Background paper for *'Communicating evidence about medicines*' workshop

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This background paper has been developed for delegates attending the Academy's '*Communicating evidence about medicines'* workshop which is being held on 6 June 2016 as part of our wider workstream on '*How can we all best use evidence to judge the potential benefits and risks of medicines*'.[1]

The aim of this background paper is to describe some of the factors to consider when exploring how to effectively communicate evidence about the potential benefits and harms of medicines. It is not an exhaustive review of current literature, nor does it cover all the factors that can influence effective communication, but has instead been developed to help foster productive and stimulating discussions at the workshop. Elements of this paper have also been informed by the responses to our call for written evidence, which was issued to inform all aspects of the wider workstream.[2]

The discussions held at the workshop will be summarised in a report which will be published to encourage wider discussion and inform the deliberations of the *'How can we all best use evidence to judge the potential benefits and harms of medicines?*' Oversight Group.

Introduction

Given the increasing access to - and breadth - of information about medicines, it is important that individuals can both understand and trust the evidence they have been given in order to make an informed choice (Box 1). However, a range of factors can impact on an individual's ability to understand evidence, and in turn make informed choices and undertake the most appropriate course of treatment for them.

People are able to access information on the potential benefits and harms of medicines not only from healthcare professionals but also from a wide number of additional sources that communicate evidence to mass populations e.g. NHS leaflets and a range of online resources. However, each is often presented and delivered in a different format. For example, evidence can be presented quantitatively i.e. risks are described in numerical terms, or qualitatively i.e. risks are described using words (Box 2). A variety of mediums and formats can also be used, for example evidence can be communicated verbally, via written text, or via the use of visual tools such as infographics. All of these factors can influence the effectiveness with which evidence is understood and can affect its perceived trustworthiness.

The *'Communicating evidence about medicines*' workshop aims to further explore the available research on how the presentation of quantitative evidence about the potential benefits and harms of medicines impacts on the understanding and trustworthiness of such evidence. It will also aim to review existing best practice guidance on the communication of evidence.

[1] Academy of Medical Sciences (2016). *How can we all best use evidence to judge the potential benefits and harms of medicines?* http://www.acmedsci.ac.uk/policy/policy-projects/how-can-we-all-best-use-evidence/
[2] Academy of Medical Science (2016). *Evidence repository.* http://www.acmedsci.ac.uk/policy/policy-projects/how-can-we-all-best-use-evidence/evidence-repository/

Throughout this paper, reference will be made to a wide range of studies (all web links were accessed in May 2016). However, where possible, there will be a focus on three exemplar medicines: hormone replacement therapy (HRT) (Annex 1), statins (Annex 2), and vaccinations (Annex 3). These medicines have been selected as case studies for the workshop as they are examples of treatments given to large proportions of the population, and for which there are a number of complex factors that can be considered when deciding whether or not to use them. The communication surrounding such medicines is therefore often particularly difficult, making them helpful scenarios on which to base discussions to explore how to improve the effective communication of medicines.

Box 1: Informed choice

Patients and the wider public have a right to receive clear information about medicines, including their potential benefits and harms, and any alternative options, before they make an 'informed choice' whether to take the treatment or not.

Definitions of informed choice, or informed decisions, vary but the process can be broadly conceptualised as one where an individual has been able to weigh up their choices after receiving relevant, accurate evidence which can inform their ultimate decision. Importantly, informed choices should be consistent with an individual's values. Therefore, informed choice can be more simply described as one that is based on relevant knowledge, consistent with the decision-makers values, and behaviourally implemented.[3]

While we acknowledge that the ability to make an informed choice is influenced by many factors, the predominant focus of the workshop will be on factors that influence the understanding and trustworthiness of quantitative evidence about the potential benefits and harms of medicines.

What influences how evidence is understood?

Impact of numerical format on the understanding of evidence

Individuals vary in the way that they interpret qualitative descriptions of risk (as detailed in Box 2), suggesting that the use of quantitative information may be preferable. Quantitative information can be presented in various formats; the most commonly used are outlined in Box 2 and include: absolute risk reduction (ARR), relative risk reduction (RRR), and numbers needed to treat (NNT).

Box 2: Quantitative vs. qualitative information

Quantitative information

Quantitative reporting of the potential benefits and harms of medicines can take a number of different forms. Whilst all are numerical, an understanding of the statistics is needed in order to accurately interpret the information. Examples of the ways in which statistical data can be presented include:

- Absolute Risk Reduction (ARR): The actual difference between the outcome of two interventions e.g. If 2% of people experience a migraine following treatment A compared to 4% taking a placebo, the ARR is 2%.
- Relative Risk Reduction (RRR): The proportional difference between the outcome of two

[3] Marteau T, Domrandy E, & Michie, S (2001). *A measure of informed choice.* Health Expectations **4(2)**, 99-108.

interventions e.g. If 2% of people experience a migraine following treatment A compared to 4% taking a placebo, the RRR is 50%.

- Number needed to treat (NNT): An estimate of the number of patients that need to be treated in order to expect that one person will avoid an adverse event e.g. if a treatment is known to save the lives of 50% of the people it is given to, two people would need to take the treatment in order for it to save one person.

Whilst the reporting of ARR and RRR are equally accurate, as can be seen in the example above, and despite the improvement being the same, the 50% RRR appears much more impactful and as such is more often the sole statistic reported in the media.

Qualitative information

Qualitative reporting of information can also involve descriptors of probabilities, with the 1998 (revised 2009)[4] EU recommended verbal descriptors being:

Very common	>10% (more than 1 in 10 people)
Common	>1% and <10% (less than 1 in 10 but more than 1 in 100)
Uncommon	0.1% to 1% (less than 1 in 100 but more than 1 in 1000
Rare	0.01% to 0.1% (less than 1 in 1,000 but more than 1 in 10,000)
Very rare	<0.01% (less than 1 in 10,000)

Whilst seemingly helpful, evidence has shown that although 'common' in EU terms refers to side effects occurring in 1-10% of people, on average patients interpret the word to mean around 45%, whilst doctors estimate the effects at around 25%. [5]

The focus of this workshop will be on the effective communication of quantitative information.

