

Utility and Adoption of Clinical Genomics: Foundations of Assessments

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- Institute of Medicine
- Facilitating Development and Utilization of Genome-Based Diagnostic Technologies: A Workshop
- November 15, 2011 Washington, DC

Genes, Coding, and Bold Action?

Palmetto GBA Designs a Medicare
Genomics Evaluation Program for 2012

NOVEMBER, 2011



Tempest in the Melting Pot: Genomics Reimbursement in 2012



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Overview

- **Canada as a Fountainhead for Evidence Based Medicine (EBM)**
 - Key role of Sackett
 - Alternative voices: Jenicek; Miettinen, Dickinson, Giacometti; in England, Worrall and Cartwright
- **Are there structural features of EBM that are worth discussing?**
- **If there are differences in doing EBM for diagnostic tests, what are they? How do we know?**

Can the “EBM Process” yield Anomalous Results?

If so, is that interesting?

- AHRQ: BRCA, breast cancer, & evidence level “fair”
- CMS recently criticized for strategic skills
 - Urban Institute (9/2011, Tunis et al.)
- TA and Oncology (O.S.)
- TA and Renal Transplant (Logical structure)
- Human beings, logic skills, and expertise
 - Evans (1992) Cognition 49:165
 - Miettinen (1998) CMAJ 158:215
 - Epstein (2004) Institute for Policy Innovation
- “Effect of Herceptin on American Indian Women”
- F. Roberts, Brit Med J, 12/16/1922

- Meta-analysis of RCT's
- Multiple RCTs
- RCT
- Cohort study
- Observational study
- Retrospective study
- Expert opinion

- Wearing shorts, eating ice cream:
High correlation
- Putting shorts on someone in Montreal in January, will not start eating ice cream
- Only a correlation

- Mid life estrogen use; getting Alzheimer's disease:
Strong negative correlation
- RCT: Giving women estrogen does not prevent Alzheimer's disease
- Need RCT!

- Meta-analysis of RCT's
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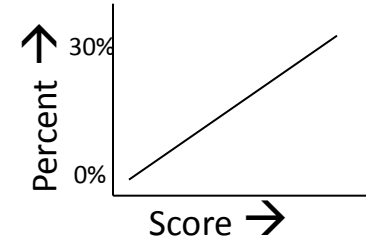
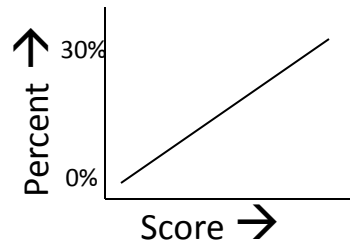
- Wearing shorts, eating ice cream:
High correlation...

- Mid life estrogen use; getting Alzheimer's disease:
Strong negative correlation...

- High troponin, having an MI:
- Strong correlation
- Giving troponin to people: does not cause an MI
- *Is this bad news??*
- One key reason for RCT is proving correlation
- Diagnostic test useful BECAUSE of a correlation

- Analytical Validity
- Clinical Validity
- Clinical Utility

- This is so general it has limited usefulness (truism)
- Book has:
 - Ink, paper, glue
 - Words, grammar, language
 - Content, meaning, usefulness
 - Each are emergent properties unrelated to prior levels
- Analytical validity: One gene measured at 2% accuracy, one at 4% accuracy, but the latter is three times better for clinical validity (r or roc)
- Clinical validity:



Moving forward

Are other test evaluation paradigms possible?

- **(A)** Two hundred-person cohorts, one in which test is used, one not; perhaps a CUI (Clinical utility index)
 - Garrison: Quantitative R/B assessment; Oullet: CUI
 - Pro's and Con's of quantified R/B: see Hughes v Temple, 2007
- **(B) Tests transform questions**
- “Transform a question we can't answer into a question we can answer”
 - “Do we need to switch your HIV drug?” transformed to:
 - “Is your HIV RNA count rising?”
 - Key is the correlation between the answer the test provides and the question that was asked
 - Explains the AHRQ/BRCA EBM paradox cited earlier

Elizabeth Anscombe



- There are two kinds of true statements
- Statements about things
 - This is a rock
 - You have leukemia
- Statements about relationships
 - Ten dimes in a dollar
 - High troponin = MI

Olli Miettinen



- Clinical Decision Making
- Specific Statements about patient
 - 58 years old
 - Male
 - Has pancreatic cancer
 - Liver mets
- General Medical Rules (principles, facts, EBM)
 - Average survival 1 year
 - No improved survival with 4 different chemotherapies
 - Net 1 year QOL better with palliative care than chemotherapy

Harley Dickinson



• Evidence Based Decision Making

(after Toulmin)



BRUTE FACT DATA (Patient)

Jack has pancreatic cancer
He is 58 years old.
The cancer is advanced, with liver mets.



