

BERYLLIUM DISEASE PROGRESSION MODELS: IMPLICATIONS FOR SCREENING

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TOPICS

- PURPOSE-WHAT ARE THE IMPORTANT QUESTIONS?
- WHY USE DISEASE MODELS?
- BERYLLIUM PROGRESSION MODEL
- SCREENING MODEL
- PRACTICAL IMPLICATIONS
- DISCUSSION CASES



PERSONALIZED MEDICINE

- OPTIMIZE FOR EACH INDIVIDUAL
- VARY OVER TIME
- CONTINUOUSLY ADJUST BASED UPON THE LAST RESULT
- TRADITIONALLY, GENETICS
- TARGET RESOURCES CAREFULLY



CURRENT APPROACH: SINGLE METHOD FOR EVERY ONE AND FOR EVERY SITUATION

- ELIGIBILITY
- COMMUNICATION
- TEST SELECTION
- TEST FREQUENCY
- TEST FOLLOW-UP
- CRITERION VALUE (ROC)



QUESTIONS

- WHAT IS THE BEST ELIGIBILITY CRITERION?
- SHOULD TESTING INTERVALS BE UNIFORMLY SPACED?
- SHOULD TESTING BE CONTINUED INDEFINITELY?
- HOW MANY NEGATIVES CONVINCED THAT DISEASE IS NOT PRESENT?
- SHOULD THE CUT POINT BE THE SAME FOR EVERYONE?



PROGRAM QUESTIONS

- WHAT IS THE BEST USE OF RESOURCES?
- PERSPECTIVES: DOES EVERYONE SHARE THE SAME VALUES/ GOALS?
 - eg, importance of job vs risk, acceptance of uncertainty
- AGGREGATE ANALYSIS: BeLPT AS A BIOLOGIC MONITOR OF EXPOSURE



AGGREGATE ANALYSIS: BeLPT AS A BIOLOGIC MONITOR OF EXPOSURE

NEW BeS → POOR CONTROL (?)

- 1ST TESTS ARE CRITICAL, SO REPEAT A FEW TIMES IN YR 1
 - BeLPT IS 'NOISY' TEST
 - FALSE POSITIVES, FALSE NEGATIVES, & NEAR MISSES OCCUR
 - TRANSITION NEG→POS IMPLIES PROBLEM
- | EXAMPLE: | <u>TRUE</u> | <u>OBSERVED</u> |
|----------|-------------|-----------------|
| TEST 1 | POS | NEG |
| TEST 2 | POS | POS |
- SUGGESTION: GET MULTIPLE BASELINE TESTS
 - (also, best chance to find cases... see later slides)



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WHY MODEL?

- EXPLICITLY EXPRESS CALCULATIONS AND CHOICES
- OVERCOME CONSTRAINTS OF SHORT-TERM FOLLOW-UP STUDIES:
 - CBD IS A 40 YEAR CONCERN, BUT FOLLOW-UPS ARE TYPICALLY FIVE YEARS
- UNDERSTAND MECHANISMS



SCIENCE = FALSIFICATION

- KARL POPPER
 - PHILOSOPHER OF SCIENCE
 - DEMARCATION PROBLEM: HOW TO DISTINGUISH PHYSICS FROM METAPHYSICS?
- SCIENCE IS BASED UPON THE ABILITY TO PROVE A THEORY IS FALSE
- APPLICATION: WE HAVE SOME FACTS ABOUT CBD. IF A THEORY LEADS TO RESULTS INCONSISTENT WITH FACTS, THE THEORY IS WRONG.