For communicating potential treatment benefits, some have suggested that quantitative information may be best understood when it is presented as number needed to treat (NNT).[6,7] However, other findings conflict with this. For example, a study by Sheridan, *et al.* (2003) found that this mode of communication is the least likely method to result in the correct interpretation of data - patients had more difficulty interpreting written information about treatment benefit when it was presented as NTT compared to ARR or RRR.[8] A study by Natter and Berry (2006) comparing the relative and absolute forms of presenting risk information about influenza and the benefits elicited from vaccination also supported this finding, but additionally found that for patients to be able to accurately understand this measure it was also important to include baseline levels of risk.[9] A more recent paper by Carling, *et al.* (2009) showed that patients are more likely to initiate statin treatment if presented with RRR rather than ARR, but as understanding was self-reported rather than tested, actual levels of comprehension are unknown.[10]

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[4] European Commission (2009). *Guideline on the readability of the labelling and package leaflet of medicinal products for human use - Revision 1*. 12 January. http://ec.europa.eu/health/files/eudralex/vol-2/c/2009_01_12_readability_guideline_final_en.pdf

[5] Berry, DC (2004). *Risk, communication and health psychology.* Open University Press, Milton Keynes.

[6] Schwartz LM, Woloshin S, Black WC & Welch HG (1997). *The Role of Numeracy in Understanding the Benefit of Screening Mammography.* Ann Intern Med. **127 (11)**, 966-972.

[7] Rajkumar S, Sampathkumar P & Gustafson A (1996). *Number needed to treat is a simple measure of treatment efficacy for clinicians.* J Gen Intern Med **11(6)**, 357–359.

[8] Sheridan HL, Pignone MP & Carmen CL (2003). *A randomised comparison of patients' understanding of number needed to treat and other common risk reduction formats*. J Gen Intern Med **18(11)**, 884–892.

[9] Natter HM & Berry DC (2006). *Effects of presenting the baseline risk when communicating absolute and relative risk reductions.* Psychol Health Med **10(4)**, 326–334.

[10] Carling CLL, Kristoffersen DT, Montori VM, *et al*. (2009). *The Effect of Alternative Summary Statistics for Communicating Risk Reduction on Decisions about Taking Statins: A Randomized Trial.* PLoS Med **6(8)**, e1000134.

These seemingly inconsistent results may, at least in part, reflect differences between the various settings, participant groups, and metrics by which understanding was assessed in individual studies. One of the earliest systematic reviews to take a more comprehensive look at the effectiveness of various formats for increasing patient understanding found that changes in risk are better understood as AAR or RRR presented with baseline risk information, rather than NNT which led to lower understanding than both ARRs and RRRs.[11] A systematic review by Zipken, *et al.* (2014) has also since reported that while RRRs increase the magnitude of perceived risks, people more accurately understand reports of risk when presented as ARR compared to RRR.[12]

Impact of presentation format on the understanding of evidence

In addition to the precise statistic by which quantitative information is described (e.g. RRR or ARR), quantitative evidence can be communicated via a variety of formats including written and verbal forms (as mentioned above) as well as in visual formats including icon arrays, graphs, infographics, and flow diagrams.

The formats in which quantitative information is communicated can also influence understanding. For example, the use of illustrations to support narrative text can increase understanding, especially in those with fewer years of formal education.[13,14] Visual formats can be particularly helpful for increasing comprehension of complex numerical concepts, and are often recommended to improve the communication of such data.[15] The majority of papers included in the recent systematic review by Zipkin, *et al.* (2014) also reported that the inclusion of visual displays improves understanding, making them a particularly attractive tool to use when communicating evidence.[16]

However, an important caveat to recognise is that individuals vary in their ability to make sense of quantitative evidence presented in different formats; not everyone benefits from the use of visual formats. Indeed, a common feature across a number of the studies reviewed for this background paper is that income and education levels (including levels of verbal, numerical, and health literacy) affect the ability to understand quantitative evidence. Individuals also vary in terms of their personal preferences for how evidence is presented; values which can be based on or influenced by race, cultural, and religious backgrounds but also medical context and disease state. Such values can play a particularly important role in informed decision-making meaning it is unlikely that a single method for communicating quantitative evidence to mass audiences will be found to be superior, especially since opportunities to tailor delivery to account for individual abilities and preferences are likely to be lacking.[17,18] For example, Fortin, *et al*. (2001) found that

[11] Trevena LJ, Barratt A, Butow P, & Caldwell P (2006). *A systematic review on communicating with patients about evidence*. J EvalClinPract. **12(1)**,13–23.
[12] Zipkin D, Umscheid C, Keating N, *et al.* (2014). *Evidence-based risk communication: A systematic review.* Ann Intern Med **161**, 270-280.
[13] Trevena L, Davey HM, Barratt A, *et al*. (2006). *A systematic review on communicating with patients about evidence.* Journal of Evaluation in Clinical Practice **12(1)**, 13-23.
[14] Galesic M, Garcia-Retamero R & Gigerenzer G (2009). *Using icon arrays to communicate medical risks: overcoming low numeracy.* Health Psychology **28(2)**, 210-216.
[15] Trevena L, Zikmund-Fisher BJ, Edwards A, *et al*. (2013). *Presenting quantitative information about decision outcomes: a risk communication primer for patient decision aid developers.* BMC Medical Informatics and Decision Making **13(2)**, S7.
[16] Zipkin D, Umscheid C, Keating N, *et al.* (2014). *Evidence-based risk communication: A systematic review.* Ann Intern Med **161**, 270-280.
[17] Trevena L, Zikmund-Fisher BJ, Edwards A, *et al*. (2013). *Presenting quantitative information about decision outcomes: a risk communication primer for patient decision aid developers.* BMC Medical Informatics and Decision Making **13(2)**, S7.

even in a small, self-selected group of women who were convened to discuss decision-making issues about HRT, no single format of graphical display was favoured by all participants (although bar graphs were overall the most popular).[19]

What makes evidence trustworthy?

