



UPPSALA
UNIVERSITET

Centre for Research Ethics & Bioethics



Challenges in benefit/risk
assessments and
communication

Mats Hansson





Risk assessment in a risk averse society – The example of Exanta[®]



- ≈ 300 patients die each year in Sweden in association with Warfarin bleedings
- Exanta was developed for the treatment and prevention of thromboembolism and approved in USA, Europe, Japan
- One patient dies in USA due to a severe adverse effect of the liver
- FDA withdraws the permit



Exanta[®]



- A patient on Exanta in Denmark dies in liver failure
- The Drug company withdraw's the drug from the market 2006
- After a careful risk assessment:
300 patients/1patient OR assessment of public relation risks?



Exanta[®]



- Recent genotyping shows: the adverse liver reactions are associated with the presence of a certain allele
- A carrier frequency of 11% in Scandinavia and 0.3 % in Japan



Life cycle approach



- Needs of treatment may bring products earlier on the market and genotyped drugs for subpopulations may be given wider indications
- Only after wide use will rare effects be recognized
- Raising the bar will exclude patients from beneficial treatment – lowering it may imply inflicting unknown risks



Risk literature not really fit for medicine



- The major bulk focuses on risks only – medical decisions are typically concerned with benefits and risks, i.e. cure and adverse reactions
- There are no medicines or medical interventions without risk of adverse effects
- There is no risk-free society



Risk communication in medicine



- Patient estimates at odds with clinicians' beliefs of understanding,
E.g. Risk communication related to breast cancer, colorectal cancer and **MEN**



Risk communication in medicine



- Different factors influence interpretations of numeric probabilities:
 - Family background, cause of disease, psycho-social factors
 - Nature of outcome (seriousness, available treatment)
 - Assymmetric loss of information (more undesirable outcome the greater cost of underestimation)



Risk communication in medicine



- Descriptors of risk (probable, improbable, likely, great/small risk) may not be related to objective risk estimates
- "Probable" may for the patient denote risk figures between 50-99%



The psychological construction of risk



- Perceptions of risk variable with regard to:
- Voluntary/involuntary
- Familiarity with the risk
- Controllability
- Affecting minors
- Temporality/immediacy of consequences



Risk and uncertainty



- From the perspective of economics:
"Risk" refers to future random adverse events that can be statistically calculated according to their probability

"Uncertainty" refers to a situation in which random events cannot be predicted on the basis of probabilistic outcomes (Knight 1921)



Risk and uncertainty



- ...the game of roulette is not subject...to uncertainty...[but] the prospect of a European war is uncertain [as is the price of copper or the rate of interest twenty years hence.
- "About these matters there is no scientific basis on which to form any calculable probability whatever. We simply do not know." (Keynes 1937)



Doug Hubbard



- Uncertainty = the existence of more than one possibility. The true outcome is not known
- Risk = a state of uncertainty where some of the possibilities involve a loss/undesirable outcome and both are quantifiable
- One can, then, have uncertainty without risk but not risk without uncertainty



Having regard to the outcome



- Risk ... a state of uncertainty where some of the possibilities involve a loss/undesirable outcome
- What constitutes a loss/undesirable outcome, e.g. a Klinefelter syndrom for a couple who have been longing for a boy for many years and are now for the first time pregnant



The catastrophic scenario



- Pascal's waiver and the problematic concept of "precautionary" principles
- A need to qualify beliefs in terms of consequences and probabilities when doing A that may lead to B but when not doing A may lead to C
- So access to this kind of information may be essential



A common perspective



- Of both economists and psychologist is the consequentialist perspective
- Implying that people make decisions on the basis of an assessment of the consequences of possible choice alternatives
- Feelings may come as a side effect, as one of the outcomes



The role of emotions



- The affect-as-information hypothesis (Schwarz & Clore 1983)
- Feelings during the decision process affect those decisions when the feelings are (correctly or wrongly) experienced as reactions to the imminent decision – sometimes diverging from cognitive evaluation
- E.g. Fear causes us to slam on the brake instead of steering away



The role of emotions and mental images in the description of outcome



1. "Jack sustained fatal injuries in an auto accident".

2. "Jack was killed by a semi-trailer that rolled over on his car and crushed his skull"



Risk and emotions



- The risk-as-feeling hypothesis (Loewenstein et al. 2001)
- Responses to risky situations and decision-making result in part from mediated emotional influences, e.g worry, fear, dread or anxiety.



Risk-as-feeling hypothesis



- Risk emotions seem not to be affected by changes in probability
- Fear and anxiety tend to favour risk-averse decisions (Lerner & Keltner 1999, 2000)
- Emotions such as fear and anxiety are sensitive to the possibility rather than the probability of risk consequences



Applied to benefit/risk research in medicine



- Information on emotional reactions should be collected in addition to probabilities and outcome values
- One should pay attention to the role of mental images when describing choice scenarios
- With the aim of identifying emotional reactions as predictors of risk behaviour/decisions



Benefit/Risk preferences



- Patients, healthcare professionals, payers and regulators may be prepared to accept different risk levels and different trade-offs between anticipated benefits and adverse reactions



Benefit/Risk preferences



- The need to incorporate different views means that a robust and reproducible method of eliciting preferences for risk is needed
- Benefit trade-offs must be used to ensure the resulting values are sufficiently robust to use the information to guide the future development of health policy



Benefit/Risk preferences



- In two programs: *IMI-PREFER* and *Mind the Risk* we use stated preference elicitation methods, i.e. discrete choice experiments (DCE) that are underpinned by robust economic theories of decision-making and preceded by qualitative studies
- E.g. On-going project on Privacy Protection vs Use of Data for patient security and research