WARRANT(S)

Pancreatic cancer is usually terminal
Pancreatic cancer patients are net better
palliative care.



CONCLUSION

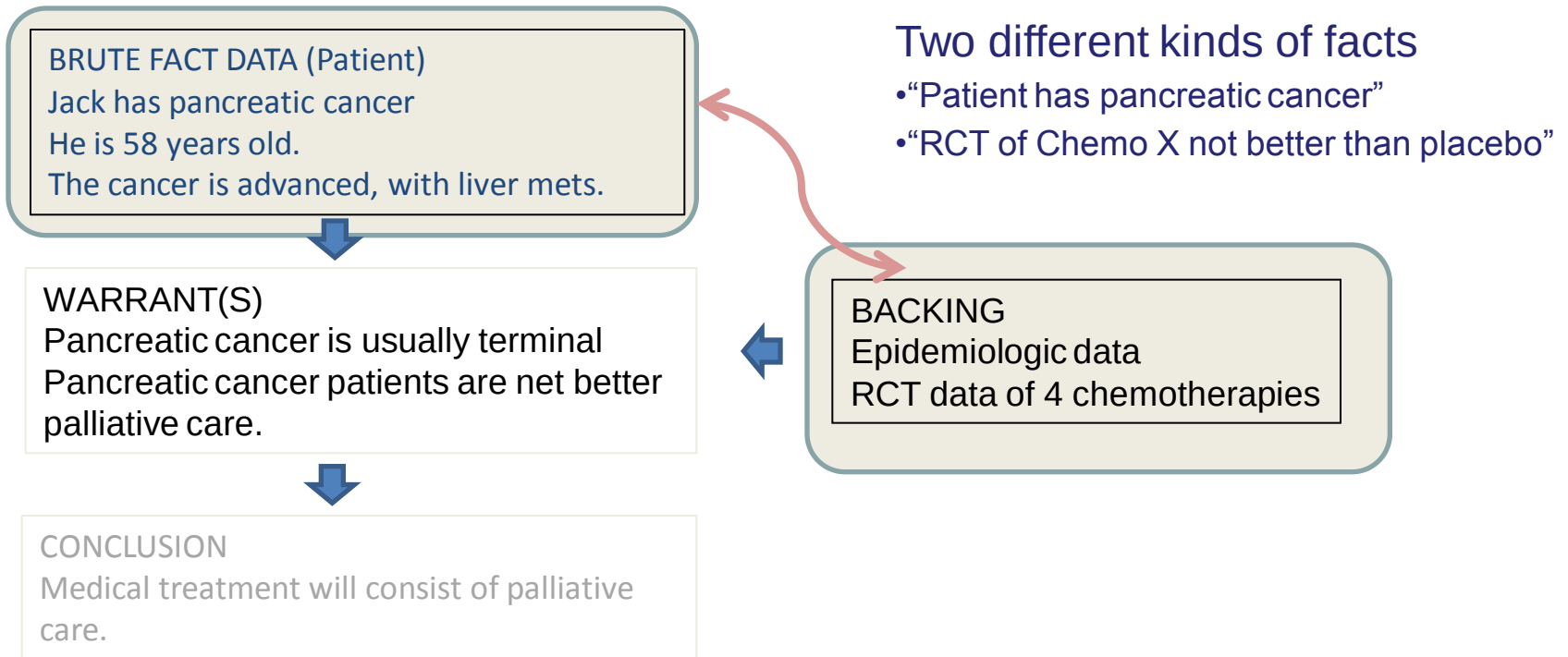
Medical treatment will consist of palliative
care.

