Paying for What Works: Comparative Effectiveness in Healthcare

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Why all the fuss about Comparative Effectiveness?

- **Effectiveness is already a part of health technology assessments … but**
- **Evidence to inform adopton / diffusion decisions and treatment decisions is sometimes lacking**
  - "insufficient evidence" vs evidence developed for other decisions
- **Therefore a key driver is recognition of the need for better evidence**
  - IOM Report on "What works"

Strategies to develop evidence must:

1. ***Ensure evidence generation is linked to the decision***
2. ***Balance the need for cost control with society's desire for new technologies***

Evidence-Based Decision Making vs Decision-Based Evidence Making

Remaining questions …

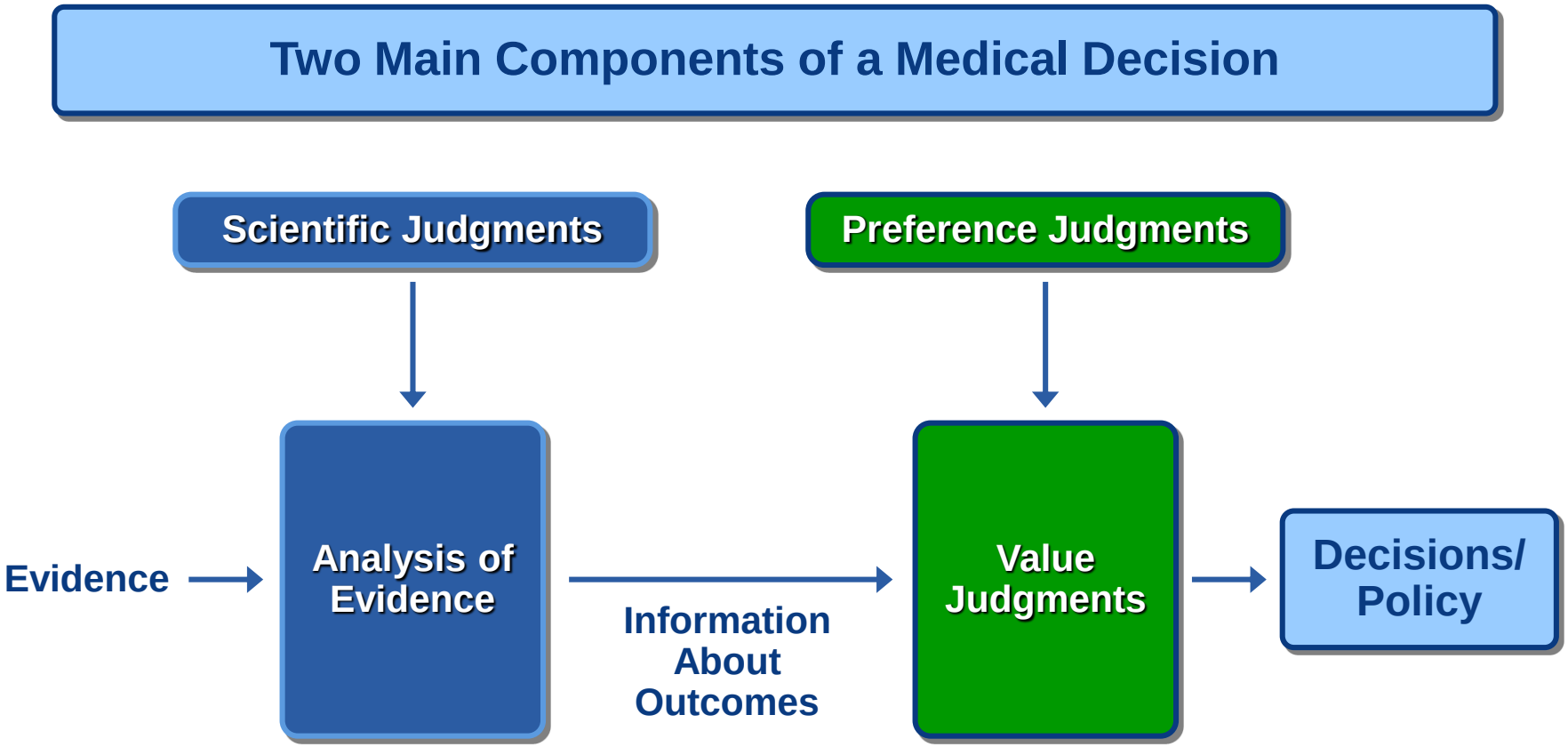
- **What if had perfect evidence? Would we have perfect decisions? Would the decisions at least be predictable?**
  - **Why do we "do the right thing" only 50% of the time when we have evidence?**
- **Can better evidence improve quality AND save money?**
  - **Why do U.S. cost savings estimates differ between the CBO and the Commonwealth Fund ($10 bil vs $368 bil over 10 yrs)?**

CER necessary but not sufficient, will need to manage expectations

Goals for today

- To propose a framework for evidence generation, assessment, and appraisal based on key decisions over the lifecycle of a healthcare technology
- To highlight areas for improvement toward better, more transparent, and more predictable decisions

Anatomy of a Decision: Analysis + Judgment = Decision



Source: D.M. Eddy: Clinical Decision Making: From Theory to Practice—Anatomy of a Decision. *JAMA 1990;* 263: 441-443.

