could be used by signatory organisations to highlight that best practice guidelines are promoted within the organisation, thereby increasing the credibility of their press releases.

4.2.2.2 *Statistics and ‘false balance’*

A further concern that has emerged repeatedly during our evidence gathering is the critical need for accurate and relevant reporting of statistical information in the media. Careful consideration should be given to communicating quantitative information in a way that is meaningful to non-specialist audiences. Researchers, press officers and journalists all agreed that absolute risks should be reported as well as relative risks, and that statistical concepts that are difficult to understand, such as odds ratios, should be avoided.⁴³⁸ A recent review into the use of statistics across the BBC found that while there were many good examples of appropriate reporting of statistics, the BBC could do more to ensure that statistics are consistently and uniformly well reported.⁴³⁹ Areas for improvement identified in the report included: contextualising statistics; presenting risk; being clear about significance; and increasing statistical capacity. The BBC has committed to increase journalists’ confidence with statistics in their day-to-day work, include BBC specific guidance on the reporting of statistics in their Editorial Guidelines, and devise online training for journalists in the use of statistics and promote relevant external guidance. We welcome these important initiatives and urge other media outlets to review their use of statistics.

Similarly, ‘false balance’ in news reports can present a distorted view of the evidence base.⁴⁴⁰ Where there is strong consensus on the evidence base and only a minority of opposing views, both sides should not misleadingly be presented on an equal standing to create more engaging reporting. Further, campaigns in medical journals can have a significant impact on health outcomes (both positive and negative).^{441,442,443} Given the authority that medical journals enjoy, it is particularly important that such campaigns base their assertions on robust and reliable evidence.

4.2.2.3 *Availability of reliable information*

We are in a time of change in terms of the channels of influence that are available for the dissemination of information, for example social media and other non-traditional online media, which are central to the current debate about ‘fake news’. In an era where information is more accessible than ever, the proliferation of online sources outside the mainstream media presents opportunities for inaccurate and potentially damaging information to find its way to the consumer. Rather than trying to regulate what is available on the internet, we feel that helping citizens and patients discern what is reliable information and giving those outlets more prominence, for example via clear kite marking, will be much more effective.

As discussed in **section 4.1.2**, we believe that establishing NHS Choices as a key provider of information about the benefits and harms of medicines, ensuring it addresses the information needs of the public, and promoting its use to the public, will allow greater access to trusted, evidence-based, reliable information about medicines.

Recommendation 10: Improving the reporting of scientific evidence in the media



To complement current initiatives to improve the reporting of scientific evidence in the media, we recommend that:

- a. The **Science Media Centre** works to develop criteria for and implement a ‘traffic light’ system for press releases of medical research that grade both the relevance of the research to clinical application and the robustness of the study. We also recommend that the **Science Media Centre** develops a series of workshops for news editors, sub-editors and non-specialist journalists to enhance their understanding and reporting of the scientific process.
- b. **Stempra** develops a code of practice for press officers to encourage best practice. Organisations that become a signatory to these principles could be authorised to use a hallmark to provide a clear signal that best practice guidelines for accuracy are promoted within the organisation, thereby increasing the credibility of the press release.
- c. **Funders** develop a code of practice for their grant awardees around how to describe the science that they fund in the media. This approach received support from the Chief Executive of the Medical Research Council (MRC). We therefore recommend that MRC leads on coordinating the development of this code of practice with the other major UK funders.
- d. **Universities** and **research institutions** play a greater role in ensuring that the research they host is portrayed accurately in the media. The **Higher Education Funding Council for England** (HEFCE, relevant functions expected to be assumed by Research England in the future) and **its counterparts in the devolved nations** should incentivise them to do so by requiring that the robustness of the approaches they adopted forms part of the institutional environment statement submitted to the Research Excellence Framework (REF), in addition to the reproducibility and ‘intelligent openness’ efforts described in **Recommendations 3** and **5** respectively.

4.3 Patient engagement in shared decision-making

4.3.1 Reception of information

Literacy and numeracy levels in many medical information sources are not appropriate for the general public.^{444,445} It is estimated that two-fifths (43%) of adults do not have sufficient health literacy to fully understand typical text-based health information, a figure that rises to three-fifths (61%) if materials include numerical information.^{446,447,448} Further, about one-fifth (15%) of adults in England have a literacy level below that of an individual expected to achieve a D–G grade in GCSE, and a quarter (23%) of English adults have numeracy levels below that expected of a 9- to 11-year-old.⁴⁴⁹ In addition to enhancing communications, parallel strategies should be put in place to help improve patients’ and the public’s understanding of science and health more widely.

There are various initiatives to enhance the capacity of the public and other audiences to interpret information about medicines, including the ‘GET-IT’ glossary of plain language definitions of health research terms and resources to enable schoolchildren and the public to appraise claims made about health.^{450,451,452} The Royal Society, the Royal Society of Biology, Wellcome Trust, and others, have influenced the content of the National Curriculum so that it better prepares children to work and think scientifically, consider the importance of evidence and critically appraise it. We support efforts within the National Curriculum to enhance numeracy, health literacy and personal responsibility for health. We encourage the Secretary of

State for Education and the Department for Education to carefully consider the outputs of current initiatives led by the Royal Society, the Royal Society of Biology and the Wellcome Trust in this regard.⁴⁵³

Most of the initiatives we have identified in this area are aimed at the next generation. However, it is older people that take the most medicines. Age UK has just started a project on polypharmacy (use of multiple medicines) and older people. They will be looking to develop a toolkit to support decision-making and questions that can be used by patients in general practitioner (GP) consultations.

4.3.2 Shared decision-making

There is compelling evidence that active participation in decisions about their health improves patients' health outcomes.⁴⁵⁴ Shared decision-making is a process where clinicians and patients work together to select tests, treatments, management or support packages, based on clinical evidence and the patient's informed preferences. It is widely viewed as a model of good practice in making choices during consultations with healthcare professionals.^{455,456} It involves the provision of evidence-based information about options, outcomes and uncertainties, together with support in decision-making and a system for recording and implementing patients' informed preferences.⁴⁵⁷

A systematic review of eight studies showed that although providing information to patients about the potential benefits and harms of medicines has no consistent effect on the number that decide to start or continue medicines, it increases patients' knowledge and the level of comfort they face when making a decision (i.e. it reduces their 'decisional conflict').⁴⁵⁸ There is also evidence that shared decision-making can improve people's knowledge about their condition and treatment options, their involvement in and satisfaction with care, and their self-confidence in their own knowledge and self-care skills.^{459,460}

Recent national surveys have shown that slightly over 50% of patients feel involved in decisions about their healthcare and treatment, but there has been almost no change in patient involvement in their health decisions over the past five years.⁴⁶¹

Through our public dialogue activities we heard that challenges to the implementation of shared decision-making, a central component of engaging the public in medical evidence, include the complexity and unfamiliarity of medical evidence, and the different interpretations of what shared decision-making is or what it ought to be. We also heard that barriers to the use of evidence in decision-making include understanding and interpretation of medical evidence, the nature of the existing healthcare professional–patient relationship, and people's current shared decision-making framework. Such concerns, as well as other evidence gaps around shared decision-making, like those identified by the Health Foundation,⁴⁶² still need to be addressed.

We support the work undertaken by the Medical Royal Colleges, including the Royal College of General Practitioners, to promote shared decision-making and ensure appropriate training. We encourage other bodies involved in the education of prescribers to do likewise.

4.4 Conclusions

A recurring theme throughout our case studies is the challenge that patients, citizens and healthcare professionals face when considering the potential benefits and harms of medicines, particularly in view of competing evidence from different sources and broader issues such as the trustworthiness of those conducting the underlying research.

