

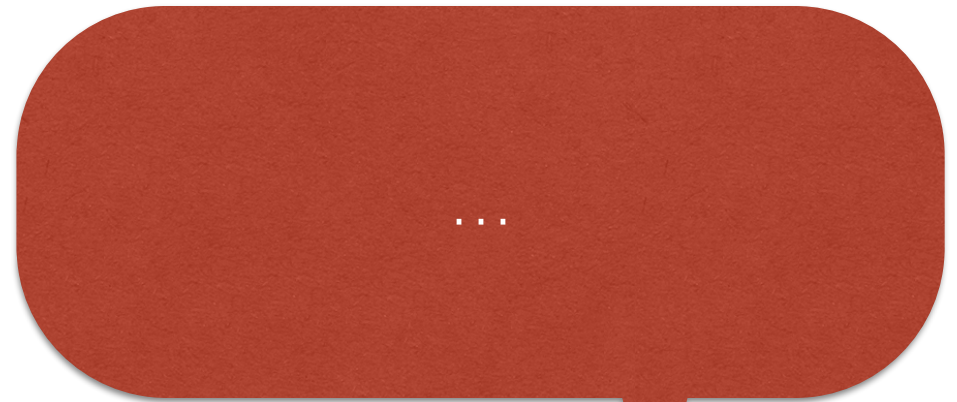
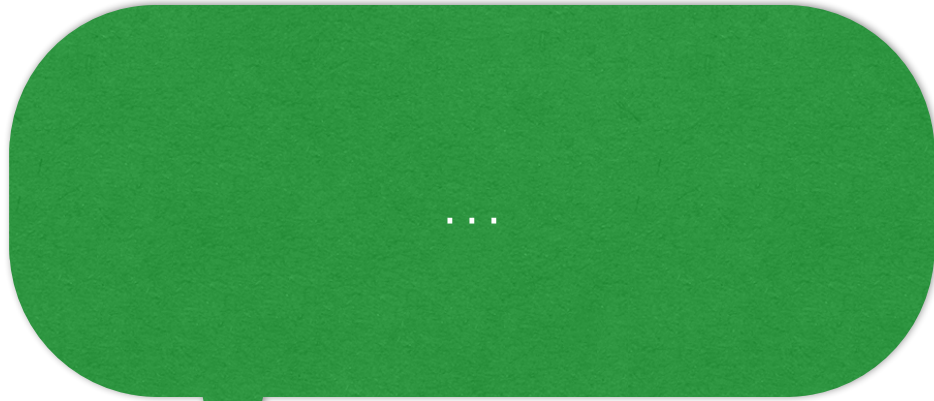
Measuring clinical impact: methodological issues and challenges

Panel discussion

Samuel G. Schumacher
McGill University

QUICK POLL

Question X?



Data on impact?

We need studies on impact!



Data on test characteristics and implementation setting are sufficient!



Final Outcomes?

We need to look at final outcomes!



Looking at key intermediate outcomes is sufficient!



RCTs?

We need RCTs!



Doing a mix of accuracy, modelling and OR is sufficient!



Settings?

Doing a few large studies representative of major epidemiological settings is sufficient!



We need many small operational research studies!



Dx or Dx+?

We need to assess the combined impact of diagnostics and downstream effects!



We should look at the impact of diagnostics, separately from the influence of downstream effects!



What are the challenges?

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1. “A major obstacle to conducting impact assessments is a lack of consensus on what **‘impact’** really means, and what patient-, population-, health systems-, and epidemiology-important **outcomes** should be measured to decide on impact.”

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2. “There is also a lack of guidance on the **methods** (i.e. study **designs**) to be used to measure them, which methods will be most rapid and cost-effective”
3. “[...] the impact of a new, more accurate diagnostic tool on tuberculosis epidemiology [is] substantially affected by **contextual factors** unrelated to tool performance.”

Challenges & Lenses

1. What is impact / which **outcomes**?
2. How to study it / which **designs**?
3. How to consider **context**?

1. **test developer**
2. **researcher**
 - primary research
 - systematic reviews
3. **policy maker / guideline developer**
 - global
 - country level
4. **Funders**

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 - country level
- 4. Funders**

1. What is impact /
which **outcomes**?

What do other say?

A quick look beyond the TB world...

What do other say?

A quick look beyond the TB world...

- World Bank

What do other say?

A quick look beyond the TB world...

- World Bank
- UPSTF / AHRQ

What do other say?

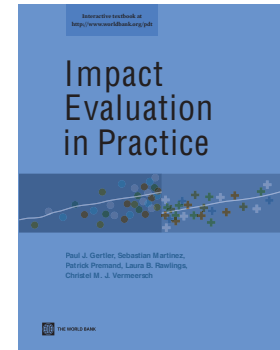
A quick look beyond the TB world...

- World Bank
- UPSTF / AHRQ
- Epidemiology/
Computer Science

What do other say?

A quick look beyond the TB world...

- World Bank



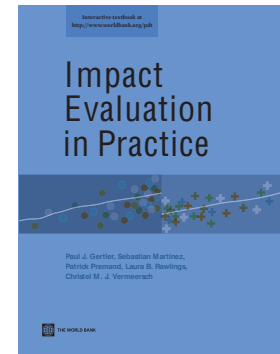
- UPSTF / AHRQ

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Computer Science

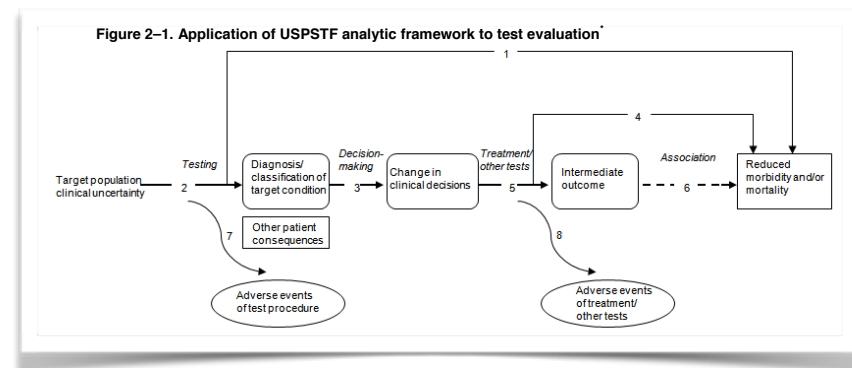
What do other say?

A quick look beyond the TB world...