Key Decisions in the Lifecycle of a Pharmaceutical Product

Investment Decision

- Decision to advance from Phase 2 to Phase 3
- Stakeholder is the product developer

Regulatory Decision

- Decision to approve a product for marketing
- Stakeholder is the regulatory agency

Adoption/Diffusion Decision

- Decision to adopt and use a product in a population
- Stakeholder is the payer or their intermediary

Treatment Decision

- Decision to prescribe a product for an individual patient
- Stakeholder is the patient and their physician

Investment Decisions by Technology Developers

- **Phase 2 – Phase 3 investment decisions are informed by financial analyses (eNPV, real options, etc.)**
  - Decisions based on opportunity costs for the portfolio
  - eNPV calculations historically based mostly on PTRS*
  - Best guess estimates of the probability of adoption and treatment use
- **Increasing emphasis on more granular input for prediction of adoption / diffusion and treatment decisions**
  - Simulation modeling to estimate the impact of policies such as CED on adoption/diffusion and eNPV (example follows)
- **Need to minimize the risk (under uncertainty) of a:**
  - ***False Positive:*** **Developing something we can't sell**
  - ***False Negative:*** **Stopping development of a beneficial treatment**

Bottom Line: **Need More Accurate Estimates of eNPV**

*** Probability of Technical and Regulatory Success**

Simple example of a hypothetical "asset" in the investment portfolio

Year	Expenses*	Revenue	Net	Phase
1	$10	0	-$10	1
2	$10	0	-$10	1
3	$20	0	-$20	2
4	$20	0	-$20	2
5	$50	0	-$50	3
6	$70	0	-$70	3
7	$70	0	-$70	3
8	$50	0	-$50	3
9	$100	$400	$300	4
10	$100	$600	$500	4
11	$80	$730	$650	4
12	$80	$760	$680	4
13	$80	$800	$720	4
14	$80	$820	$740	4
15	$80	$840	$760	4
16	$60	$750	$690	4
17	$1	$300	$299	5
18	$1	$100	$99	5
19	$1	$50	$49	5
20	$1	$40	$39	5

* $ values in millions

** Values hypothetical, made up by me

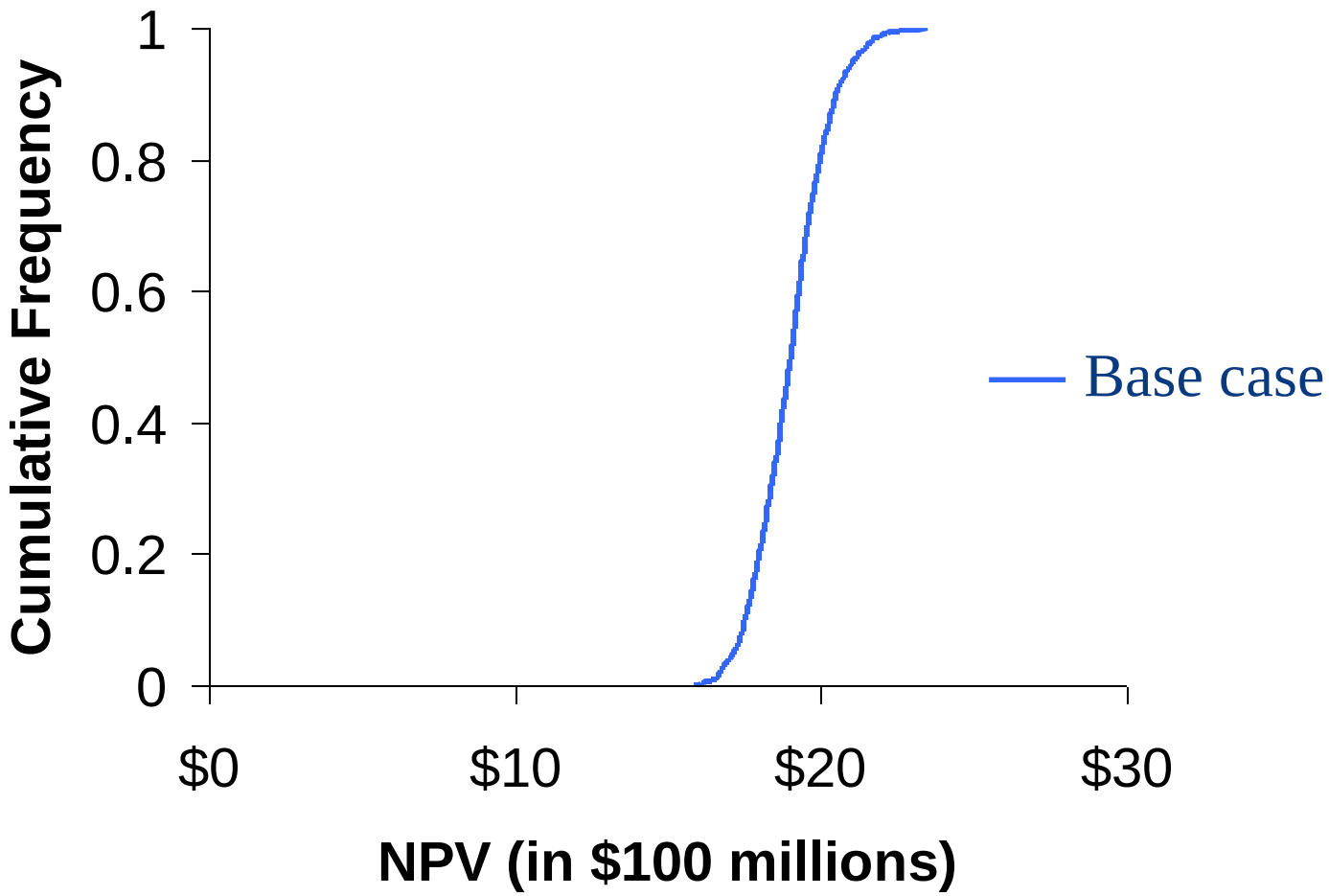
Brief Illustration: The impact of CED on eNPV

