Office of the National Coordinator for Health Information Technology

ONC Tech Forum
Clinical Decision Support Series Session 3

Creating Value by Modernizing and Measuring Clinical Decision Support

Nov. 8, 2023

Overview of session 1

- What to Know About Clinical Decision Support through Real World Examples
- Overview of CDS
- How to Implement CDS Locally
- Examples of Interoperable CDS in the Real World
  - Medical University of South Carolina's implementation of the CDC Clinical Practice Guideline for Prescribing Opioids for Pain
  - University of Washington's COSRI and PainTracker
  - HealthPartners Institute's Priority Wizard

Overview of session 2

- The Future of Clinical Decision Support in September
- CDS Hooks and SMART Apps
- CDS Connect
- Patient-centered Decision Support
- Clinical Decision Support Innovation Collaborative
- Building Co-design
- Fall TIPS
- Charts-on-FHIR
- CDS in Social Determinants of Health and Guideline-concordant Care

Agenda

- Predictive algorithms and decision support
- How new technologies add value to CDS
- Break at 1:40 p.m. ET
- Examples of CDS
- Measuring and evaluation successes in CDS development

Predictive Algorithms and Decision Support

Jeff Smith, ONC

Office of the National Coordinator for Health Information Technology

Predictive Algorithms & Decision Support

Tech Forum

Jeffery Smith, M.P.P. Deputy Division Director, Certification & Testing Division, Office of the National Coordinator for Health IT

ONC Activities & Objectives

ONC Activities

- Standards
- Certification
- Exchange

- Federal
- Coordination
- State & Public

ONC Objectives

- Advance the development and use of health IT capabilities
- Establish expectations for data sharing

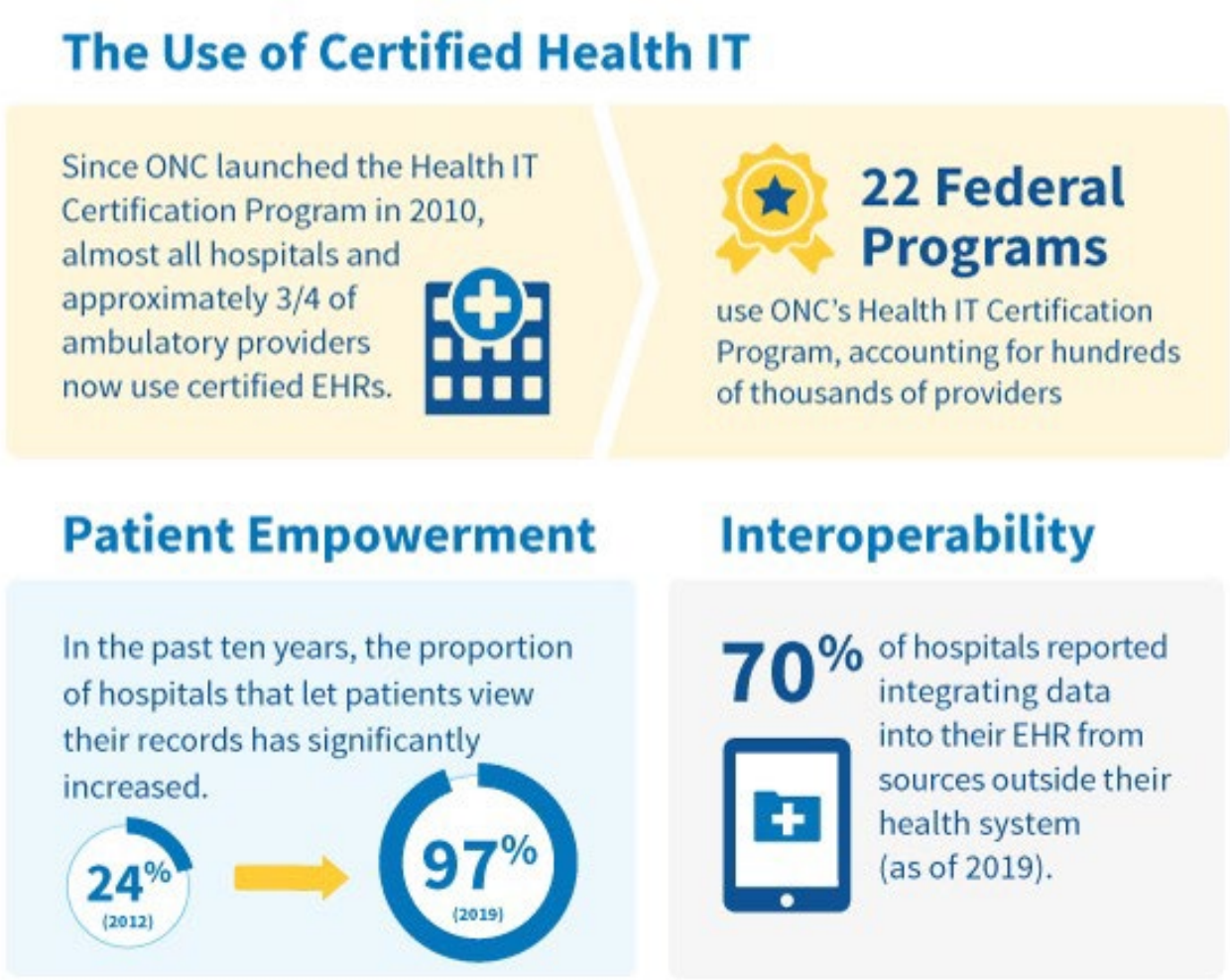
ONC Health IT Certification Program

ONC Certification is:

- Voluntary, standards-based, and solutions-agnostic
- Participation requires a programmatic requirement or be funding contingent

Through the combination of CMS payment incentives and ONC's Health IT certification program, hospitals and providers rapidly adopted certified EHRs and ushered the modernization of the U.S. health care system. This promoted:

- A more effective marketplace, greater competition, increased consumer choice, and improved health outcomes
- Seamless exchange of electronic health information across a variety of methods and platforms
- A safe and secure health IT infrastructure for patients and healthcare providers
- Increased ease-of-use of health IT



Current View of Artificial Intelligence in Health Care

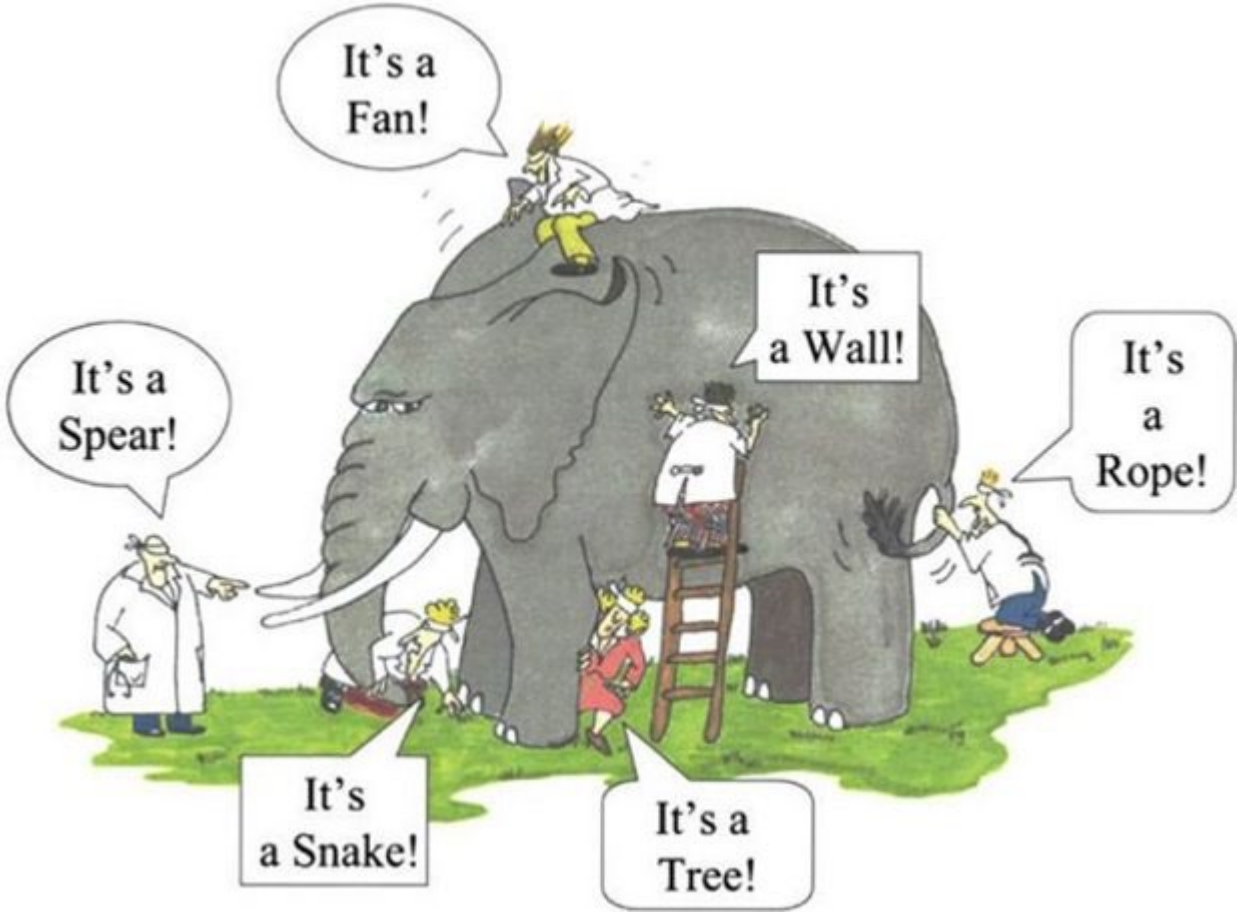
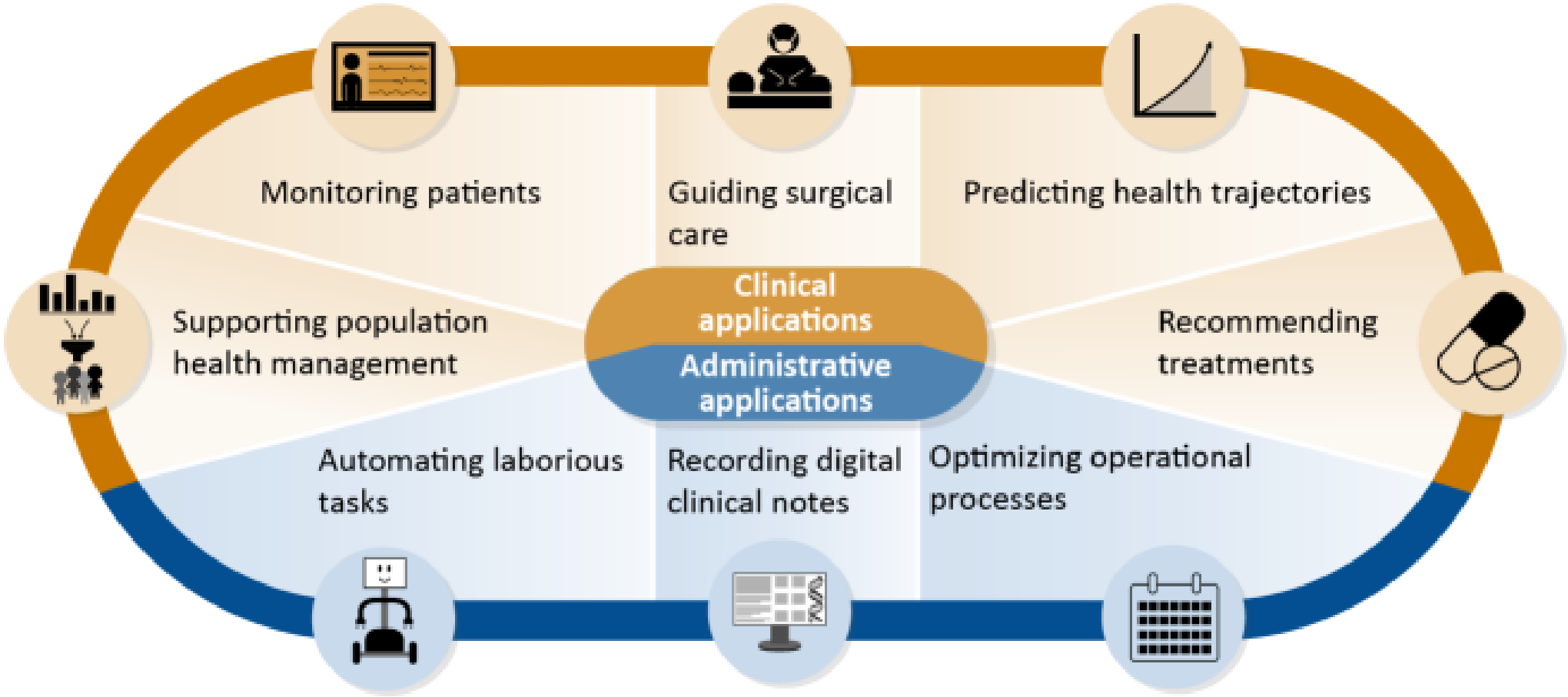


Image Source: https://medium.com/analysts-corner/companies-are-elephants-d9bf807bf217



Source: GAO. | GAO-21-7SP

An inclusive framing of the promise & the peril of AI

To optimize the use of AI in health care we must address fundamental and far-reaching challenges associated with predictive algorithms that:

- Reproduce or amplify implicit and structural biases
- Magnify existing ethical, legal, and social concerns related to data collection and use
- Repeat the ills of history by reinforcing common, non-evidence-based practices or baking-in existing inexplicable differences in health outcomes
- Perpetuate fundamental information asymmetries regarding an algorithm's quality, performance (including its fairness and validity)
- Lead to recommendations that are ineffective or are unsafe

HTI-1 Proposals for Predictive Decision Support Interventions

Objective: Enable improved information transparency on the trustworthiness of predictive DSIs to support their responsible and widespread use in health care.

Improve Transparency

Regarding how a predictive DSI is designed, developed, trained, evaluated, and should be used

Enhance Trustworthiness

Through transparency on how certified health IT developers manage potential risks and govern predictive DSIs that their certified Health IT Modules enable or interface with

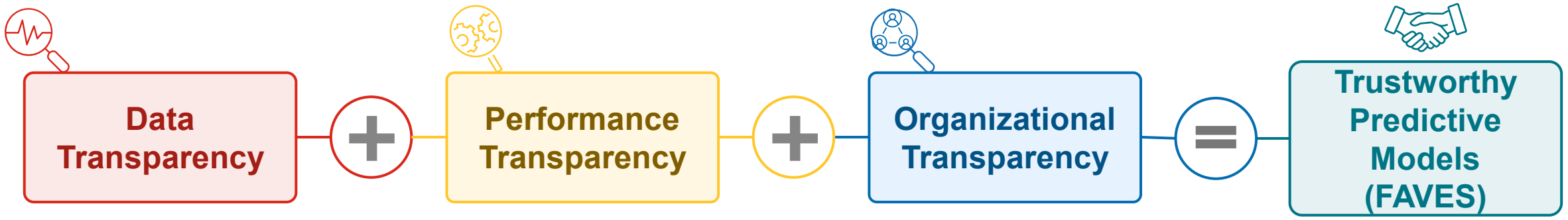
Support Consistency

In the availability of predictive DSI information to users, so that users may determine the DSI's quality and whether its recommendations are fair, appropriate, valid, effective, and safe (FAVES)

Advance Health Equity by Design

By addressing bias and health disparities, potentially propagated by predictive DSIs, to expand the use of these technologies in safer, more appropriate, and more equitable ways

Transparency Is a Prerequisite for Trustworthy AI



Data Transparency

Proposed requirements would enable users to know when a DSI uses specific data elements relevant to health equity, including:

- Race, Ethnicity, & Language (REL)
- Gender Identity & Sexual Orientation
- Social Determinants of Health (SDOH)
- Disability
- Date of Birth

Performance Transparency

Proposed source attributes would enable users to have consistent and routine electronic access to technical and performance information on predictive DSIs

- Intended use, training data descriptions, measures of fairness, maintenance, etc.
- Establishes baseline ingredients for a model "nutrition label"
- Information available to users in plain language and via "direct display," "drill down" or "link out" functionality

Organizational Transparency

Proposed requirement for certified health IT developers to employ or engage in risk management of predictive DSIs

- Analyze risks; mitigate risks; and establish governance for predictive DSIs spanning 8 socio-technical characteristics including Validity, Reliability, Robustness, Fairness, Intelligibility, Safety, Security, & Privacy
- Disclose summary information publicly

Policy Benefits for Patients, Providers, and Industry

Patients

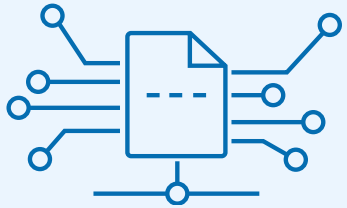
- Enables patients to benefit from the use of FAVES predictive models related to their care
- Avoids preventable harms, such as errors in decision making, health inequities, bias, and discrimination
- Clarifies patient access to underlying information

Providers

- Enables access to information necessary to trust predictive DSIs for patient care
- Ensures consistent availability on how predictive DSIs are intended to work and perform
- Enables clinicians to use PDSIs in more appropriate, equitable, and safer ways for patients and populations

Developers / Industry

- Drive consensus on how to communicate the “ingredients” of predictive DSIs consistently
- Promote developers with high quality models
- Establish an information ecosystem that enables an actionable and widely accepted approach for transparency and trustworthiness of algorithms in health care



Office of the National Coordinator for Health Information Technology

Contact ONC

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Health IT Feedback Form: https://www.healthit.gov/form/healthit-feedback-form

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Questions

Extra Slides

High-level Overview Points

- Introduced in April 2023, the HHS Office of the National Coordinator for Health IT (ONC) proposed first-of-its-kind regulations in the US for artificial intelligence- and machine learning-based predictive software in health care.
- The rule would apply to companies that sell electronic health records, or EHRs, which are certified by ONC and used by more than 96% of hospitals and 78% of office-based clinicians in the US.
- The rule would require transparency regarding the performance and quality of predictive decision support software, including how the model or algorithm behind the prediction was designed, developed, tested, and evaluated.
- This information would give users of predictive decision support software an opportunity to determine if the model was fair, appropriate, valid, effective, and safe for use on their patients.
- In addition to transparency regarding the performance and quality of predictive decision support software, the proposed rule would require transparency regarding the risk management and governance practices of organizations that develop these tools.
- The rule would make performance and quality information available to users of predictive decision support software, and summary information about risk management and governance practices would be available publicly.
- If finalized as proposed, the rule would come into effect beginning January 1, 2025.