If informed decisions rely (at least in part) on the availability of accurate and relevant information (Box 1), then it follows that there is a need for individuals to consider the information they receive as trustworthy.

When determining if an individual considers evidence as trustworthy, two aspects of trust emerge: trust in the source of information (e.g. a doctor) and a more fundamental trust in the evidence itself. Whilst seemingly simple concepts, they actually interlink and become complex. Indeed, extensive literature searches performed for the development of this background paper yielded little in the way of studies which focus solely on patient trust in the information they receive from their doctors, with studies instead largely focussing on trust in the doctor as a source of evidence.

The doctor-patient relationship is particularly complex as it involves interaction between individuals in non-equal positions, is often non-voluntary, concerns issues of vital importance, is therefore emotionally laden, and requires close cooperation.[20] It is not unreasonable to assume that if a patient believes the information that their doctor has given them then this can be considered as finding the evidence trustworthy. However that does not mean that they need to trust their doctor, or that they need to understand the evidence they are being given. Acting on the evidence received from a source and thereby being influenced by that information does not require a belief that the source is reliable. In 1994, Foley stated that *'it can be reasonable for us to be influenced by others even when we have no special information indicating that they are reliable.'*[21]

Placing trust in a doctor to provide accurate information about medicinal evidence raises a number of interesting points that are relevant to this workshop, and highlights an overlap with the importance of ensuring such evidence is communicated to all stakeholders in a way that is easily understood. Firstly it suggests that patients are assuming that doctors understand the evidence they are presenting. However, a number of studies have demonstrated that doctors may not fully understand the statistics themselves.[22,23] In 2000, Schwartz and Woloshin tested physicians at Dartmouth Hitchcock Medical Centre on basic numeracy with the use of three simple test questions (outlined in Box 3).[24] Whilst all were correct for the basic probability question, only 91% could

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[18] Tait AR, Voepel-Lewis T, Brennan-Martinez C, *et al*. (2012). *Using Animated Computer-generated Text and Graphics to Depict the Risks and Benefits of Medical Treatment.* The American Journal of Medicine **125(11)**, 1103-1110.
[19] Fortin JM, Hirota LK, Bond BE, *et al.* (2001). *Identifying patient preferences for communicating risk estimates: A descriptive pilot study.* BioMed Central. **1**, 2.
[20] Chaitchik S, Kreitler S, Shaked S, *et al*. (1992). *Doctor-patient communication in a cancer ward*. J. Cancer Educ **7**, 41 as cited in Ong LML, De Haes JCJM, Hoos AM & Lammes FB (1995). *Doctor-patient communication: A review of the literature*. Soc. Sci. Med **40(7)**, 903-18.
[21] Foley, R (1994). *Egoism in Epistemology* in F. Schmitt, ed., Socializing Epistemology. Lanham, MD: Rowman & Littlefield
[22] Wegwarth O, Schwartz LM, Woloshin S, *et al*. (2012). *Do Physicians Understand Cancer Screening Statistics? A National Survey of Primary Care Physicians in the United States.* Ann Intern Med **156(5)**, 340-349.
[23] Wulff HR, Andersen B, Brandenhoff P & Guttler F (1987). *What do doctors know about statistics?* Statistics in Medicine **6**, 3-10.
[24] Schwartz LM & Woloshin S (2000). Physician Grand Round Survey (unpublished data) cited in Gigerenzer G, Gaissmaier W, Kurz-Milcke E, *et al*. (2007). *Helping Doctors and Patients Make Sense of Health Statistics.* Psychological Science in the Public Interest **8(2)**, 53-96.

convert 1% to 1 in 100 while only 75% could convert 1 in 1,000 to 0.1% - only 72% of physicians tested were able to answer all three questions correctly. If physicians are unable to interpret data correctly how can they be expected to communicate it accurately, and in doing so inspire a sense of trust?

Box 3: Testing numeracy

Studies assessing peoples comprehension of quantitative information commonly rely on tests of numeracy to determine understanding of data formats and probabilities such as those developed by Schwartz, *et al.* (1997):[25]

1. A person taking Drug A has a 1% chance of having an allergic reaction. If 1,000 people take drug A, how many would you expect to have an allergic reaction? (Asks participants to convert a percentage to a proportion).
2. A person taking drug B has a 1 in 1,000 chance of an allergic reaction. What percent of people taking drug B will have an allergic reaction? (Asks participants to convert a proportion to a percentage).
3. Imagine I flip a coin 1,000 times. What is your best guess about how many times the coin would come up heads in 1,000 flips? (Asks participants about basic probability).

Secondly, it implies that doctors are neutral in their presentation of evidence. As described in more detail below, an individual's beliefs can influence how receptive they are to evidence and preconceived beliefs held by doctors have also been shown to impact on the evidence that is given to patients. In the case of statins, a paper by Foley, *et al.* (2006) examined physician attitudes and beliefs about hyperlipidaemia and whether they are associated with lipid treatment decisions.[26] It was found that when treating patients whose serum cholesterol levels exceeded the desired level, if physicians believed that 'close enough to goal is good enough' patients had a 47% lower odds of having a dose increase compared to those patients whose physicians believed that 'statins are effective'. Given that the impact of belief translated in clinical practice, it is not unreasonable to assume that this also impacts on the neutrality with which information is presented to patients.

A paper by Benin, *et al.* (2006) encompasses the overlap between trust and understanding after studying how parents decide whether to vaccinate their infants.[27] It was found that knowledge about vaccinations was similarly low in both vaccinator and non-vaccinator groups, but that the key concept underpinning all of the themes about decision-making was trust in the medical profession. The authors concluded that *'trust or lack of trust and a relationship with a paediatrician or another influential person were pivotal for decision-making of new mothers and about vaccinating their children.'* The study also found that pre-existing beliefs about whether or not to vaccinate impacted on trust and understanding. While non-vaccinators felt that the evidence they had been given was unsatisfactory (both in quality and quantity), vaccinators were conversely willing to trust the doctor even if they did not fully understand it. Indeed, such individuals were often found to not want too much information because they trusted the doctor to make the decision on their behalf.