To enhance the quality of the information about medicines to inform decision-making, we recommend that the comprehension and readability of patient information leaflets should be improved to include a balanced appraisal of the potential benefits and harms (**Recommendation 8**). This should help patients arrive at a clearer understanding of the potential benefits and risks, helping avoid situations like the one described in our case study on statins. We also recommend that NHS Choices should be developed as a central repository for clear and up-to-date information on the potential benefits and harms of medicines (**Recommendation 9**). Such a recommendation should prevent situations where confusion over the safety of the therapy significantly affects the use of medicines, such as in the case of hormone replacement therapy and statins. Further, to ensure that the potential benefits and harms of medicines, risk and uncertainty are clearly communicated to patients, we support higher education institutions, Medical Royal Colleges and other professional bodies in their training of healthcare professionals.

We call on all those involved in the generation and communication of research, including researchers, press officers and journalists, to enhance the reporting of scientific evidence in the media. It is incumbent on all parties to ensure that reporting is responsible, accurate and balanced, and does not cause undue concerns or unfounded hype. To do so, we recommend that a 'traffic light' system for press releases is established to grade the relevance of research to clinical application and the robustness of the study. We also recommend that codes of practice are developed for press officers and for researchers to encourage best practice in press releases. We strongly encourage journalists to adhere to the Science Media Centre's '10 best practice guidelines for reporting science & health stories'.⁴⁶³ The REF has an important role to play in galvanising change and ensuring that higher education institutions are more engaged in ensuring that the research they host is accurately portrayed in the media.

The role of the media in influencing public discourse and, ultimately, people's decisions about medicines is exemplified in our case studies on hormone replacement therapy, statins, Tamiflu, human papilloma virus (HPV) vaccine and, perhaps most famously, measles, mumps and rubella (MMR) vaccine. In this last example, the mainstream media gave disproportionate coverage to a study that several subsequent studies failed to replicate, and that has since been fully retracted. The result was a notable drop in vaccine coverage in the UK. It is situations like this that we hope will be avoided if we improve the reporting of scientific evidence in the media (**Recommendation 10**).

Finally, we believe that patients and the public should be better equipped to make sense of the information about the medicines they are given. We support efforts to enhance patients' and the public's understanding of science and health so that they can make full use of medical information sources. We also support shared decision-making as a model of good practice for evidence-based decision-making during consultations but recognise that much needs to be done, including research into determinants of its uptake, to enhance its utility.

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The generation, trustworthiness and communication of scientific evidence can be improved so it can play a greater role in decisions about medicines.



5. Implications and conclusions

This report was initiated in response to recent high-profile debates over the use of medicines, such as statins to prevent cardiovascular disease, Tamiflu to treat flu and the human papilloma virus vaccine to prevent cervical cancer, among others (see Box 1). All of these controversies left patients and, to a certain extent, healthcare professionals confused as to whether such treatments were safe and effective.

In this report, we have explored how the generation, trustworthiness and communication of scientific evidence can be improved so that it can play a more significant role in decisions by patients, carers, healthcare professionals and others about the benefits and harms of medicines. In doing so, we engaged extensively with the public, patients and healthcare professionals to ensure that we address the areas of most concern. We are confident that we have identified some actions that could avoid similar controversies from occurring in the future, which we summarise below.

5.1 Deciding whether to use a medicine

In this report, we consider how the public, patients and professionals can better be enabled to use scientific evidence to judge the potential benefits and harms of medicines. The surveys of general practitioners (GPs) and the general public, and the public engagement we conducted, endorsed the concerns that precipitated the report, but also revealed the complexity of the issues involved and the need for collective responsibility to address them. We describe the roles and responsibilities of the different parties involved that have arisen from the recommendations of this report in detail in **Annex II**.

It is clear that for many people, scientific evidence plays a lesser part in the decisions they make about medicines than other forms and sources of information. It is also clear that people's perceptions of illness and treatment, which ultimately shape their decisions, are influenced by a wide range of factors, of which scientific evidence is just one. While it was not within the remit of this report to explore this complex area, it became clear that there are many unresolved issues involved that need to be addressed as a priority. Effective communication of scientific evidence is likely to be informed by a clearer understanding of the broader array of factors that influence people's decisions. It is proposed that the Academy hosts a symposium on the topic (jointly with the other United Kingdom National Academies) to characterise current understanding of decision-making about medicines and to agree research priorities.

5.2 The role of scientific evidence in decision-making

Notwithstanding the many factors and types of information that contribute to decision-making, we contend that the public is entitled to expect high-quality, trustworthy scientific evidence about the potential benefits and harms of medicines they might choose to take; and healthcare professionals have a responsibility to provide patients with such evidence in clear, intelligible ways, tailored as appropriate for the particular circumstances of the patient in front of them.⁴⁶⁴ Further, we suggest that high-quality, trustworthy scientific evidence should play a major role in influencing people's choices about medicines, for the simple reason that it is the only source of evidence that can be subject to systematic check and challenge according to a rigorous scientific process. Scientific advice is also what is expected of healthcare professionals. Accordingly, our recommendations are predicated on the need to elevate the role of scientific evidence in decision-making about medicines, both at the individual and population level, and the understanding of its role in the formulation of treatment guidelines.

5.3 Demonstrating the trustworthiness of scientific evidence

A principal concern that precipitated this report, and was confirmed by our surveys and deliberative public dialogue work, relates to the confusion engendered in the minds of patients, citizens and healthcare professionals by controversies over the trustworthiness and applicability of scientific evidence on the potential benefits and harms of medicines. In addressing these issues, the integrity of the scientific process, and the reliability of scientific evidence and its relevance to questions that matter to patients, are crucial. We stress the need to improve the trustworthiness of scientific evidence if it is to play a greater role in decision-making. We also highlight the fundamental importance of applying appropriate research design and methods, and conducting research rigorously, all of which have notable implications for scientists and those that host or fund research.

Significant concerns exist around the influence of competing and conflicting interests on the trustworthiness of scientific evidence, particularly when the generation of the evidence involves commercial bodies. We emphasise the importance of declaration and management of competing interests, as opposed to the condemnation of relations between academia and industry. New drug development is likely to be increasingly dependent on transparent, constructive alliances between academia and industry, each of which brings different skills to the process of medical innovation. Society should be made more aware of the need for this interdependence to better address unmet clinical need. We propose a set of principles to govern the relationship between academia and commercial partners when developing evidence related to the use of medicines in clinical trials (see **Online annex F**).⁴⁶⁵

5.4 Improving the communication of scientific evidence

If scientific evidence is to achieve greater use in decision-making by healthcare professionals, citizens and patients, we argue that in addition to being trustworthy it should be accessible, assessable and usable,⁴⁶⁶ as well as accurate and relevant. The only written information automatically administered to patients with a prescription is the patient information leaflet contained within the drug packaging that lists all the potential side effects. Discussions with the Medicines and Healthcare products Regulatory Agency (MHRA) reveal laudable efforts to achieve a more balanced view of benefits and harms that conform to the characteristics of accessibility, assessability and usability, and we encourage their implementation. Further efforts are needed at a European Union (EU) level to improve the comprehension and readability of these leaflets. We also commend the wider use of NHS Choices in this context, with greater emphasis placed on contemporary scientific evidence and working with patient charity groups and other sectors, as appropriate.

5.5 Cross-cutting concerns: patients with multimorbidity and the medicalisation debate

During the course of our work, two general (and somewhat related) concerns stood out: the challenge of treating patients with multiple conditions (multimorbidity); and medicalisation (too great a reliance placed on medicines over non-drug alternatives or lifestyle changes) and both over- and under-medication in relation to perceived clinical need.

5.5.1 Addressing the challenge of multimorbidity

In routine clinical practice, the decisions that healthcare professionals and patients need to make are very often not confined to one illness or drug. It is estimated that 44% of patients attending general practice aged 75 years or over have more than one condition, with 9% having four or more conditions, and will potentially be prescribed multiple drugs.⁴⁶⁷ The implications of multimorbidity (which is set to increase given demographic trends) should be addressed if better decision-making leading to the most appropriate treatment approach in which all parties have confidence is to be achieved.