- World Bank



- USPSTF / AHRQ

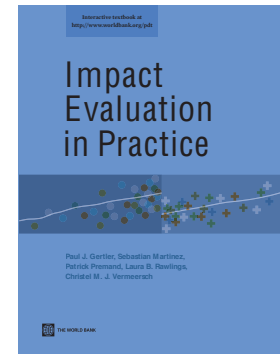


- Epidemiology/
Computer Science

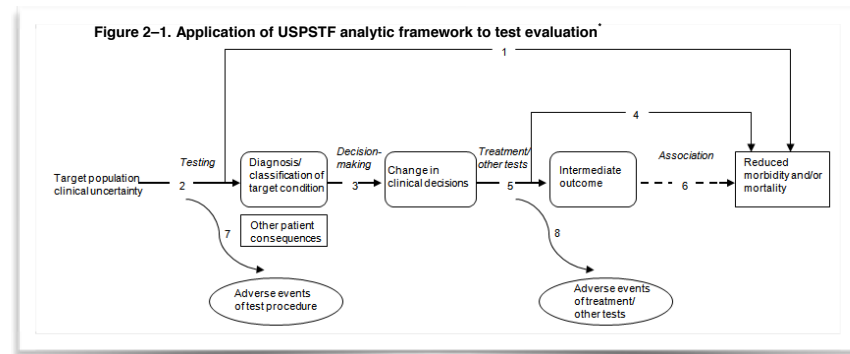
What do other say?

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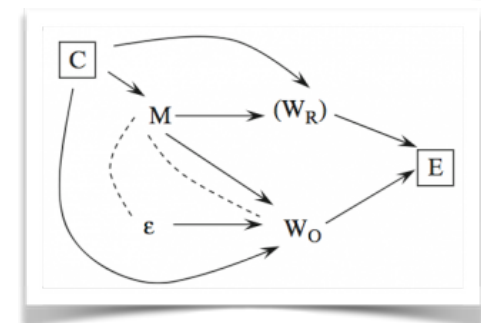
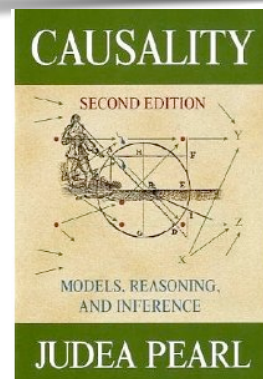
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How to Assess Impact

3 important points

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 - ▶ logical framework connecting intermediate (surrogate) to final outcomes

How to Assess Impact

3 important points

1. impact = **causal effect** on **final outcomes**
 - ▶ comparison group (risk of bias)
 - ▶ extrapolation (indirectness)
2. importance of mapping out the **causal chain**
 - ▶ logical framework connecting intermediate (surrogate) to final outcomes
3. importance of **context**
 - ▶ need to understand reasons for heterogeneity

2. How to study it / which **designs**?

Study Design Examples

RCTs

OPEN ACCESS Freely available online

PLOS MEDICINE

A Multi-Country Non-Inferiority Cluster Randomized Trial of Frontloaded Smear Microscopy for the Diagnosis of Pulmonary Tuberculosis

Luis Eduardo Cuevas^{1,2*}, Mohammed Ahmed Yassin¹, Najla Al-Sonboli³, Lovett Lawson⁴, Isabel Arbide⁵, Nasher Al-Aghbari⁶, Jeevan Bahadur Sherchand⁷, Amin Al-Absi⁶, Emmanuel Nnamdi Emenyonu⁴, Yared Merid⁸, Mosis Ifenyi Okobi⁹, Juliana Olubunmi Onuoha⁴, Melkamsew Aschalew⁸, Abraham Aseffa¹⁰, Greg Harper¹, Rachel Mary Anderson de Cuevas¹, Kristin Kremer¹¹, Dick van Soolingen¹¹, Carl-Michael Nathanson², Jean Joly², Brian Faragher¹, Stephen Bertel Squire¹, Andrew Ramsay²

OPEN ACCESS Freely available online

PLOS MEDICINE

LED Fluorescence Microscopy for the Diagnosis of Pulmonary Tuberculosis: A Multi-Country Cross-Sectional Evaluation

Luis Eduardo Cuevas^{1,2*}, Najla Al-Sonboli³, Lovett Lawson⁴, Mohammed Ahmed Yassin¹, Isabel Arbide⁵, Nasher Al-Aghbari³, Jeevan Bahadur Sherchand⁶, Amin Al-Absi⁷, Emmanuel Nnamdi Emenyonu⁴, Yared Merid⁸, Mosis Ifenyi Okobi⁹, Juliana Olubunmi Onuoha⁴, Melkamsew Aschalew⁸, Abraham Aseffa¹⁰, Greg Harper¹, Rachel Mary Anderson de Cuevas¹, Sally Jane Theobald¹, Carl-Michael Nathanson², Jean Joly², Brian Faragher¹, Stephen Bertel Squire¹, Andrew Ramsay²

Feasibility, accuracy, and clinical effect of point-of-care Xpert MTB/RIF testing for tuberculosis in primary-care settings in Africa: a multicentre, randomised, controlled trial



Grant Theron, Lynn Zijenah, Duncan Chanda, Petra Clowes, Andrea Rachow, Maia Lesosky, Wilbert Bara, Stanley Mungofa, Madhukar Pai, Michael Hoelscher, David Dowdy, Alex Pym, Peter Mwaba, Peter Mason, Jonny Peter, Keertan Dheda, for the TB-NEAT team*

Comparison of two methods for acquisition of sputum samples for diagnosis of suspected tuberculosis in smear-negative or sputum-scarce people: a randomised controlled trial



Jonathan G Peter, Grant Theron, Anil Pooran, Johnson Thomas, Mellissa Pascoe, Keertan Dheda

Study Design Examples

Quasi-experimental studies

OPEN ACCESS Freely available online

PLOS ONE

A Multi-Site Evaluation of Innovative Approaches to Increase Tuberculosis Case Notification: Summary Results

Jacob Creswell^{1*}, Suvanand Sahu¹, Lucie Blok², Mirjam I. Bakker³, Robert Stevens⁴, Lucica Ditiu¹

OPEN ACCESS Freely available online

PLOS ONE

Impact of Xpert MTB/RIF Testing on Tuberculosis Management and Outcomes in Hospitalized Patients in Uganda