[25] Schwartz LM, Woloshin S, Black WC & Welch HG (1997). *The role of numeracy in understanding the benefit of screening mammography.* Ann Intern Med **127(11)**, 966-972.
[26] Foley KA, Denke MA, Kamal-Bahl S, *et al*. (2006). *The impact of physician attitudes and beliefs on treatment decisions.Lipid therapy in high-risk patients.* Med Care **44**, 421-428.
[27] Benin AL, Wisler-Scher DJ, Colson E, *et al.* (2006). *Qualitative analysis of mothers' decision-making about vaccines for infants: the importance of trust.* Pediatrics **117(5)**, 1532-1541.

The wider public now has access to a breadth of sources about medicinal evidence beyond GPs, not all of which are accurate, balanced, or complete. It can, therefore, be of particular importance to ensure that the mass communication of evidence is performed in a way that is credible and trustworthy, as public mistrust can be a valid barrier to effective communication.

As detailed in the 2009 Wellcome Trust Monitor, the public has varying levels of trust in professionals and institutions as sources of information about medical research.[28] 64% of respondents said they have high levels of trust in doctors, nurses and other medical practitioners, making them the most trusted of the professions in terms of providing accurate and reliable information about medical research. Scientists followed next, although trust in scientists was found to more intricately vary depending on the institution they work for - while 59% of people have high levels of trust in university scientists only 29% of respondents maintained trust in industry scientists. Medical charities are also trusted to some extent, with 37% of people reporting they trust them completely or a 'great deal' although journalists were viewed as the least trustworthy source of information with 59% of people not trusting them at all or very little. Although the Wellcome Trust Monitor investigated medical research in a broad sense, it is not unreasonable to speculate that similar levels of perceived trust exist when communicating more specifically about medicinal evidence.

Interestingly, there is also some evidence that the format of information (in addition to its source) may impact on trustworthiness as well as understanding. For example, a study by Tait, *et al.* (2013) looked at various forms of presenting risk/benefit information to parents about paediatric postoperative pain medication and found that pictographics were deemed to be significantly more trustworthy than numbers or tables.[29]

Initiatives for communicating quantitative evidence to mass audiences

A number of initiatives have been, or are being, developed by different stakeholders to effectively communicate summaries of relevant and balanced evidence about medicines to mass audiences. These include the American Drugs Fact Box, the European Medicine Agency's Effects Table, and Cochrane's Summary of Findings Table. Some additional information is provided below, although there will be an opportunity to discuss these initiatives (amongst others) during the workshop.

In recognition that the general public has increasingly become an audience for prescription drug information, but have historically not been given access to precise numerical information about potential benefits and harms, Swartz and Woloshin have developed a written resource termed the Drug Facts Box: a simple one-page summary of both the benefits and side effects, and uncertainties, of a given indication of a drug.[30] Each Drugs Fact Box provides prose descriptions to communicate what the drug is for and who might consider taking it, together with simple, tabulated quantitative information from publicly available Food and Drug Administration (FDA) trials on the drug's potential benefits and harms. Please see http://www.informulary.com for examples of the Drugs Fact Box.

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[28] Wellcome Trust Monitor (2009). http://www.wellcome.ac.uk/stellent/groups/corporatesite/@msh_grants/documents/web_document/wtp060289.pdf

[29] Tait AR, Voepel-Lewis T, Zikmund-Fisher BJ & Fagerlin A. (2010). *The Effect of Format on Parents' Understanding of the Risks and Benefits of Clinical Research: A Comparison between Text, Tables, and Graphics.* J Health Commun **15(5)**, 487-501.

[30] Schwartz LM & Woloshin S (2013). *The Drug Facts Box: Improving the communication of prescription drug information.* PNAS **11(3)**, 14069-14074.

Despite initial concern, studies have revealed that the majority of consumers are able to comprehend numerical information, presented as percentages, as available on the Drugs Fact Box leaflets. Indeed, the use of percentages alone has been found to result in greater levels of comprehension compared to the use of percentages together with frequencies (i.e. x in 1000).[31] However, even when presented in this format, there was still a proportion of study participants who failed to understand the evidence, highlighting the difficulties faced when attempting to optimise the format in which numerical information is given to ensure it is widely understood.[32] While this background paper has so far predominately discussed the impact of numerical format on understanding, research involving the Drugs Fact Box has also revealed the importance of remembering that such information is often best applied alongside narrative explanations that take into account patient-relevant preferences (i.e. clinical rather than surrogate outcomes).[33]

An initiative from the European Medicines Agency (EMA), the Effects Table (ET), has been developed as part of the EMA's Benefit-Risk Methodology Project which aims to enhance the transparency of the benefit-risk decision-making process, and facilitate the communication of the rationale for each decision both within the regulatory system and to the public.[34] The ET also provides a description of both the benefits and risks which contribute to the benefit-risk balance, along with supporting quantitative data (including comparison between treatment groups). Details on uncertainties and the strength of evidence - both of which also influence decisions - are also presented, and references allowing further information to be sought are included. Following an initial pilot, during which the ET was received positively, the template of the ET is being updated to incorporate feedback.[35]

The Cochrane 'Summary of findings' (SoF) tables present the main findings of a given review (most often a Cochrane systematic review) in a transparent and simple tabular format.[36] Specifically, they are headed by information on the structure of trials (participants, intervention etc) and contain quantitative data on outcomes (including both potential benefits and potential harms) to aid decision making, as well as providing a metric of evidence quality on a clear scale out of four. Space for comments is also provided.[37] Additional information and explanations about the numerical information included in such tables are provided in clear language on the Cochrane website.[38] Two small randomised-controlled trials have shown that the use of SoF tables is associated with improved understanding, and faster recall, of the key findings presented in the review.[39]