Predictive Decision Support Intervention – Source Attributes

Intervention Details (3)	• Output • Intended use • Cautioned out of scope use(s)
Intervention Development (3)	• Input features including description of training and test data • Process used to ensure fairness in development • External validation process, if available
Quantitative Performance Measures (5)	• Validity and Fairness of prediction in test data • Validity and Fairness of prediction in external data, if available • References to evaluation of use of the model on outcomes, if available
Ongoing Maintenance & Intervention Use (3)	• Update and continued validation or fairness schedule • Validity of prediction in local data, if available • Fairness of prediction in local data, if available

Pillars of IRM Practices

Risk Analysis

- Analyze potential risk(s) and adverse impact(s) associated with the predictive DSI

Risk Mitigation

- Implement practices to minimize or mitigate risk(s) identified in the Risk Analysis associated with the predictive DSI

Governance

- Establish policies and implement controls for predictive DSI, including how data are acquired, managed, and used in the predictive DSI

Note: Generally, many of the proposed terms and concepts in the IRM proposal rely on the National Institute of Standards and Technology (NIST) AI Risk Management Framework and U.S. Department of the Treasury's Office of the Comptroller of the Currency (OCC) Model Risk Management Guidance & Handbook.

AI Accountability in Health Care: What Federal Regulations May Apply to Me?

Who Must Comply with What?

	Developer of an AI-enabled Medical Device	Developer of Certified Health IT & AI	User of AI	Patient
Is my AI activity potentially the focus of federal oversight?	*If you are developing an AI-enabled digital health or software products that are considered a medical device:*	*If you are developing AI technology, based on any USCDI standards, and it is enabled by or interfaces with certified health IT:*	*If you are using AI to support decision-making in health care or covered health programs and activities*:*	*If you are wondering if you receive health care and human services through the use of AI or if there is federal oversight of AI in healthcare:*
Applicable Federal Regulation	• **FD&C Act** • *Clinical Decision Support Guidance* • *Policy for Device Software Functions and Medical Applications – Function Guidance* • *Predetermined Change Control Plan for AI/ML-enabled device software functions*	**ONC HTI-1 Proposed Rule** *Health IT Certification Program*	• **Sec. 1557 Nondiscrimination in Health Programs and Activities Proposed Rule** • **HIPAA Privacy & Security Rule** (e.g., patient right of access)	• **Sec. 1557 Nondiscrimination in Health Programs and Activities Proposed Rule** • **HIPAA Privacy & Security Rule** (e.g., patient right of access) • **FD&C Act** • **ONC HTI-1**

**If you are a health program or activity that receives HHS funding, or a health insurer that participates in the Health Insurance Marketplaces, or from health care provider using technology a health care provider or plan, then…*

How can new technologies add value to CDS

Bryn Rhodes, Smile, Dr. Michael Pencina, Duke AI Health, and Dr. Irbaz Riaz, Mayo Clinic

Duke
AI HEALTH

Measuring Clinical Decision Support: Duke ABCDS

Michael J. Pencina, PhD

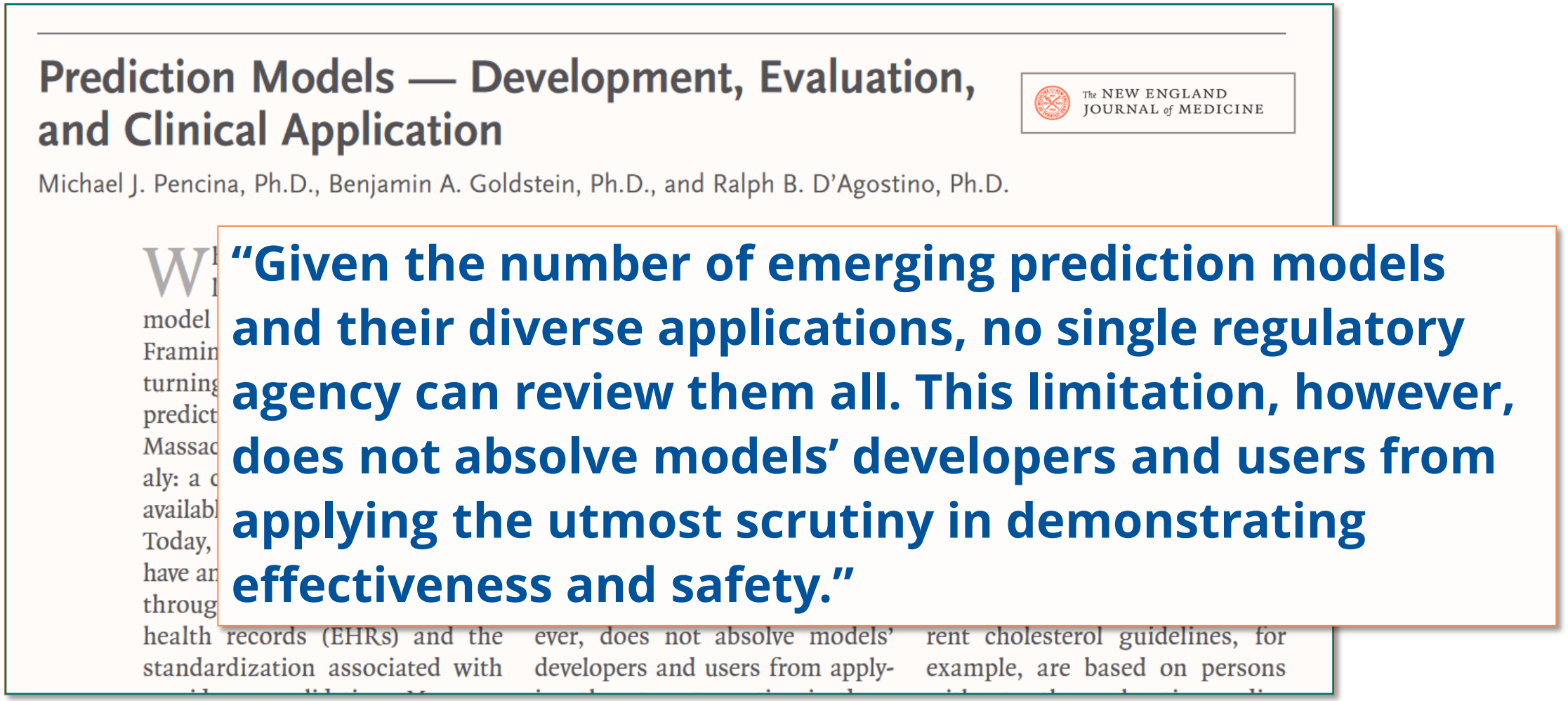
November 8, 2023

"Wild West" of Algorithms

"We have a Wild West of algorithms," said Michael Pencina, coalition co-founder and director of Duke AI Health. "There's so much focus on development and technological progress and not enough attention to its value, quality, ethical principles or health equity implications."

Politico, April 4, 2023

We need to do better



Prediction Models — Development, Evaluation, and Clinical Application

Michael J. Pencina, Ph.D., Benjamin A. Goldstein, Ph.D., and Ralph B. D'Agostino, Ph.D.

The NEW ENGLAND JOURNAL of MEDICINE

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"Given the number of emerging prediction models and their diverse applications, no single regulatory agency can review them all. This limitation, however, does not absolve models' developers and users from applying the utmost scrutiny in demonstrating effectiveness and safety."

Pencina MJ, Goldstein BA, D'Agostino RB. *N Engl J Med*. 2020 Apr 23;382(17):1583-1586. doi: 10.1056/NEJMp2000589.

Considerations for CDS development

- Population at risk
- Outcome of interest
- Time horizon
- Predictors
- Mathematical model
- Model evaluation
- Translation to CDS
- Clinical implementation

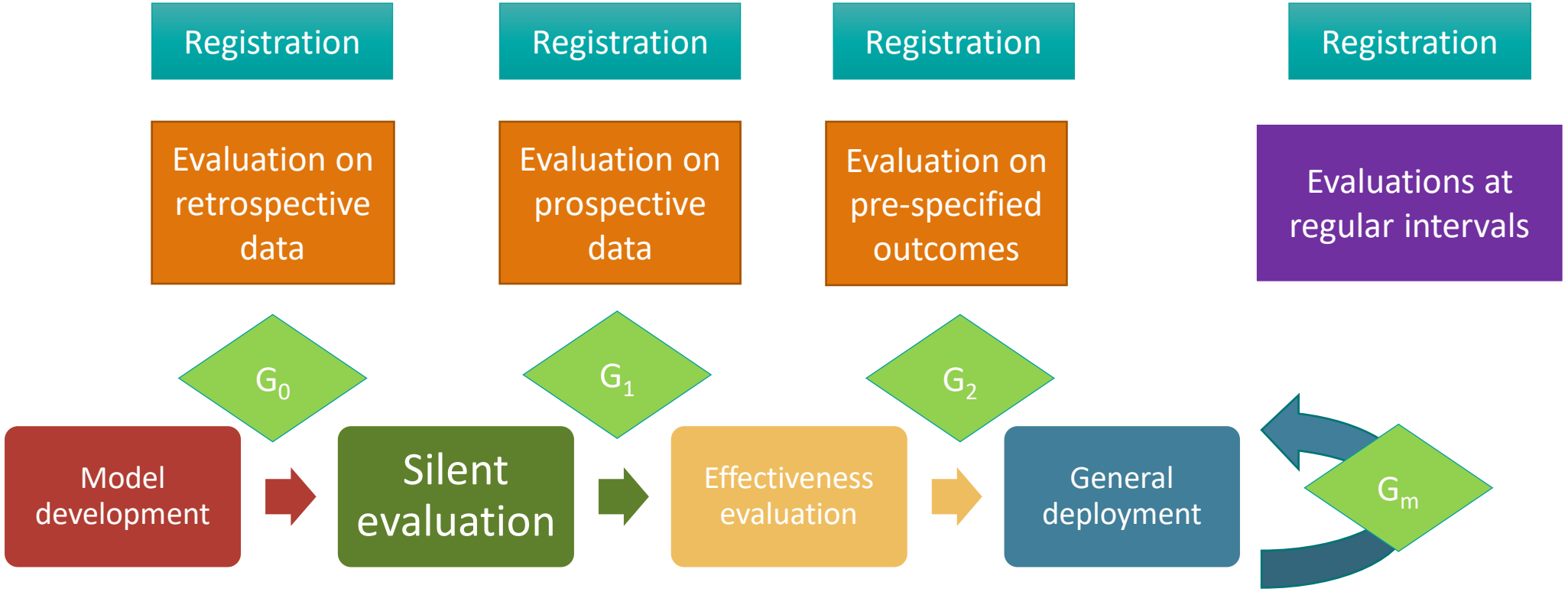
Pencina et al., *NEJM*. 2020;382:1583-1586. doi:10.1056/NEJMp2000589

Health System Example: Duke ABCDS

Algorithm-Based Clinical Decision Support (ABCDS) Mission Statement:

Out of our primary focus on patient safety and high-quality care, our mission is to guide algorithm-based clinical decision support (ABCDS) tools through their lifecycle by providing governance, evaluation, and monitoring.

ABCDS Overall Framework

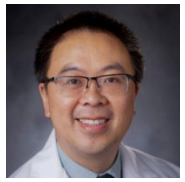


Bedoya et al., *JAMIA*. 2022; 1-6, https://doi.org/10.1093/jamia/ocac078

ABCDS Committee Structure

Co-Chairs:


M Pencina


E Poon

Program Director:

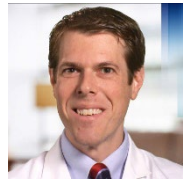

N Economou

ABCDS Oversight Committee

Additional Committee Members:


S Balu


M Cary


M Lipkin


K Lytle

ABCDS Regulatory Subcommittee

Co-Chairs:


A Parrish

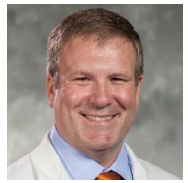

S Elengold

S Ellison

ABCDS Evaluation Subcommittee

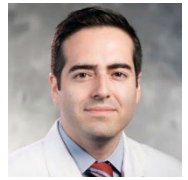
Co-Chairs:


B Goldstein


E Jelovsek

ABCDS Implementation and Monitoring Sub-Committee

Co-Chairs:


A Bedoya

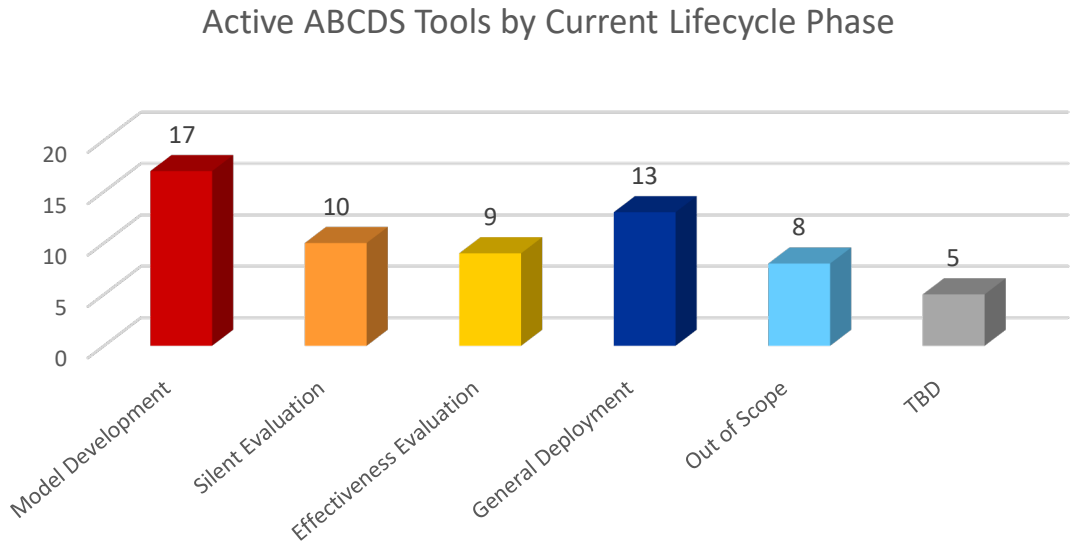

C O'Brien

Evaluation Lead:

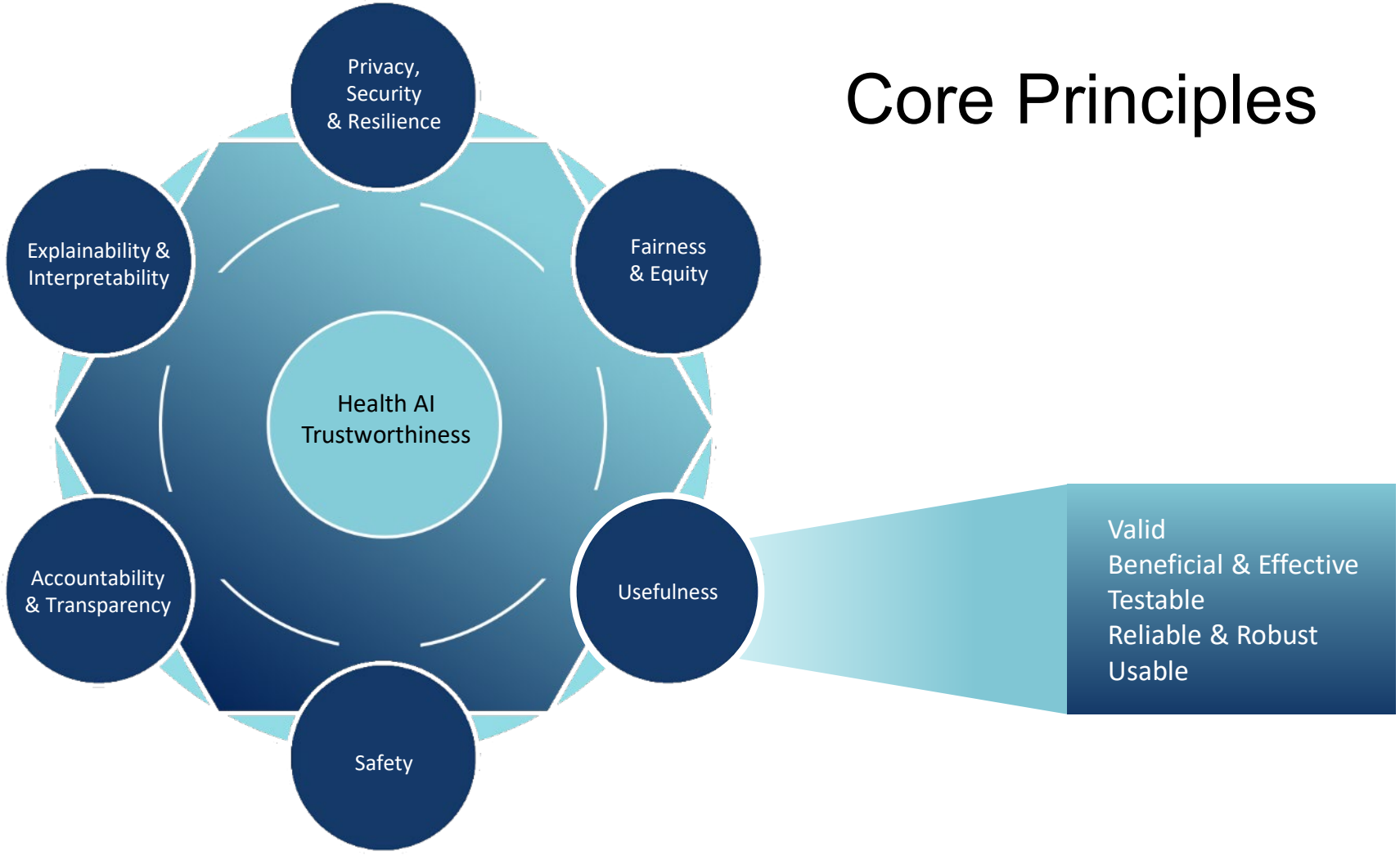

S Bessias

Duke ABCDS Oversight Portfolio Metrics

ABCDS Model Registration and Review	Total
Number of active tools* (includes unregistered)	62
Number of active tools registered	43
Number of active tools evaluated	28



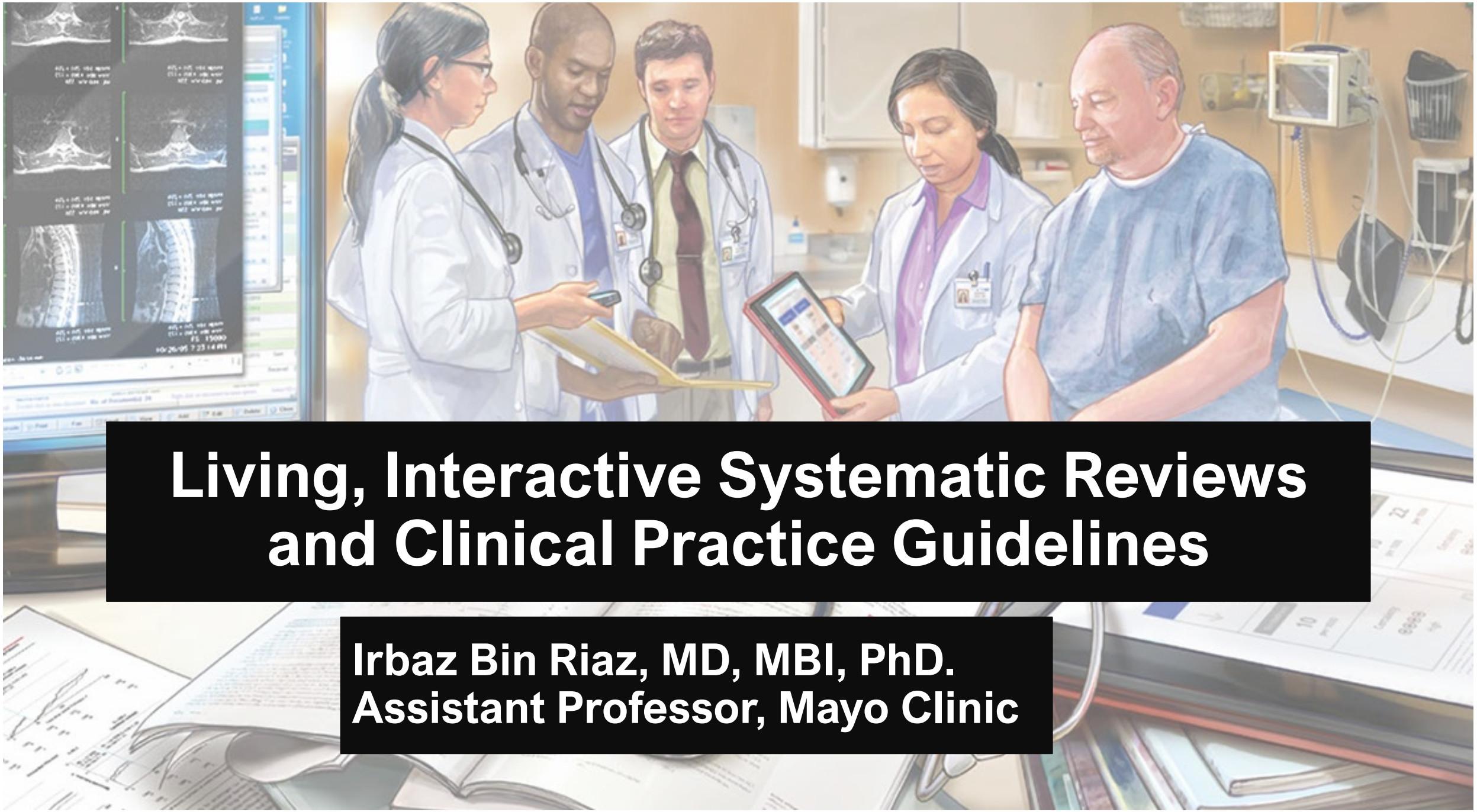
** Tools currently in use or proposed for use at DUHS (excluding retired, on hold)*



CHAI Blueprint for Trustworthy AI

Duke
AI HEALTH

Thank you!



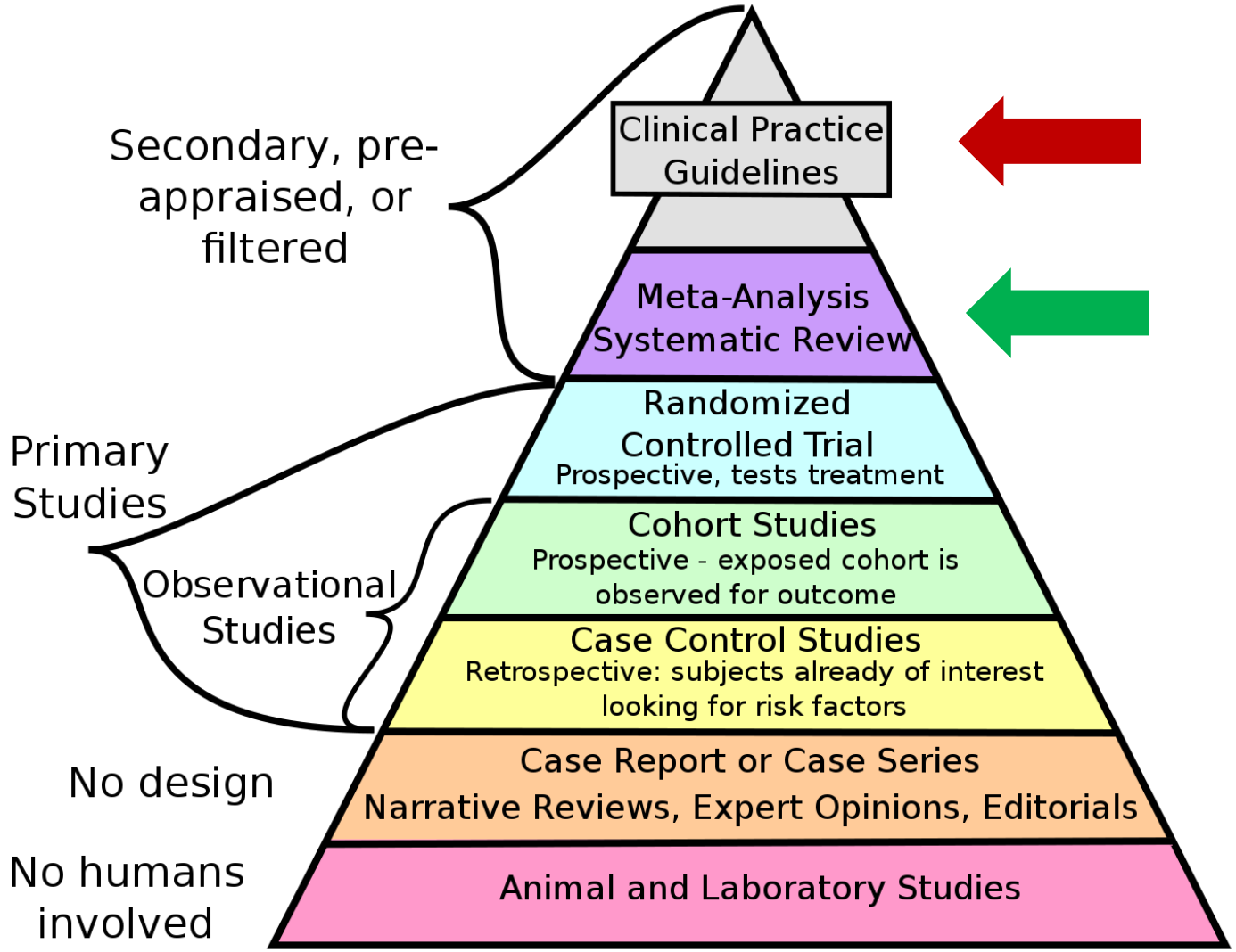
Living, Interactive Systematic Reviews and Clinical Practice Guidelines

Irbaz Bin Riaz, MD, MBI, PhD.
Assistant Professor, Mayo Clinic

Evidence Hierarchy

- Significant Expertise
- Painstaking
- Time-consuming
- Expensive

- Outdated quickly
- Updates restart from scratch
- No use of technology
- Wasted Efforts



EVIDENCE SYNTHESIS WORKFLOW

5000 citations

Ovid MEDLINE

Screening

Data Extraction

Systematic Review & Meta-Analysis

Clinical Guidelines Development

ASCO Guidelines(2009) - mCRPC

VOLUME 25 · NUMBER 33 · NOVEMBER 20 2007

JOURNAL OF CLINICAL ONCOLOGY | ASCO SPECIAL ARTICLE

American Society of Clinical Oncology Endorsement of the Cancer Care Ontario Practice Guideline on Nonhormonal Therapy for Men With Metastatic Hormone-Refractory (castration-resistant) Prostate Cancer

Ethan M. Basch, Mark R. Somerfield, Tomasz M. Beer, Michael A. Carducci, Celestia S. Higano, Maha H.A. Hussain, and Howard I. Scher

New studies

10000 citations

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See accompanying article on page 3391; listen to the podcast by Drs Suzman and Antonarakis at www.jco.org/podcasts

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ASCO Guidelines – prostate cancer


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ASCO Guidelines (update)- prostate cancer


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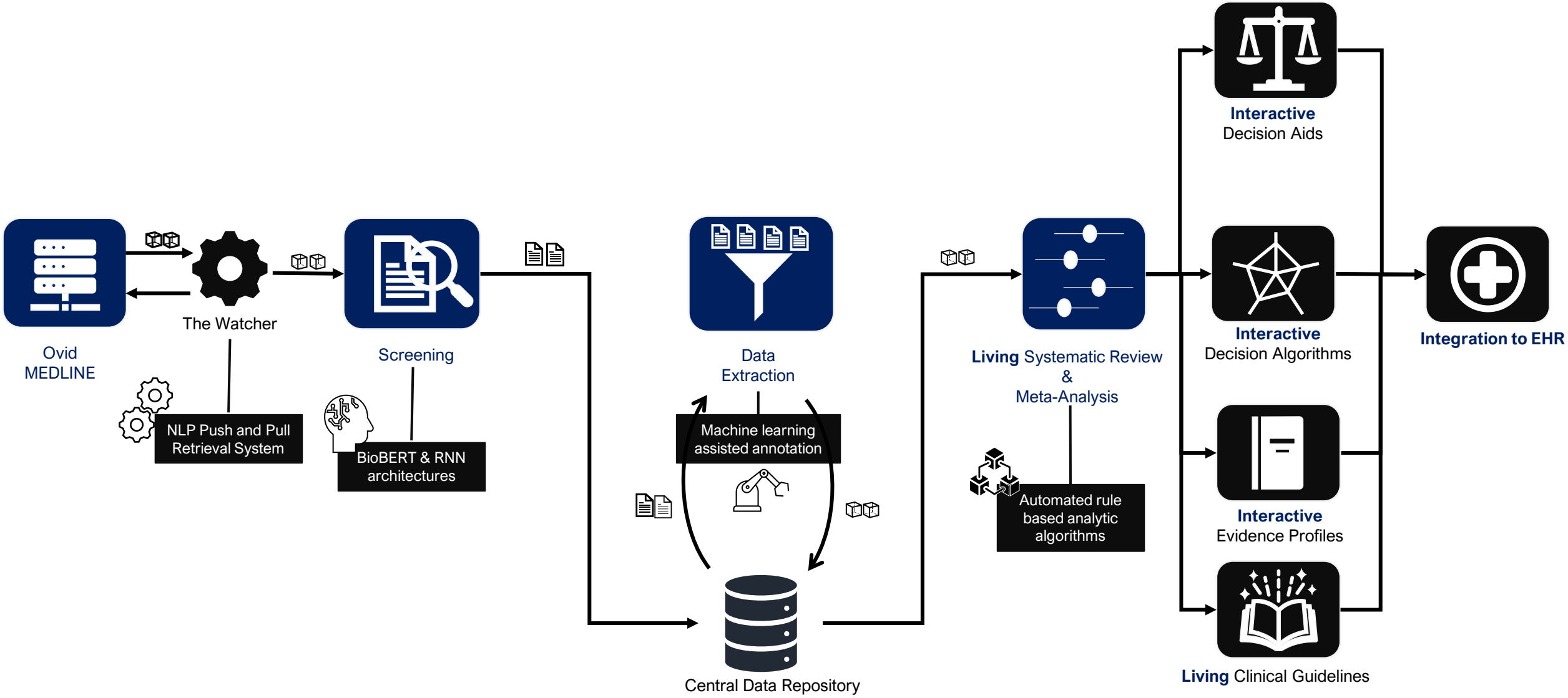
EVIDENCE SYNTHESIS WORKFLOW

LIVING EVIDENCE WORKFLOW



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What are the optimal systemic treatments for men with metastatic, hormone-sensitive prostate cancer? A STOPCaP systematic review and network meta-analysis