Christina Yoon^{1,3}, Adithya Cattamanchi^{1,2,*}, J. Lucian Davis^{1,2}, William Worodria^{4,5}, Saskia den Boon⁶, Nelson Kalema⁶, Wincelaus Katagira⁶, Sylvia Kaswabuli⁶, Cecily Miller¹, Alfred Andama⁴, Heidi Albert⁷, Pamela Nabeta⁸, Christen Gray⁹, Irene Ayakaka⁶, Laurence Huang^{1,3}

Engaging the private sector to increase tuberculosis case detection: an impact evaluation study



Aamir J Khan, Saira Khowaja, Faisal S Khan, Fahad Qazi, Ismat Lotia, Ali Habib, Shama Mohammed, Uzma Khan, Farhana Amanullah, Hamidah Hussain, Mercedes C Becerra, Jacob Creswell, Salmaan Keshavjee

ORIGINAL ARTICLE

Accuracy and impact of Xpert MTB/RIF for the diagnosis of smear-negative or sputum-scarce tuberculosis using bronchoalveolar lavage fluid

Grant Theron¹, Jonny Peter¹, Richard Meldau¹, Hoosain Khalfey¹, Phindile Gina¹, Brian Matinyena¹, Laura Lenders¹, Gregory Calligaro¹, Brian Allwood¹, Gregory Symons¹, Ureshnie Govender¹, Mashiko Setshedi¹, Keertan Dheda^{1,2}

Feasibility, diagnostic accuracy, and effectiveness of decentralised use of the Xpert MTB/RIF test for diagnosis of tuberculosis and multidrug resistance: a multicentre implementation study



Catharina C Boehme, Mark P Nicol, Pamela Nabeta, Joy S Michael, Eduardo Gotuzzo, Rasim Tahiri, Ma Tarcefa Gler, Robert Blakemore, William Worodria, Christen Gray, Laurence Huang, Tatiana Caceres, Rafail Mehdiyev, Lawrence Raymond, Andrew Whitelaw, Kalaiselvan Sagadevan, Heather Alexander, Heidi Albert, Frank Cobelens, Helen Cox, David Alland, Mark D Perkins

Study Design Examples

Studies of clinical decision-making

INT J TUBERC LUNG DIS 15(5):641-646
© 2011 The Union
doi:10.5588/ijtld.10.0195

Does solid culture for tuberculosis influence clinical decision making in India?

N. Stall,* T. Rubin,† J. S. Michael,‡ D. Mathai,§ O. C. Abraham,§ P. Mathews,§ K. Thomas,§
M. John,* P. Daley§

INT J TUBERC LUNG DIS 15(3):405-407
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SHORT COMMUNICATION

Implementation of liquid culture for tuberculosis diagnosis in a remote setting: lessons learned

P. Hepple,* J. Novoa-Cain,† C. Cheruiyot,† E. Richter,‡ K. Ritmeijer§

ORIGINAL STUDIES

Evaluation of the Impact of Interferon-Gamma Release Assays on the Management of Childhood Tuberculosis

Daphne I. Ling, MPH,* Claire A. Crépeau, BScN,† Marieke Dufresne, RN,† Shazia Khan, BA,†
Caroline Quach, MD, MSc,*‡ Nandini Dendukuri, PhD,§ Kevin Schwartzman, MD, MPH,*¶
Dick Menzies, MD, MSc,*¶¶ Larry C. Lands, MD, PhD,† and Madhukar Pai, MD, PhD*¶¶

Use of Drug-Susceptibility Testing for Management of Drug-Resistant Tuberculosis, Thailand, 2004–2008

Eugene Lam, Sriprapa Nateniyom, Sara Whitehead, Amornrat Anuwatnonthakate, Patama Monkongdee, Apiratee Kanphukiew, Jiraphan Inyaphong, Wanlaya Sitti, Navarat Chiengsorn, Saiyud Moolphate, Suporn Kavinum, Narin Suriyon, Pranom Limsomboon, Junya Danyutapolchai, Chalinthorn Sinthuwattanawibool, and Laura Jean Podewils

Effect of Nucleic Acid Amplification for *Mycobacterium tuberculosis* on Clinical Decision Making in Suspected Extrapulmonary Tuberculosis*

Renda Soylemez Wiener, MD; Phyllis Della-Latta, PhD; and Neil W. Schluger, MD, FCCP

Study Design Examples

uncontrolled/hypothetical/model-based

Test and Treat: A New Standard for Smear-Positive Tuberculosis

To the Editors:

THE PROBLEM

Despite its limited sensitivity, sputum smear microscopy is the principal method of tuberculosis (TB) diagnosis in high-burden settings around the world. It will likely remain so for many years because more cost-effective and affordable diagnostic techniques are unlikely to be developed soon. Optimizing smear microscopy by improving rates of testing, completion, and reporting is

Supported by National Institutes of Health Grants K23HL094141 (to A. Cattamanchi) and K23AI080147 (to J. L. Davis); National Center for Research Resources Grant NIH KL2RR024130 (for the technical support by UCSF Clinical and Translational Sciences Institute Career Development Program).

The authors have no conflicts of interest to disclose.

J. L. Davis and D. W. Dowdy contributed equally to this work.

Correspondence to: Adithya Cattamanchi, MD, MAS, San Francisco General Hospital, Room 5K1, 1001 Potrero Avenue, San Francisco, CA 94110 (e-mail: acattamanchi@medsfgh.ucsf.edu).

Integrated Strategies to Optimize Sputum Smear Microscopy

A Prospective Observational Study

Adithya Cattamanchi^{1,2}, Laurence Huang^{1,3}, William Worodria^{4,5}, Saskia den Boon⁶, Nelson Kalema⁶, Wincelaus Katagira⁶, Patrick Byanyima⁶, Samuel Yoo⁶, John Matovu⁴, Phillip C. Hopewell^{1,2}, and J. Lucian Davis^{1,2}

Impact of GeneXpert MTB/RIF[®] on Patients and Tuberculosis Programs in a Low-Burden Setting: A Hypothetical Trial

J. Lucian Davis^{1,2}, L. Masae Kawamura³, Lelia H. Chaisson¹, Jennifer Grinsdale³, Jihane Benhammou⁶, Christine Ho⁵, Anna Babst⁴, Houmpheng Banouvong³, John Z. Metcalfe^{1,2}, Mark Pandori⁴, Phillip C. Hopewell^{1,2}, Adithya Cattamanchi^{1,2}