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[31] Woloshin S & Schwartz LM (2011). *Communicating data about the benefits and harms of treatment: a randomized trial*. Ann Intern Med **155(2)**, 87-96.
[32] *Ibid.*
[33] Schwartz LM & Woloshin S (2011). *Communicating uncertainties about prescription drugs to the public: a national randomized trial.* Arch Intern Med. **171(16)**,1463-1468.
[34] European Medicines Agency (2008). *Benefits-risk methodology research project.* http://www.ema.europa.eu/ema/index.jsp?curl=pages/special_topics/document_listing/document_listing_000314.jsp
[35] European Medicines Agency (2014). *Benefit-risk methodology project. Update on work package 5: Effects Table pilot (Phase 1).* http://www.ema.europa.eu/docs/en_GB/document_library/Report/2014/02/WC500162036.pdf
[36] Langendam MW, Akl EA, Dahm P, *et al*. (2013). *Assessing and presenting summaries of evidence in Cochrane Reviews.* Systematic Reviews. **2**,81.
[37] Cochrane Library. *Explanations for Cochrane Summary of Findings tables.* http://www.cochranelibrary.com/about/explanations-for-cochrane-summary-of-findings-sof-tables.html
[38] *Ibid.*
[39] Rosenbaum SE, Glenton C, & Oxman, AD (2010). *Summary-of-findings tables in Cochrane Reviews improved understanding and rapid retrieval of key information.* J Clin Epidemiol **63**, 620-626.

Best practice guidance for communicating evidence

Despite the complexities in doing so, a number of resources are available which recommend or detail effective approaches to evidence communication. We have allowed plenty of time during the workshop to discuss such approaches in more detail, and we are particularly keen to explore whether there are any limitations, and if so, further discuss ways to address them in order to improve the effective communication of evidence about medicines.

In this context, the following resources may be helpful to consider ahead of the meeting:

1. Table 4 (*'Recommended Approaches to Risk Communication'*) in a systematic review by Zipkin, *et al.* (2014).[40]
2. Table S1 (*'Key Messages for Presenting Quantitative Information about Decision Outcomes'*) in a review by Trevena, *et al.* (2013).[41]
3. A summary of recommendations for risk communication in a commentary by Fragerlin, *et al*. (2011).[42]
4. Currently unpublished guidance from a review by Professor Sir David Spiegelhalter OBE FRS titled *'Risk and Uncertainty Communication'.*[43] These have been informed, in part, by published guidance from Fragerlin, *et al*. (2011) and Trevena, *et al.* (2013).[44,45]
5. A summary of the relevant responses that were received to the Academy's call for evidence, which was issued to inform all aspects of the wider *'How can we all best use evidence to judge the potential benefits and harms of medicines*' workstream.[46]

These resources have been reproduced below for convenience.

Table 4 ('Recommended Approaches to Risk Communication') in a systematic review by Zipkin, et al. (2014)[47]

Recommended Approaches to Risk Communication
To improve understanding: • Express probabilities as event rates (percentages) or natural frequencies (numerator/denominator as whole numbers). • When using natural frequencies, use a denominator of 1000 participants. • Express benefits and risks in absolute terms, such as ARRs. • Avoid expressing benefits as NNTs. • Add bar graphs or icon arrays to natural frequencies or event rates. • Consider the use of icon arrays with smaller numerators and bar graphs with larger

[40] Zipkin D, Umscheid C, Keating N, *et al.* (2014). *Evidence-based risk communication: A systematic review.* Ann Intern Med **161**, 270-280.
[41] Trevena L, Zikmund-Fisher BJ, Edwards A, *et al*. (2013). *Presenting quantitative information about decision outcomes: a risk communication primer for patient decision aid developers.* BMC Medical Informatics and Decision Making **13(2)**, S7.
[42] Fragerlin A, Zikmund-Fisher, BJ, & Ubel, PA (2011). *Helping patients decide: ten steps to better risk communication*. J Natl Cancer Inst. 103(19).
[43] Spiegelhalter, D (2016). *Risk and Uncertainty Communication: Annual Review of Statistics.* In preparation.
[44] *Ibid.*
[45] Trevena L, Zikmund-Fisher BJ, Edwards A, *et al*. (2013). *Presenting quantitative information about decision outcomes: a risk communication primer for patient decision aid developers.* BMC Medical Informatics and Decision Making **13(2)**, S7.
[46] Academy of Medical Science (2016). *Evidence repository.* http://www.acmedsci.ac.uk/policy/policy-projects/how-can-we-all-best-use-evidence/evidence-repository/
[47] Zipkin D, Umscheid C, Keating N, *et al.* (2014). *Evidence-based risk communication: A systematic review.* Ann Intern Med **161**, 270-280.

numerators.
- Place a patient's risk in context by using comparative risks of other events.
- Avoid the use of qualitative risk descriptors alone (such as 'high risk').

To improve satisfaction:
- Supplement numerical risks with icon arrays or bar graphs.
- Use an incremental risk format with icon arrays (risk with and without intervention displayed in the same array).
- Avoid the use of NNTs.
- Avoid the use of qualitative risk descriptors alone.

To influence acceptance of interventions:
- Realize that expressing numerical benefits as RRRs has the greatest effect on decision making.
- Add baseline risks to both ARRs and RRRs to equalize their effects on decision making.
- Realize that positive framing (stating benefits rather than harms) increases acceptance of therapies.

Table S1 ('Key Messages for Presenting Quantitative Information about Decision Outcomes') in a review by Trevena, et al. (2013).[48]

Key Messages for Presenting Quantitative Information about Decision Outcomes	
Communication Issues In Presenting Quantitative Information	Key Messages

Presenting the Chance an Event Will Occur	• Ideal formats depend on the task that the recipient faces.
	• Use simple frequency (e.g., x in 100) or simple percentage (e.g., x%) formats that explicitly specify the reference class over time.
	  o Using both formats together does not appear to provide benefits.
	• When comparing two independent events, the simple percentage format appears to be better understood than the simple frequency format, possibly because fewer numbers are simpler to process.
	  o Specifying the reference class over time is essential.
	  o Format biases may exist with very small numbers and for the less numerate. These may be partly corrected by use of appropriate visual display formats.
	  o Use consistent denominators with simple frequency formats (i.e., no '1 - in -X' formats").

