EXPERT REVIEW

Guidance on Communicating Risk and Uncertainty in the Context of Genomic Testing

The content for this expert review document is based on a presentation by Professor Dame Lesley Fallowfield given on October 23, 2024.

Communicating Risk and Uncertainty in the Context of Genomic Testing

Key Summary Points:

How to discuss numbers with patients:

- Use a combination of percentages (40%), fractions (2/5ths), and frequencies (4 in 10) to communicate risk.
- Be mindful of denominator neglect; patients often focus on the numerator alone.
- Frame risk comparisons clearly. For example, instead of saying, “With Drug A, 5 in 20 people experience diarrhea, and with Drug B, 5 in 40 do,” reframe as, “With Drug A, 50 in 200 experience diarrhea, compared to 25 in 200 with Drug B.”

How to share information on risks:

- Avoid vague terms like “rare” or “common,” as they are interpreted inconsistently.
- When using percentages, pair them with verbal descriptors and frequencies, e.g., “This is very rare, affecting fewer than 1 in 1,000 patients”.
- Recognize that patients often struggle with statistical information, so simplify numerical concepts and provide visual aids when possible.

How to help patients make decisions about chemotherapy:

- Clearly outline the probabilities of benefits and harms with and without chemotherapy.
- Be aware of optimism bias; patients may acknowledge potential harms but believe they are personally at lower risk.
- Confirm patient understanding by asking them to explain the information in their own words.
- Offer gene expression profiling tests to provide personalized risk assessments and support decision making.

How to explain the results of gene expression profiling tests to patients:

- Familiarize yourself with commonly used gene expression profiling tests (e.g., Oncotype DX, EndoPredict, Prosigna) and how they categorize risk.
- Assess patient comfort with numerical information before discussing test results (e.g., “I am going to share some statistics about your risk—how comfortable are you with numbers?”).
- Adapt communication based on patient response and level of numeracy.
- Supplement verbal explanations with easy-to-read written materials and visuals.
- Research shows that short educational videos improve patient understanding when compared with written materials.

How to enhance communication strategies with patients:

- Undergo training in effective risk communication, such as “Talking about Risk in the Context of Genomic Tests” (TARGET) workshops.
- Be self-aware of unconscious biases that may impact how risk is conveyed.
- Recognize that standard patient education materials may be too complex; aim for readability at an 8th-grade level.
- Incorporate multimedia resources like short informational videos, which have been shown to improve patient comprehension and reduce consultation time.

Background

Complexity of Modern Medicine

Over the past few decades, significant progress has been made in our understanding of cancer—particularly breast cancer— as well as genetics and molecular biology, leading to numerous therapeutic advancements. Additionally, there have been improvements in diagnostics, surgical and radiotherapy techniques, as well as in targeted systemic therapies. However, the advantages and disadvantages of these new advances and different treatments are not always simple to explain to patients and caregivers. This is especially true in our current climate where patient centricity and shared decision making is an expectation. It is often difficult for providers to explain complex treatment options in a busy clinic and the information that is passed on to patients is often set in a backdrop of fear and anxiety. Therefore, patients, who are often experiencing emotional turmoil, are entering a world of esoteric language and concepts which makes discussing risk and uncertainty tricky.