- Estimated Base Case eNPV* and the impact of Coverage with Evidence Development in years 9 - 11
  - Scenario 0 = Base case + probability of trial success of 0.5
  - Scenario 1 = Base case + probability of trial success of 0.7
  - Scenario 2 = Base case + probability of trial success of 0.9
- Winners get 5% “prize”, losers get 75% “penalty” in years 12 - 16
- Estimated the impact of more efficient drug development (production) costs for each scenario
- Monte Carlo simulation with 1,000 trials

* Estimated from Year 1

Scenario 0

(p trial success = 0.5)



Scenario 0

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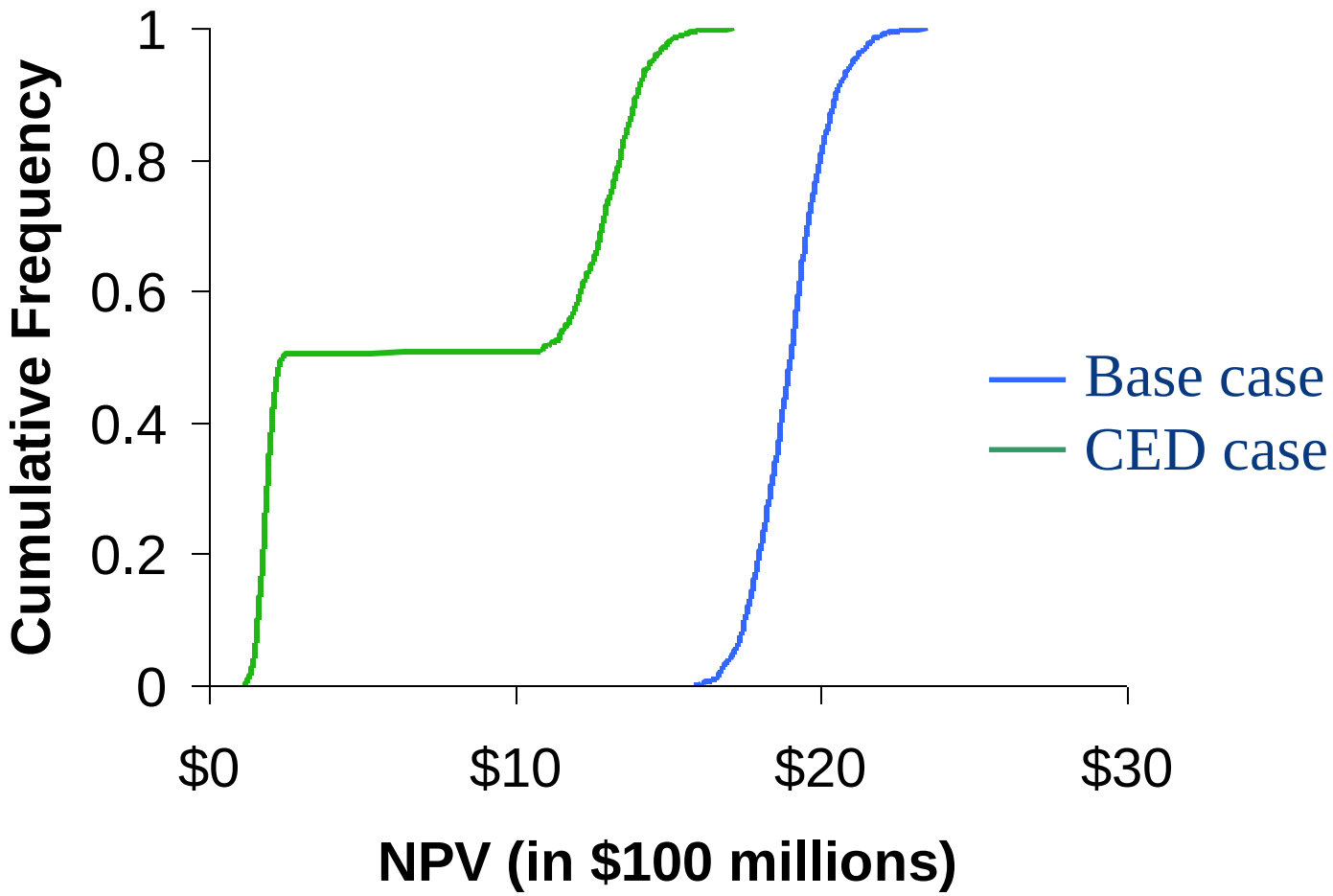