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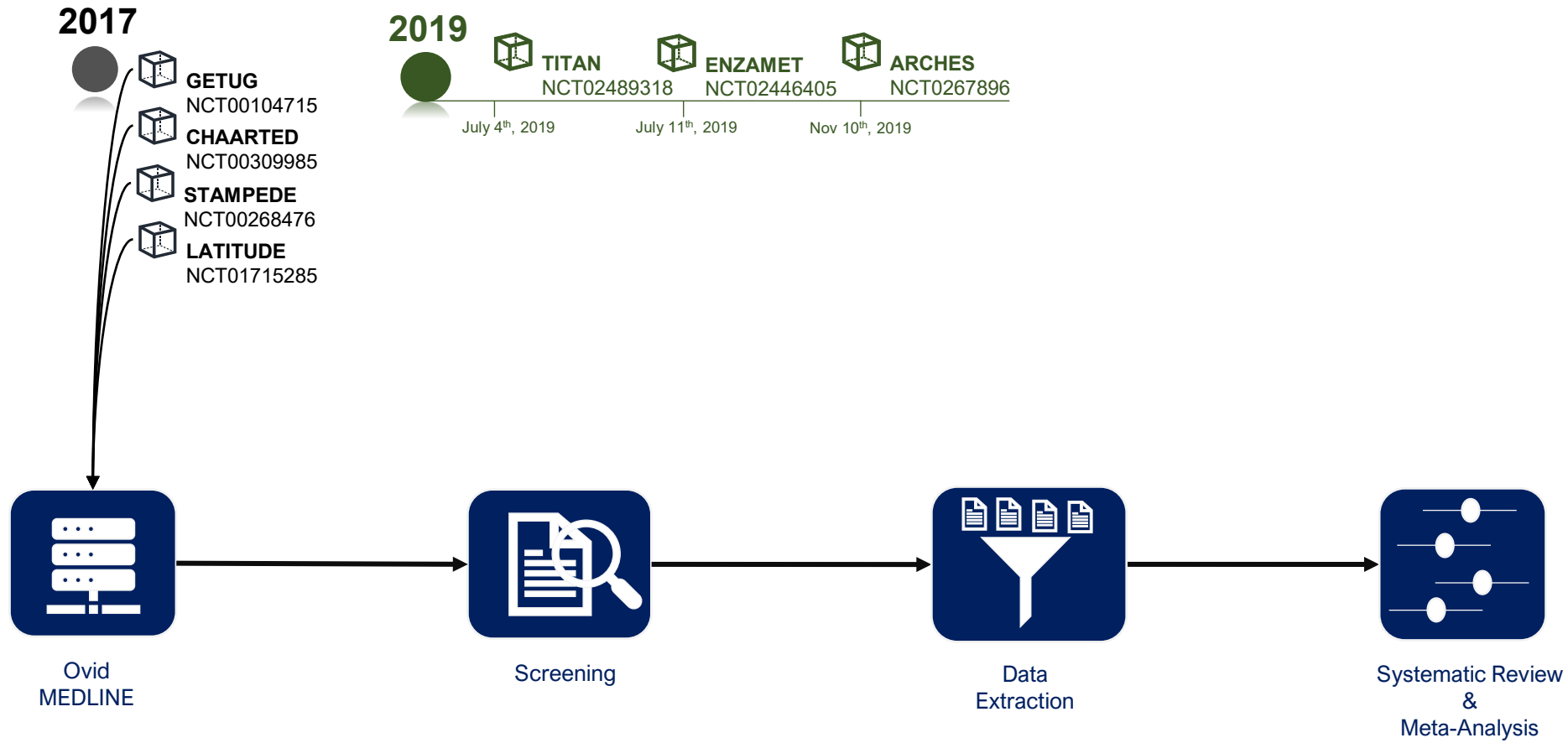
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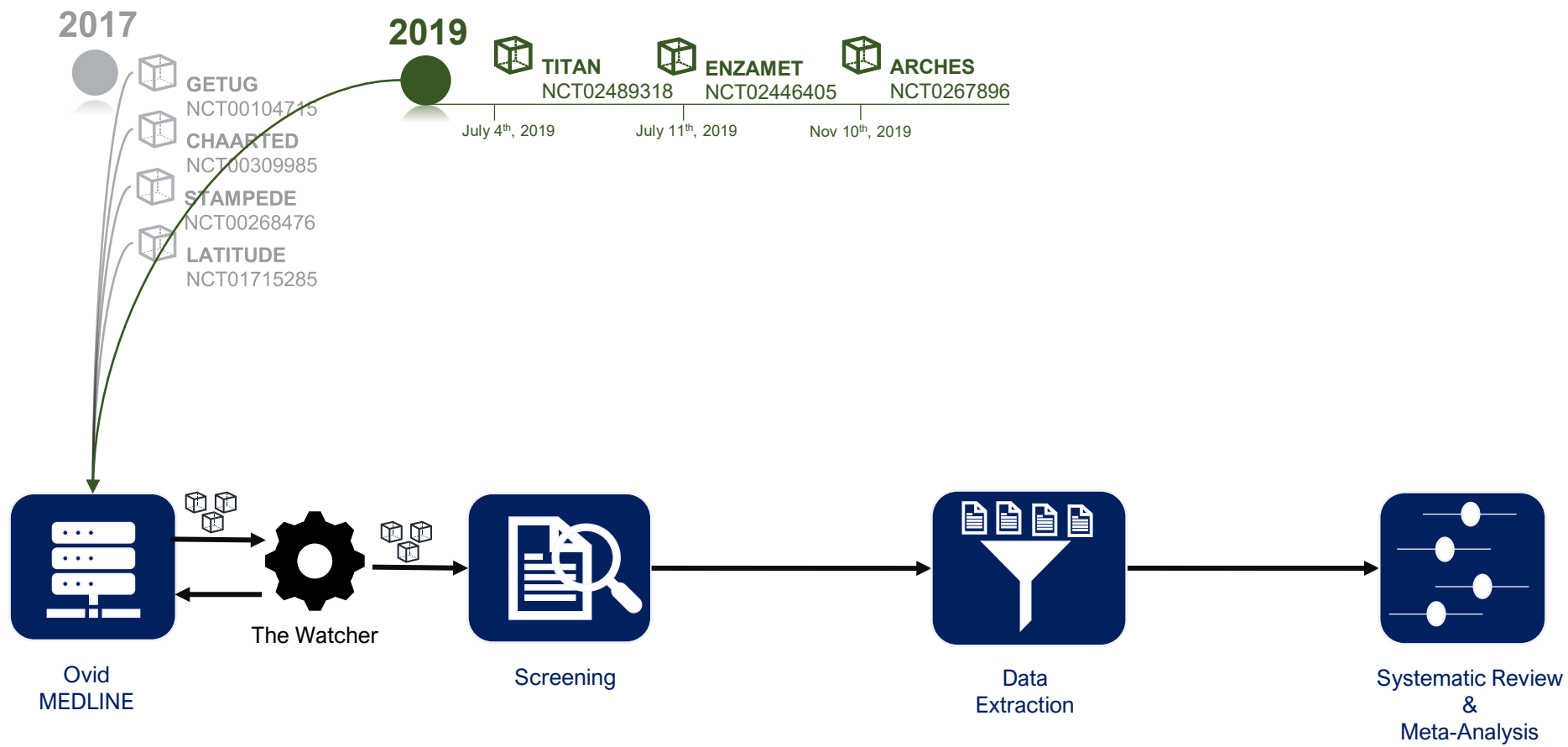
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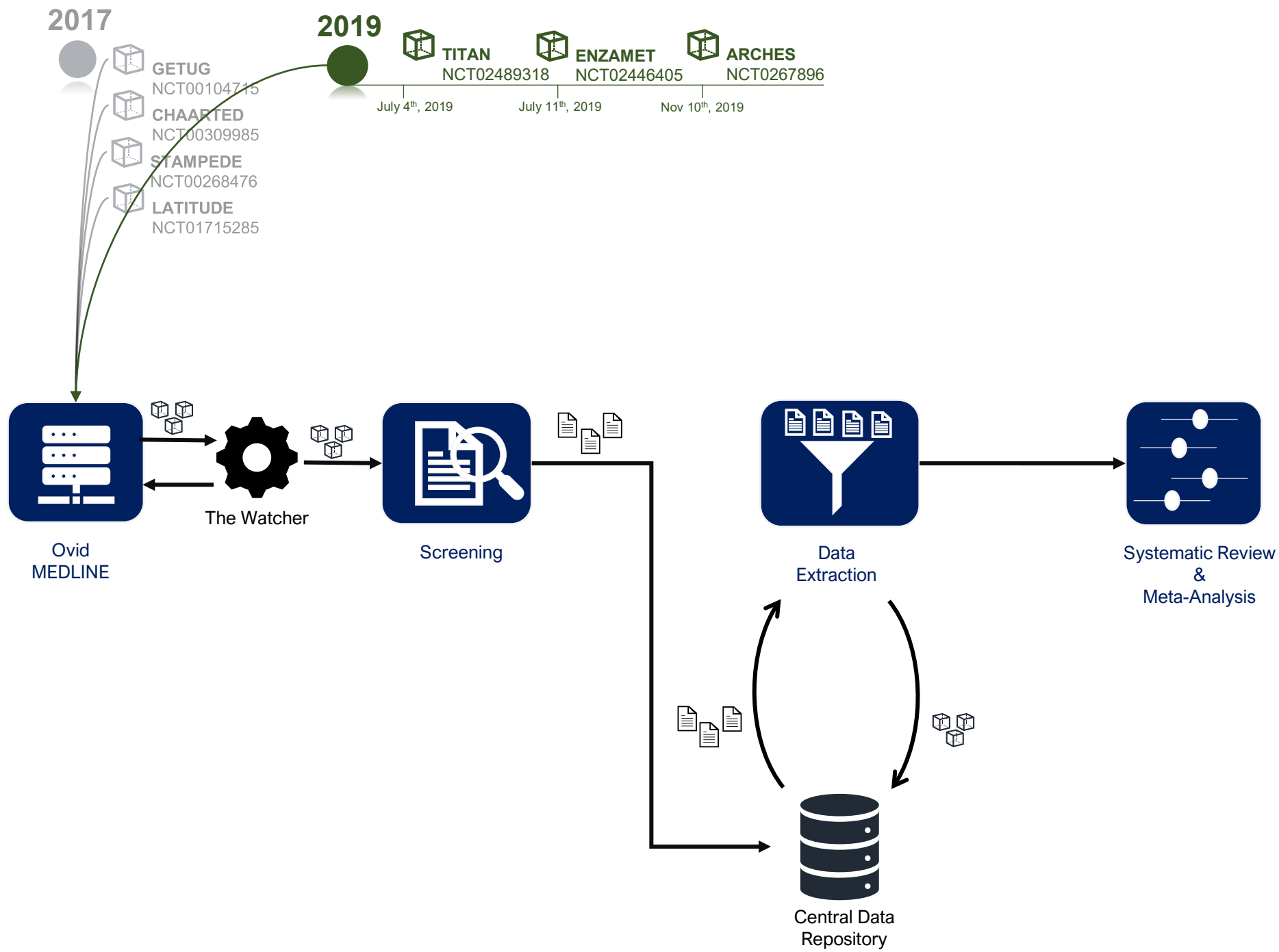
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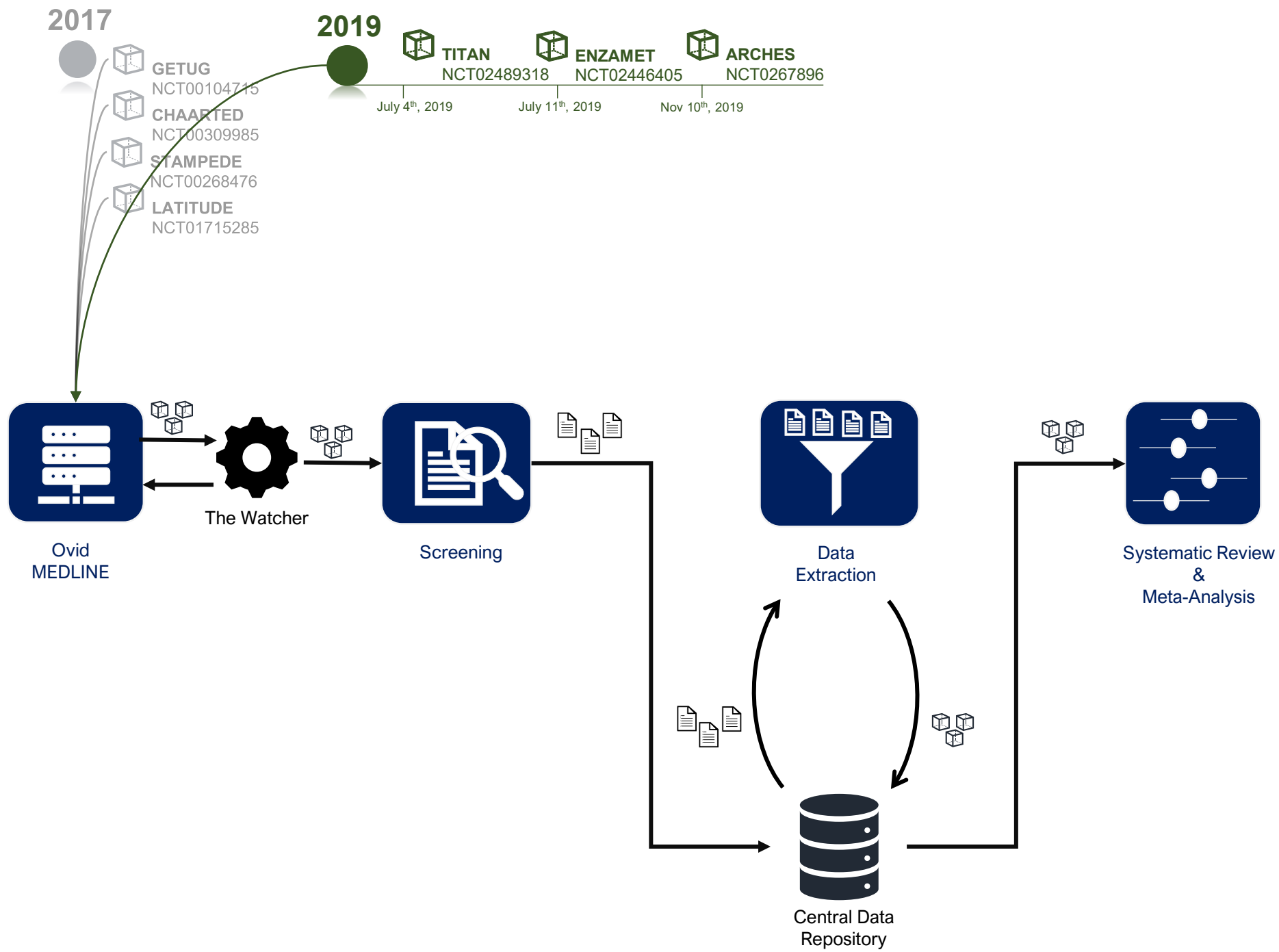
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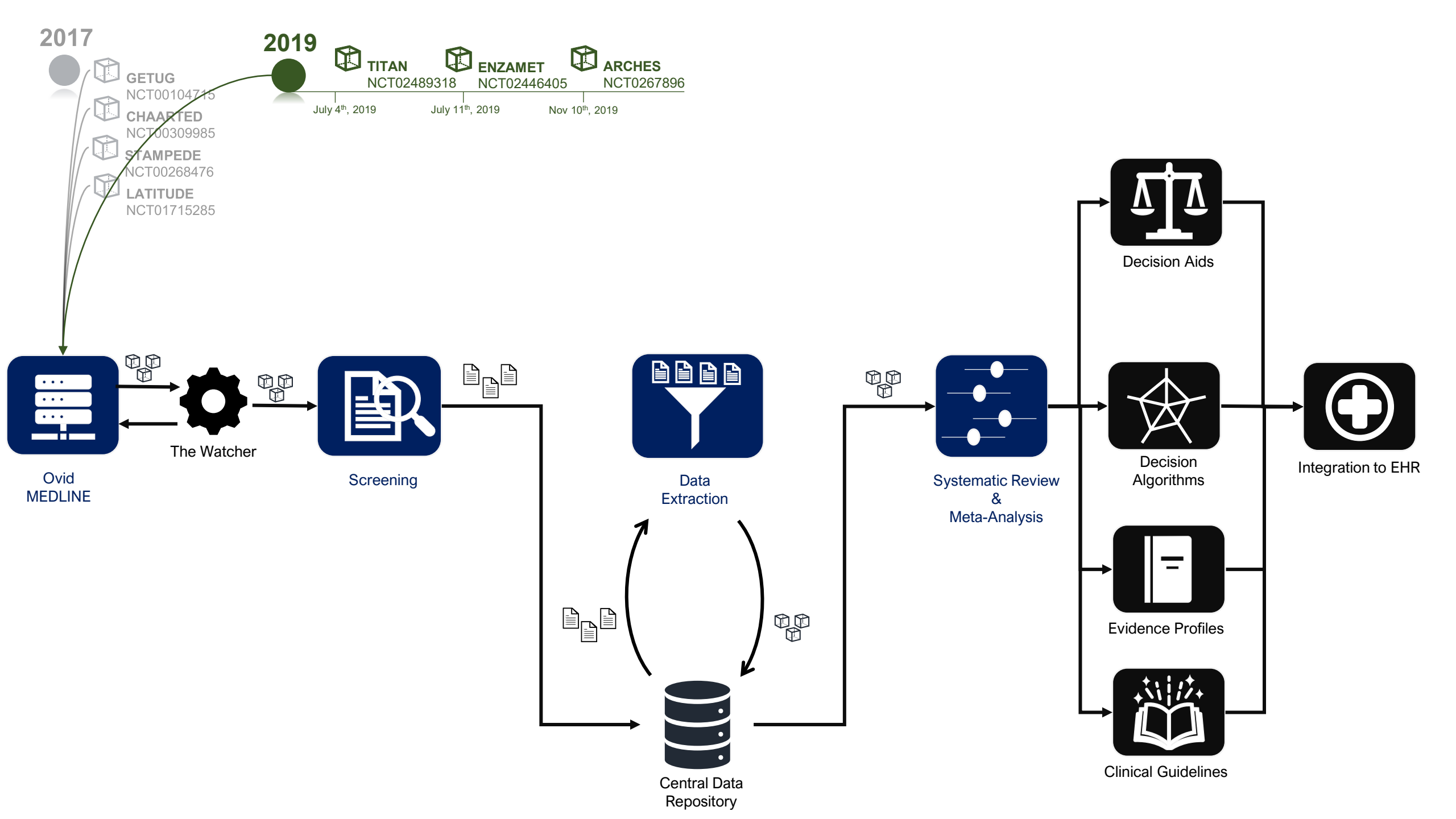
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Nov 10th, 2019
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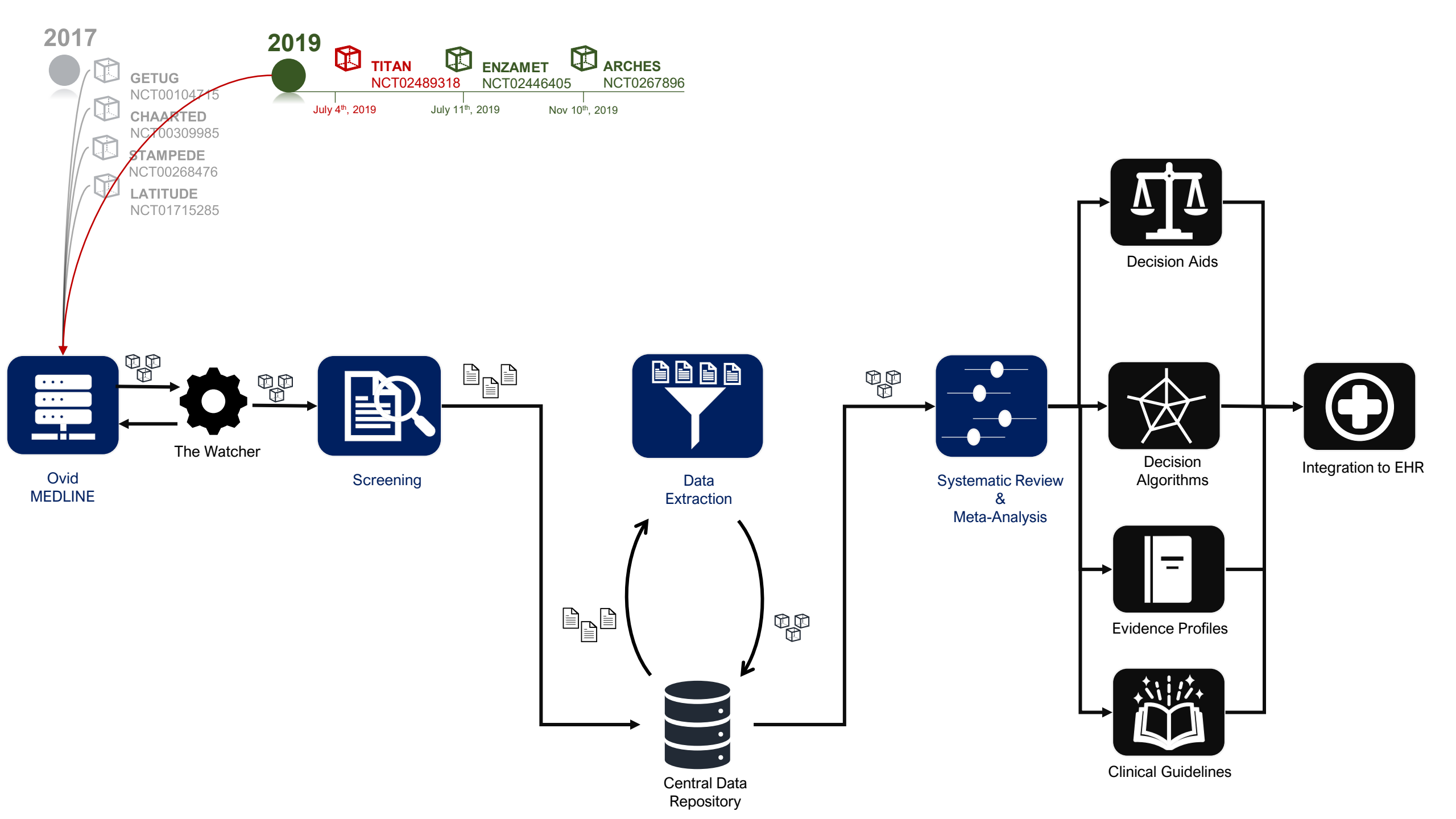
Systematic Review
&
Meta-Analysis
Decision Aids
Decision
Algorithms
Evidence Profiles
Clinical Guidelines
Integration to EHR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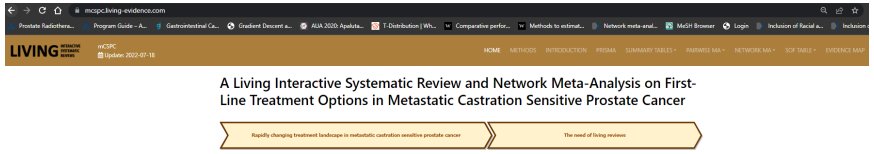