Clinical Infectious Diseases Advance Access published January 14, 2014

Xpert MTB/RIF testing in a low TB incidence, high-resource setting: limitations in accuracy and clinical impact

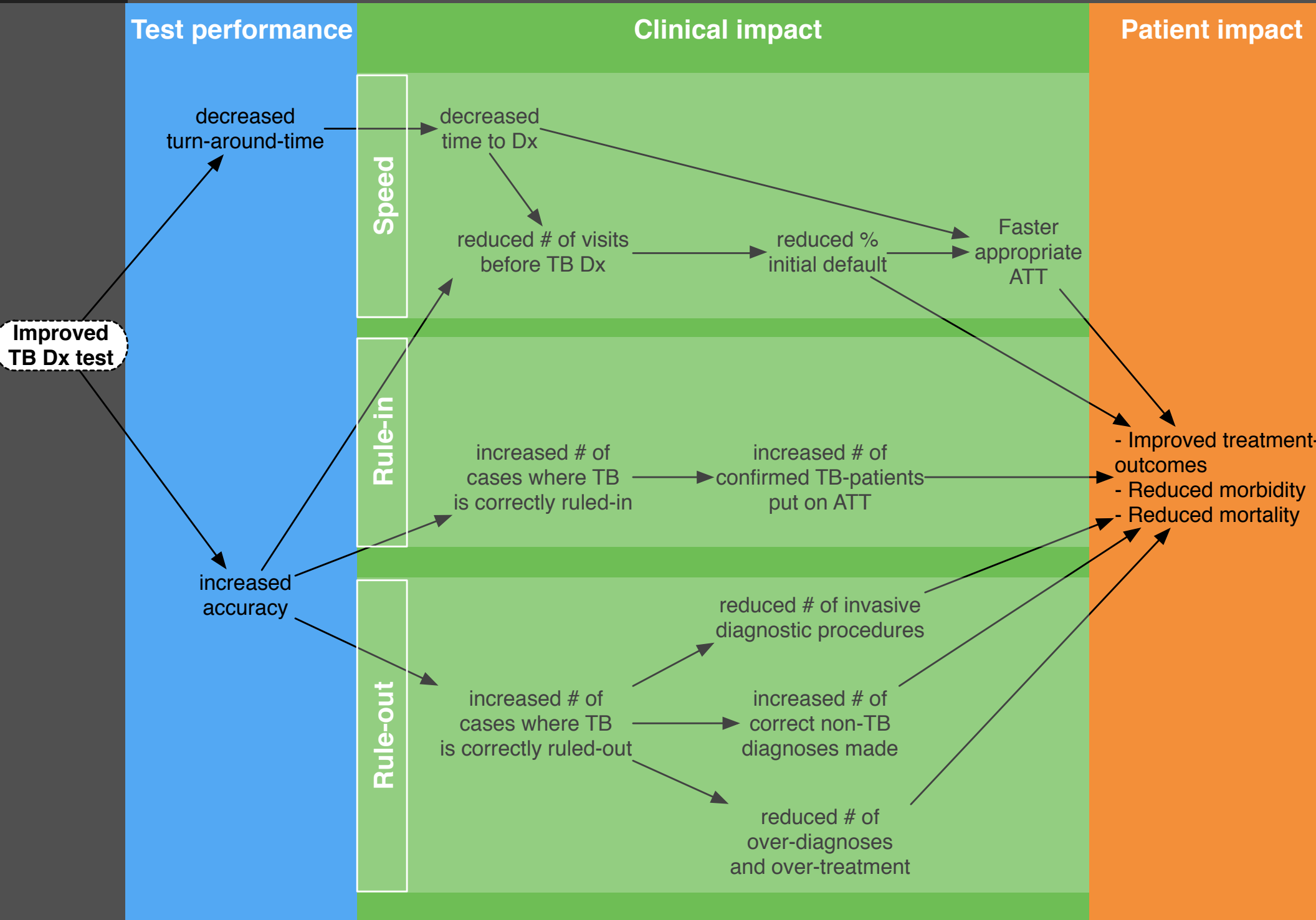
Hoon Sohn^{1,2}, Abebech D. Aero^{1,2}, Dick Menzies^{1,2}, Marcel Behr^{1,2}, Kevin

Schwartzman^{1,2}, Gonzalo G. Alvarez^{1,3}, Andrei Dan¹, Fiona McIntosh^{1,2}, Madhukar

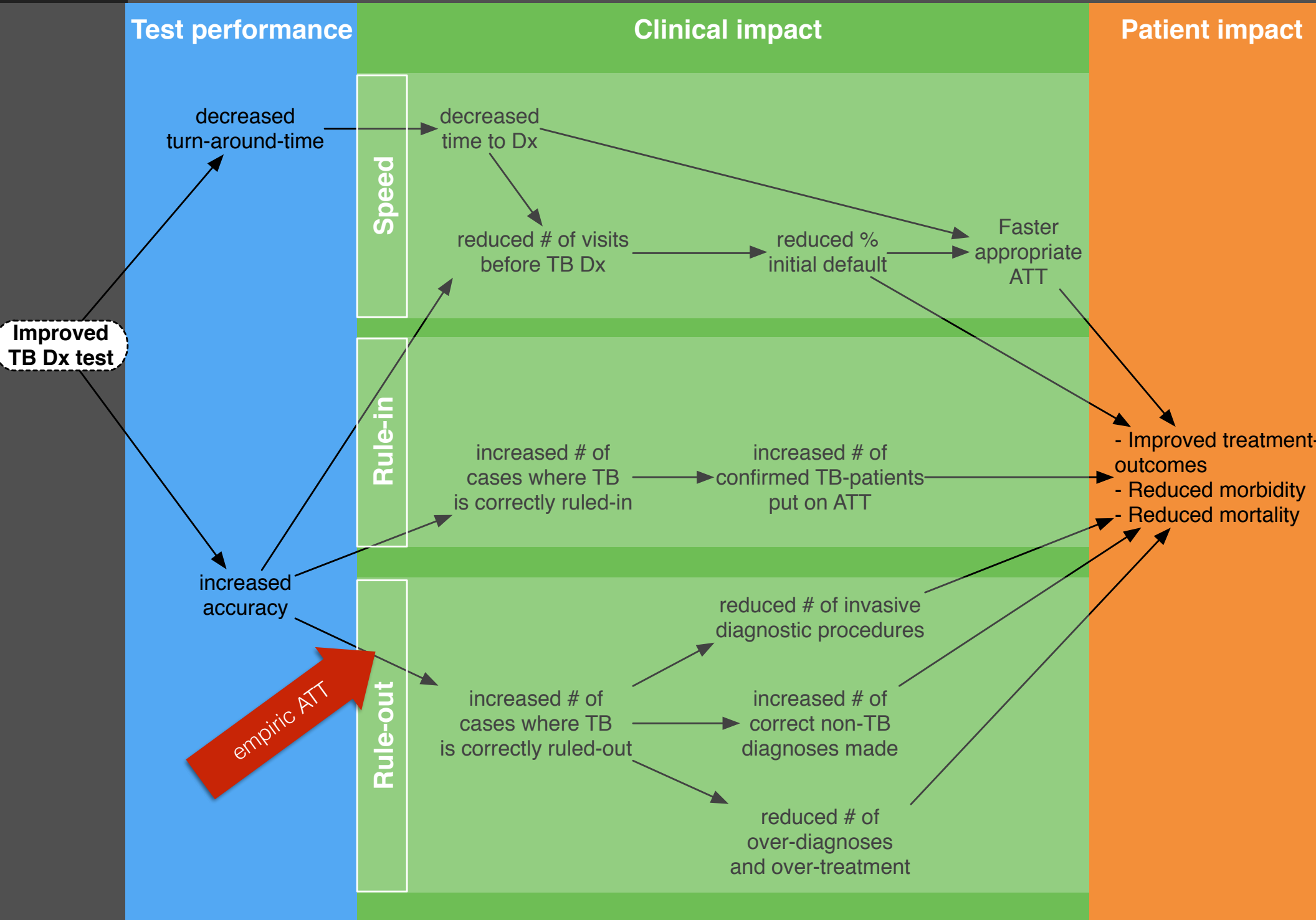
Pai^{1,2,*}, Claudia M. Denlinger^{1,4,*}