A recent report by the Royal College of General Practitioners highlighted GPs' concerns about the multiple medicines patients with multimorbidity are often prescribed and the challenges they face in medicines prioritisation.⁴⁶⁸ Wider apprehension about over-medication and medicalisation has been echoed across the community, with organisations such as the Academy of Medical Royal Colleges compiling a list of commonly used treatments and procedures that are of questionable value.⁴⁶⁹ Whereas each medicine in

isolation may have a logical basis, the possibility of drug interaction will need to be considered, as will support for lifestyle changes that may limit the need for some drugs.

Despite the National Institute for Health and Care Excellence's (NICE's) recent guidelines on multimorbidity, there is a paucity of support structures and robust, evidence-based decision aids to help patients and healthcare professionals make decisions in the face of this complexity.⁴⁷⁰ Since patients with multiple conditions are typically excluded from randomised clinical trials (RCTs), questions have also been raised about the applicability of RCT data to patients with multimorbidity.⁴⁷¹ The Academy has recently launched a project exploring the gaps in the existing evidence and the associated research priorities in this area.⁴⁷²

Evidence suggests that decision aids improve people's knowledge of options and the level of comfort a person experiences when making a decision. They can also help stimulate people to take a more active role in decision-making and improve the accuracy of their perception of risk.⁴⁷³ They are also needed to assist healthcare professionals make sense of myriad guidelines and directives and a burgeoning evidence base, which will ever increase. We heard clearly from many healthcare professionals that they were struggling to cope with the avalanche of data that could inform their practice, potentially limiting the adoption of newer, beneficial therapeutic approaches.

Promising strides are being made in the development of machine learning and artificial intelligence (AI) to support healthcare professionals in assimilating relevant data.^{474,475,476} It is our contention that, with the appropriate checks and balances, such approaches will become ever more necessary to support evidence-based practice. Such systems are unlikely to replace the need for healthcare professionals as a key interface with patients in support of shared decision-making that takes account of a patient's particular circumstances and priorities. Accordingly, we recommend that decision aids, algorithms and other tools should be developed to assist patients and healthcare professionals make decisions about treatment strategies and discuss non-drug alternatives. Clearly, such tools will need to be informed by robust and relevant primary evidence about treatment effects, the source of which should be open to scrutiny (including for those developed by private companies). However, much of the currently available evidence focuses on single disease states and there is a paucity of evidence collected in the context of multimorbidity, making it difficult for these tools to be developed. We also recommend that research efforts are enhanced to establish the role that machine learning and AI can safely play in the clinical decision-making process.

A complementary practical approach to multimorbidity is the pursuit of so-called 'goal-oriented patient care', in which advice from healthcare professionals and treatment decisions are informed by what really matters to patients and the quality of life they seek to achieve,⁴⁷⁷ so that priorities can be established rather than resorting to 'a pill for every ill'. Such an approach resonates with that promoted by Atul Gawande concerning treatment decisions towards the end of life.⁴⁷⁸ Ultimately, limiting the expression of multimorbidity and the use of multiple drugs is likely to rely on rebalancing the health and social care system. Such rebalancing would see more proportional investment in primary prevention and public health measures that tackle the wider drivers of ill-health. This would allow health-promoting behaviours to flourish.⁴⁷⁹

Currently, the average GP consultation lasts 9.2 minutes and deals with an average of 2.5 issues.⁴⁸⁰ This does not allow sufficient time for conversations about treatment options and lifestyle changes guided by decision aids, or about the patient's goals and priorities,⁴⁸¹ particularly in the context of multimorbidity, where there may be many questions and potential treatments to be explored. We support the measures proposed by the Royal College of General Practitioners in better addressing multimorbidity in general practice.⁴⁸² We also recommend that, where necessary, extended consultations for patients with multimorbidity or chronic or long-term conditions are implemented to allow a more personalised approach to care planning, which has been shown to result in improved health and enhance people's capability to self-manage their condition.⁴⁸³

Recommendation 11: Supporting joint decision-making between healthcare professionals and patients



To support joint decision-making between healthcare professionals and patients, we recommend that:

- a. **General practices** ensure that enough time is available through care planning and that adequate resourcing is provided by commissioners of primary care services to address patients' priorities and concerns regarding medication decisions. As proposed in **Recommendation 9**, the evidence provided by NHS Choices should assist in informing patients alongside their discussions with healthcare professionals.
- b. The **National Institute for Health and Care Excellence (NICE)**, in discussion with **NHS Choices** (or its equivalents in the devolved nations), coordinates the development of decision aids based on robust evidence, the source of which is open to scrutiny. These aids should be used to inform the decision-making process, helping patients and healthcare professionals decide on the most suitable course of action, including optimising treatment strategies and supporting the discussion of non-drug alternatives, such as lifestyle changes. The effectiveness of different forms of decision aids, including the use of machine learning and artificial intelligence, and their relative utility, should be subject to research evaluation and supported by funders, including the **National Institute for Health Research (NIHR)**.

5.5.2 Achieving the right level of medication for preventative purposes

A potent stimulus for this report was the debate in the specialist and general media regarding the over- or under-use of medicines for preventive purposes. Statins took centre stage in this debate with the suggestion from NICE that their use should be considered for the primary prevention of cardiovascular disease (CVD) for those with a 10% or greater 10-year risk of developing CVD rather than the existing threshold of a 20% risk or greater.⁴⁸⁴ A detailed discussion of the debate and the evidence that underpins statin use is provided in **Online annex A**.⁴⁸⁵

The change in NICE guidance was informed by high-quality evidence of the worthwhile benefits of statins (including in low-risk patients) and the low rate of adverse side effects. There is evidence that the widespread coverage questioning the risk–benefit balance for statins increased the numbers of people stopping statin treatment. As a result, it has been estimated that there may be over 2,000 excess CVD events over 10 years in the UK.⁴⁸⁶ Surveys have also suggested that patients were confused about the role of statins for CVD as a result of media coverage, and that GPs' confidence in discussing statins with patients or in prescribing statins was affected.^{487,488} While there may be a legitimate concern that there is a reduced need for preventing CVD if the base rate of CVD risk is low, the fundamental requirement is to assist patients in making a properly informed decision about whether or not to take statins by discussing with them the most up-to-date and robust evidence.

The benefits of preventative treatments, such as statins and vaccines (see **Box 1** for an account of the measles, mumps and rubella, MMR, and human papilloma virus, HPV, vaccine debates) are often invisible as, by definition, they aim to prevent a disease from appearing. In contrast, the potential side effects are apparent, especially to the patient. Nonetheless, the fact that such treatments are used preventatively in individuals who may not have any clinical signs or symptoms should not affect the underlying evidence that supports their use. Patients should be presented with all the information available on the benefits and harms, which they should consider with their clinician in order to make an informed decision, a point well acknowledged in the NICE guidance.⁴⁸⁹ Ultimately, the choice to use a treatment that is offered lies with the patient and is likely to be affected by their personal preferences and health beliefs (see an online discussion paper on decision-making about medicines for further details).⁴⁹⁰

5.6 The future: keeping pace with evolving attitudes

Scientific output is increasing at an unprecedented rate, and it is the hope of many in the field that genomics and new biological and data analysis capabilities will spawn a ‘precision medicine’ era that could not only cure certain diseases but also, applied pre-emptively, even prevent them from being expressed. Such potential needs to be balanced against the health gains to be had through influencing health-related behaviour at a population as well as individual level, but we contend that the optimal preventative strategy will exploit synergy between both approaches. However, advances that relate to the use of medicines may never be realised if we do not achieve better ways of generating, evaluating, communicating and using scientific evidence in a manner that builds public trust, acknowledging the central role of the citizen in co-developing their health. We propose certain changes now, but it is crucial to appreciate that scientific potential and public attitudes will continue to evolve.