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The Watcher

Screening

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Central Data Repository

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&
Meta-Analysis

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Algorithms

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Evidence Profiles

Living Clinical Guidelines

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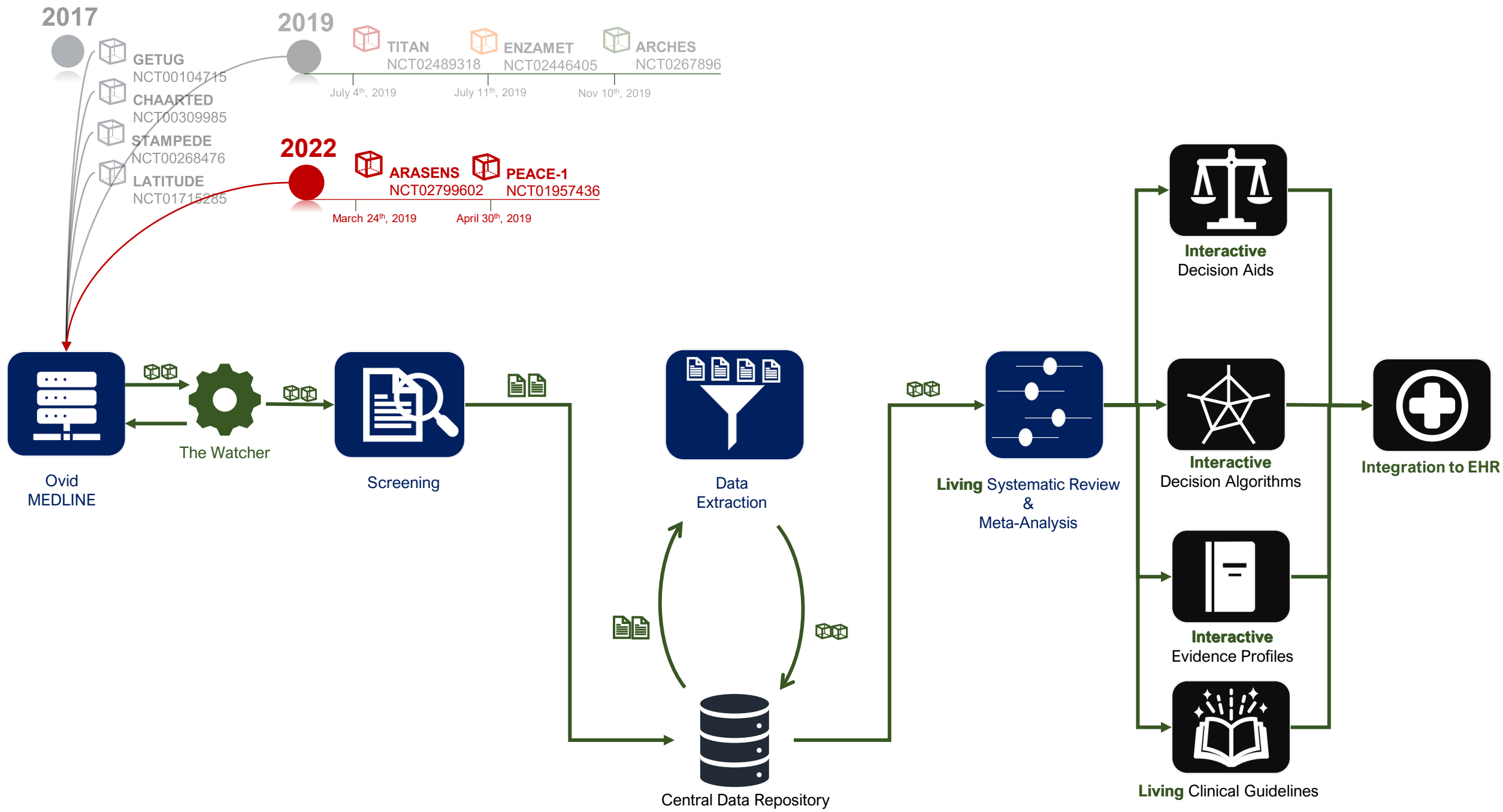
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March 24th, 2019
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Decision Aids
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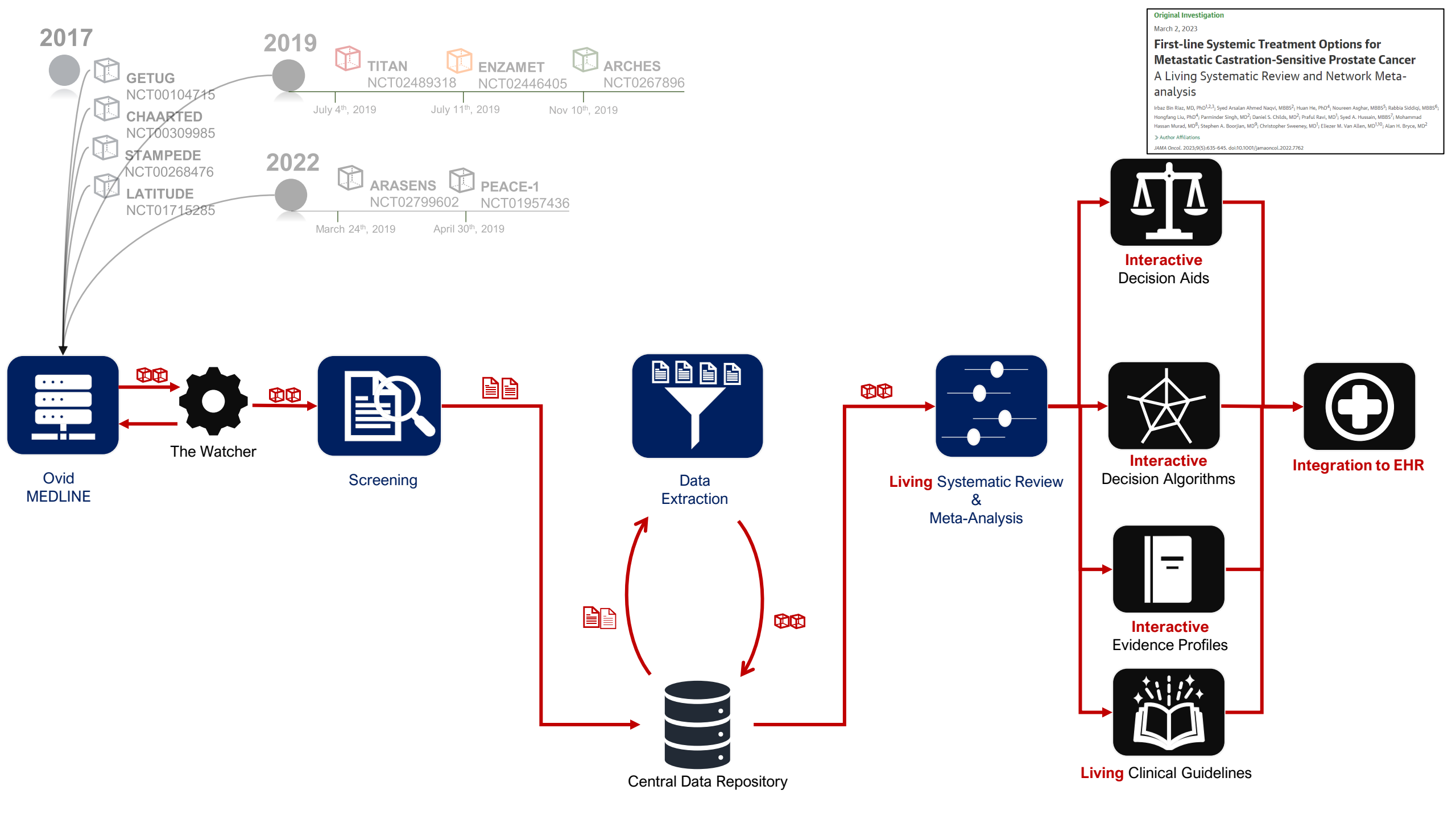
Interactive
Evidence Profiles
Living Clinical Guidelines
Integration to EHR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March 24th, 2019
PEACE-1
NCT01957436
April 30th, 2019
Original Investigation
March 2, 2023
First-line Systemic Treatment Options for Metastatic Castration-Sensitive Prostate Cancer
A Living Systematic Review and Network Meta-analysis
Irbaz Bin Riaz, MD, PhD[1,2,3]; Syed Arsalan Ahmed Naqvi, MBBS[2]; Huan He, PhD[4]; Noureen Asghar, MBBS[5]; Rabbia Siddiqi, MBBS[6]; Hongfang Liu, PhD[4]; Parminder Singh, MD[2]; Daniel S. Childs, MD[2]; Praful Ravi, MD[1]; Syed A. Hussain, MBBS[7]; Mohammad Hassan Murad, MD[8]; Stephen A. Boorjian, MD[9]; Christopher Sweeney, MD[1]; Elliezer M. Van Allen, MD[1,10]; Alan H. Bryce, MD[2]
Author Affiliations
JAMA Oncol. 2023;9(5):635-645. doi:10.1001/jamaoncol.2022.7762
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Screening
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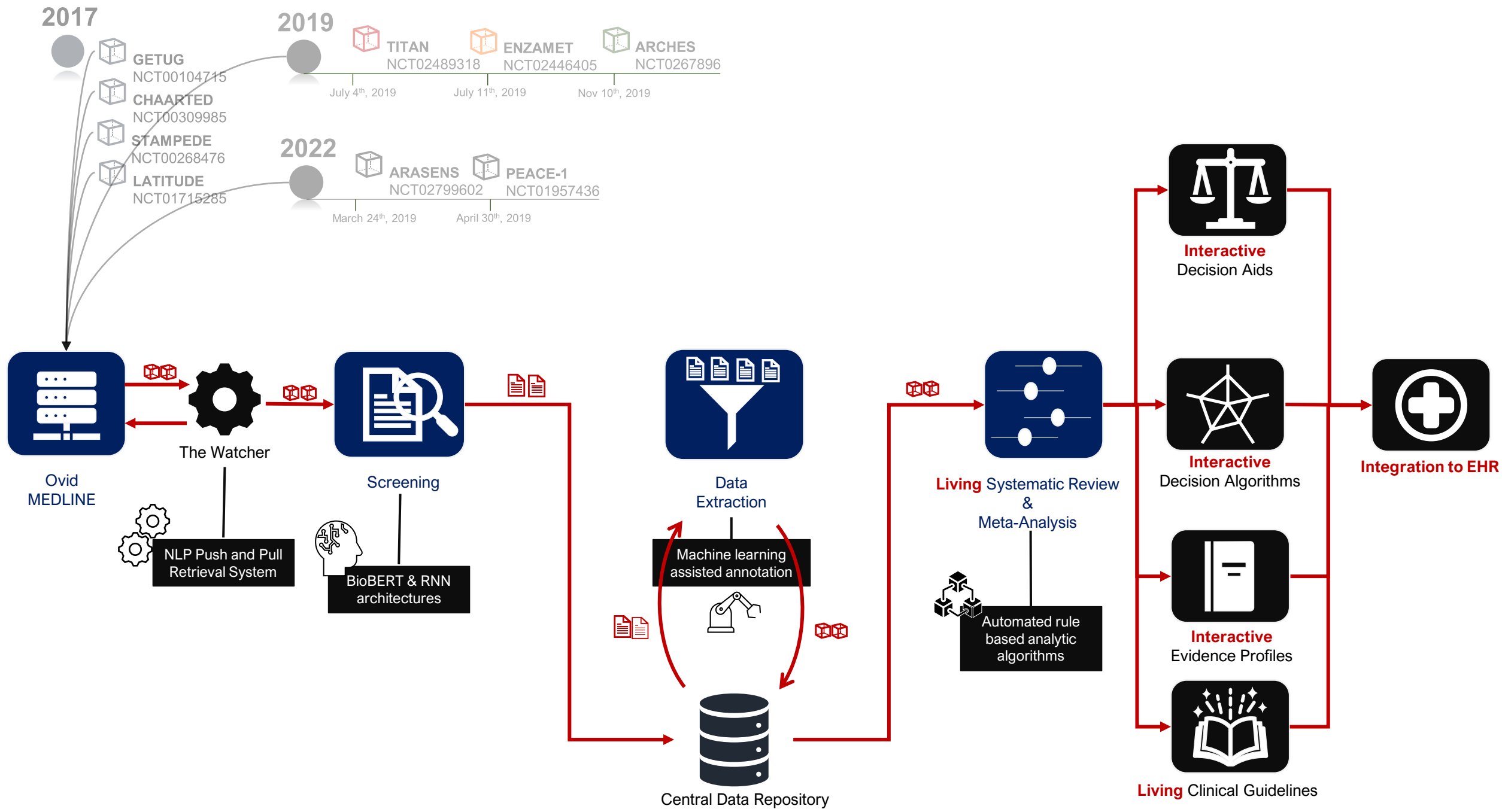
Central Data Repository
Living Systematic Review & Meta-Analysis
Interactive Decision Aids
Interactive Decision Algorithms
Interactive Evidence Profiles
Living Clinical Guidelines
Integration to EHR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2022
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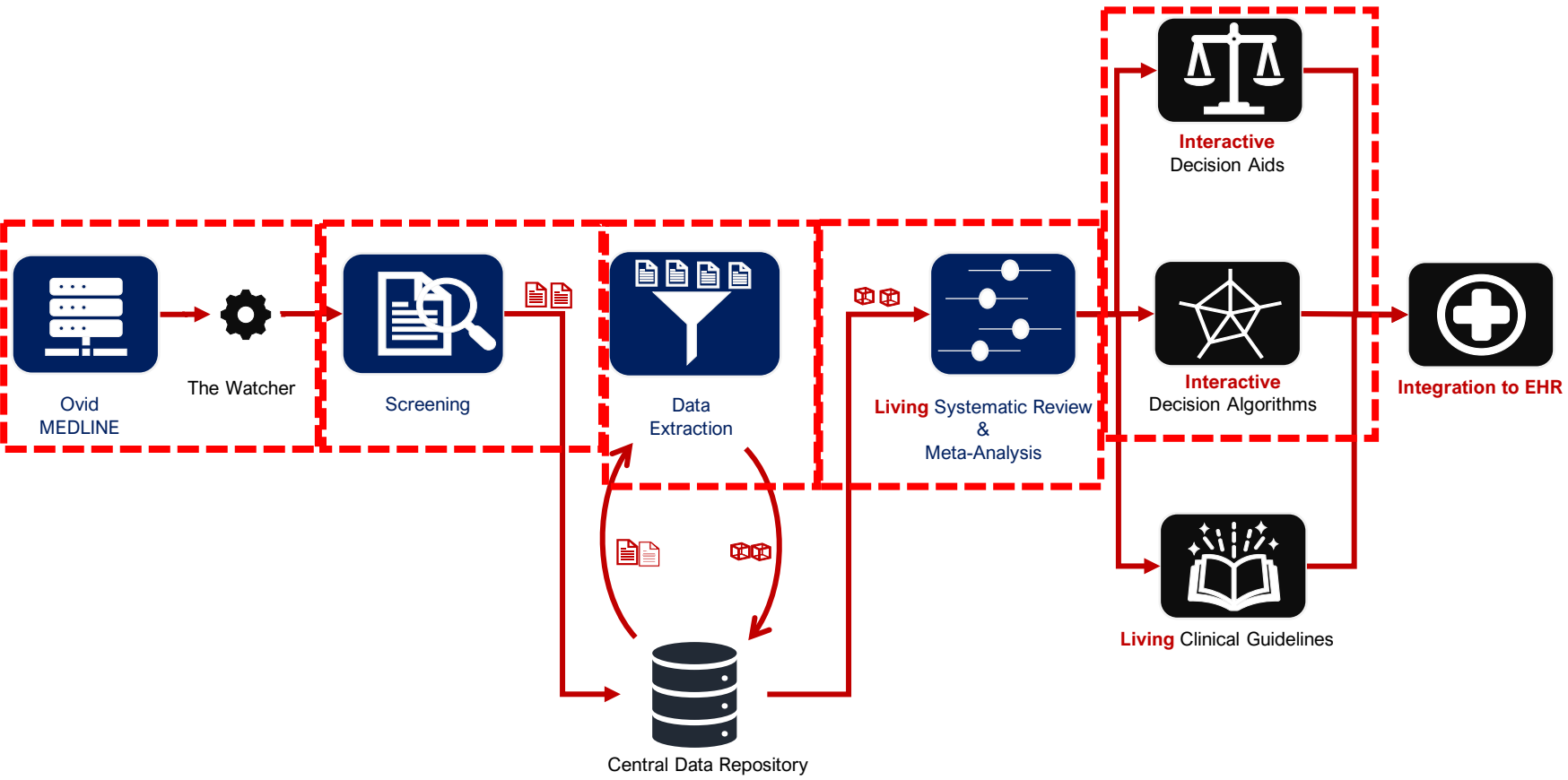
The Watcher
NLP Push and Pull
Retrieval System
Screening
BioBERT & RNN
architectures
Data
Extraction
Machine learning
assisted annotation
Central Data Repository
Living Systematic Review
&
Meta-Analysis
Automated rule
based analytic
algorithms
Interactive
Decision Aids
Interactive
Decision Algorithms
Interactive
Evidence Profiles
Living Clinical Guidelines
Integration to EHR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MEDLINE
The Watcher
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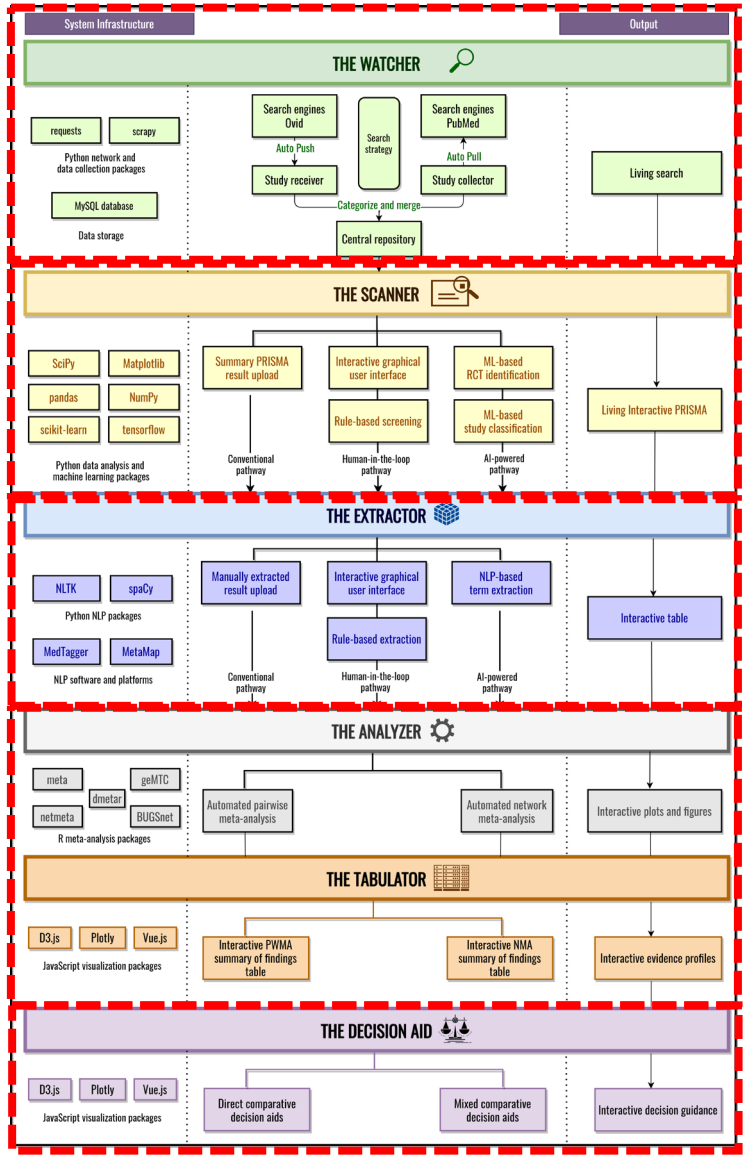
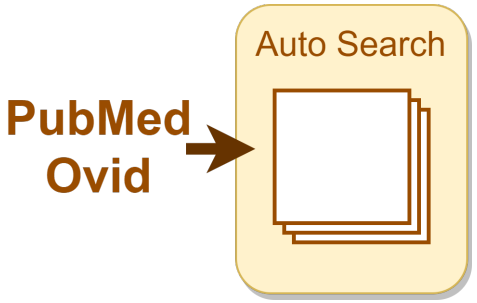