BACKING

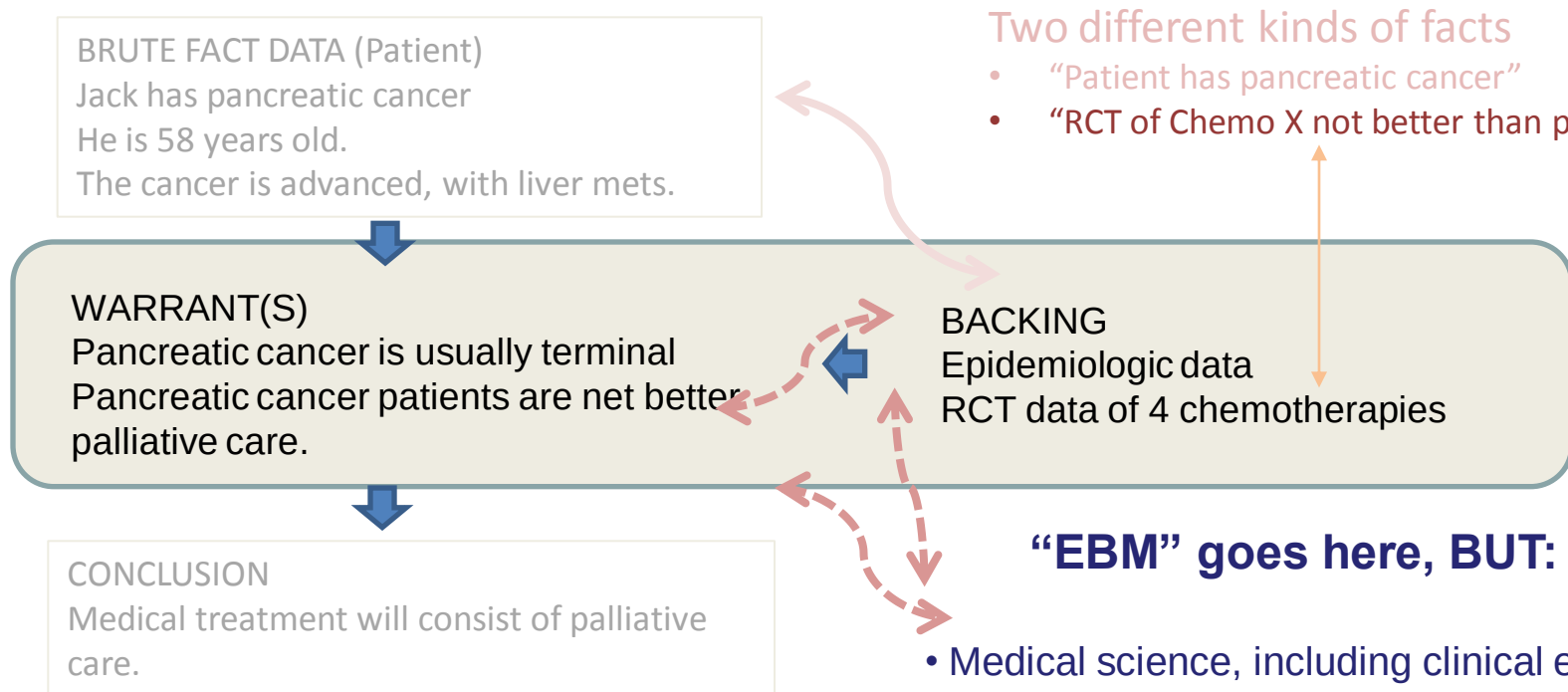
Epidemiologic data
RCT data of 4 chemotherapies



Evidence Based Decision Making



Evidence Based Decision Making



Two different kinds of facts

- “Patient has pancreatic cancer”
- “RCT of Chemo X not better than placebo”

“EBM” goes here, BUT:

- Medical science, including clinical epidemiology, is very hard and requires a lot of thought and expertise
- Not clear that “clunky” EBM adds or subtracts value; Miettinen and others have been adamant on this (also earlier AHRQ/BRCA example)
- Recent example of two meta-analyses being wrong
 - *DVT & travel: AnnIM (2009) 151:180*
- Real science: Watson & Crick 5 warrants; S. Haack

Specific Patient Facts
(Brute Facts)

BRUTE FACT DATA (Patient)

- Mary is 55 years old. Mary had 1 cm breast cancer, grade 2, NØ.
- Mary is uncertain/open to options re chemotherapy.



Warrants
(Clinical Rules)

WARRANT(S)

- ODX/MP test correlates well with BrCa recurrence.
- Low recurrence risk = no chemotherapy.