Our report is a snapshot of the current status of the use of scientific evidence in the context of decisions about the use of medicines. There must be a commitment to an ongoing relationship with society to address the perceived concerns that precipitated the report. A more profound commitment to public dialogue will be crucial as a prerequisite for a new social contract to sustain a healthcare system fit for the 21st century, as will ongoing monitoring of the attitudes and concerns of citizens and healthcare professionals.

Recommendation 12: Continuing dialogue and engagement with patients and the public



To ensure the health system remains responsive to evolving public attitudes towards health, the use of medicines and the role played by scientific evidence in decisions about their use, we recommend that:

- a. **Health-related organisations** continue their dialogue and engagement with the public to ensure that they are responsive to evolving public attitudes and patient needs, and that they are engaging communities in enhancing the use of evidence as part of the decision-making process.
- b. **The Wellcome Trust** incorporates questions into its regular survey of public attitudes to science to monitor the impact of the recommendations made in this report on the use of evidence within the healthcare sector and in decision-making.⁴⁹¹

The late social historian Roy Porter at the end of his treatise on medical advances over the centuries concluded: *‘Medicine has led to inflated expectations, which the public eagerly swallow. Yet as those expectations become unlimited, they are unfillable; medicine will have to redefine its limits even as it extends its capacity.’*⁴⁹² To defy that somewhat pessimistic prognosis and reap the rewards of modern science will require a collective effort on the part of all the constituencies identified in this report. The Academy is prepared to play its role.

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Glossary of acronyms and abbreviations

- ABPI:** Association of the British Pharmaceutical Industry
ADRN: Administrative Data Research Network
AI: artificial intelligence
AMRC: Association of Medical Research Charities
APPROVE: Adenomatous Polyp PRevention On Vioxx
ARRIVE: Animal Research: Reporting of In Vivo Experiments
BBSRC: Biotechnology and Biological Sciences Research Council
CHM: Commission on Human Medicines
CONSORT: Consolidated Standards of Reporting Trials
CPD: continuing professional development
CPRD: Clinical Practice Research Datalink
CRPS: complex regional pain syndrome
CVD: cardiovascular disease
DMC: data monitoring committee
EFPIA: European Federation of Pharmaceutical Industries and Associations
EMA: European Medicines Agency
EU: European Union
FDA: Food and Drugs Administration (United States)
GP: general practitioner
HEFCE: Higher Education Funding Council for England
HPV: human papilloma virus
HRT: hormone replacement therapy
ICMJE: International Committee of Medical Journal Editors
ICR: Institute of Cancer Research
IMPRESS: The Independent Monitor for the Press
IPD: individual patient data
INVOLVE: INVOLVE is the public involvement programme of the National Institute for Health Research
IPSO: Independent Press Standards Organisation
MHRA: Medicines and Healthcare products Regulatory Agency
MMR: measles, mumps and rubella
MRC: Medical Research Council
NC3Rs: National Centre for the Replacement, Refinement and Reduction of Animals in Research
Nesta: Formerly known as NESTA, the National Endowment for Science Technology and the Arts
NICE: National Institute for Health and Care Excellence
NIHR: National Institute for Health Research
POTS: postural orthostatic tachycardia syndrome
PPI: patient, carer and public involvement
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROTECT: Pharmacoepidemiological Research on Outcomes of Therapeutics by a European Consortium
RCT: randomised controlled trial
REF: Research Excellence Framework
STROBE: STrengthening the Reporting of OBServational studies in Epidemiology
TS: thymidylate synthase
UK: United Kingdom
UKRI: UK Research and Innovation
US: United States
VIGOR: Vloxx Gastrointestinal Outcomes Research

Glossary of terms

'Intelligent openness' terms

'Intelligent openness' terms	Definition ⁴⁹³
Accessible	Information must be located in such a manner that it can readily be found and in a form that can be used. It should also be comprehensible for those who wish to scrutinise it. Audiences need to be able to make some judgment or assessment of what is communicated and the nature of the claims made.
Assessable	Information must provide an account of the results of scientific work that is intelligible to those wishing to understand or scrutinise it. Information must therefore be differentiated for different audiences. Information should also be in a state that allows judgments to be made as to its reliability. Assessability also includes the disclosure of attendant factors that might influence public trust.
Usable	Information should be in a format that readily enables others to use it, including for different purposes. This will require proper background, explanatory information and metadata, as appropriate.

Others terms

Absolute risk

The absolute probability that a given outcome will occur in an individual exposed to a treatment.

Adherence to medicines

Observing a recommended course of treatment, as prescribed by a healthcare professional.

Conflict of interest

A set of circumstances by which a reasonable person would consider that an individual's ability to apply judgement or act, in the context of his/her work is, or could be, impaired or influenced by another competing interest they hold.⁴⁹⁴

'Interests' can arise in a number of different contexts. A material interest is one which a reasonable person would take into account when making a decision because the interest has relevance to that decision.

Interests can be:

- **Financial:** where an individual may get direct financial benefit⁴⁹⁵ from the consequences of a decision they are involved in making.
- **Non-financial:** where an individual may obtain a non-financial benefit (either professionally or personally) from the consequences of a decision they are involved in making, such as increasing their professional reputation or promoting their professional career.
- **Indirect:** where an individual has a close association⁴⁹⁶ with another individual who has a financial or non-financial interest and would stand to benefit from a decision they are involved in making.

Decisional conflict

The level of comfort a person faces when making a decision.

Medicalisation

The process by which some aspects of human life come to be considered as medical problems, thereby becoming the subject of medical study, diagnosis, prevention, or treatment.

Natural frequencies

The number of people affected per unit of population (e.g. ten in every 1,000 women have breast cancer).

Number needed to treat (NNT)

The average number of patients who will need to be treated to get an additional positive outcome. For instance, if the NNT is 20, then 20 patients on average would have to be treated to ensure an additional positive outcome in one patient. The lower the NNT, the more effective the treatment.

Odds ratio

The odds that an outcome will occur given a particular exposure, compared to the odds of the outcome occurring in the absence of that exposure.

Over-medication

The overuse of medicines over other non-medical alternatives such as lifestyle changes. Over-medication includes:

- Treatments that are known from the evidence to be ineffective but are still prescribed (e.g. prescribing antibiotics for viral infections).
- Treatments that, given the evidence, are inappropriately used in a particular patient or context (e.g. if the evidence has poor external validity).

Persistence with medicines

Persevering with the recommended medication schedule over the course of treatment, as prescribed by a healthcare professional.

Relative risk

The fraction by which the risk after exposure to an intervention is greater or lesser than that amongst those not so exposed.

Shared decision-making

A process where clinicians and patients work together to select tests, treatments, management or support packages, based on clinical evidence and the patient's informed preferences. It involves the provision of evidence-based information about options, outcomes and uncertainties, together with decision support counselling and a system for recording and implementing patients' informed preferences.

Termination of treatment

Ending a course of treatment, whether or not this was recommended by a healthcare professional.

The public

In the report, the term 'the public' is used to encompass the many different people, publics and perspectives within society.

Transfers of value

Payments made to professionals for activities such as consultancy and advisory boards, speaker fees, and sponsorship to attend meetings.⁴⁹⁷

Under-medication

Underuse of medicines in patients where the evidence suggests it would be beneficial to use them. This could be due to healthcare professionals being reluctant to prescribe a medicine, or due to patients choosing not to take a medicine that could be beneficial to them.

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495. In these bullets, 'benefit' encompasses those that may arise from making a gain or avoiding a loss.
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Annex I. Report preparation

Terms of reference

This work stream examined the evaluation of scientific evidence for medicinal products and how this evidence is interpreted and assimilated by different groups (including, but not limited to, patients, the public, healthcare professionals, researchers and communicators). It aimed to better align evidence generation with user expectations, and facilitate decision-making about therapeutic options. In doing so, the work stream explored:

1. How different groups' perspectives and perceptions affect their evaluation of evidence. This formed the basis of dialogue activities throughout the project.
2. The strengths and limitations of results and conclusions that originate from different study types or data sources to evaluate the benefits and harms of medicinal products. This was examined by a sub-group study launched in summer 2015.
3. How interests (including, but not limited to, different models and sources of funding) impact on the validity, or the perception of validity, of evidence. This was informed by a workshop in November 2015.
4. How to effectively communicate research findings to improve the understanding of evidence about the benefits and harms of medicinal products. This was informed by two workshops in April and June 2016.