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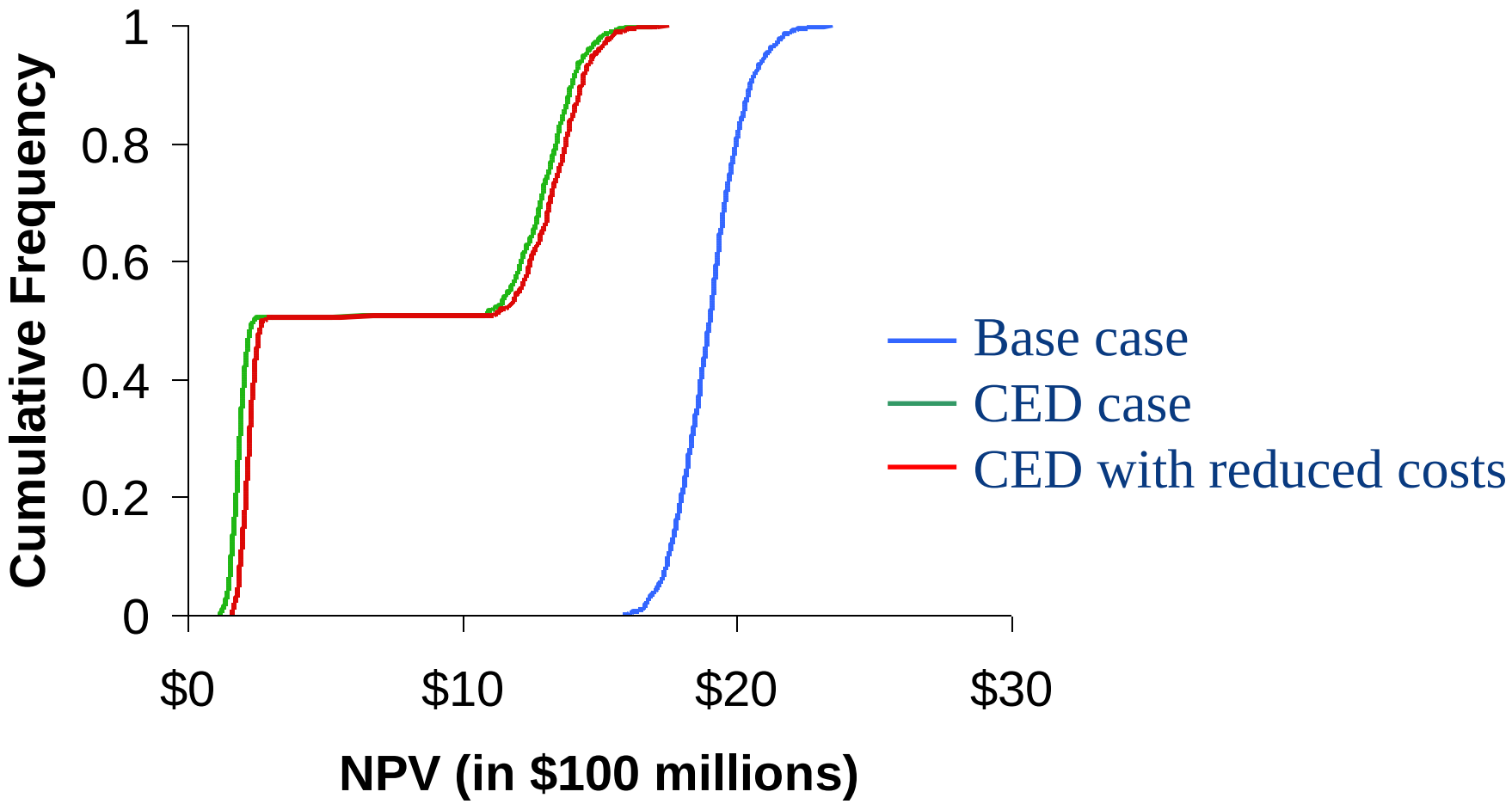
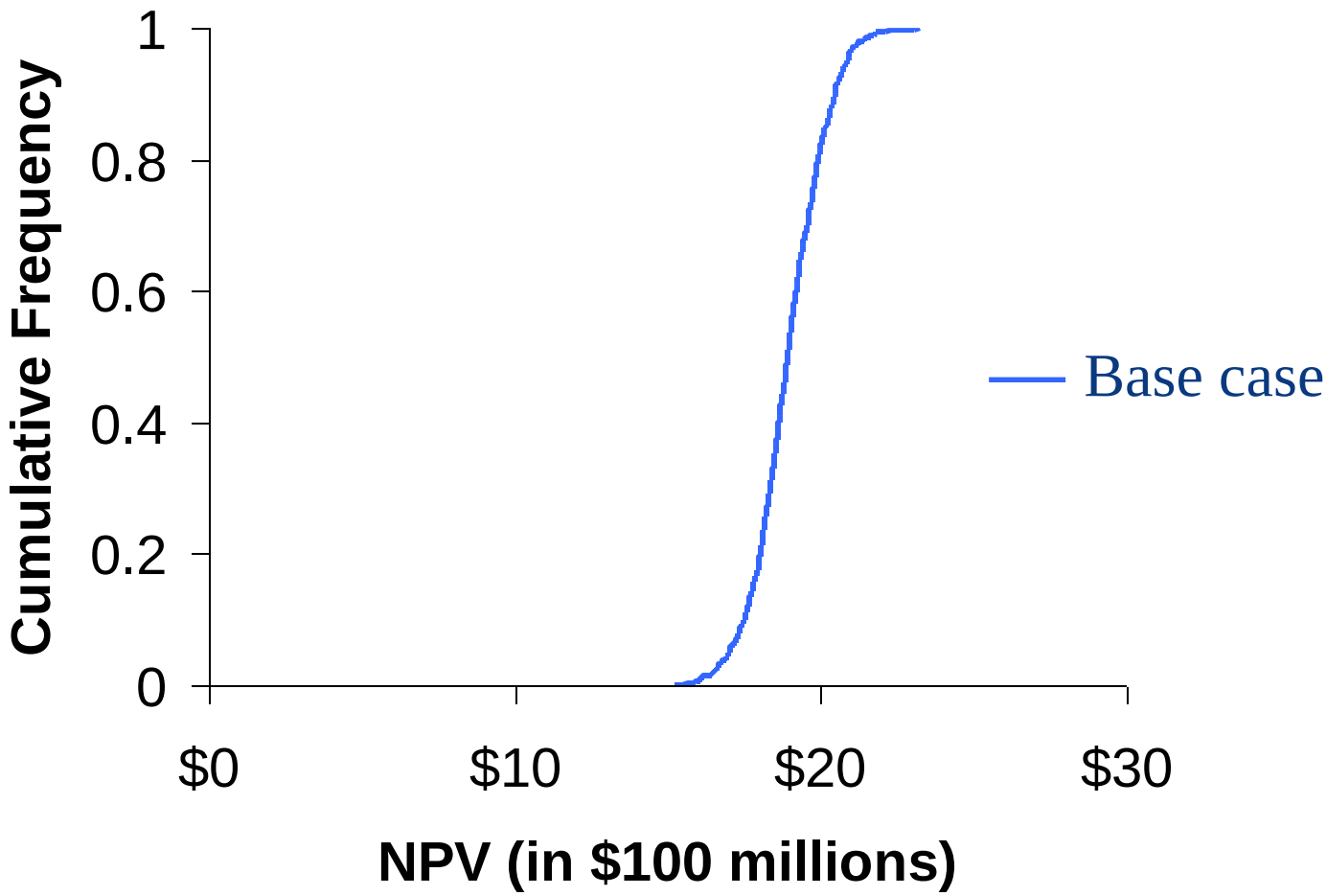