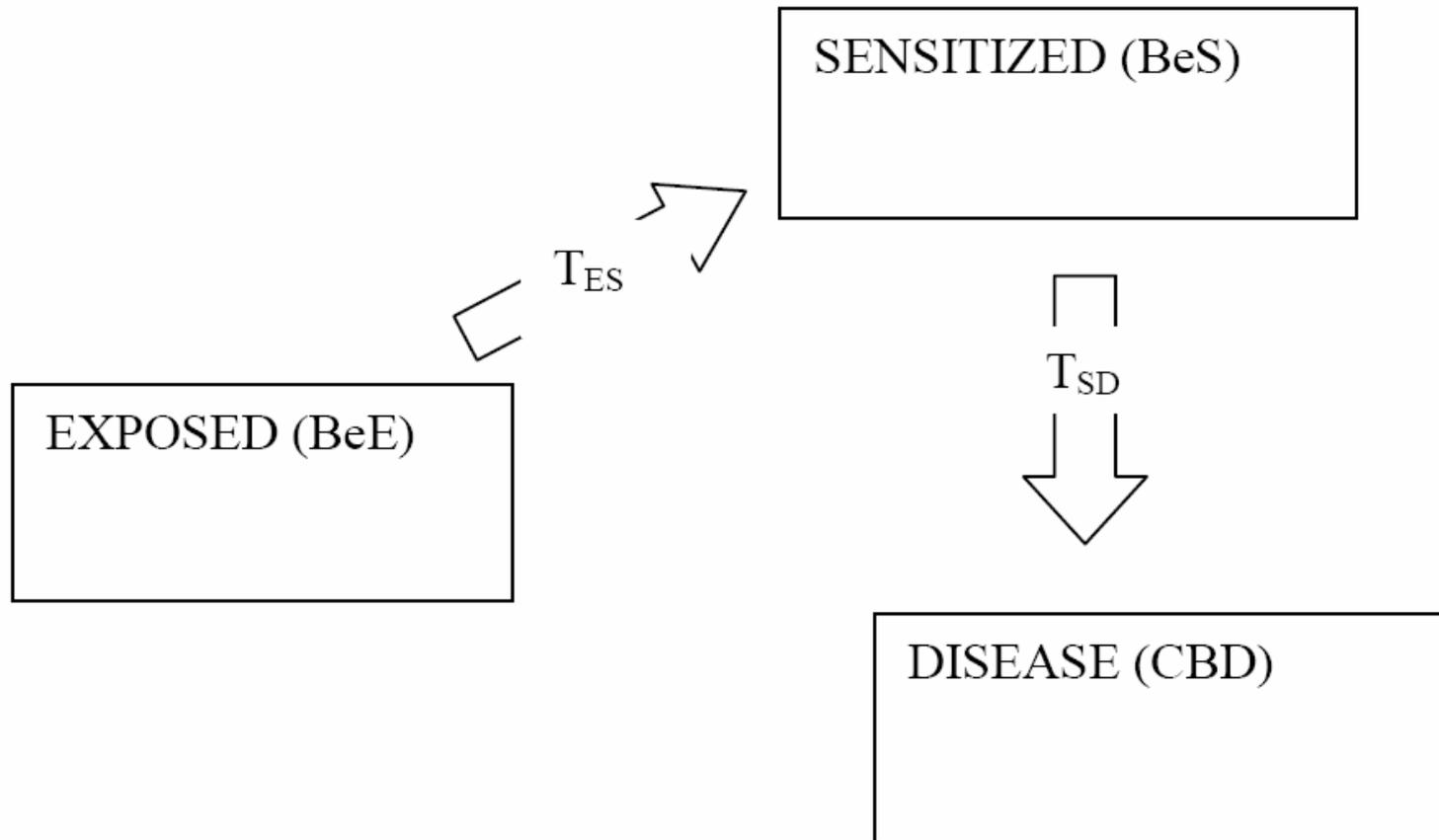


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