The overarching report embraces and informs decision-making about medicines and develops a list of practical and impactful recommendations relating to the interpretation, weighting and communication of evidence. These aim to enable a wide range of groups (as described above) to better consider the benefits and harms of medicinal products. The report draws on examples of dilemmas in current therapeutic practice, but does not seek to address all such areas of contention, nor to replicate the work performed by the Medicines and Healthcare products Regulatory Agency and the National Institute for Health and Care Excellence. The remit of this project required expertise from outside of the Academy, and we therefore engaged widely via a call for evidence, workshops and further dialogue with a broad range of stakeholders.

Oversight Group membership

This report was prepared by an Oversight Group of the Academy of Medical Sciences. Members participated in a personal capacity, not as representatives of the organisations listed. A summary of the Oversight Group members' interests is provided below.

Chair

Professor Sir John Tooke FMedSci (Chair of the Oversight Group) is Co-Chair of the Centre for the Advancement of Sustainable Medical Innovation, a joint initiative between Oxford University and University College London (UCL). His research interests relate to the pathogenesis of diabetic complications and their management, and the development of academic health science systems. He was Vice Provost (Health) at UCL and Academic Director of UCL Partners until July 2015, and in the past has served as Chair of the Medical Schools Council. He is a Non-Executive Director of Bupa and Executive Chairman of Academic Health Solutions, a company that offers advice to international governments, universities and other agencies on the development of academic health science systems. He served as President of the Academy of Medical Sciences for four years until December 2015. He was in receipt of a National Institute for Health Research (NIHR) grant for the UCL Hospitals Biomedical Research Centre. He serves on the International Advisory Boards for both the Qatar Academic Health System and the National University of Singapore Medical School and is a member of Google DeepMind Health's Independent Advisory Board.

Members

Professor Dorothy Bishop FRS FBA FMedSci is a Wellcome Trust Principal Research Fellow and Professor of Developmental Neuropsychology at the University of Oxford, where she heads a programme of research into children's communication impairments. Her main interests are in the nature and causes

of developmental language impairments, with a particular focus on psycholinguistics, neurobiology and genetics. She is a supernumerary fellow of St John's College Oxford. She has honorary degrees from the Universities of Lund, Western Australia, and Newcastle upon Tyne. As well as publishing in conventional academic outlets, she writes a popular blog with personal reactions to scientific and academic matters. She is in receipt of a Wellcome Trust Programme Grant and is Director of Scholars Mews Residents.

Michael Blastland is a writer and broadcaster. Now freelance, he devised the 'More or Less' programme and continues to present 'The Human Zoo', both on Radio 4, and 'The Inquiry', on BBC World Service. He also recently produced and co-wrote with Andrew Dilnot for Radio 4 two series of 'A History of Britain in Numbers'. He presents and advises widely about data, statistics and risk, and also about journalism and communication. This has included work for the Said Business School Executive Leadership programme, at the BBC's College of Journalism, and for business, the public sector and in academia. He has written three books – the first about autism, the second about making sense of numbers in the news, and most recently a book about risk, co-authored with Professor Sir David Spiegelhalter OBE FRS. He has received payment for conference presentations on the representation of risk by Biogen Idec Limited and by the Association of the British Pharmaceutical Industry. A member of his family is a Non-Executive Director of the Hillingdon Hospitals NHS Foundation Trust.

Professor Dame Nicky Cullum DBE FMedSci (from August 2016) is Professor of Nursing and Head of the Division of Nursing, Midwifery and Social Work at the University of Manchester and Honorary Professor of Nursing at Central Manchester University Hospitals NHS Foundation Trust. Her research mainly focuses on the epidemiology and management of complex wounds such as leg, foot and pressure ulcers and non-healing surgical wounds. She was a founding member of the Cochrane Collaboration and has been Coordinating Editor of the Cochrane Wounds Group since 1995. A particular interest is how research evidence of relevance to clinical nursing decisions is produced and that evidence is translated into practice. She founded the Centre for Evidence-Based Nursing at the University of York in 1995. She has been a NIHR Senior Investigator since 2008, is a member of the Royal College of Nursing and a Fellow of the American Academy of Nursing. She has a number of current grants, either as a principal or co-applicant, from NIHR.

Professor Sarah Cunningham-Burley is Professor of Medical and Family Sociology, and Dean of Molecular, Genetic and Population Health Sciences at Edinburgh Medical School, University of Edinburgh. Her research spans the study of health and family life and the analysis of social issues in relation to new technologies and health, including developments in genomic medicine. She combines the disciplines of medical sociology and science and technology studies with methodological expertise in qualitative research. She currently holds a Wellcome Trust Senior Investigator Award, jointly with Professor Anne Kerr, University of Leeds. She is strongly committed to public engagement in research as well as wider knowledge exchange for and with policy and practice communities. She was elected to the Academy of Social Sciences in 2012, the Royal Society of Edinburgh in 2014 and the Faculty of Public Health in 2015. She is or has recently been a member of the Medical Research Council (MRC) Methodology Research Panel (Deputy Chair), Wellcome Trust Society and Ethics Investigator and Collaborative Award Expert Review Group, Ireland's Health Research Board Expert Panels and the French National Cancer Institute's Scientific Evaluation Committee for Social and Human Sciences, Epidemiology and Public Health (Co-Chair). She has grants for her current work, either as a principal or co-applicant, from the Wellcome Trust, the Economic and Social Research Council (ESRC)/Ministry of Defence, the Chief Scientist Office, NIHR Health Technology Assessment, and leads the public engagement research programmes for the ESRC Administrative Data Research Centre, Scotland and MRC-led Farr Institute, Scotland.

Professor Jane Dacre is President of the Royal College of Physicians (RCP), an Honorary Consultant Physician and Rheumatologist at the Whittington Hospital in North London, Professor of Medical Education and was former Director of UCL Medical School. She was also the Medical Director of the Membership of the RCP of the United Kingdom examination until December 2013, and prior to that Academic Vice-President of the RCP. She was a General Medical Council (GMC) Council Member, chaired the GMC Education and Training Committee (2008–2012) and leads a research programme in medical education focussing on assessment. Professor Dacre has been instrumental in the development, implementation and evaluation of assessment systems in medicine. She is a Trustee of the RCP.

Simon Denegri is National Director for Patients and the Public in Research at the National Institute for Health Research (NIHR), and Chair of INVOLVE – the national advisory group for the promotion and support of public involvement in research funded by NIHR. He was Chief Executive of the Association of Medical Research Charities (AMRC) from 2006 until 2011 and, prior to this, Director of Corporate Communications at the RCP from 2003. He also worked in corporate communications for Procter & Gamble in the United States from 1997 to 2000. He has a long-standing personal and professional interest in the needs and priorities of people with dementia and their carers, and currently chairs the Lay Champions Group for the national portal on dementia research that is to be launched this year. He is a member of the NIHR Advisory and Strategy Boards, and a Board member of the UK Clinical Research Collaboration, Farr Institute and care.data programme respectively. He also writes a blog about the public and health research. He is Chair of the UK Clinical Trials Gateway Project Board, the NIHR Collaboration for Leadership in Applied Health Research and Care (CLAHRC) North Thames International Expert Advisory Board, and the Patient and Public Involvement Strategic Group at the North Thames Genomic Medicine Centre. He is a member of a number of Advisory Boards and Groups (Clinical Practice Research Datalink, British Medical Journal, WEB-RADR, Open Trials, Engineering and Physical Sciences Research Council MeDe Innovation, EU Joint Programme on Neurodegenerative Disease Research). He is also a member of the NIHR Greater Manchester Primary Care Patient Safety Translational Research Centre, COMET Patient and Public Involvement and Engagement Working Group, the Canadian Institutes for Health Research Adjunct Panel for Support for Patient Orientated Research Units, and sits on the editorial boards of the International Journal for Engagement and Involvement and Research for All.