Scenario 2

(p trial success = 0.9)



Scenario 2

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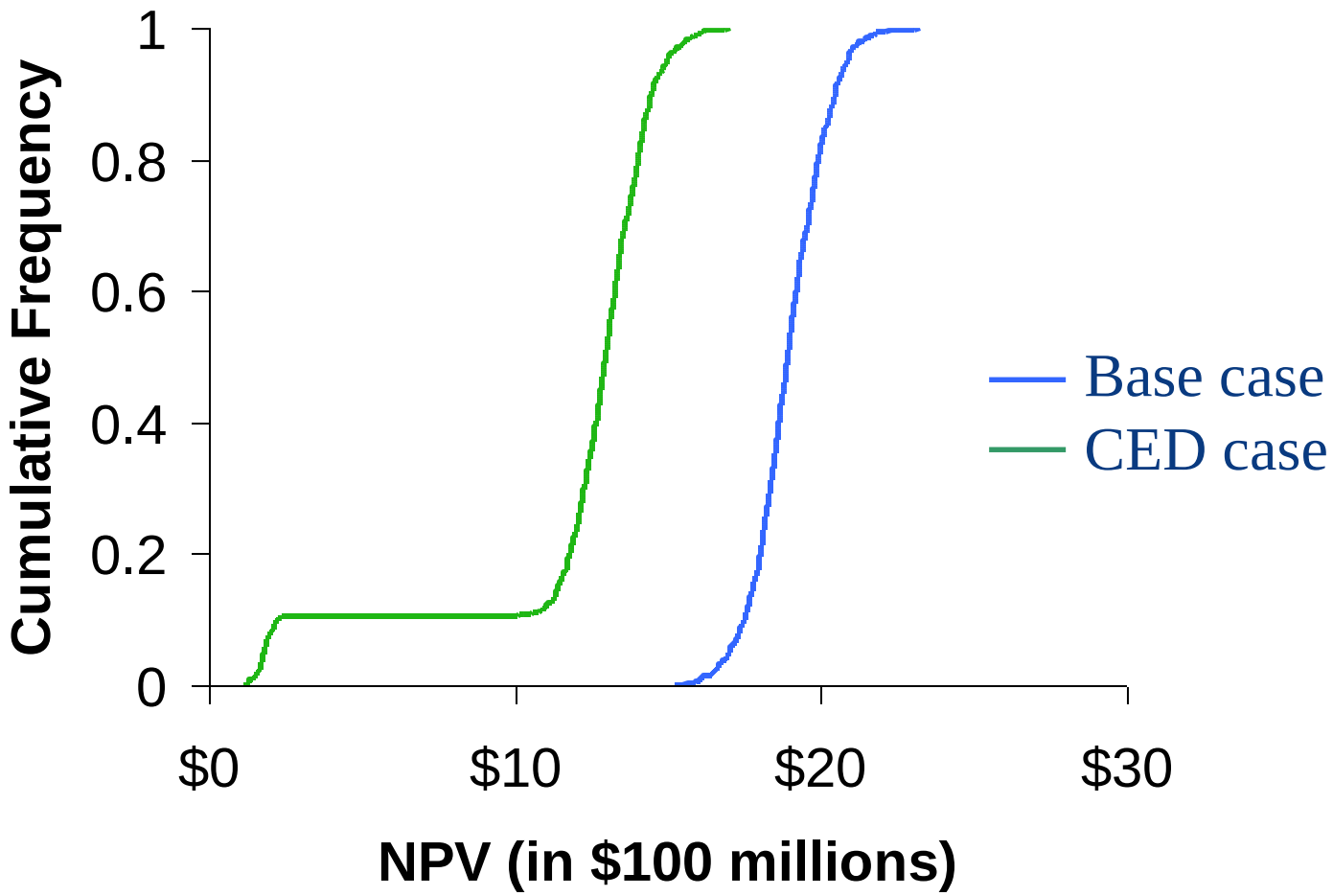

