Why do we care?

Challenges of real-world randomized trials:
• Any true differences are typically modest
• Heterogeneous patient populations
• Complex causal pathways
• Competing effects of treatments
Does randomization create or increase risk?

• Randomization should be treated as one of many factors in a study that influence (or mitigate) risk
• Randomization influences the treatment received – and any effect on risk is mediated by its effects on treatment
• Constraints on provider’s and patient’s subsequent decision are study-specific, not inherent to randomization
• Randomization may mitigate risk due to suboptimal treatment assignments by gender, race, or ethnicity resulting from implicit bias
• Bottom line – It depends
Other consequences of study participation

• Constraints on treatment choices
• Providers’ dual allegiances
• Risks or burdens of non-therapeutic procedures

These are consequences of study participation – not specifically related to random assignment of treatment
Compared to what? – Ideal view

Personalized Treatment
(systematic, guided only by evidence and patient preferences)

Research Treatment
(systematic, randomly selected)
Compared to what? – Realistic view

Personalized Treatment
(systematic, guided by evidence and patient preferences)

Haphazard Treatment
(cryptically selected, guided by provider’s habits & prejudices and by economic factors)

Research Treatment
(systematic, randomly selected)
Compared to what? – Realistic view, and

Personalized Treatment (systematic, guided by evidence and patient preferences)

Haphazard Treatment (cryptically selected, ? guided by provider’s preferences and interests)

Research Treatment (systematic, randomly selected)

Sub-Standard Treatment (cryptically selected, and limited by social and economic disadvantage)
Two ways that altering treatment choice might alter “risk”

• Change in average expectation – This is study-specific. If we are in clinical equipoise, then any average effects are likely small.

• Change in individual experience – This is almost certain. Net effect could be positive or negative for any individual, and this is often unpredictable.

We certainly must consider and communicate the first type. What about the second type? And how would we communicate it?
Communication challenges

• More comprehensible descriptions of random assignment
• More accurate descriptions of alternatives (What really would happen to you if you didn’t join this study?)
Therapeutic misconception

• Misconceptions regarding research are remarkably resilient (e.g., believing that my doctor will still pick the treatment that’s best for me.)

• BUT – Misconceptions regarding ‘usual’ treatment may be just as problematic