System Infrastructure
Output
THE WATCHER
requests
scrapy
Python network and data collection packages
MySQL database
Data storage
Search engines Ovid
Auto Push
Study receiver
Search strategy
Search engines PubMed
Auto Pull
Study collector
Categorize and merge
Central repository
Living search
THE SCANNER
SciPy
Matplotlib
pandas
NumPy
scikit-learn
tensorflow
Python data analysis and machine learning packages
Summary PRISMA result upload
Interactive graphical user interface
ML-based RCT identification
Rule-based screening
ML-based study classification
Conventional pathway
Human-in-the-loop pathway
AI-powered pathway
Living Interactive PRISMA
THE EXTRACTOR
NLTK
spaCy
Python NLP packages
MedTagger
MetaMap
NLP software and platforms
Manually extracted result upload
Interactive graphical user interface
NLP-based term extraction
Rule-based extraction
Conventional pathway
Human-in-the-loop pathway
AI-powered pathway
Interactive table
THE ANALYZER
meta
geMTC
dmetar
netmeta
BUGSnet
R meta-analysis packages
Automated pairwise meta-analysis
Automated network meta-analysis
Interactive plots and figures
THE TABULATOR
D3.js
Plotly
Vue.js
JavaScript visualization packages
Interactive PWMA summary of findings table
Interactive NMA summary of findings table
Interactive evidence profiles
THE DECISION AID
D3.js
Plotly
Vue.js
JavaScript visualization packages
Direct comparative decision aids
Mixed comparative decision aids
Interactive decision guidance

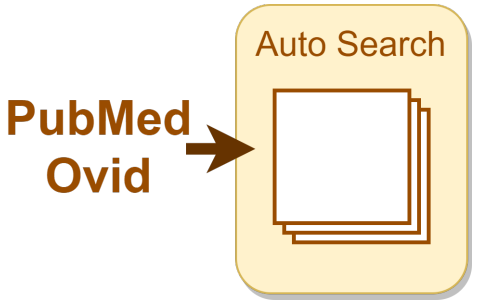
LIVING EVIDENCE WORKFLOW

PubMed
Ovid

LIVING EVIDENCE WORKFLOW



LIVING EVIDENCE WORKFLOW



#	Searches	Results
1	exp *Prostatic Neoplasms/	283331
2	exp Clinical Trial/	2498364
3	exp Meta-Analysis/	353101
4	1 and (2 or 3)	27693
5	exp animals/ not exp humans/	9641145
6	4 not 5	27634
7	limit 6 to (letter or editorial or erratum or note or addresses or autobiography or bibliography or biography or blogs or comment or dictionary or directory or interactive tutorial or interview or lectures or legal cases or legislation or news or newspaper article or overall or patient education handout or periodical index or portraits or published erratum or video-audio media or webcasts) [Limit not valid in Embase, Ovid MEDLINE(R), Ovid MEDLINE(R) Daily Update, Ovid MEDLINE(R) PubMed not MEDLINE, Ovid MEDLINE(R) In-Process, Ovid MEDLINE(R) Publisher; records were retained]	1039
8	6 not 7	26595

LIVING EVIDENCE WORKFLOW

PubMed
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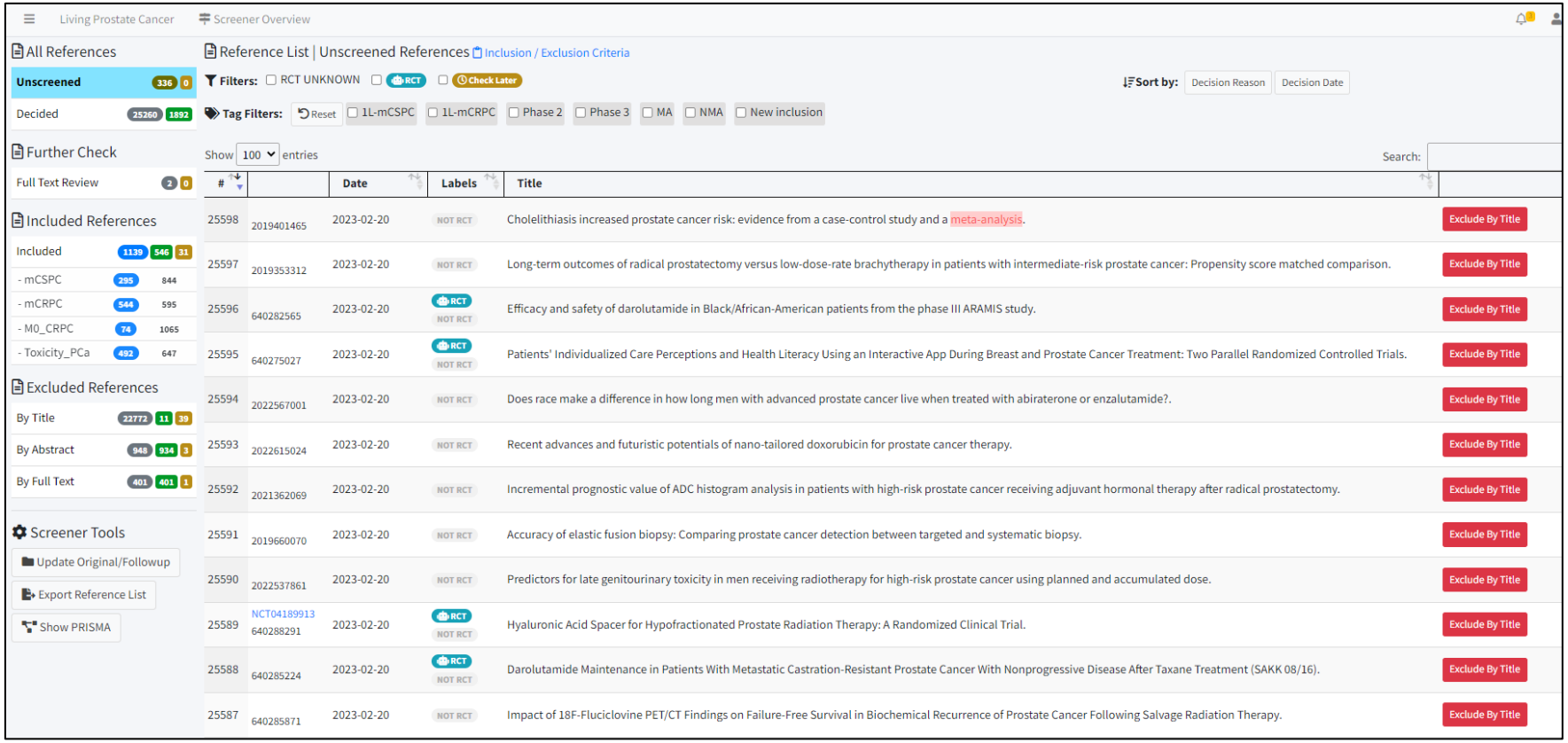

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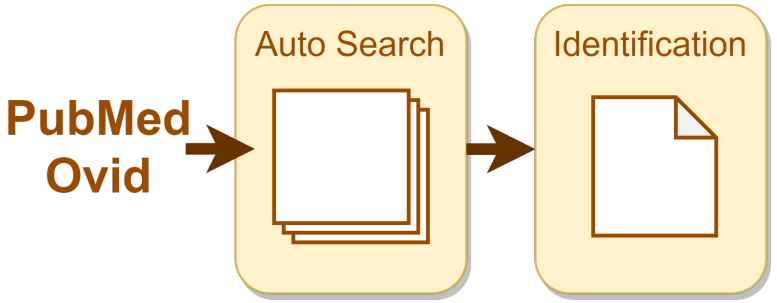

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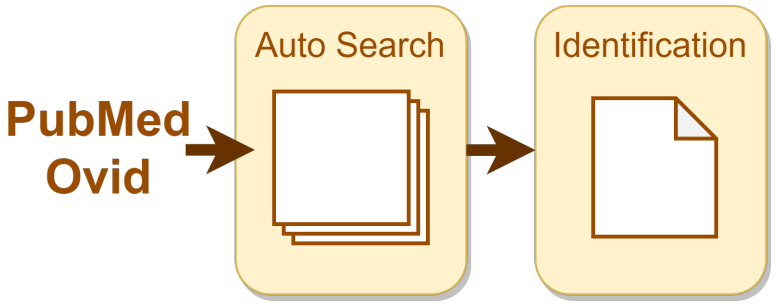