Scenario 2
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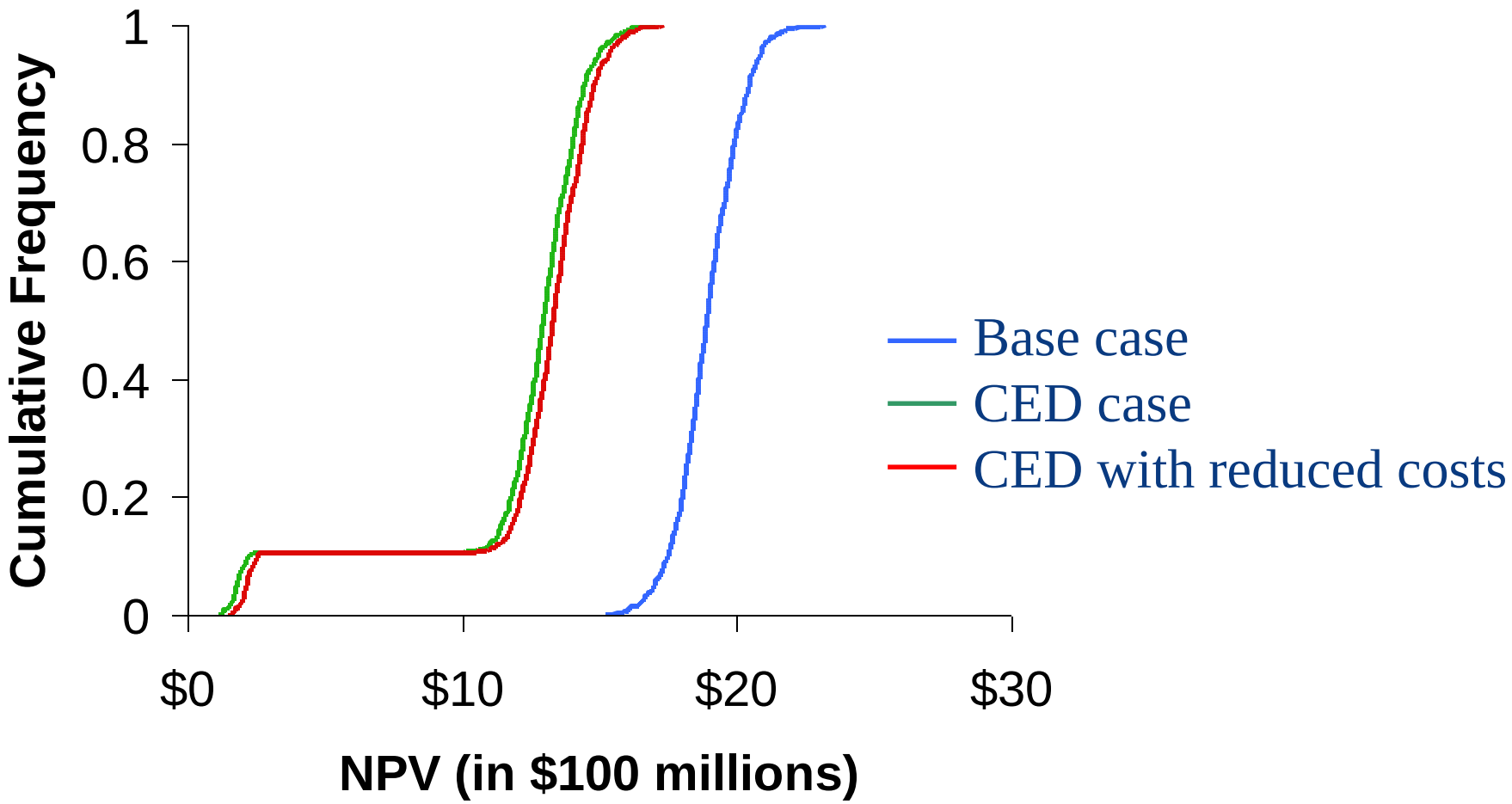