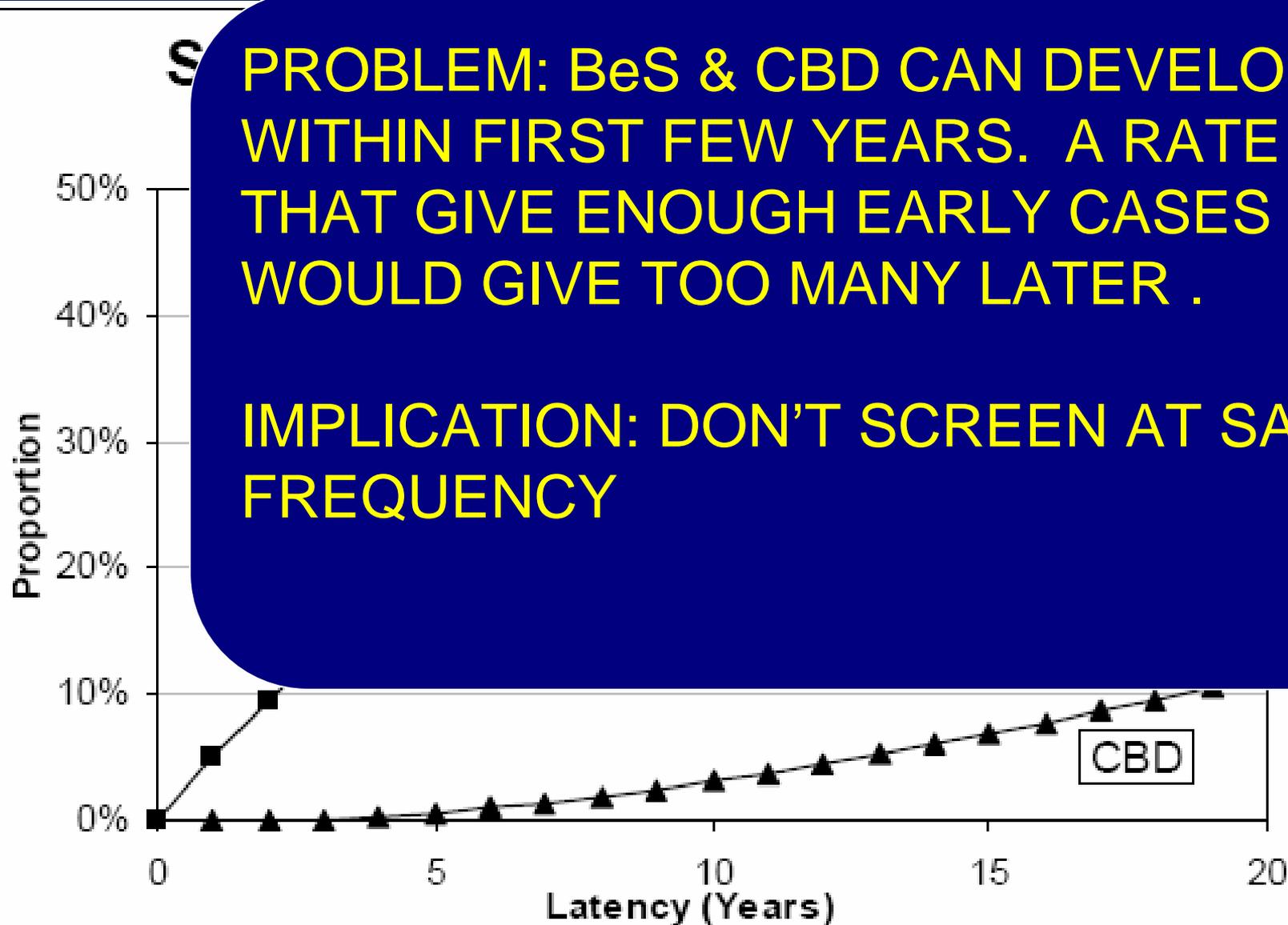
3 STATE MODEL