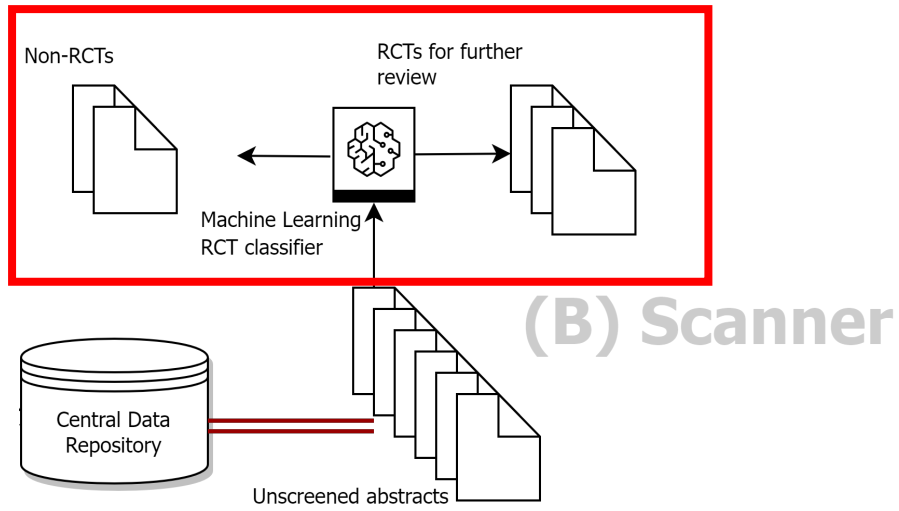

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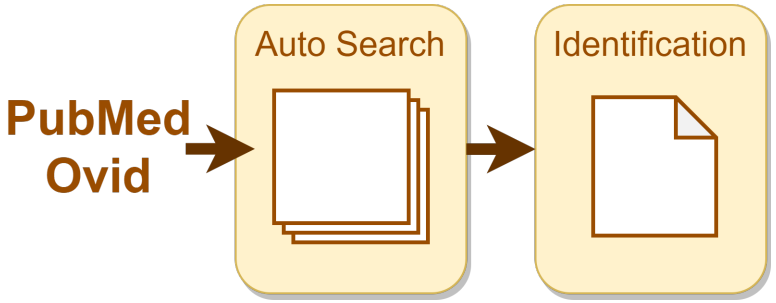

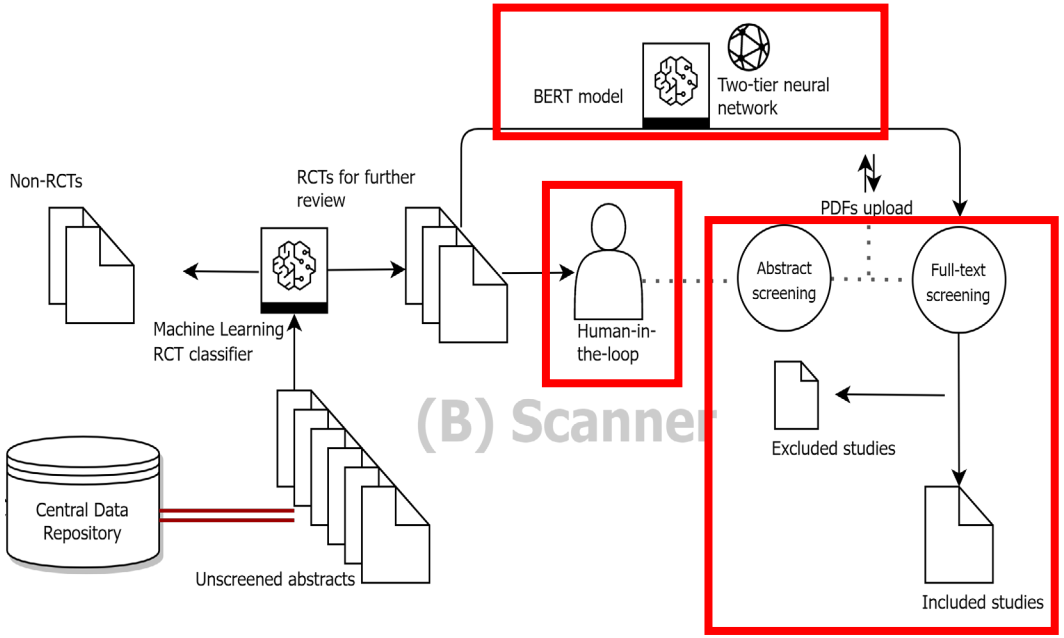

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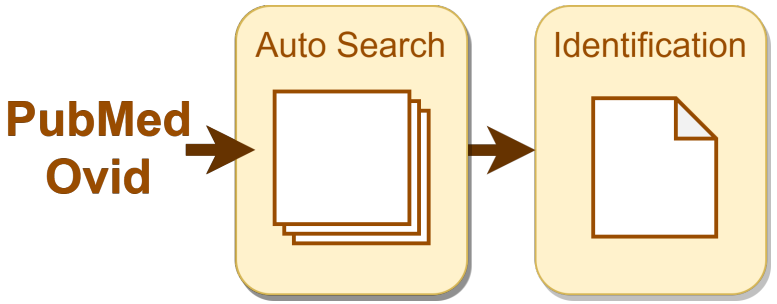
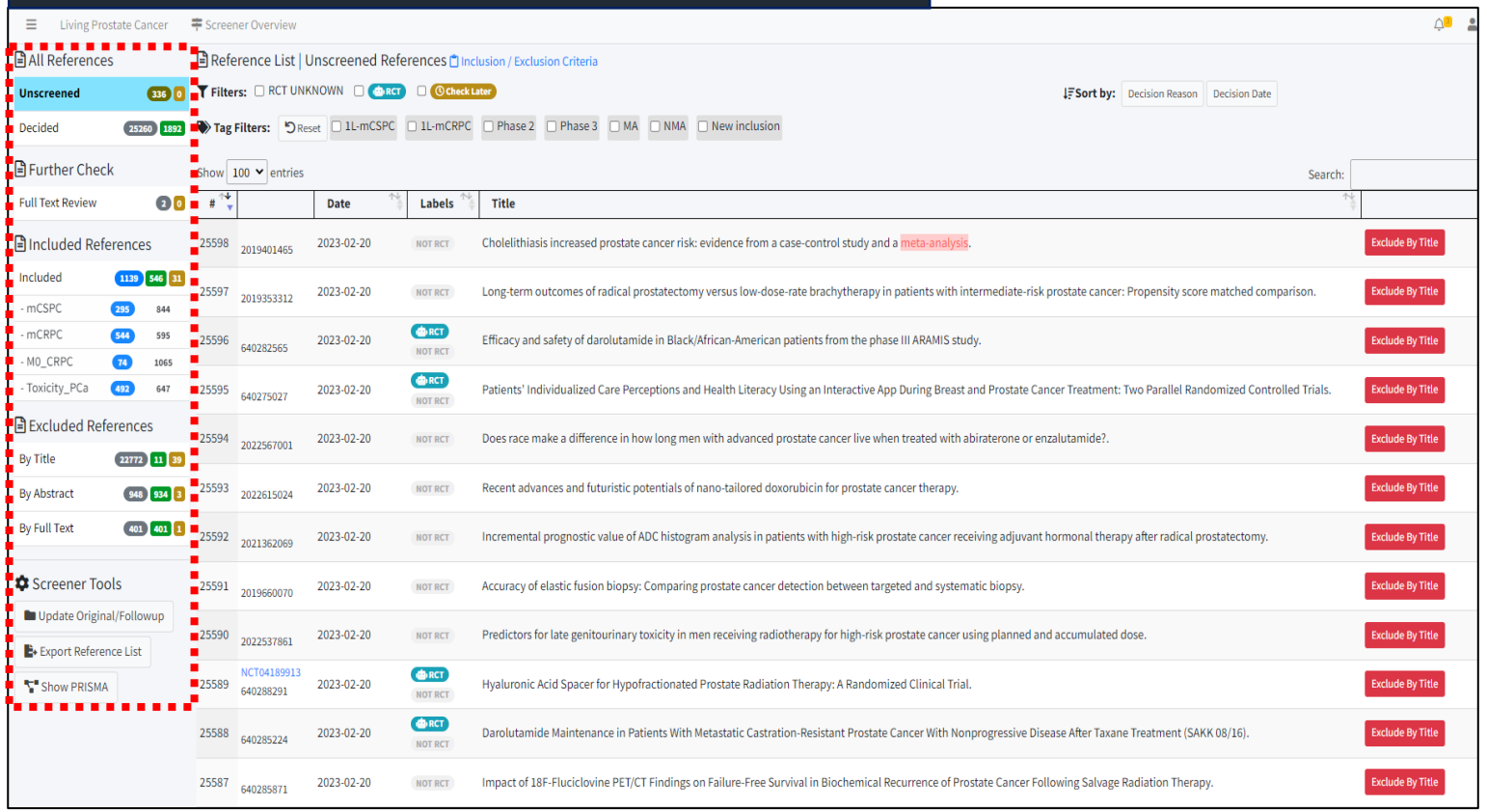


Screening Categories: Categorized by screening levels with numbers indicating the screening progress



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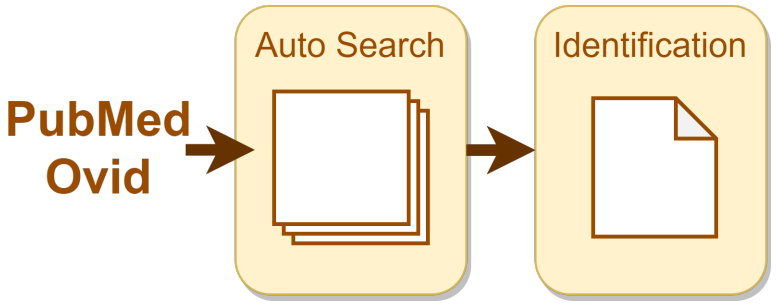
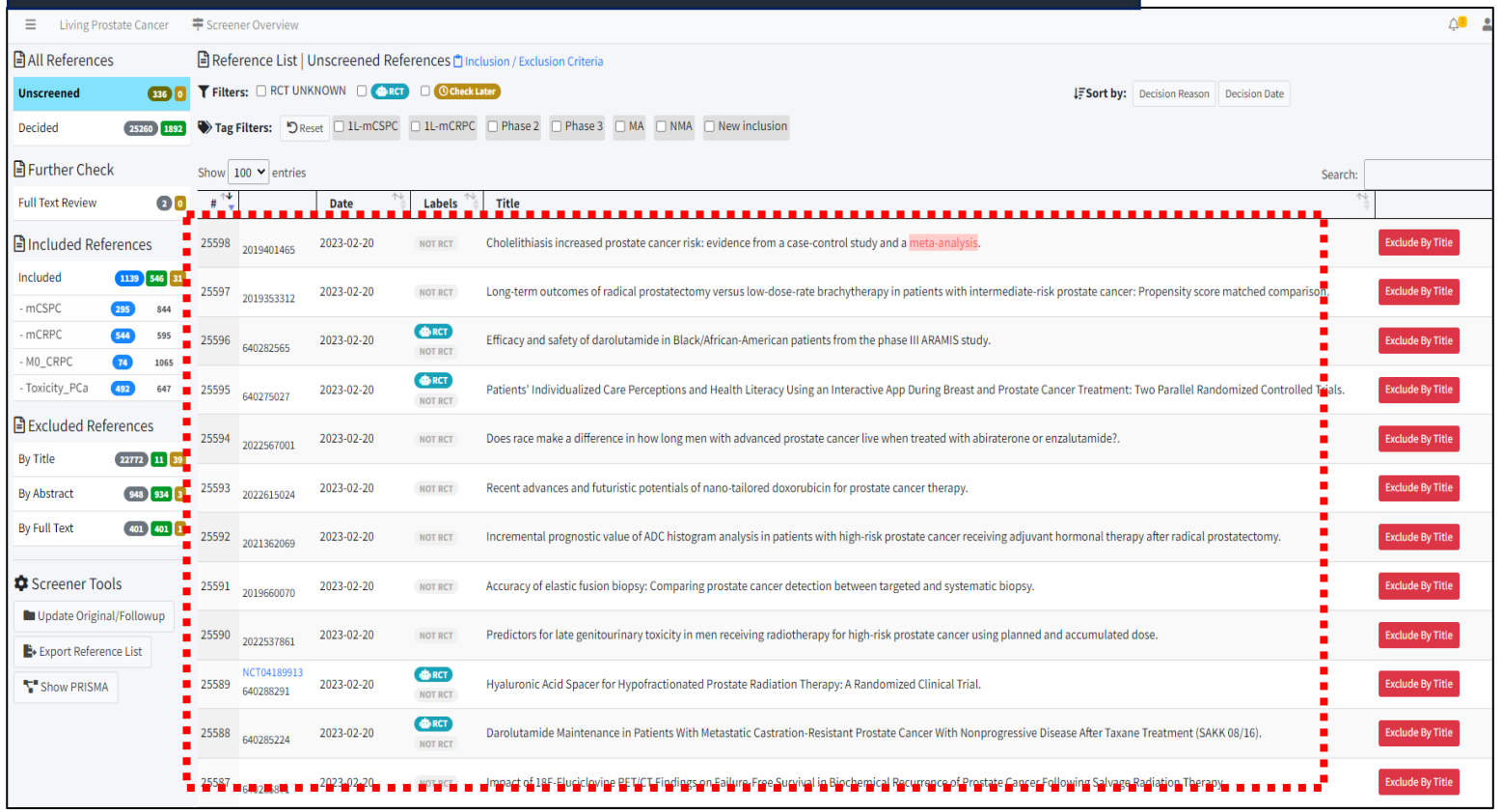


List of Studies: Studies are listed with unique study identification information and machine-learning based classifiers to facilitate decisions



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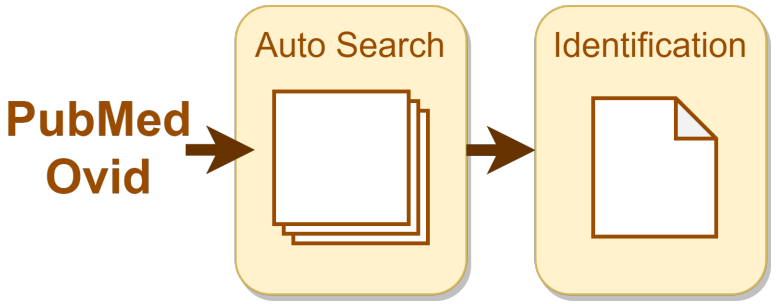
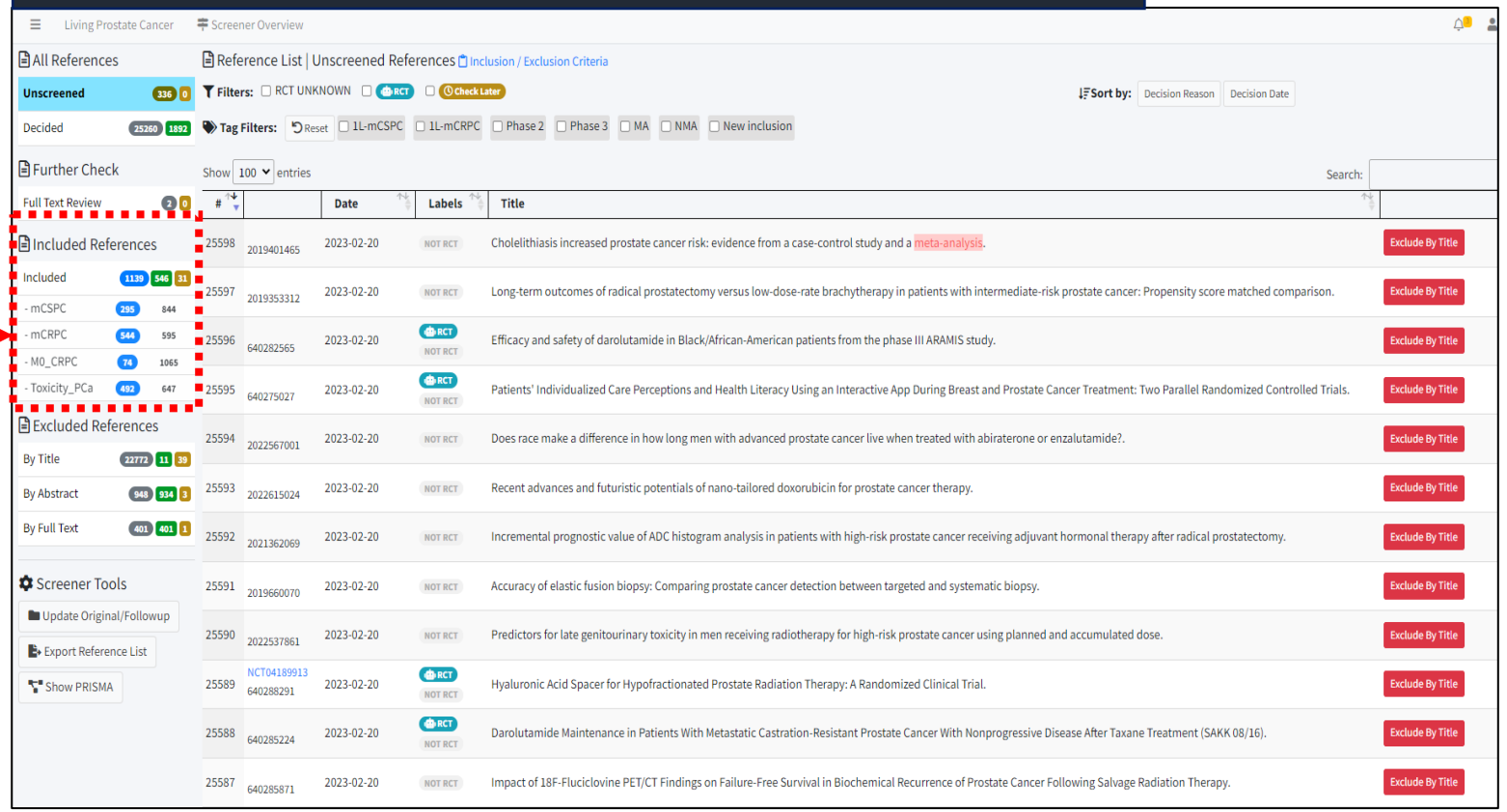