Conclusions

- Loss of revenue during CED decreased eNPV from base case
- eNPV partially, but not completely, restored by better predicting “winners”
- Improved production efficiency had little impact on eNPV

Marketing Approval Decisions by Regulatory Agencies

- **The evidence requirements for a given product label and the subsequent approval decision are relatively predictable**
  - **Phase 3 evidence requirements are agreed in the EOP2* meeting with the regulatory agency**
  - **Appraisal uncertainty → External advisory boards**
- **Regulatory agencies have historically focused more on benefit (efficacy and safety) than cost**
  - **Value is in the context of clinical value, not economic value**
  - **Trend in some markets toward comparative or relative benefit**
  - **Willing to trade off external validity for internal validity**

*** EOP = End of Phase 2**

Adoption/Diffusion Decisions by Payers

- Adoption decisions not as predictable as regulatory decisions
- No "rules of the road" or defined evidence requirements
  - Historically, input in Phase 2 has been informal
  - NICE "consultation": Based on EOP2 regulatory process
- Evidence requirements are different and more challenging than for a regulatory decision
  - Willing to trade internal validity for external validity (context sensitive)
  - Lack of "real world" experience for new products
  - Lack of methodological standards for observational studies of benefit
- In the U.S., clinical value and budget impact assessments are more common than economic value assessments

Issues in Adoption and Diffusion Decisions

- Most of the discussion is on evidence assessment; the appraisal process has received little attention

Evidence Assessment

- Methodological issues
- Lack of real world data for new products
- Reproducibility of evidence reviews not well studied
- Effectiveness endpoint for CER controversial

Evidence Appraisal

- Few value judgment studies
- No guidelines or certification requirements for decision makers (including P&T)
- Ripe for additional research: Ongoing project using a modified Rand Appropriateness criteria approach to evaluate the impact of quality of evidence, health impact, and cost on decisions

Need to Understand Both Assessment and Appraisal in Order to Estimate Evidence Requirements and Predict Decisions

EBM Best Practices Study (on-going): Round 1

- Experts (11) from academia and payer community
- Methods: modified RAND Appropriateness criteria approach
- 8 Scenarios: 6 drugs and 2 devices
- Scenarios varied by:
  - The quality of evidence on efficacy
  - The quality of evidence on safety
  - Whether the intervention extends life
  - Whether the intervention improves quality of life
  - Whether the intervention has a higher cost than available ones
- 42 individual sub-scenarios rated
- "Agreement" in 21 of the ratings
  - cluster within a range of 3 after excluding high and low scores
- "Disagreement" in 5 of the ratings
  - 3+ from 1-3 and 3+ from 7-9