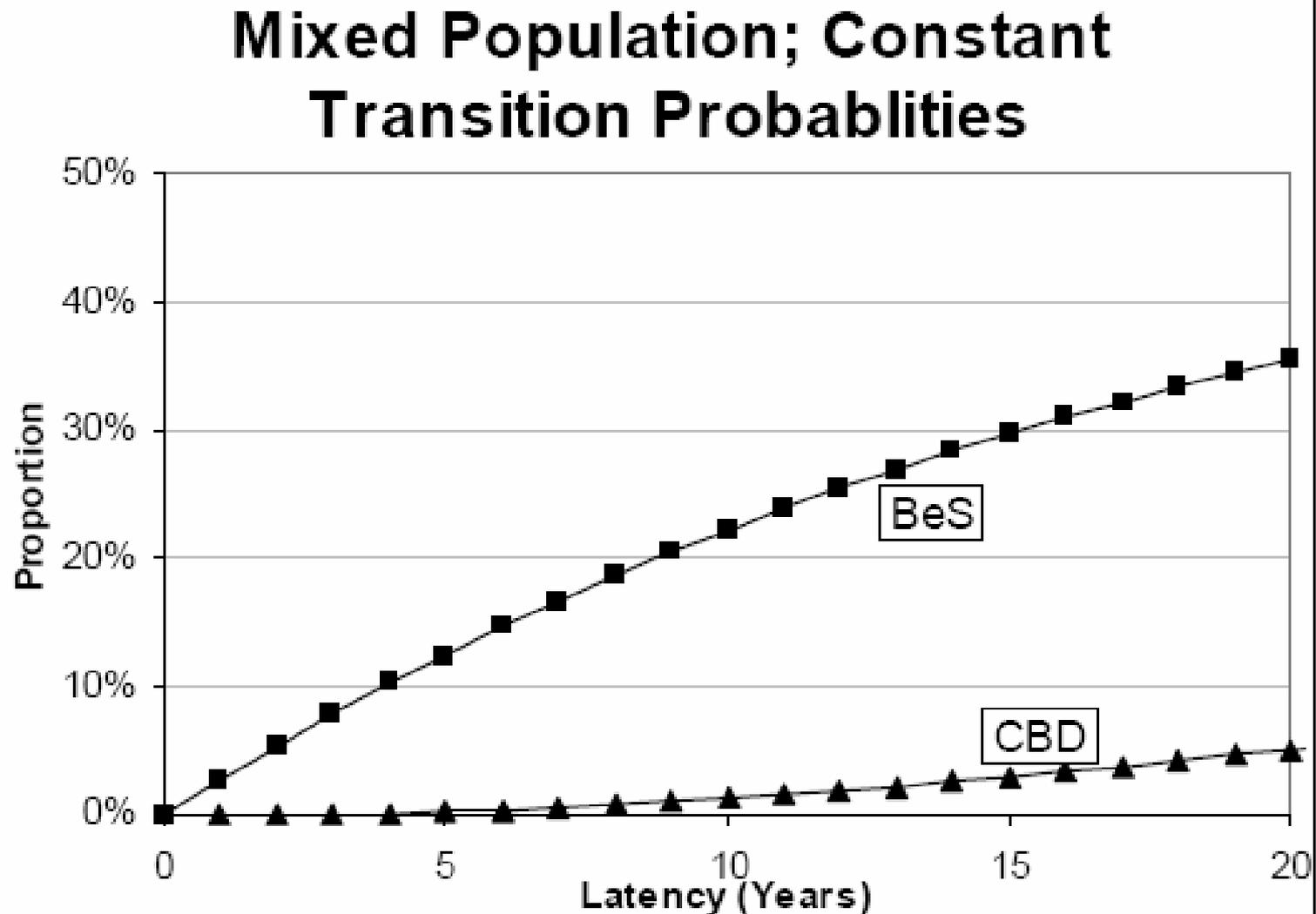
SINGLE POPULATION; CONSTANT RISK OVER TIME

PROBLEM: BeS & CBD CAN DEVELOP WITHIN FIRST FEW YEARS. A RATE THAT GIVE ENOUGH EARLY CASES WOULD GIVE TOO MANY LATER .