Professor Rob Horne is Professor of Behavioural Medicine at UCL School of Pharmacy, where he is Director of the Centre for Behavioural Medicine. Following an initial decade in clinical pharmacy and medicines management within the NHS he completed a PhD in health psychology at Guys Medical School followed by a 17-year programme of research in behavioural medicine, focussing on the role of psychological and behavioural factors in explaining variation in response to treatment. His current interests centre on the development of interventions to support optimal engagement with essential treatments and effective medical innovations and on optimising the non-specific effects (placebo and nocebo components) of medicines. Professor Horne was appointed as a Founding Fellow of the Royal Pharmaceutical Society of Great Britain in 2010 and, in 2011, a NIHR Senior Investigator. In 2012, Professor Horne became UCL's academic lead for the Centre for the Advancement of Sustainable Medical Innovation (CASMI), a joint undertaking with the University of Oxford. He is also academic lead for CASMI's Medical Innovation Academic Consortium and lead for the UCL School of Pharmacy Research Cluster. He is on the Management Board for the UCL Centre of Behaviour Change and the Steering Committee for the UCL Institute of Digital Health and UCL Personalised Medicine Health Domain. He is a member of the Management Group for the NIHR North Thames Collaboration for Leadership in Applied Health Research and Care (CLAHRC) and of the Management Board for Asthma UK Centre for Applied Research. He is an Honorary Fellow of the RCP and the Faculty of Pharmaceutical Medicine, a Fellow of the Royal Pharmaceutical Society, a member of the Martin Fisher Foundation Board of Trustees and the Asthma UK Research Board. He has received grants for his work, either as a principal or co-applicant, from Amgen, Asthma UK, Bupa Foundation, Crohn's and Colitis UK, Department of Health, Health Foundation, MRC, NIHR, NIHR North Thames CLAHRC, and the Wellcome Trust. He is Director of a Spoonful of Sugar Ltd (a UCL business spinout company) and Pharmed Research Ltd. He has received consultancy fees from GlaxoSmithKline (Salford Lung Study and Medication Taking Behaviour in COPD Advisory Board), Merck Sharp & Dohme (Summer Summit and Workshop Adherence Concept), the Norwegian Association of Pharmacists, Pfizer (Consumer Men's Health Advisory Board) and the Swiss Society for Infectious Diseases.

Professor Peter Johnson FMedSci is Professor of Medical Oncology at the University of Southampton and Chief Clinician for Cancer Research UK. He is responsible for bringing together a broad multidisciplinary group of basic, translational and clinical researchers, and linking the research of the academic unit to the extensive clinical practice in cancer treatment in the Southampton Cancer Centre. His research interests are in applied immunology and immunotherapy, lymphoma biology and clinical trials. He is Chief Investigator for lymphoma trials ranging from first in man novel antibody therapeutics to international randomised studies, and for the Cancer Research UK Stratified Medicine Programme. He was Chair of the UK National Cancer Research Institute Lymphoma Group from 2005 to 2011 and has been a member of national trials committees for the MRC, Cancer Research UK, and Leukaemia and Lymphoma Research. He has received grants from Bloodwise, Cancer Research UK, Eisai and Janssen for his scientific work, and is a Director of Cancer Research UK. He has carried out advisory work for Boehringer Ingelheim, Bristol-Myers Squibb, Epizyme and Pfizer.

Professor Martin Marshall CBE is Professor of Healthcare Improvement at UCL and leads Improvement Science London, an initiative to promote and embed the science of improvement across both the health service and academic sectors. Previously he was Director of Research and Development at the Health Foundation, Deputy Chief Medical Officer and Director General in the Department of Health, and a clinical academic at the University of Manchester. He has been a General Practitioner for 27 years, now serving an inner-city community in Newham, East London. He is a Fellow of the Royal College of General Practitioners (RCGP), RCP and Faculty of Public Health Medicine, and was a Non-Executive Director of the Care Quality Commission until 2012. He was awarded a CBE in the Queen's Birthday Honours for Services to Health Care. He is a member of Tower Hamlets Clinical Commissioning Group Primary Care Commissioning Board, the Newham Health and Wellbeing Board and the RCGP's Council, and was elected Vice-Chair for External Affairs of the RCGP in November 2016. He is also an External Examiner at Imperial College London.

Professor Theresa Marteau FMedSci is Director of the Behaviour and Health Research Unit in the Clinical School at the University of Cambridge, Director of Studies in Psychological and Behavioural Sciences at Christ's College, Cambridge, and a NIHR Senior Investigator. Her research focuses on: the development and evaluation of interventions to change behaviour (principally diet, physical activity, tobacco and alcohol consumption) to improve population health and reduce health inequalities, with a particular focus on targeting non-conscious processes; risk perception and communication, particularly of biomarker-derived risks and their weak links with behaviour change; and acceptability to the public and policymakers of government intervention to change behaviour. She is a member of the Academy of Medical Sciences' Council, the International Scientific Advisory Board of the French National Cancer Institute and the Scientific Advisory Panel of the Behavioural Insights Team (Cabinet Office and Nesta). She is a Fellow of the Academy of Social Sciences and the Royal College of Physicians of Edinburgh, and is an Associate Fellow at the Cambridge Centre for Science and Policy. She has funding from the Department of Health Policy Research Programme.

Professor Jonathan Montgomery is Chair of the Health Research Authority and Professor of Health Care Law at UCL. His research work concerns healthcare law and bioethics governance systems. His previous national Chair roles include the Advisory Committee on Clinical Excellence Awards (2005–14), the Human Genetics Commission (2009–12), and the Nuffield Council on Bioethics (2012–17). He has been involved in the preparation of ethical guidance in a number of areas of health practice and chaired a task and finish group for the GMC overseeing the revision of its guidance on confidentiality published in 2017. He is an Honorary Fellow of the Royal College of Paediatrics and Child Health. In his role as Chair of the Nuffield Council on Bioethics, he was in receipt of grants from the Nuffield Foundation, MRC and Wellcome Trust, which co-fund the organisation.

Baroness Onora O'Neill CH CBE HonFRS FBA FMedSci combines writing on political philosophy and ethics with a range of public activities. She was Principal of Newnham College, Cambridge from 1992 to 2006, President of the British Academy from 2005 to 2009, chaired the Nuffield Foundation from 1998 to 2010 and has been a crossbench member of the House of Lords since 2000 (Baroness O'Neill of Bengarve). She currently chairs the UK's Equality and Human Rights Commission and is on the Boards of the MRC and the Banking Standards Review. She lectures and writes on justice and ethics, accountability and trust, justice and borders, as well as on the future of universities, the quality of legislation and the ethics of communication. She is Emeritus Professor of Philosophy at the University of Cambridge. She chairs the University of London's Institute of Philosophy Advisory Board, is a Council Member for the Royal Institute of Philosophy and the Foundation for Science & Technology, a Trustee of the American University of Sharjah, and a member of the Demos Advisory Group. She is a member of the University of London/British Academy Panel advising on an inquiry into the future of Public Service Broadcasting and of the advisory Board for the Huxley Summit (a British Science Association event), was a member of the Royal United Services Institute Independent Surveillance Review and the Nurse Review Reference Group, and is on the Committee for the appointment of the next British Judge on the European Court of Human Rights.