Variability across Experts, all scenarios

Likelihood of Reimbursement

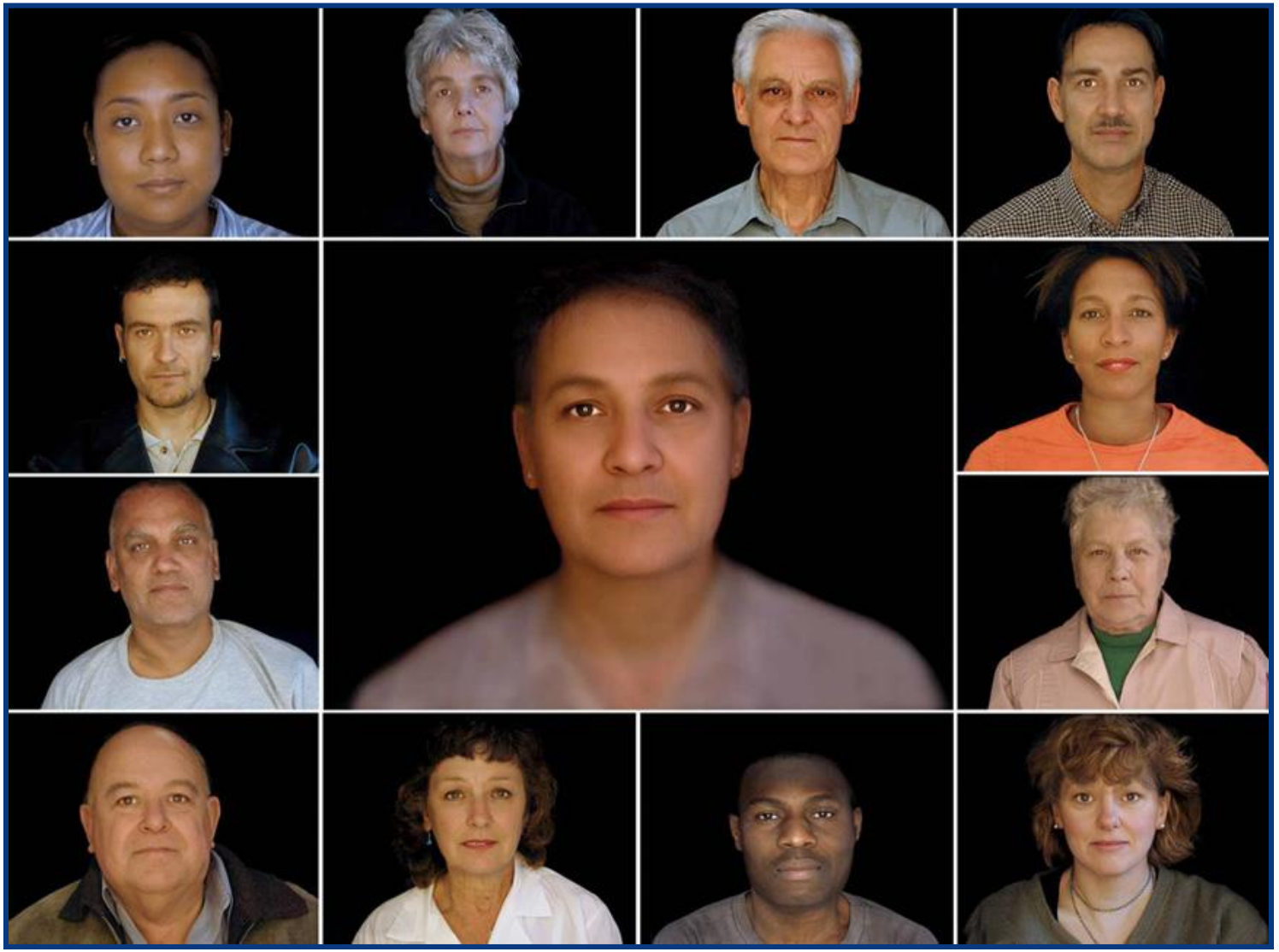
	A	B	C	D	E	F	G	H	I	J	K
Median	5.3	5.0	4.5	4.5	4.3	4.1	4.1	4.1	3.2	2.9	2.1

1 = Very unlikely
9 = Very likely

Treatment Decisions by Patients and Their Physicians

- Decisions ideally informed by best evidence, physician expertise, and patient preferences (Sackett EBM definition)
- Formal incorporation of patient preferences into individual treatment decisions is rarely done but important
- Getting from population based “best evidence” to the best choice for a given patient is difficult when heterogeneity exists
  - Genotyping: Reduction of uncertainty at the individual patient level
  - Actuarial diagnostics: Reduction of uncertainty at the sub-group level using patient phenotype and / or other available data

How much is your patient like the average?



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Summary

- Value for pharmaceuticals may be assessed and appraised differently depending on
  - The type of decision
  - The preferences of the decision maker
- We need thoughtful policies that balance cost control with broad access and continued innovation
  - Requires more predictability and transparency in adoption and diffusion decisions
  - Requires developers to partner with stakeholders from early development through the product lifecycle
- Individual treatment decisions could be improved by better incorporating patient preferences and heterogeneity of treatment effect into the (treatment) decision

Decision-Based Evidence Making, then Evidence-Based Decision Making