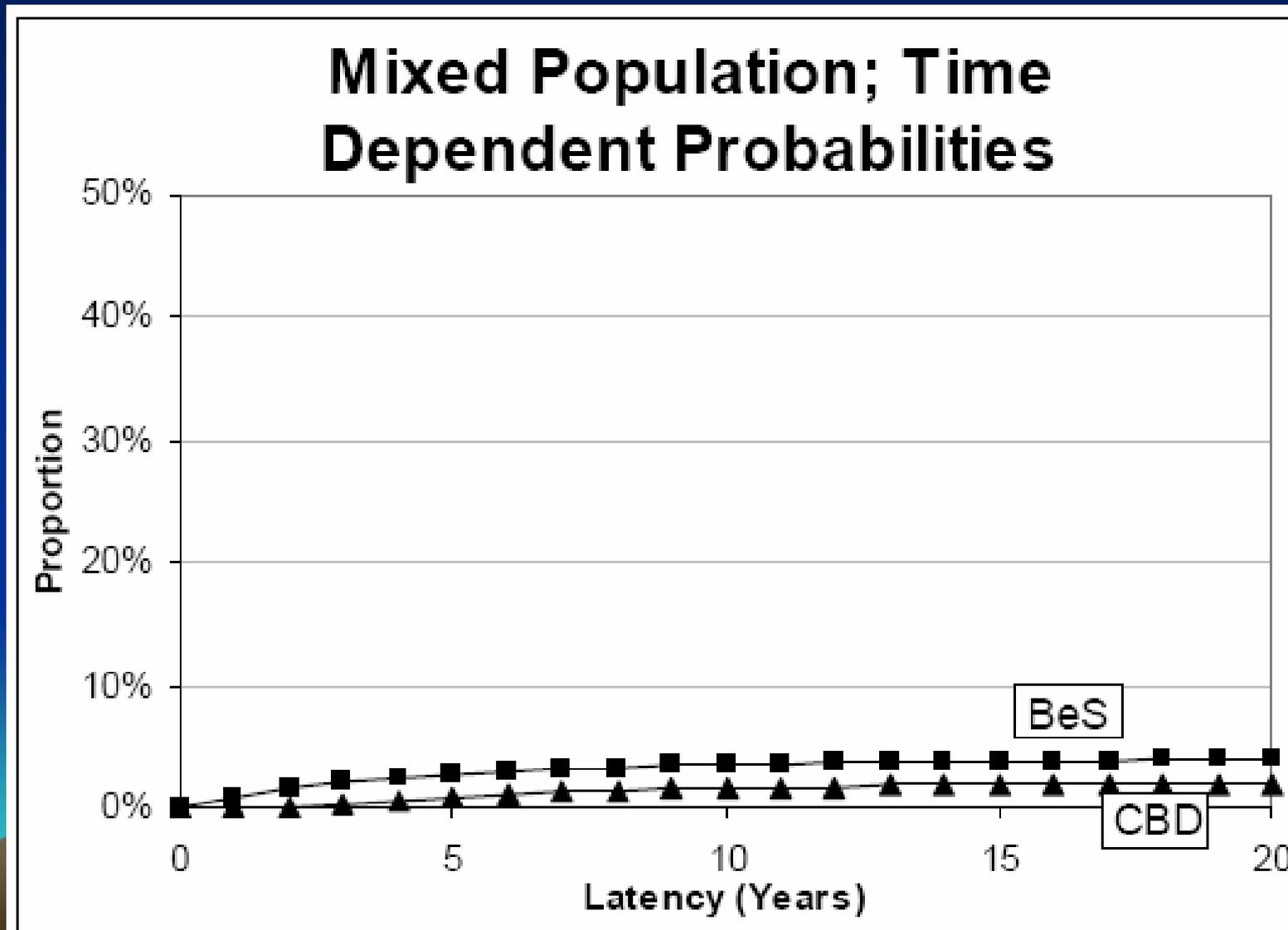
IMPLICATION: DON'T SCREEN AT SAME FREQUENCY



MIXED POPULATION; CONSTANT RISK