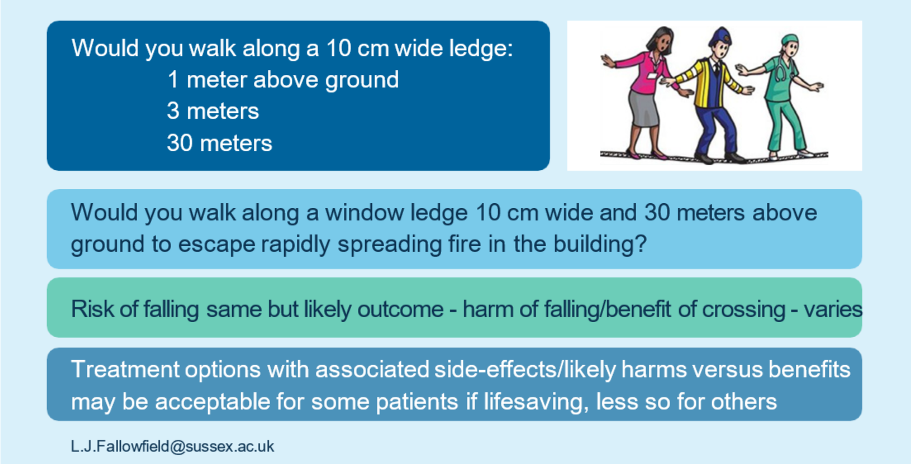
To address this complex interaction between patients and providers, this expert review document will discuss the basics of information processing and how risk and uncertainty impact decision making.

Discussing Risk

Risk is a feature of everything we do in both life and medicine; however, almost everyone dislikes uncertainty. Medicine is an uncertain science, where most facts are probabilities defined or refined by repeated hypothesis testing in studies. There is also much confusion regarding health literacy and numeracy. Most patients would prefer that benefits and harms of treatment options were definitive. The tolerance of health care providers to uncertainty impacts information exchange and decision-making. If tolerance is low, healthcare providers are less likely to disclose ambiguous results, communicate uncertainty, or feel confident disclosing facts that are uncertain (Fallowfield et al, Br.Ca.Res & Tmt, 2019;177:641-649). Health care professionals who have a low tolerance to uncertainty are likely to order more unnecessary tests or treatments and may offer patients more aggressive treatments (Luther et al, Acad. Med, 2011;86:799-800).

Discussing Decision-Making

Decision making is rarely rational. There are two ways that we process information, 1) cognitively (i.e., we evaluate information received verbally or in written form) and 2) emotionally (i.e., we react to risks and harms presented for general or medical purposes). Both approaches are inter-related; cognitive appraisal gives rise to emotions and these emotions can influence appraisal. There is also something called optimism bias, which complicates things further. For example, although an individual may feel less at risk than his or her peers, they may also have overly optimistic expectations about a drug. Finally, in all these decisions, there exists a *predominance of affect* – which refers to the notion that statistical information may be ignored, if medical choices are seen as serious or scary, which leads to a probability neglect.



Would you walk along a 10 cm wide ledge:
1 meter above ground
3 meters
30 meters

Would you walk along a window ledge 10 cm wide and 30 meters above ground to escape rapidly spreading fire in the building?

Risk of falling same but likely outcome - harm of falling/benefit of crossing - varies

Treatment options with associated side-effects/likely harms versus benefits may be acceptable for some patients if lifesaving, less so for others

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When it comes to decision making, it is important to take into consideration patient expectations around benefits and harms of interventions. It is important to understand the probability of something happening as well as what the consequences may be. Patients must calculate the risks from the numbers and concepts given to them by providers and then use their own personal preferences to make a decision. When patients are often asked about their own decision making, they tend to dichotomize risk into either high or low and ignore intermediate risks, which are hard to process. A systematic review of expectations of benefits and harms of treatments, screening, and tests showed that most patients overestimated intervention benefit and underestimated harms. This was often due to optimism bias giving patients unrealistic hope and a sense of control, the patient being given incorrect or incomprehensible information, or it reflects the provider's own optimism bias when communicating with the patient about harms.

Discussing Numbers and Data

Many scientific presentations and/or publications provide sub-optimal information about absolute risk and benefits. Healthcare providers often have many misconceptions themselves about absolute risk and relative risk (Gigerenzer & Edwards 2003, BMJ 327(741-744). Health care providers are also more likely to recommend chemotherapy if the data show relative risk, instead of absolute risk or the number needed to treat (Chao et al, 2003, JCO 21(23), 4299-4305). Patients cannot make informed decisions if they have a poor understanding regarding the absolute risk of recurrence, without treatment for example, and the absolute harms of the treatment that is being offered.