3. How to consider **context?**

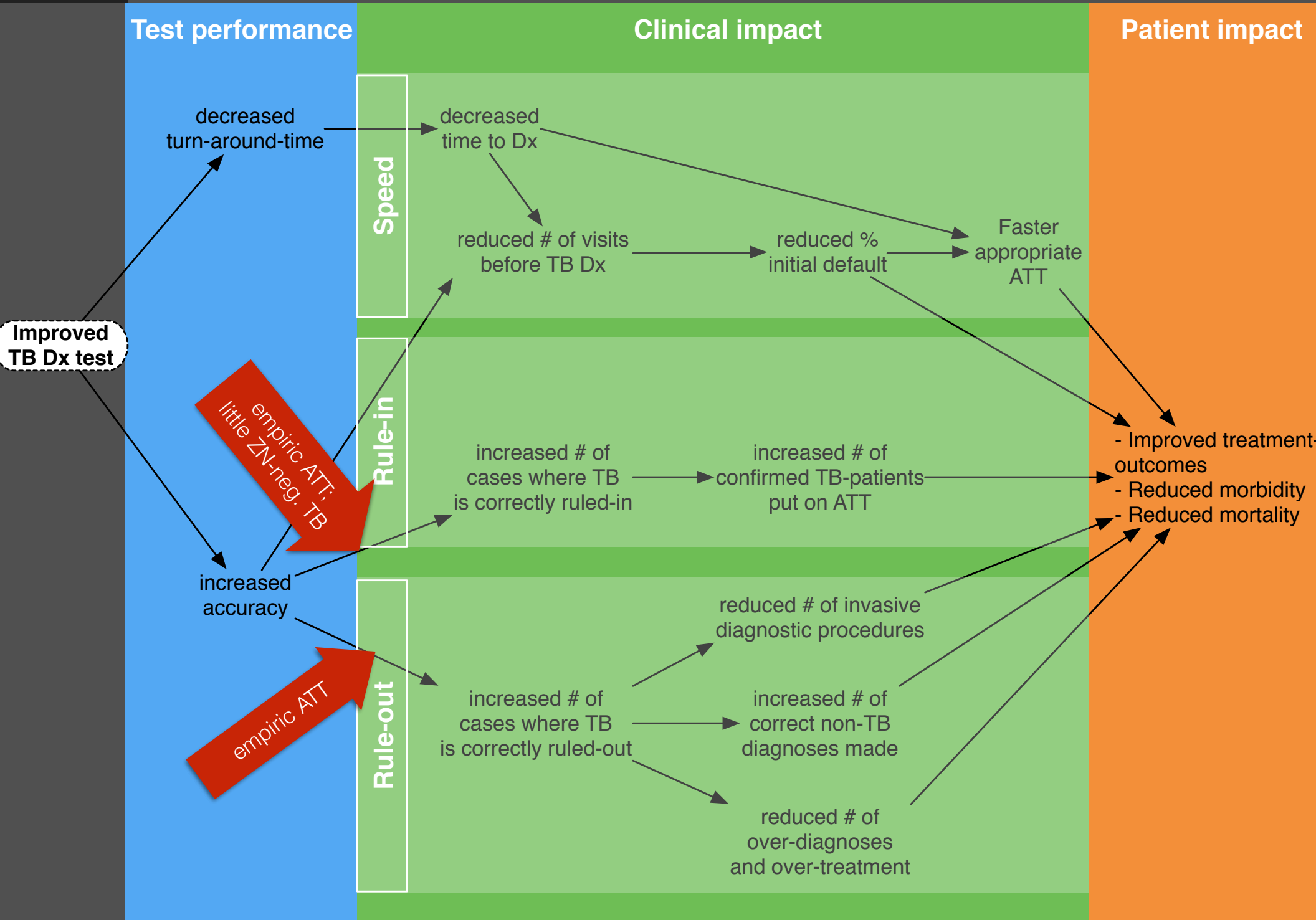
Diagnostic Causal Chain & Spectrum of diagnostic research