Presenting Changes in Numeric Outcomes	• Use absolute risk presentations (either simple frequencies or percentages) rather than relative risk presentations (e.g. "30% lower risk"), as the latter tend to magnify risk

[48] Trevena L, Zikmund-Fisher BJ, Edwards A, *et al*. (2013). *Presenting quantitative information about decision outcomes: a risk communication primer for patient decision aid developers.* BMC Medical Informatics and Decision Making **13(2)**, S7.

	perceptions and decrease understanding. o Maintain constant denominators across statistics. • Incremental risk formats (absolute risk increase or decrease) may be valuable if accompanied by visual displays.
Outcome Estimates for Tests and Screening Decisions	• Use of 'natural frequencies' (frequency representations that use a common, fixed reference class of cases) can improve peoples' understanding and estimates of joint occurrence risks (e.g., the probability of having breast cancer given an abnormal mammography result). o Representations of the calculated 'post-test probability' may be communicated as percentages if that simplifies the user's task.
Numerical Estimates in Context and with Evaluative Labels	• Contextual data (e.g., providing the risk of conditions other than the target condition) can help users get perspective on their risk of disease. o Providing such data should be considered when feasible. • Directly interpreting the meaning of risk data (e.g., by providing evaluative labels such as "poor") has a substantial impact on people's reactions. o Because the appropriateness of such reactions varies, evaluative labels should be applied carefully.
Communicating Uncertainty	• Care should be taken to distinguish between the randomness of future events and 'ambiguity' (a lack of knowledge needed to predict the likelihood of future outcomes). • Many people exhibit 'ambiguity aversion,' avoiding decision making and showing affective responses to situations described as having epistemic uncertainty. • Little consensus exists regarding how best to communicate these concepts.
Visual formats	• Visual displays such as pictographs/icon arrays and bar charts can improve understanding, especially among the less numerate. o People vary in their graph literacy, i.e., their ability to extract data and meaning from visual displays. • Visual displays convey essential or 'gist' information more than precise information. o Bars and pictographs are perceived most accurately and easily, especially when they depict the part-whole relationship by showing the entire population.
Tailoring Estimates to Individual Characteristics	• Research is mixed regarding the effect of tailoring risk information.
Formats for Understanding Outcomes Over Time	• Efforts to estimate risk over time are often hampered by a lack of data.

	• Multiple approaches can show risk over time, including chance of a specific outcome at a single point in the future, mortality or survival graphs, and lifetime risk estimates. o Research is needed to assess the relative strengths and weaknesses of different approaches.
Narrative Methods for Conveying the Chance of an Event	• The proportion of favorable vs. unfavorable narratives can influence perceptions of risk and treatment choices. o When used to present risk or benefit information, they should be accompanied by a visual display such as pictographs. • Narratives should be used with caution until research better clarifies their effects (both positive and negative).
Important Skills for Understanding Numerical Estimates	• Higher numeracy facilitates computations, interpretations of numbers, information seeking, depth of processing and, trust in numerical formats. o Lower numeracy is associated with overestimation of risk probabilities, higher susceptibility to other factors such as format, and denominator effect. • Both objective and subjective measures of numeracy are now available.
Interactive, Web-based Formats	• While interactive, web-based formats can use motion cues or game-like interfaces to potentially reinforce risk messages, they may degrade knowledge unless these elements reinforce the most critical gist message.

A summary of recommendations for risk communication in a commentary by Fragerlin, et al. (2011).[49]

Summary of recommendations for risk communication to patients
• Use plain language to make written and verbal materials more understandable. • Present data using absolute risks. • Present information in pictographs if you are going to include graphs. • Present data using frequencies. • Use an incremental risk format to highlight how treatment changes risks from pre-existing baseline levels. • Be aware that the order in which risks and benefits are presented can affect risk perceptions. • Consider using summary tables that include all of the risks and benefits for each treatment option. • Recognise that comparative risk information (e.g. what the average person's risk is) is persuasive and not just informative. • Consider presenting only the information that is most critical to the patient' decision making, even at the expense of completeness. • Repeatedly draw patients' attention to the time interval over which a risk occurs.

[49] Fragerlin A, Zikmund-Fisher, BJ, & Ubel, PA (2011). *Helping patients decide: ten steps to better risk communication*. J Natl Cancer Inst. 103(19).

Currently unpublished guidance from a review by Professor Sir David Spiegelhalter OBE FRS titled 'Risk and Uncertainty Communication'.[50] These have been informed, in part, by published guidance from Fragerlin, et al. (2011) and Trevena, et al. (2013).[51,52]

General issues when communicating risks based on statistical analysis:

- Be clear about objectives.
- Segment audience into target groups and identify their needs, beliefs and skills.
- Develop, test and evaluate material with target groups.
- Build trust by being trustworthy.
- Use plain language and limit information to only what is necessary.
- Allow for different levels of interest, knowledge and numeracy, for example a top 'gist' level, then numerical information, and then evidence and uncertainty.
- Have humility to admit uncertainty.

Communicating numerical risks:

- Use absolute risks (but also provide relative risks when dealing with potential catastrophic events).
- For single unique events, use % chance if possible, or if necessary '1 in X'.
- When appropriate, express chance as a proportion, a frequency or % - crucial to be clear about reference class.
- To avoid framing bias, provide percentages or frequencies both with and without the outcome.
- Keep denominator fixed when making comparisons with frequencies, and use an incremental risk format.
- Be explicit about the time interval.
- Be aware that comparators can create an emotional response.
- For more knowledgeable audiences, consider providing quantitative epistemic uncertainty about the numbers, and qualitative assessment of 'confidence' in analysis.
- More sophisticated metrics can be made for technical audiences, but this only serves to exclude others.