Dr Imran Rafi is a General Practitioner and Principal and Senior Lecturer in Primary Care Education at St George's, University of London. He is Chair of the RCGP Clinical Innovation and Research Centre (CIRC), which oversees the clinical priority programme, and programmes that support research and promote quality improvements in general practice. CIRC receive the bulk of their funding from other charities and foundations, NHS England, Public Health England, Department of Health and the European Commission.

Historically, CIRC have received unrestricted educational grants from Pfizer, Novartis and Grunenthal Pharma. Dr Rafi has an interest in genetics and has been a member of the Health Education England Genome Advisory Board and the Human Genome Strategy Group Service working group. He was a founder member of the Primary Care Genetics Society and the World Organisation of Family Doctors specialist interest group in primary care genetics, as well as the Society for Academic Primary Care specialist group on primary care genetics. He is currently funded by Health Education England on the Masters Medical Genomics course at the University of Cambridge. He is a member of the RCGP and a fellow of the RCP.

Professor Sir Michael Rutter CBE FRS FBA (until June 2016) is Professor of Developmental Psychopathology at the Social Genetic and Developmental Psychiatry (SGDP) Research Centre at the Institute of Psychiatry, Psychology and Neuroscience, King's College London. His research interests include the use of natural experiments and animal models to test hypotheses about causation, the use of epidemiological longitudinal studies for the same purpose, gene-environment interplay, and studies of psychosocial risk. He founded the SGDP in 1994 and was its first honorary director. He retired from his administrative posts in 1998 but remains active in research and teaching. His textbook on child and adolescent psychiatry remains distinctive in attention to both conceptual and statistical issues, as well as the integration of science and clinical work. He is Governor of the Coram Foundation and Chair of the Scientific Advisory Group for the Canadian Institute for Advanced Research programme on Children and Brain Development.

Suzie Shepherd is outgoing Lay Chair of the RCP Patient and Carer Network, a Member of the RCP Future Hospital Commission Implementation Group, a full Member of RCP Council, and sits on the Clinical Standards Accreditation Board at a national level. In these roles she works to influence health and public health policy and organisational development within healthcare. Prior to retiring, Ms Shepherd worked for the NHS as a Senior Dental Nurse and, in her role as Improving Working Lives Lead for Leeds Community and Mental Health Trust, supported staff through service reconfigurations, modernisation and redesign. Drawing on her experiences as a patient, carer, parent and former member of NHS staff, she has maintained a key interest in ensuring that the lay patient and carer voice is heard during times of service change and development. She is Director of Leeds Occupational Health Advisory Service and Vice-Chair of the Clinical Services Accreditation Alliance. She is a lay member of a number of national, regional and local Boards and Committees, including at the RCP.

Professor Sir David Spiegelhalter OBE FRS is Winton Professor for the Public Understanding of Risk and Professor of Biostatistics at the University of Cambridge. His background is in medical statistics, particularly the use of Bayesian methods in clinical trials, health technology assessment and drug safety. He leads a small team, attempting to improve the way in which the quantitative aspects of risk and uncertainty are discussed in society. In collaboration with the Millennium Mathematics Project, he is developing an exciting treatment of probability and risk for mathematics education. He advises organisations and government agencies on risk communication and is a regular commentator on current risk issues. He is a Fellow of Churchill College Cambridge, an Honorary Fellow of the Institute for Risk Management, an Honorary Fellow of the RCP and a Fellow of the Royal Society. He was awarded an OBE in 2006 and knighted in 2014, both for Services to Medical Statistics. In 2013, he received an honorarium for a talk on the public perception of risk at a meeting supported by Pfizer.

Dr Julian Treadwell is a General Practitioner based in Wiltshire and an NIHR In-Practice Fellow at the Nuffield Department of Primary Care Health Sciences. He is Vice-Chair of the RCGP Standing Group on Overdiagnosis and a member of the editorial board of the Drug and Therapeutics Bulletin. He has an interest in evidence-informed prescribing and shared decision-making. He is a member of the RCGP and of the British Medical Association.

Professor Patrick Vallance FRS FMedSci is President, R&D at GlaxoSmithKline (GSK). Prior to this, he was Senior Vice President, Medicines Discovery and Development. He joined the company in May 2006 as Head of Drug Discovery. He is a member of the GSK Board and the Corporate Executive Team. Prior to joining GSK, he was a clinical academic and led the Division of Medicine at UCL. He has over 20 years' experience of research clinical medicine, general internal medicine, cardiovascular medicine and clinical pharmacology. He was elected to the Academy of Medical Sciences in 1999 and to the Royal Society in 2017. He was on the Board of the UK Office for Strategic Co-ordination of Health Research

(OSCHR) from 2009 to 2016. He is an Honorary Fellow at both UCL and Imperial College London, a Non-Executive Director and Board member for UK Biobank, a Non-Executive Board member for Genome Research Limited and a Member of the Dementia Discovery Fund, which is managed by SV Life Sciences. He is also a GSK shareholder.

Project team

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Review Group membership

The report was reviewed by a group on behalf of the Academy's Council. Reviewers were asked to consider whether the report met the terms of reference and whether the evidence and arguments presented in the report were sound and supported the conclusions. Reviewers were not asked to endorse the report or its findings. Review Group members were:

Professor Christopher Day FMedSci (Chair), Vice-Chancellor and President, Newcastle University and Vice-President of the Academy of Medical Sciences

Professor Deborah Ashby OBE FMedSci, Professor of Medical Statistics and Clinical Trials, Co-Director of Clinical Trials Unit, Imperial College London

Professor Nick Barber, Emeritus Professor, University College London School of Pharmacy

Professor Christopher Butler FMedSci, Professor of Primary Care, University of Oxford

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Professor Graeme Laurie FRSE FMedSci, Professor of Medical Jurisprudence, University of Edinburgh

Dr Fiona Marshall FMedSci, Chief Science Officer, Heptares Therapeutics

Derek Stewart CBE, Associate Director for Patient & Public Involvement and Engagement, National Institute for Health Research

Annex II. Roles and responsibilities of all those involved in the generation and communication of scientific evidence

Although improving the use of scientific evidence is a collective responsibility, we make specific recommendations in the report for the different constituencies involved. In our deliberations, we have come across many examples of good practice, which we applaud. As such, rather than relying on a regulatory approach, in most instances we believe good practice spread through peer pressure and alignment of incentives is likely to be more fruitful. Below we summarise the implications for different sectors.

The scientific community



Researchers

In both academia and industry, it is ultimately the scientist who is responsible for the integrity of their research. This means that researchers must ensure that the study is methodologically sound, recognises prior knowledge and presents findings in a justifiable manner, with due account given of the limitations of the research. It also means that interests should be declared and that data, methods and the roles of the parties involved in the research should be available for public scrutiny. Clinical research should strive to address the issues that matter most to patients with the condition under study. We describe below the role of researchers in communicating scientific evidence (see **'Communicators of evidence'** below).



Universities and research institutions

Universities and research institutes are in a position to foster the conditions that allow the scientists they host to fulfil the responsibilities described above. As the Higher Education Funding Council for England (HEFCE, relevant functions expected to be assumed by Research England in the future) develops proposals for the conduct of the next Research Excellence Framework (REF), there is an opportunity to enshrine some of our requirements and motivate their widespread adoption through the new proposed (auditable) institutional environment statement. For example, these should reflect the institution's reproducibility efforts, 'intelligent openness' initiatives and the robustness of the approaches taken to ensure accurate portrayal of their research in the media. Career progression criteria should also place greater emphasis on these attributes.

Training and continuing professional development (CPD) for scientists should ensure appropriate understanding of established and emerging research designs and methodologies and their relative values and limitations. Curricula for healthcare professionals should be reviewed to ensure that they embrace an adequate appreciation of the process of choice and the means to achieve informed decision-making, advocating better use of scientific evidence while respecting the citizen's viewpoint.