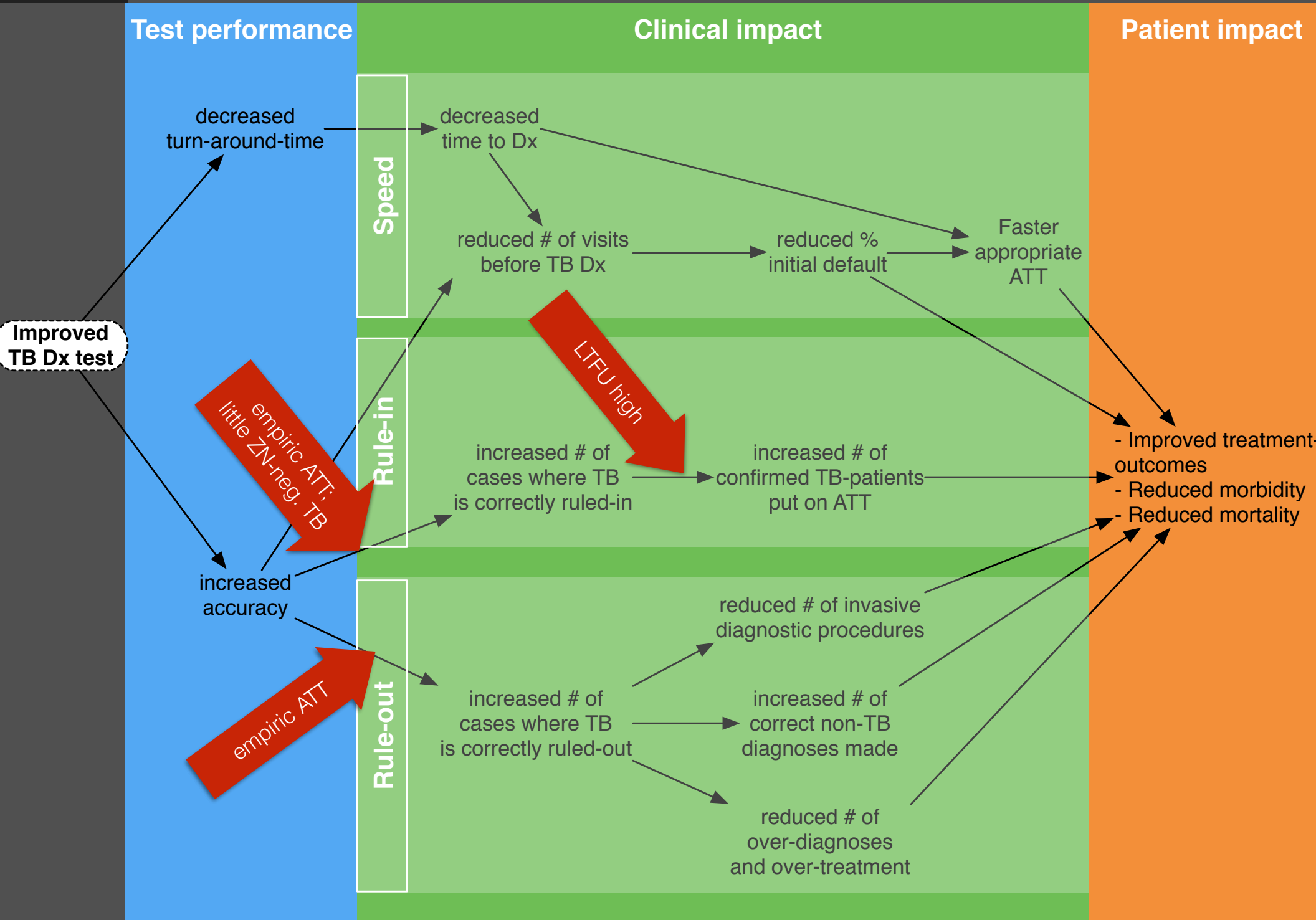
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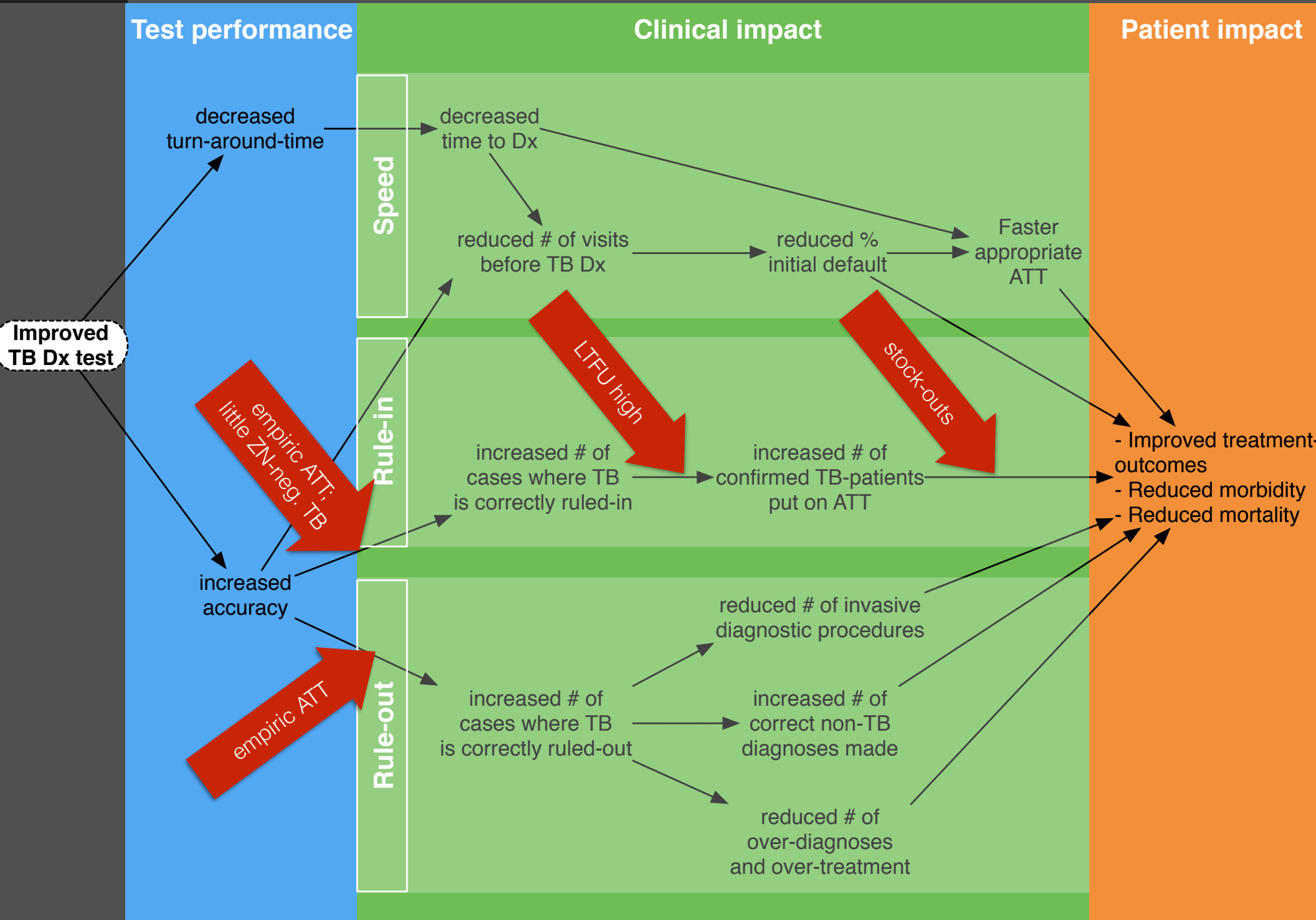
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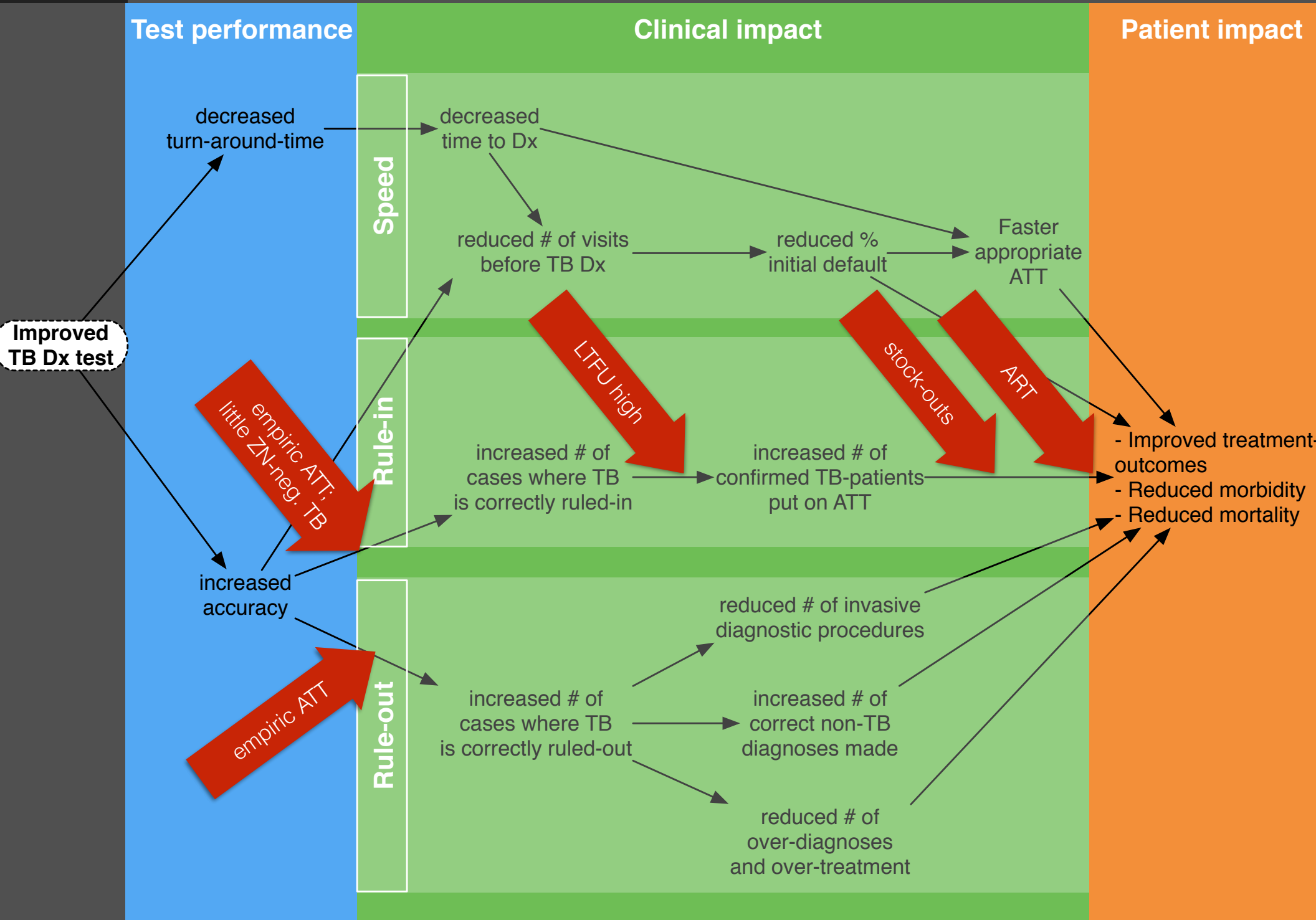
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