When considering the impact of numeracy on risk and decision making, there is a lot of research showing that a collective statistical illiteracy exists among society, patients, journalists, politicians, and health care professionals (Gigerenzer, 20210, Arch Int med). Risk is often presented in consultation with patients as a percentage, but one study showed that 20% of people don't know which of 1%, 5% or 10% represents a higher risk. About 30% of respondents were unsure if 1 in 10, 1 in 100, or 1 in 1,000 represented the biggest risk. When cumulative risks were discussed, as it often is during a standard medical consultation, it was even more difficult to understand for patients (Galesic & Garcia-Retamero, Arch Int Med 2010; 462- 468.) A study of 450 women in the United States, where the median age was 68 and 96% of participants had a high school diploma, found that 46% were unable to convert percentages to proportions. About 80% were unable to convert proportions to percentages, and 46% could not estimate coin flip probability (Woloshin et al, 2001).

Patients will often receive written information, but the complexity of text and numerical formats are often confusing. We know from research that icon arrays are generally easier to comprehend and have more impact than abstract numbers. Sometimes risk will only be discussed in terms of probability of occurrence, but providers should focus more on probability and consequences of treatments. Finally, providers having these discussions should be aware that low numeracy individuals are very susceptible to framing effects (Levin & Gaeth, J Cons. Res. 1988). In a focus group held with patients and family members with *BRCA* pathogenic gene alterations few remembered the diagrams or pictures in educational materials given to them. However, retaining the gist of what patients need to understand for decision-making was found to be more important than remembering the exact numbers shared (Shilling et al, 2020).

How should providers discuss numbers with patients?

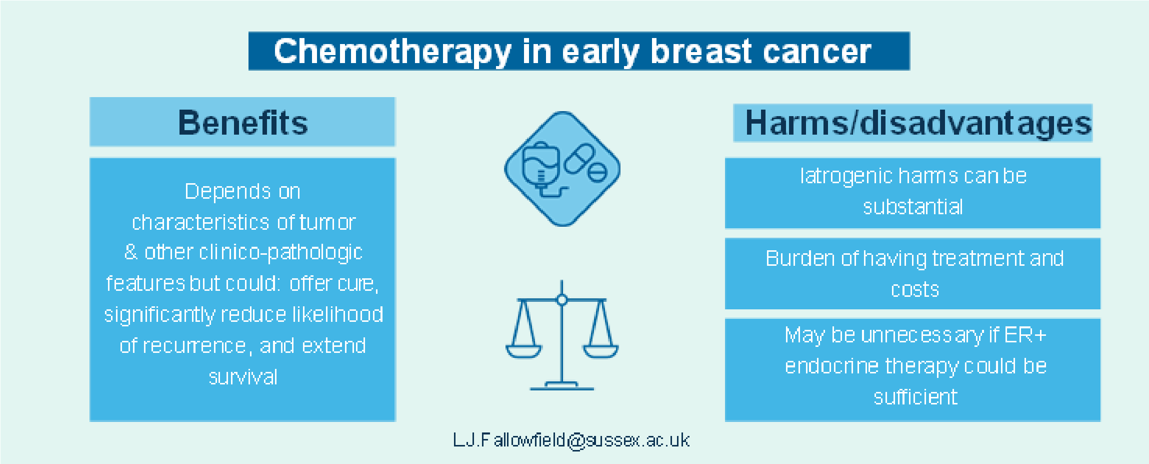
Percentages confuse many, as do fractions (2/5ths). Frequencies are usually easier to understand, but remember denominator neglect (where patients tend to dismiss the denominator and focus on the numerator). Try to use the same denominator each time, especially when sharing many different numbers with the patient. For example, instead of saying "With Drug A – around 5 in every 20 people get diarrhea, whereas with Drug B 5 in 40 do", compare Drug A (50 in 200) with Drug B (25 in 200).

How should providers express risk information to patients?