Research funders

There are many good examples of funders promoting, through award conditions and training programmes, scientific behaviours that help to improve research practice. We suggest that best practice is promulgated, particularly in relation to data openness; open access; and patient, carer and public involvement. Patient and disease-specific charities have an important role in raising awareness of concerns of their patient populations, ensuring their needs and priorities are clearly identified and that the research they fund acts upon this agenda. Funders' help will be required in addressing knowledge gaps by, for example, funding more research programmes in clinical shared decision-making about medicines, the management of medicines in the context of multimorbidity and the implications of a medicines-based approach to prevention for wider public health strategies combining 'precision prevention' with public health strategies.



Industry

Industry is a vital part of the research ecosystem for the development and introduction of new medicines. Although considerable effort has been made in recent years to address societal concerns about the role of industry in the generation of scientific evidence on the potential benefits and harms of medicines, much remains to be done to build public trust. 'Intelligent openness' and data sharing, as described in the report, will be crucial in that regard. Industry should work with academic collaborators better to explain the benefits of working together and the measures put in place to manage competing interests. The measures that we suggest universities adopt to encourage the integrity of the research process and the robustness of research findings should be replicated in the industrial sector where this is not already the case.

Communicators of evidence

We recognise that there is an increasing number of online sources outside the mainstream media that present opportunities for inaccurate and potentially harmful information to become available. It would be an impossible task to regulate online content. As such, we feel that helping citizens and patients discern what reliable information is and giving those outlets more prominence will be much more effective. For example, establishing NHS Choices as a key provider of information about the benefits and harms of medicines should allow greater access to trusted, evidence-based, reliable information about medicines.



The media

The media have a vital role in portraying a non-sensationalist, balanced view of the weight of scientific evidence, as well as in avoiding undue emphasis being given to counter views that misrepresent a balanced interpretation of the evidence, in the interest of stoking controversy and media interest. We strongly encourage journalists to adhere to the Science Media Centre's '10 best practice guidelines for reporting science and health stories' and recommend that the independent press regulators adopt these principles as their standards for use in the newsrooms.⁴⁹⁸ We call upon scientists with relevant expertise to publicly counter unjustifiable claims. Science and health specialist journalists can play an important role in ensuring responsible reporting of research findings and should be championed and better utilised by both the research community and non-specialist journalists.



Journals and publishers

Journals and publishers have a responsibility to make sure that the research they publish is sufficiently reliable and reproducible. This means ensuring it receives adequate methodological scrutiny, mandating that sufficient information is available in the final publication to allow a study to be independently repeated, and ensuring that authors adhere to internationally agreed publication guidelines. Additionally, to ensure the validity, accuracy and trustworthiness of reporting, they should take responsibility for correcting errors when these occur in an open and timely fashion (as should researchers and the mainstream media). Journals and publishers also have a crucial role in the shift towards 'intelligent openness'. They should commit to publishing data from rigorous research even if the results may have been traditionally viewed as less interesting, including 'negative', null and inconclusive results. They should also consider publishing lay summaries of data or patient perspectives so that results are intelligible to a wider audience. In addition, they should be open about and declare their interests. We support journals that only publish findings from trials that have been appropriately registered, and recommend that all journals adopt such a policy. Campaigns in medical journals can have a significant impact on health outcomes (both positive and negative). Given the authority that journals enjoy, it is particularly important that such campaigns base their assertions on robust and reliable evidence.



Researchers, universities and funders

Researchers should recognise the importance of communicating their work and engaging with the media. In communicating their findings, scientists should not make exaggerated claims and, where it concerns their area of expertise, they should not shy away from challenging misrepresentation of scientific evidence in the media. Researchers should be supported by their organisation's press offices in their engagement with journalists. Funders also have a role to play in ensuring responsible and accurate portrayal in the media of research they fund. They should encourage best practice by developing a code of practice for their grant awardees, describing how they expect the research that they fund to be represented. Universities and research institutions should provide leadership on public engagement and communication of science and evidence, supporting researchers and research teams appropriately to act responsibly and in the public interest when communicating their work.



Healthcare professionals

Healthcare professionals are often at the frontline in providing information on the potential benefits and harms of medicines, and in dealing with patient queries or concerns. It is therefore critical that they are able to clearly communicate evidence, risk and uncertainty about the use of medicines. Such conversations should be tailored to the individual as far as possible, and take into consideration their understanding of the illness and treatment. We recommend training efforts to ensure that healthcare professionals can clearly communicate the potential benefits and harms of medicines, risk and uncertainty to patients. Healthcare professionals should be supported by robust and evidence-based decision aids, algorithms and other tools in their decisions about treatment strategies and discussion of non-drug alternatives. In the future, it is likely that artificial intelligence will have an increasingly important role in this regard. We also encourage efforts to equip both healthcare professionals and patients better to engage in shared decision-making.

The public

Our work, particularly our public engagement, has emphasised that the concept of 'one public' fails to acknowledge the diversity of views and the impact of health beliefs and prior experience within society. These views and beliefs may also vary depending on factors such as age, ethnicity and the severity of disease. While some may wish to take more control of their healthcare, others may be content to be guided by a trusted healthcare professional. In this case, it is crucial that the trust is sustained, particularly for vulnerable elderly people who often have multiple co-occurring conditions requiring a number of medicines.

Being a citizen in a health system founded on the principle of social solidarity – i.e. shared practices reflecting a collective commitment to carry costs to support others – implies both rights and responsibilities. We contend that it is unrealistic for citizens to fully fulfil these unless they have sufficient health literacy and numeracy skills to appreciate the scientific evidence informing their choices, as well as having the opportunity, capability and capacity to modify health-related behaviour. We highlight the crucial part to be played by the education establishment, building on reforms to the National Curriculum to address these issues. Much more could be done by universities, institutions, researchers and funders to recognise the important role that patients, carers and the public can play in helping to design, deliver and disseminate scientific evidence. The Academy has also noted the part they will play in helping society meet future health challenges in its 'Improving the health of the public by 2040' report.⁴⁹⁹

Health services



The relationship between society and the healthcare system

In a preliminary workshop exploring the societal implications of more personalised medicine,⁵⁰⁰ many delegates believed that the assimilation of modern practice and the evidence that underpinned it was not possible without considering ways in which the healthcare system, including the NHS, might need to change.

The collective responsibilities alluded to above argue for the creation of a new social contract between science, society and health services. Although this is clearly beyond the brief of this report, certain issues deserve emphasis. Drug use for many long-term conditions could be reduced if greater attention were paid to diet, lifestyle, personal behaviours and the wider social, political and environmental determinants that underpin them. Moving to a health- as opposed to sickness-orientated service will require better ways of combining more targeted prevention, personalised for the individual, with conventional population-orientated approaches.

An average general practitioner (GP) consultation time of 9.2 minutes, which on average deals with 2.5 issues, does not give sufficient time for conversations about treatment options guided by evidence-based decision aids, or about the patient's goals and priorities. We support calls for a care planning approach that allows adequate consultation times to enable patients to be fully engaged in addressing their treatment needs. As mentioned above, we commend NHS Choices as an established vehicle to help address many of these issues. Curricula for the training of healthcare professionals need to take account of the implications of this report, increasing capacity to assimilate and communicate scientific findings while remaining sensitive to patient goals and priorities.



GPs

GPs are the key clinical interface for the majority of care for most patients, particularly those with chronic long-term conditions. Responding to the recommendations in this report will require increased efforts to improve the understanding of the strengths and limitations of different forms of scientific evidence, critical appraisal skills and a deep appreciation of the many factors that influence decision-making about the use of medicines. Undergraduate, postgraduate and CPD opportunities should better reflect these needs.

As discussed above, particular attention should be paid to enhancing communication skills such that scientific evidence on the potential benefits and harms of medicines and lifestyle change initiatives can be presented in ways that are relevant, intelligible and usable. These conversations should be supported by robust and evidence-based decision aids where appropriate. As more sophisticated algorithms, machine learning and artificial intelligence support mechanisms become available, GPs should play their part in their evaluation and integration into clinical practice, as necessary.

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