Visualisations (these are derived primarily from Spiegelhalter, *et al*. (2011)[53]

- Consider a good summary table as a visualisation.
- Use multiple formats, because no single representation suits all members of an audience.
- Illuminate graphics with words and numbers.
- Design graphics to allow part-to-whole comparisons on an appropriate scale.
- Helpful narrative labels are important. Compare magnitudes through tick-marks, and clearly label comparators and differences.
- Use narratives, images and metaphors that are sufficiently vivid to gain and retain attention, but which do not arouse undue emotion. It is important to be aware of affective responses.
- Assume low numeracy of a general public audience and adopt a less-is-more approach by reducing the need for inferences, making clear and explicit comparisons, and providing

[50] Spiegelhalter, D (2016). *Risk and Uncertainty Communication: Annual Review of Statistics.* In preparation.
[51] *Ibid.*
[52] Trevena L, Zikmund-Fisher BJ, Edwards A, *et al*. (2013). *Presenting quantitative information about decision outcomes: a risk communication primer for patient decision aid developers.* BMC Medical Informatics and Decision Making **13(2)**, S7.
[53] Spiegelhalter D, Pearson, M, & Short, I (2011). *Visualizing Uncertainty About the Future*. Science **333**, 1393 –1400.

optional additional detail.
- Be cautious about interactivity and animations – they may introduce unnecessary complexity.

A summary of the relevant responses that were received to the Academy's call for evidence, which was issued to inform all aspects of the wider 'How can we all best use evidence to judge the potential benefits and harms of medicines' workstream.[54]

Effective communication mechanisms should, where possible:

- Be targeted and disseminated to specific audiences. A method of effectively communicating evidence to one group may not be suitable for another.
- Use a wide range of different communication mediums to ensure it is distributed widely.
- Involve end-users. Involving the public and patients as active collaborators in evidence generation and communication is vital.
- Include interaction/mutual dialogue between stakeholders, especially when behaviour changes are desired and public trust is low.
- Come from a credible source so that intended stakeholders perceive the information to be trustworthy.
- Be consistent.
- Be clear and concise using simple English language, but not overly-simplistic or patronising.
- Be empowering and promote independence. The public in particular should be taught to effectively understand and interpret evidence. Education is vital for effective communication, and will help the public be resilient to scaremongering or adverse marketing mechanisms.
- Use language that is able to recognise and reflect the uncertainty associated with evidence of effectiveness derived from clinical trials.
- Be personally relevant or relatable.

Effective communication mechanisms should consider:

- Psychological/social factors. Pre-existing beliefs and experiences influence the interpretation and use of evidence. Cultural background, professional training, personal experiences, and illness will all affect individual views of medicinal products.
- Involving neutral third parties. The involvement of neutral third parties, advisory bodies, members of the public, patient groups etc can help improve public trust and demonstrate shared values.
- Engaging children. Efforts to engage children will help create awareness of key points from an early age.
- The recipients of public trust. An understanding of which authorities patients (for example) trust and perceive to be credible to give advice might help inform who is best placed to give particular information.
- Formatting. Layering content from simple-to-complex (especially online) can have an influence on the effectiveness of evidence communication. Visual aids can help improve recall and be beneficial for certain audiences (e.g. those with poor English language proficiency).

[54] Academy of Medical Science (2016). *Evidence repository.* http://www.acmedsci.ac.uk/policy/policy-projects/how-can-we-all-best-use-evidence/evidence-repository/

Annex 1: Hormone replacement therapy (HRT) case study

Target treatment group

Women undergoing menopause. The most common symptom of the menopause is hot flushes, occurring in three in every four menopausal women. Other common symptoms include night sweats, sleeplessness, vaginal dryness, irritated skin, more frequent urinary incontinence and urinary tract infections, low mood and a reduced interest in sex. Symptoms vary hugely in duration, severity and what impact they have between women.[55]

What treatment involves

First introduced in the UK in 1965, HRT replaces the oestrogen levels that naturally fall during the menopause thereby reducing the symptoms experienced. There are more than 50 types of HRT available that can be given orally as tablets; transdermally through a patch or gel on the skin; subcutaneously via a long-lasting implant; or vaginally. It can be given either as oestrogen-alone, or in combination with progestogen.[56]

Potential side effects

Some women experience side effects when taking HRT for the first time, such as breast tenderness, leg cramps, nausea, bloatedness, irritability and depression. Usually these symptoms resolve after a few months, but change in type, or route of HRT may be required. Furthermore, HRT has been shown to lead to increased rates of breast cancer (2 per 1000 when single therapy is taken for 5 years from the age of 50, with a higher risk for combined therapy) [57] and ovarian cancer (1 per 1000 when taken for 5 years from the age of 50; similar rates for single/combined therapy) and to increase the risk of other conditions such as heart disease and strokes. [58] However, it should be noted that the risks vary according to HRT type (single or combined), age at first starting treatment and mode of delivery.

Complexity of communicating evidence

There are a number of confounding factors for risk estimates with HRT which can impact on both the communication and comprehension of the evidence e.g. age at first taking, body mass index (BMI), single/combined therapy, mode of delivery. In the early 2000s, two studies, the Women's Health Initiative and Million Women Study published their findings on the its effect on certain aspects of women's health (for details of the findings of both studies see [59]). Some differences in findings between studies were reported, and possible study flaws may have contributed to overestimation of changes to risk.[60] Confusion among both patients and doctors surrounding the safety of HRT leading to a significant reduction in the number of women in the UK taking HRT during the next 5 years from over 2 million to less than 1 million.[61] There is still some disagreement amongst the healthcare community about the evidence base relating to the balance

[55] https://www.womens-health-concern.org/help-and-advice/factsheets/menopause/
[56] https://www.womens-health-concern.org/help-and-advice/factsheets/hrt-know-benefits-risks/
[57] Banks E, Canfell K, Reeves G (2008). *HRT and breast cancer: recent findings in the context of evidence to date.* Women's Health (Part of Future Medicine Group). **4(5)**, 427-431.
[58] http://www.cancerresearchuk.org/about-cancer/causes-of-cancer/hormones-and-cancer/hrt-and-cancer
[59] https://www.womens-health-concern.org/help-and-advice/factsheets/hrt-the-history/
[60] *Ibid.*
[61] *Ibid.*

of risks and benefits and how it is used for guideline development, but in recent years opinion has shifted in favour of prescribing HRT.[62]

The role of individual values in decisions about medicines

Perception of the magnitude of risk increase of cancer is clearly important in decision making for HRT, but values attached to that may vary. Some women will value the lack of hot flushes over what they perceive to be a minor increased risk, but others will find *any* increase in the risk of cancer unacceptable.