Consider how information is provided to patients. For example, when you say “with this drug constipation is rare” without further explanation, the provider and the patient may have different ideas of what the word ”rare” means. These verbal descriptions such as “common” or “rare” are known as *elastic* concepts that produce very different estimates and are often grossly overestimated by patients. Providers often use percentages, but these can confuse many people (especially if they are low percentages or less than 1%). Natural frequences, e.g. “this affects 1 in 100 patients”, tend to be better understood by patients. The best approach is to combine a verbal descriptor with a frequency, for example “this is very rare, it happens to fewer than 1 in every 1,000 patients.”

How can providers help patients make decisions about chemotherapy?

When patients are making decisions about chemotherapy, they need to understand the probabilities of harms and consequences with and without chemotherapy. They need to be able to compute their “risk” from numbers and concepts provided by the providers and be able to couple that information with their own personal preferences. It is important to keep in mind that due to optimism bias, individuals can sometimes acknowledge the likelihood of harms but still believe themselves to differ in some way. There is also the possibility that an intended message given by the provider is not the same message that the patient understood, as explaining risks and benefits clearly is not always simple. In the case of chemotherapy, offering patients a gene expression profiling test may help clarify risk and explain the likely benefits.



Chemotherapy in early breast cancer

Benefits

Depends on characteristics of tumor & other clinico-pathologic features but could: offer cure, significantly reduce likelihood of recurrence, and extend survival

Harms/disadvantages

Iatrogenic harms can be substantial

Burden of having treatment and costs

May be unnecessary if ER+ endocrine therapy could be sufficient

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How can providers effectively explain the results of gene expression profiling tests to patients?

There are several different gene expression profiling tests; they differ somewhat in the numbers and specific genes looked at, but all provide scores that categorize the risk of recurrence and the likely benefit of adjuvant chemotherapy. In the U.S., Oncotype DX is the most commonly used test; others include EndoPredict and Prosigna. Not all health care providers are adept at communicating GEP risk of recurrence scores and their implications for treatment recommendations with patients. Talking about risk in the context of genomic tests (TARGET) workshops with trained facilitators were found to significantly improve attendees’ competence when communicating about gene expression profiling test results (Fallowfield, et al 2019). These evidence-based workshops employed a robust pedagogical model focusing on improving healthcare providers’ knowledge, their behavioral skills, self-awareness, and self-confidence to efficiently communicate these test results to patients.

Patients’ perceptions and preferences are also influenced by written information, which usually takes the form of leaflets and brochures (often written by industry). However, most health information is too complex for most adults, especially when numerical information is included. In fact, 1 in 4 adults feel anxious when information is presented in numerical format (National Numeracy Report). In the United States, just 12% of adults demonstrate proficient health literacy, and lower health literacy has been linked to higher all-cause mortality among cancer patients (Al Hussein, et al 2025).

Furthermore, readability tests on the brochures that come with gene expression profiling tests show that most of these materials are written at fairly difficult to very difficult levels (i.e. college graduate reading level). A randomized cross-over study (IMPARTER) done with women without breast cancer found that short (8-minute) patient information videos, using a conversational style of dialogue and simple explanatory graphics, showed that knowledge scores were significantly higher following the video viewing compared to those who read a leaflet ($p<0.0001$); furthermore, individuals preferred the video to leaflets. (Fallowfield, et al 2022). The subsequent IMPARTER4 randomized study of women with early breast cancer given standard hospital information plus or minus the video (Fallowfield et al, BMJ Oncology 2025) similarly found that cancer patients’ knowledge was significantly higher in the groups who were shown the film versus those receiving the standard information alone. Clinicians also reported that patients in the group which received standard information asked more difficult and unexpected questions and felt that their consultations took longer.

Conclusion

Discussing genomic and genetic testing can be complex, especially when patients’ anxiety may be high, and numeracy and literacy levels are low. Healthcare providers’ own communication about risks, harms, and benefits may be subject to unconscious bias and misunderstandings. There is a need for improved repertoires when explaining information, and well-designed training workshops can help providers. There is also evidence that short informal videos for patients are better, or can complement, written material and verbal explanations.