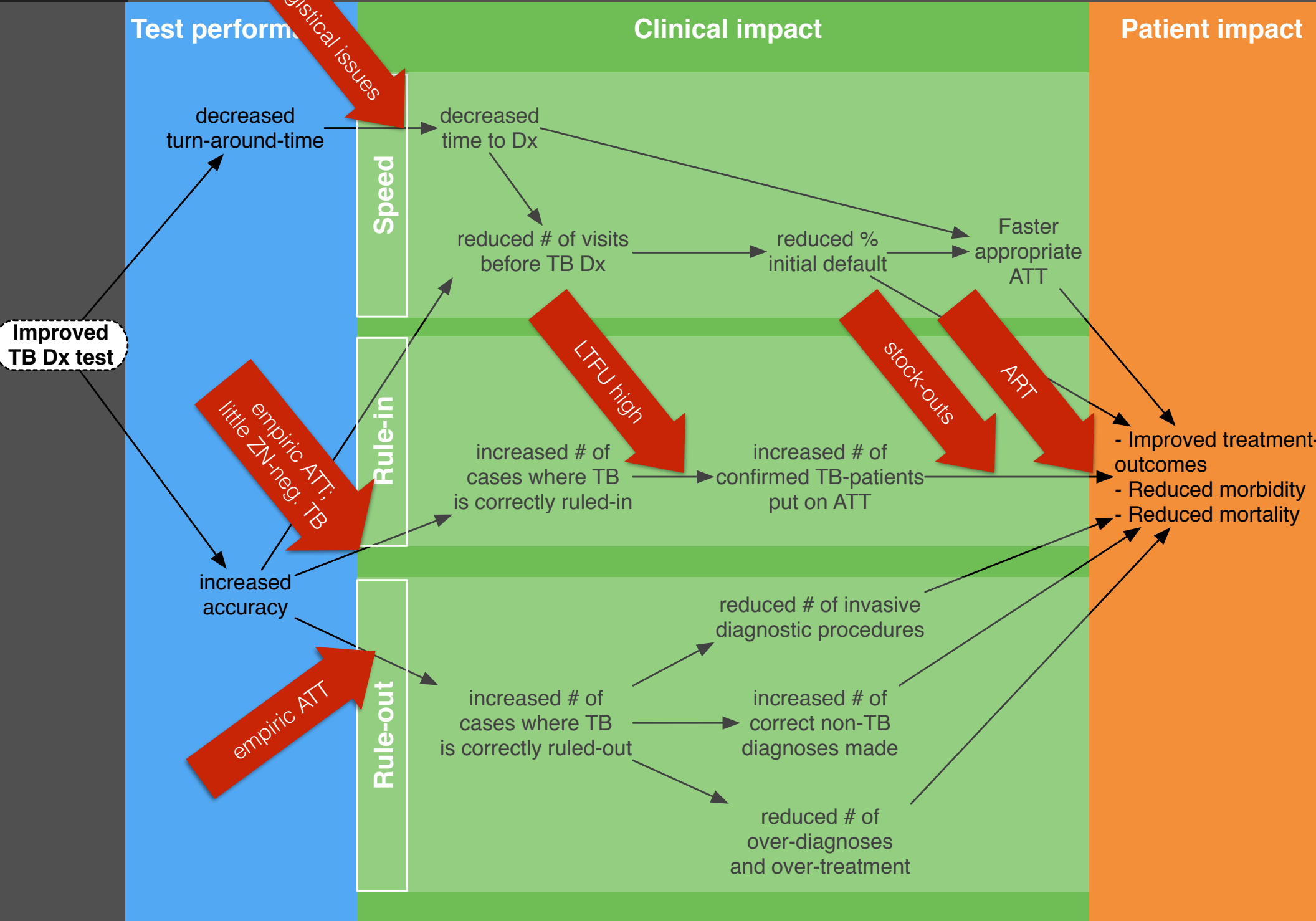
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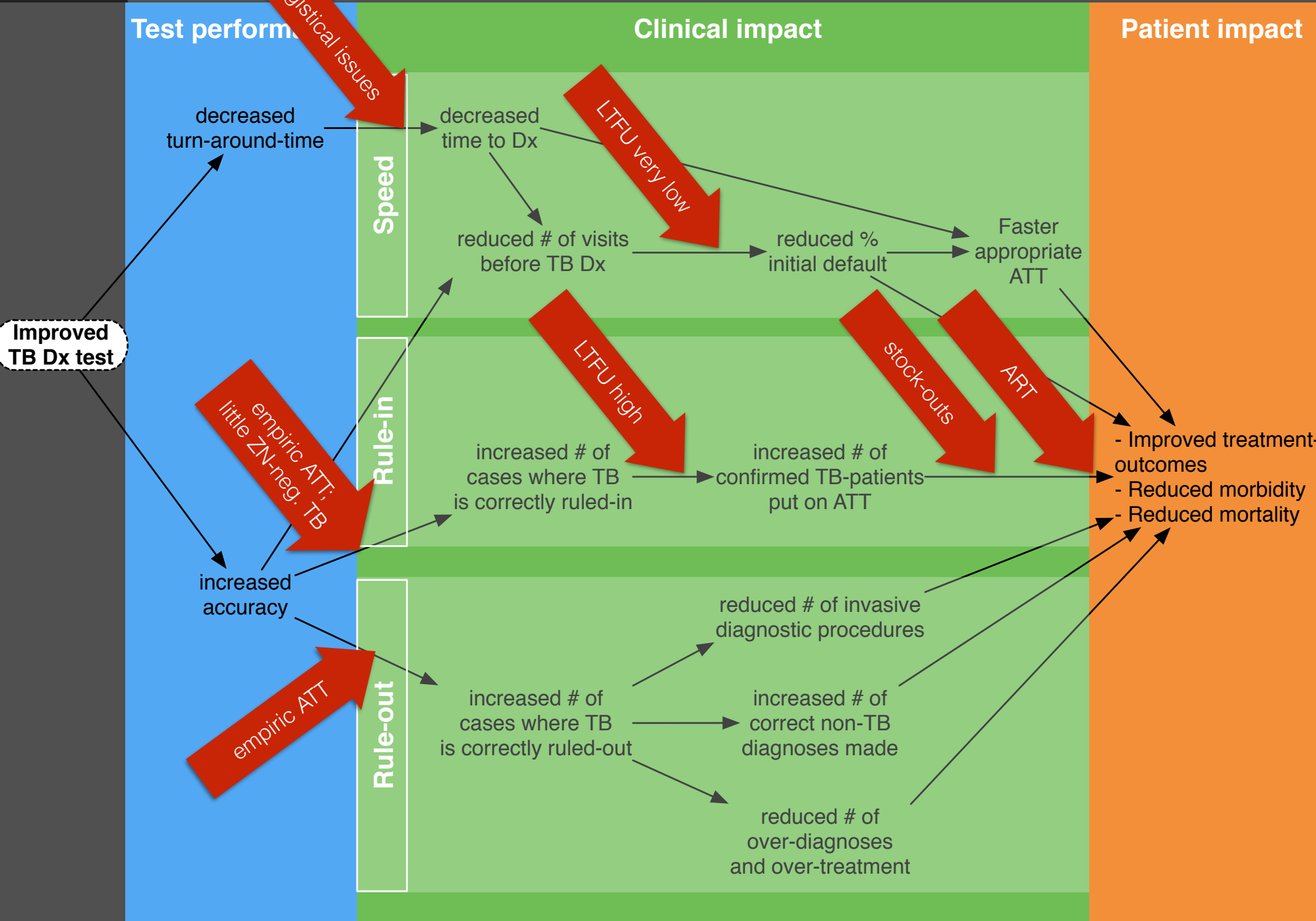
Diagnostic Causal Chain & Spectrum of diagnostic research



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Diagnostic Causal Chain & Spectrum of diagnostic research



Panel Discussion

Panel Members

Adithya Cattamanchi	UCSF
Claudia Denking	FIND
Afrânio Kritski	Universidade Federal do Rio de Janeiro
Andrew Ramsay	TDR
Grant Theron	UCT

Challenges & Lenses

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