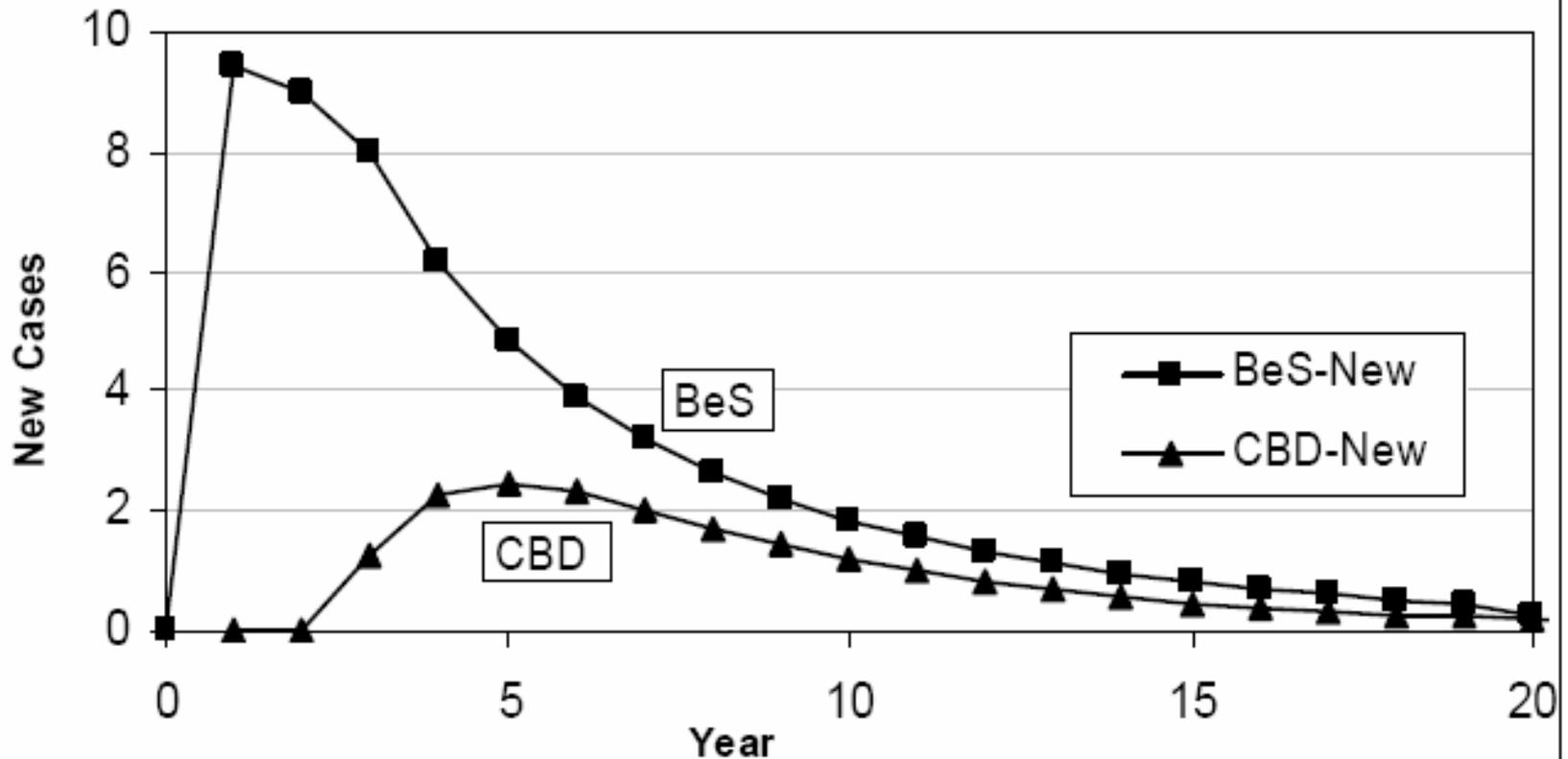


MIXED POP; TIME VARYING RISK



INCIDENCE (NEW CASES)