Guidance Statements

The guidance statements in this expert review can be subject to future variations and periodic updates based on new research. Therefore, the information provided in this document should not be considered as being complete or inclusive of all available information. This information does not mandate any particular course of medical care and is not intended to be a substitute for the independent professional judgment of a health care provider. The document does not represent the official institutional position of Dana-Farber Cancer Institute.

References

Fallowfield L, Solis-Trapala I, Starkings R, Catt S, May S, Jenkins V. Talking about risk in the context of genomic tests (TARGET): development and evaluation of an educational program for clinicians. Breast Cancer Res Treat. 2019 Oct;177(3):641-649. doi: 10.1007/s10549-019-05316-7. Epub 2019 Jun 14. PMID: 31201584; PMCID: PMC6745030.

Luther VP, Crandall SJ. Commentary: ambiguity and uncertainty: neglected elements of medical education curricula? Acad Med. 2011 Jul;86(7):799-800. doi: 10.1097/ACM.0b013e31821da915. PMID: 21715991.

Gigerenzer G, Edwards A. Simple tools for understanding risks: from innumeracy to insight. BMJ. 2003 Sep 27;327(7417):741-4. doi: 10.1136/bmj.327.7417.741. PMID: 14512488; PMCID: PMC200816.

Chao C, Studts JL, Abell T, Hadley T, Roetzer L, Dineen S, Lorenz D, YoussefAgha A, McMasters KM. Adjuvant chemotherapy for breast cancer: how presentation of recurrence risk influences decision-making. J Clin Oncol. 2003 Dec 1;21(23):4299-305. doi: 10.1200/JCO.2003.06.025. Epub 2003 Oct 27. PMID: 14581440.

Woloshin S, Schwartz LM, Moncur M, Gabriel S, Tosteson AN. Assessing values for health: numeracy matters. Med Decis Making. 2001 Sep-Oct;21(5):382-90. doi: 10.1177/0272989X0102100505. PMID: 11575488.

Fallowfield L, Solis-Trapala I, Starkings R, Catt S, May S, Jenkins V. Talking about risk in the context of genomic tests (TARGET): development and evaluation of an educational program for clinicians. Breast Cancer Res Treat. 2019 Oct;177(3):641-649. doi: 10.1007/s10549-019-05316-7. PMID: 31201584; PMCID: PMC6745030.

National Numeracy Report (2018) https://mathsanxietytrust.com/

Al Hussein Al Awamlh B, Moses KA, Whitman J, Stewart T, Kripalani S, Idrees K. Health literacy and all-cause mortality among cancer patients. Cancer. 2025 Mar 15;131(6):e35794. doi: 10.1002/cncr.35794. PMID: 40045673; PMCID: PMC11883198.

Fallowfield LJ, Farewell D, Jones H, May S, Catt S, Starkings R, Jenkins V. IMPARTER, Phase 1 of an intervention to improve patients' understanding of gene expression profiling tests in breast cancer. Breast Cancer Res Treat. 2022 Apr;192(2):265-271. doi: 10.1007/s10549-021-06491-2. Epub 2022 Jan 4. PMID: 34982321; PMCID: PMC8750374.

Shilling V, Catt S, Jenkins V, Fallowfield L. Using patient perspectives to inform communication training materials for health care professionals discussing BRCA mutation testing. Breast Cancer Res Treat. 2020 Nov;184(2):491-498. doi: 10.1007/s10549-020-05871-4. Epub 2020 Aug 18. PMID: 32812179; PMCID: PMC7599138.

Fallowfield L, Solis-Trapala I, Starkings R, et al. Improving patient understanding of GEP test results (IMPARTER4): an RCT. BMJ Oncol. 2025;4:e000689. doi: 10.1136/bmjonc-2024-000689.