# Do Patients REALLY Want More Risk?

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# What is a Patient?

- **Word "patient" comes from Latin root for "one who suffers"**
- **Basic principle of medicine since time of Hippocrates has been "first do no harm"**
- **All medical interventions (drugs, vaccines, devices, procedures) have some associated harm**
- **The goal is to maximize benefit and decrease harm – how to do this?**

# What is "Increased Risk"

- **Recently senior FDA managers have stated that in their view "patients are willing to accept increased risk" with new drugs**
- **Raises several important questions:**
  - **What does "risk" mean?**
  - **Risk of what? Lack of effectiveness or adverse effects?**
  - **How do FDA mangers know what patients are willing to accept?**

# Concept of "Risk"

- Risk = potential negative impact on some asset/characteristic of value arising from some present process or future event
- Differentiate risk from uncertainty
  - Risk implies a measurable value
  - Uncertainty implies something that is not measured
- Confusion occurs when there is uncertainty about measurement of risk; often the case with new drugs

# Concept of "Risk"

- **Drug companies talk of "regulatory uncertainty" regarding whether their drug will receive approval or not**
- **Now discussing that greater "uncertainty" for patients is acceptable when there are "unmet medical needs"**
- **Uncertainty is not measured – therefore unclear what one is accepting under such conditions**

# Concept of "Risk"

- **Risk consists of two factors:**
  - **Impact:**
    - **What happens to you? death vs less serious morbidity**
  - **Probability: how often it happens; likelihood of event occurring**

- **Probability refers to outcomes in groups of subjects, not outcome in an individual**
  - **Probability of outcome in an individual is either 0% or 100%**
  - **"You have a 1 in 100 chance of an adverse event" is an incorrect statement**

- **If probability of event is 1 in 100, who is the one and who is the other 99?**

# Risk of What?

- **Since 1962 the law since 1962 requires the drug companies show their drug is effective in order to justify any harms – even minor harms**
- **This conforms to "first do no harm" - evaluate clear benefits first then discuss potential harms**
- **Difference between a hypothesis and results – hypotheses need to be tested to provide evidence for or against them**

# Learning from History

- *"If the drug that killed one person in ten thousand was of only minor use therapeutically, it might still be judged to be unsafe, whereas the drug that killed one in a thousand persons, if it had marked and undisputed therapeutic value it would still be a safe and valuable drug"*
  - **J.J. Durett, Chief, Drug Division, FDA, December 1938**

- **Safety and effectiveness dependent upon conditions of use – not just if a drug "works" but in whom, when and on what outcomes**

# Where does FDA get information from Patients?

- FDA officials speak with drug companies on regular basis
- FDA has several mechanisms to obtain information from patients:
  - Representatives on advisory committees – how are these chosen?
  - Public hearings at advisory committees – short time for people to speak and often supported by companies
  - Other types of public hearings and workshops – invitation only or majority of time devoted to drug companies
- Are all "patient groups" created equal?

# Trust and Risk

- People more willing to accept risk if they trust source of information
- Is information from drug companies reliable and truthful – over 20 companies have been fined since 2008 for marketing their drugs for diseases for which FDA has not granted approval
- "Ask your doctor"
  - Where do doctors get reliable information?
  - If FDA accepts less evidence how will doctors provide information to patients?