MORE
BRUTE FACT DATA
(Patient/Tumor)

- Gene expression is (a,b,c,d,e...)
- Algorithm result is <8%.

Backing
(Trials or Other Solid Knowledge)

BACKING
Multiple large studies



Clinical Utility
(Impact)
(Change in Mgt)
(Change in Outcome)

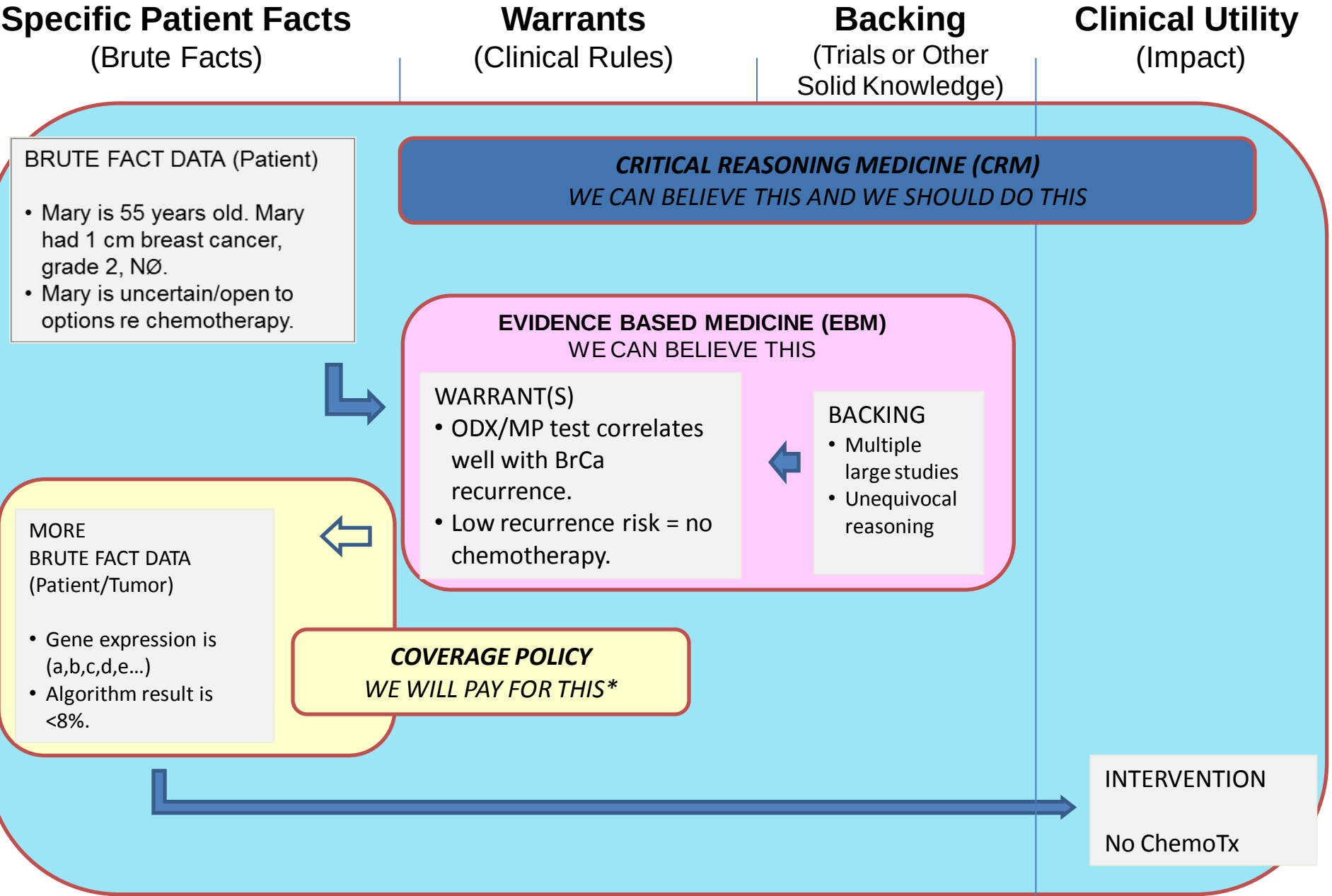


INTERVENTION

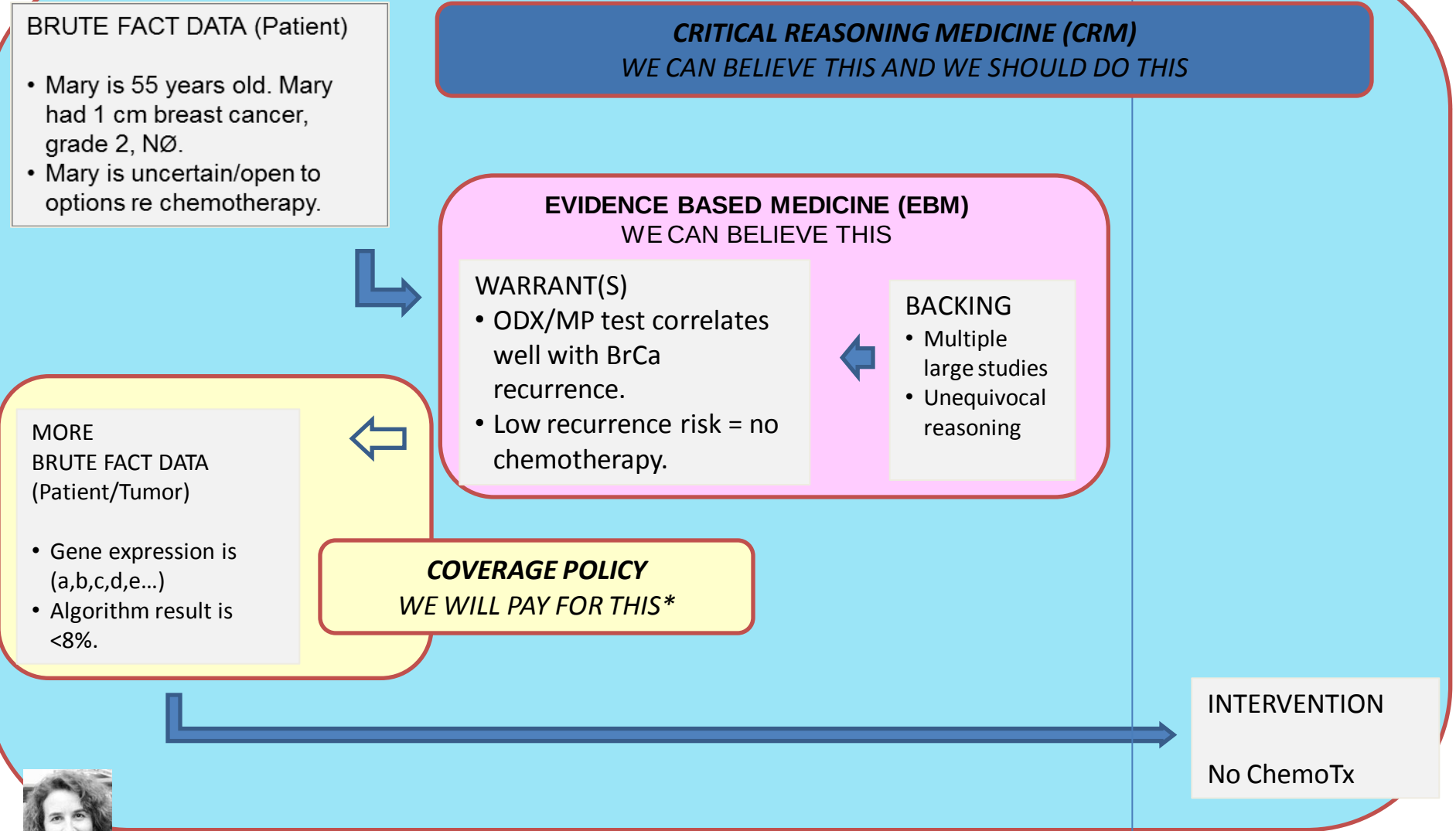
No ChemoTx



See also: Milos Jenicek urging from “Evidence Based Medicine” (EBM) to “Critical Reasoning Medicine” (CRM)
Med Sci Monit (2006) 12:149; (2011) 17:12; several books



• In relationship to the whole box, funds, priorities, and available alternatives (e.g. incremental clinical utility index)
• E.g. Giacomini M (2007) How good is good enough? Standards in policy decisions to cover new health technologies, Health Pol 3 :91.



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Thank you.

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