Incidence of BeS and CBD

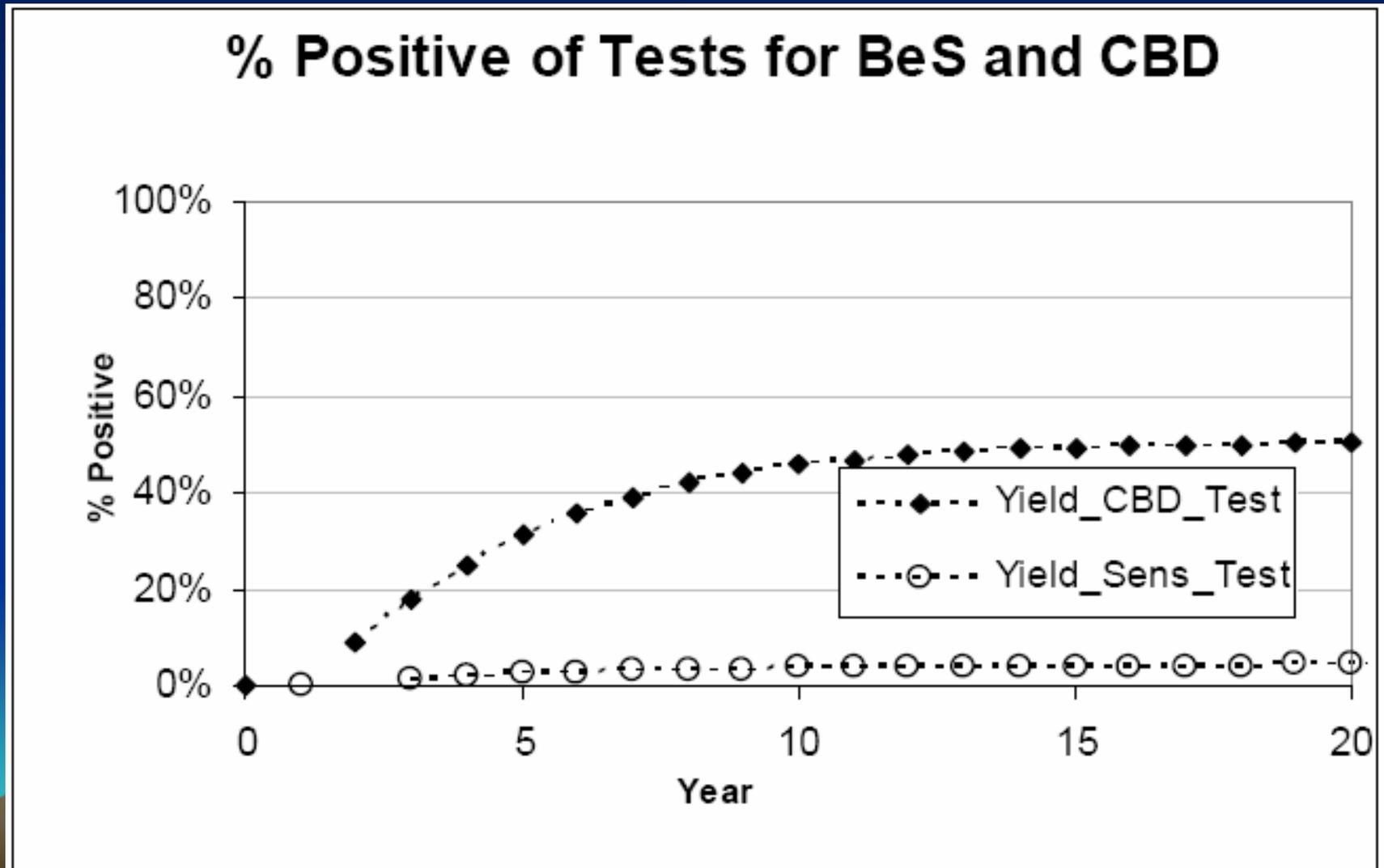


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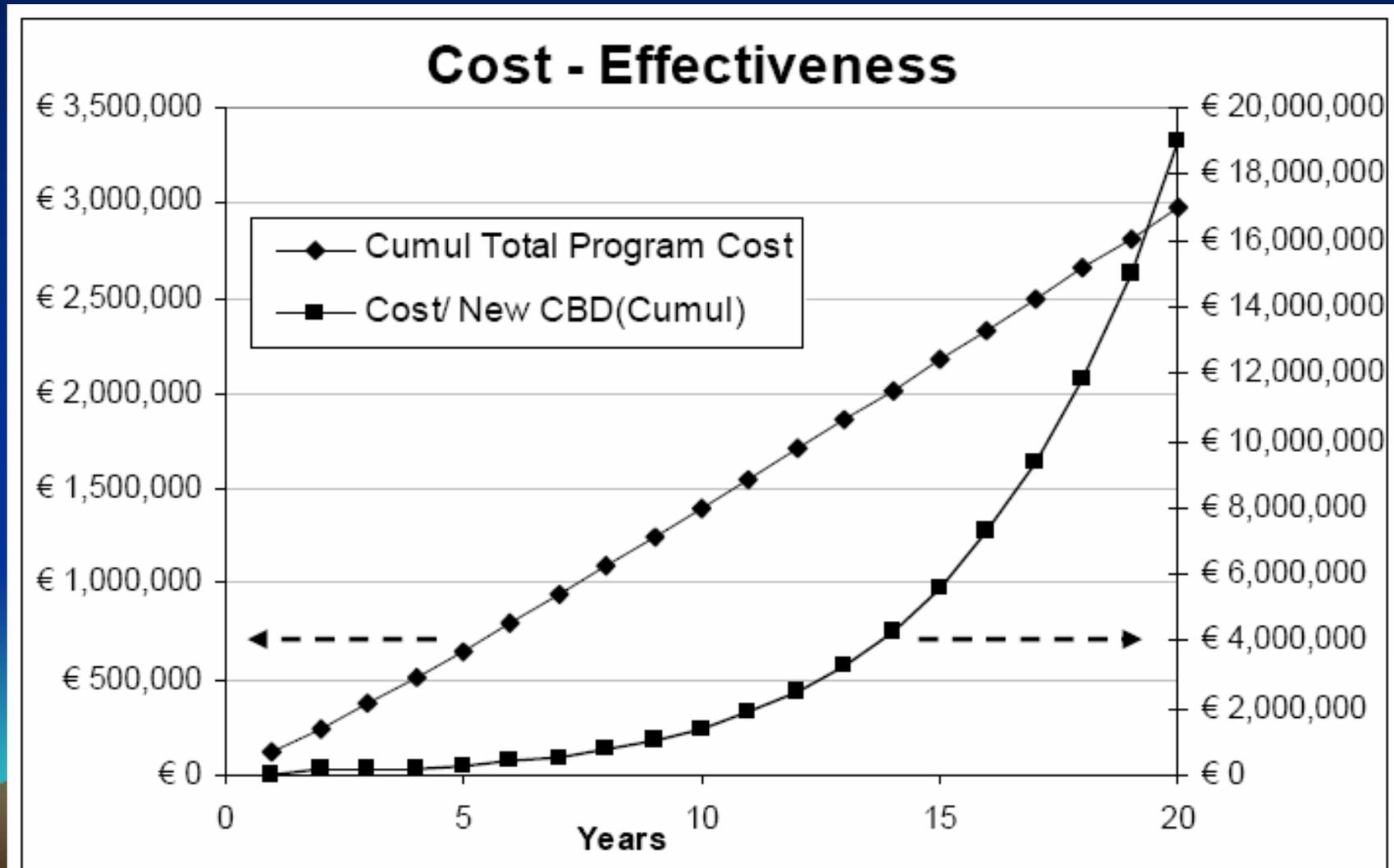
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SCREENING IMPLICATIONS: yield of testing varies by year



COST-EFFECTIVENESS



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PRACTICAL IMPLICATIONS

- The risk of developing BeS among exposed individuals is greatest in the first few years after exposure and then declines.
- The annual risk of progressing from BeS to CBD declines over time.
- , there is a persistent risk of developing new BeS and new CBD even with long latency.
- Screening intensity should be adjusted according to years of latency in order to optimally use resources.
- Screening is useful for exposed workers who have not been previously tested.



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HYPOTHETICAL CASES

- 2 pos
- 2 pos
- 1 pos
- 1 pos

SUGGESTION : ADD TIME CRITERION:
Eg "POS" MEANS 2 POS WITHIN 2
YEARS...