[62] https://www.womens-health-concern.org/help-and-advice/factsheets/hrt-know-benefits-risks/

Annex 2: Statins case study

Target treatment group

Statins are recommended to patients who are at risk of coronary vascular disease (CVD), based on the QRISK2 calculation for patients up to and including 84 years of age. The QRISK2 algorithm calculates the risk of having a heart attack or stroke over the next decade, based on factors such as smoking and diabetes status, ethnicity and social background. Those with a 10% risk of developing heart disease over 10 years are recommended for treatment (following lifestyle advice).[63]

What treatment involves

The first commercially available statin, lovastatin, was given FDA approval in 1987[64], and since then a number of statins have been developed, of which 5 are available via NHS prescription in the UK [65]: atorvastatin (Lipitor), fluvastatin (Lescol), pravastatin (Lipostat), rosuvastatin (Crestor) and simvastatin (Zocor). Statins are a class of medicines that reduce plasma levels of low density lipoproteins (LDL), a high concentration of which is potentially dangerous as it can lead to atherosclerosis and cardiovascular disease. In a review of multiple studies on the efficacy of statins, with follow-up time ranging from 1-5 years, overall nine fewer people died per 1000 due to cardiovascular disease compared to a placebo.[66]

Potential side effects

A number of possible side effects have been reported, including muscular aches and pains, upset stomach, headache and feeling sick. There is some suggestion, however, that some of these may be experienced due to so-called 'nocebo' effects, where non-pharmacological effects arise due to negative expectations.[67]

Complexity of communicating evidence

According to NICE, in 2014 around 7 million people in the UK were taking statins, at an estimated annual cost of £285 million.[68] Statins are often prescribed as a preventative treatment, and are therefore used despite the patient not feeling unwell. Individuals prescribed statins will often be on the medication for life, as stopping has been shown to result in rapid rise in serum LDL levels and an increased risk of CVD; therefore even minor side effects can be a significant consideration with respect to long-term adherence. There is also considerable uncertainty with regard to which individuals will benefit from statin treatment. As it is, some people taking statins will suffer a coronary death, just as people who are eligible for statins but decide not to take them will live.[69]

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[63] NICE guidelines [CG181]. *Cardiovascular disease: risk assessment and reduction, including lipid modification.* Published date: July 2014

[64] Tobart JA (2003). *Lovastatin and beyond: The history of the HMG-CoA reductase inhibitors.* Nat Rev Drug Disc 2. 517-526

[65] http://www.nhs.uk/Conditions/Cholesterol-lowering-medicines-statins/Pages/Introduction.aspx

[66] https://www.nice.org.uk/guidance/cg181/evidence/lipid-modification-update-full-guideline-243786637 Table 41

[67] Goldacre B. *Meta-analysis of side effects of statins shows need for trial transparency.* BMJ. **348**:g2940

[68] https://www.nice.org.uk/news/press-and-media/nice-advises-much-wider-use-of-statins-in-draft-guidance

[69] Skolbekken J-A (1998). *Communicating the risk reduction achieved by cholesterol reducing drugs.* BMJ **316**,1956–8.

The role of individual values in decisions about medicines

While there is strong evidence to support the benefits of statins in reducing mortality, the decision to medicate apparently healthy individuals for life has been controversial. When changes to NICE guidelines raised the possibility of substantial increases in the proportion of the population prescribed statins, concerns were expressed by healthcare professionals amongst others about the 'overmedicalisation' of society.[70] Individuals may judge benefits to be distant or unlikely, whereas side effects are more immediate, and indeed concerns about side effects may be an important factor in non-adherence to statins.[71]

[70] http://www.nationalhealthexecutive.com/Health-Care-News/nice-lowers-threshold-for-statins-prescriptions
[71] http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2912713/pdf/prjl.14.1.004.pdf

Annex 3: Vaccinations case study

Target treatment group

The NHS has a routine schedule for vaccinations for all members of the public, from childhood through to old age. In addition, non-routine vaccines are available for people who fall into certain risk groups such as hepatitis B for healthcare workers. An additional category of vaccines are for those travelling to areas at high risk of infection, some of which e.g. hepatitis A/typhoid can be administered free on the NHS, whilst others e.g. yellow fever are only available privately.

What treatment involves

Vaccination is the administration of a biological preparation to improve immunity to a particular disease. Vaccines typically contain an agent that resembles a disease-causing microorganism, and is often made from weakened or killed forms of the microbe, its toxins or one of its surface proteins.[72] Discovered by Edward Jenner in its modern form in 1796, vaccination became more popular towards the late 1800s and by the end of the 1920s, vaccines were available for diphtheria, tetanus, whooping cough and tuberculosis. Since then, vaccines have been developed for a range of infections including polio, human papillomavirus (HPV), influenza, shingles and most recently, meningitis B.[73]

Potential side effects

These include injection site reactions (pain, swelling), mild fever, shivering, fatigue, headache and muscle and joint pain. Anaphylaxis can occur following vaccination but is reported in fewer than 1 in 1,000,000 cases.

Complexity of communicating evidence

Vaccines are a category of medicine for which (in the case of childhood vaccination) consent is given usually by a parent on behalf of the recipient (the child). As such, information regarding safety, efficacy and possible risks needs to accommodate parental concerns. Because of the role of herd immunity in vaccine efficacy, risk-benefit calculations must take into account the population as well as the individual – refusing a vaccine in a population with high herd immunity will not increase risk to the individual in the same way as not taking a preventative medicine. Therefore where the introduction of vaccines has led to a dramatic reduction in childhood diseases and as such, where parents have little or no experience, memories, or knowledge of many of the diseases that childhood immunisations prevent, conveying the benefits of vaccination, as opposed to the side effects, represents a significant challenge.

The role of individual values in decisions about medicines

As with all preventative medicines, individuals may place greater value on immediate impacts (adverse effects) rather than more temporally distant or unlikely ones (protective effects). However, this is complicated by the role of herd immunity: subjective value judgements are important in determining how the balance is weighted between risks.

[72] http://www.who.int/topics/vaccines/en/
[73] www.nhs.uk/conditions/vaccinations/pages/the-history-of-vaccination.aspx