LOOK AT WHAT HAPPENS ONCE
POSITIVE



YET MORE HYPOTHETICALS

FOR HOW LONG IS A NEGATIVE CBD EVALUATION ADEQUATE TO ASSURE ABSENCE OF DISEASE?

- JONES: PROGRESSES FROM BeS to EARLY CBD IN 4 YEARS
- SMITH: PROGRESSES FROM BeS to EARLY CBD IN 40 YEARS



HYPOTHETICAL CASES

- 2 pos
- 2 pos
- 1 pos
- 1 pos

GOAL OF SCREENING AND EARLY TREATMENT:

1. REDUCE EXPOSURE POTENTIAL(?)
2. PREVENT DISABLING DISEASE
3. RAPID PROGRESSORS AND YOUNG MAY BE AT GREATER RISK (and need more careful followup..."nonstationary Markov...")



WHAT ARE THE VALUES?

- “UTILITY ANALYSIS”
- EARLY DETECTION OF DISEASE
 - USEFUL IF TREATMENT HELPFUL
- TREATMENT BENEFIT
 - BALANCE RISK OF TREATMENT VERSUS BENEFIT VERSUS YEARS OF LIFE SAVED



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THEORIES

- EVERYONE EXPOSED HAS COMPARABLE RISK, ADJUSTED FOR EXPOSURE
- RISK OF BeS and CBD DEVELOPMENT IS CONSTANT OVER TIME
- PROGRESSION RISK IS TIME INVARIANT
- BeS & CBD DEVELOPED DE NOVO



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