Different Clinical Questions: Studies are included/excluded at full-text review for multiple clinical questions



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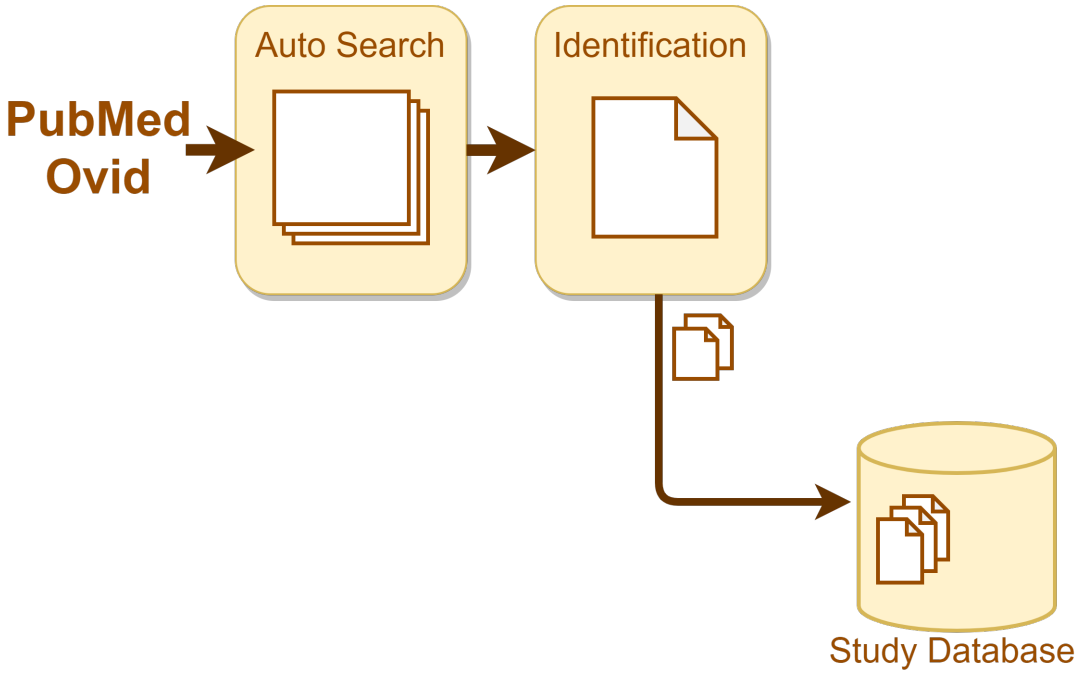

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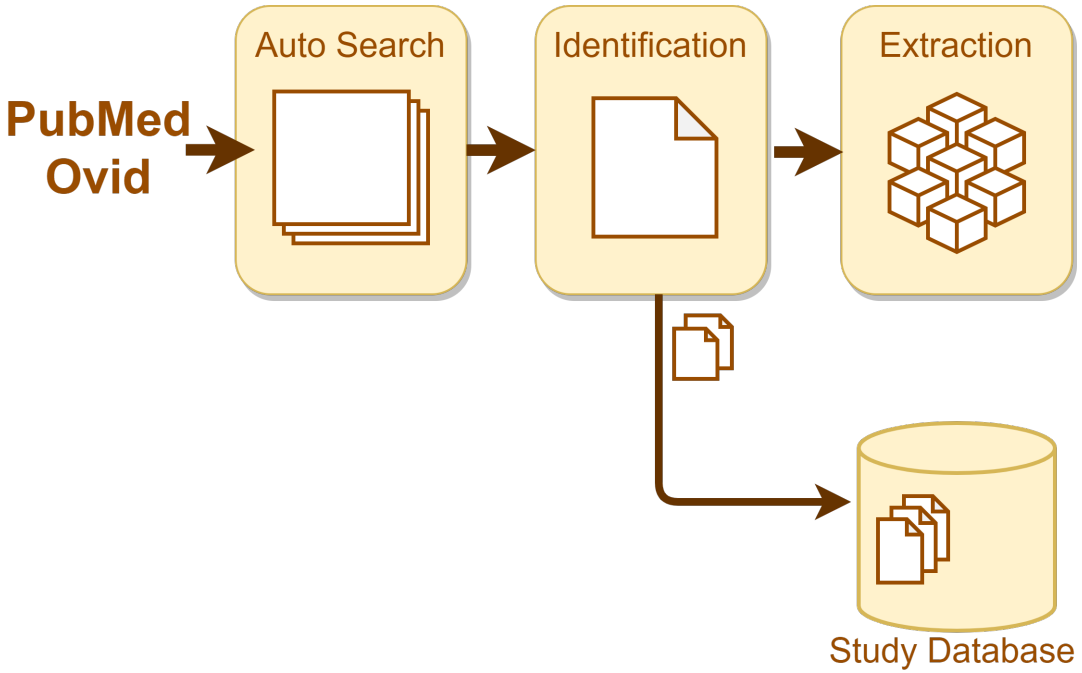

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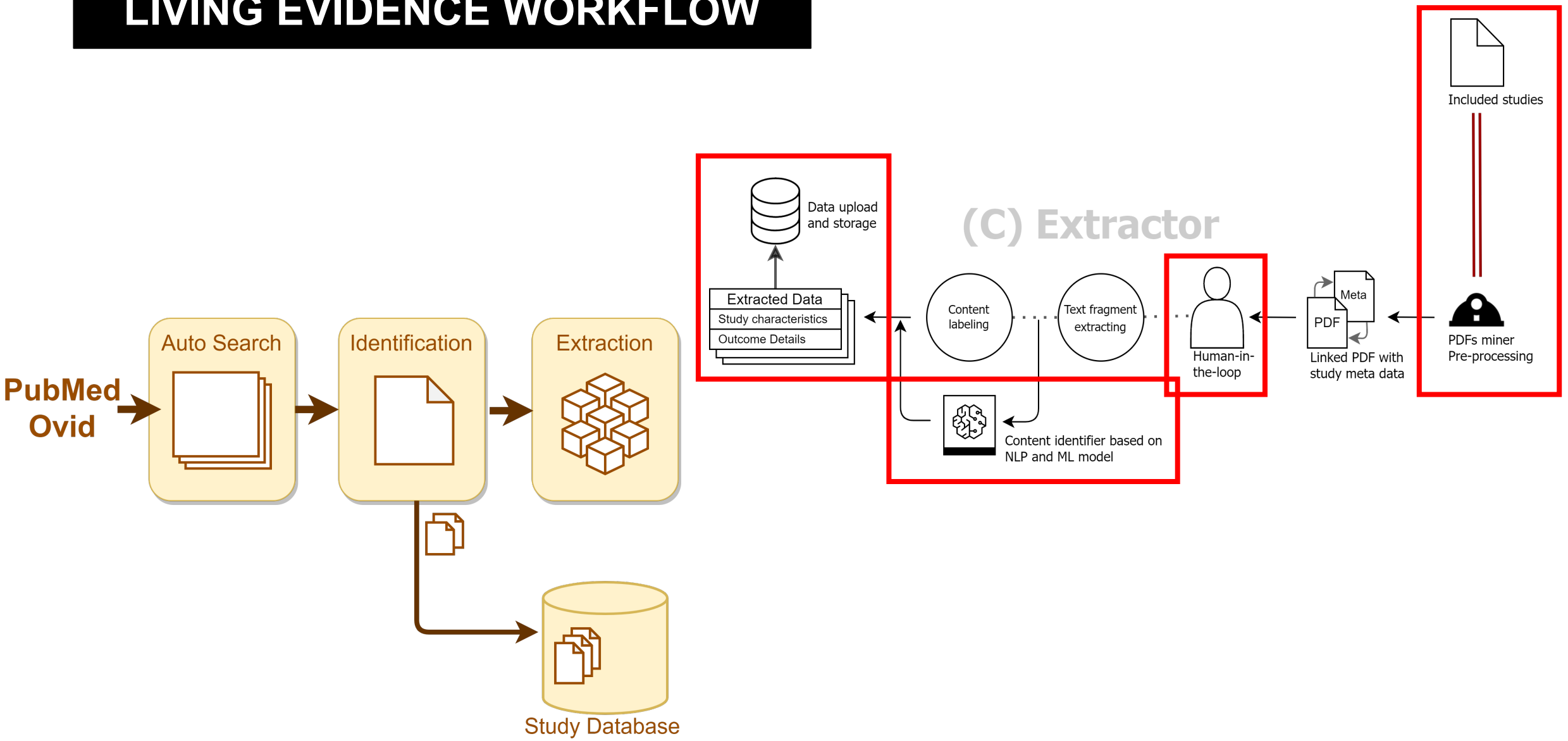

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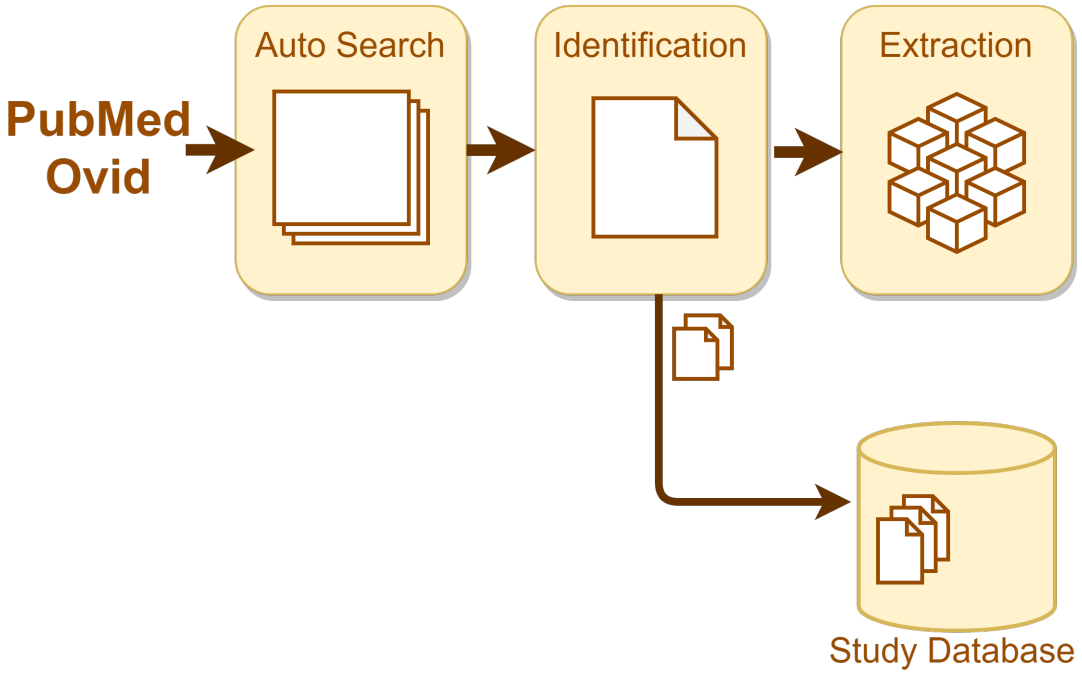


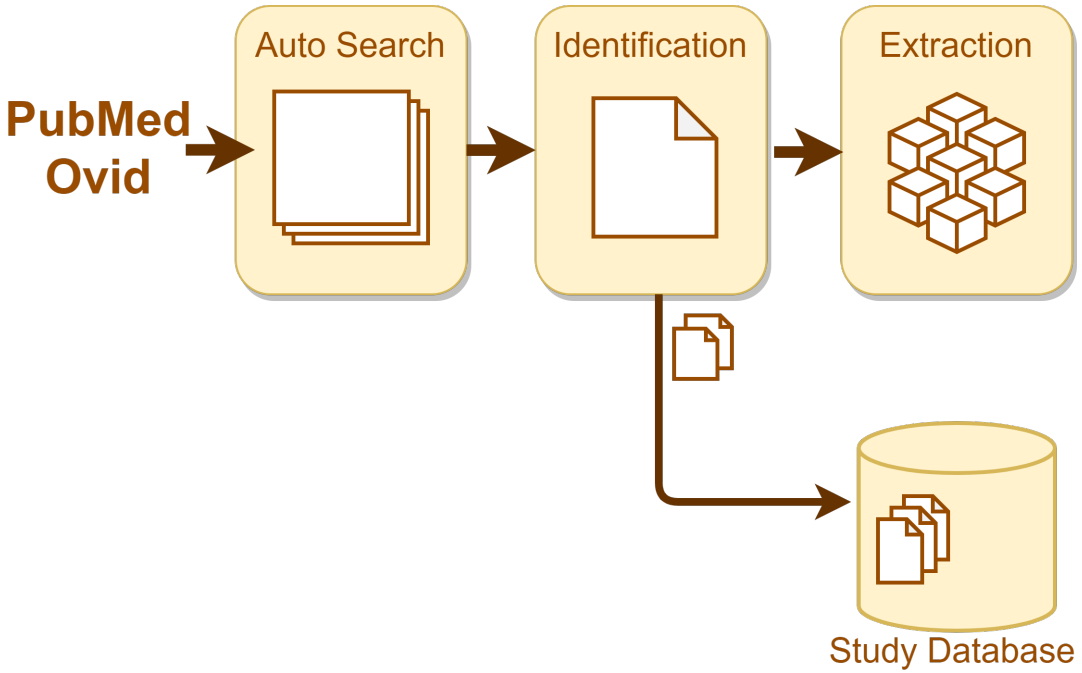
Study list panel

Renal Cell Carcinoma | Adjuvant Renal Cell Carcinoma | Extract by paper

9 studies (included in SR) PMID, short #, first author name

#	PID	9 studies	Outcomes	
503	34407342	Toni K Choueiri et al 2021	7	Adjuvant Pembrolizumab after Nephrectomy in Renal-Cell Carcinoma.
530	28967554	Robert J Motzer et al 2017	1	Adjuvant Sunitinib for High-risk Renal Cell Carcinoma After Nephrectomy: Subgroup Analyses and Updated Overall Survival Results.
531	28902533	Robert J Motzer et al 2017	9	Randomized Phase III Trial of Adjuvant Pazopanib Versus Placebo After Nephrectomy in Patients With Localized or Locally Advanced Renal Cell Carcinoma.
532	33052759	Tim Eisen et al 2020	9	Adjuvant Sorafenib for Renal Cell Carcinoma at Intermediate or High Risk of Relapse: Results From the SORCE Randomized Phase III Intergroup Trial.
533	27718781	Alain Ravaud et al 2016	11	Adjuvant Sunitinib in High-Risk Renal-Cell Carcinoma after Nephrectomy.
534	30412222	M Staehler et al 2018	1	Adjuvant sunitinib in patients with high-risk renal cell carcinoma: safety, therapy management, and patient-reported outcomes in the S-TRAC trial.
535	26969090	Naomi B Haas et al 2016	7	Adjuvant sunitinib or sorafenib for high-risk, non-metastatic renal-cell carcinoma (ECOG-ACRIN E2805): a double-blind, placebo-controlled, randomised, phase 3 trial.
536	33461782	Robert J Motzer et al 2021	3	Adjuvant Pazopanib Versus Placebo After Nephrectomy in Patients With Localized or Locally Advanced Renal Cell Carcinoma: Final Overall Survival Analysis of the Phase 3 PROTECT Trial.
537	30346481	M Gross-Goupil et al 2018	13	Axitinib versus placebo as an adjuvant treatment of renal cell carcinoma: results from the phase III, randomized ATLAS trial.

LIVING EVIDENCE WORKFLOW



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535	26969090	Naomi B Haas et al 2016	7	**Adjuvant sunitinib or sorafenib for high-risk, non-metastatic renal-cell carcinoma (ECOG-ACRIN E2805): a double-blind, placebo-controlled, randomised, phase 3 trial.**
536	33461782	Robert J Motzer et al 2021	3	**Adjuvant Pazopanib Versus Placebo After Nephrectomy in Patients With Localized or Locally Advanced Renal Cell Carcinoma: Final Overall Survival Analysis of the Phase 3 PROTECT Trial.**
537	30346481	M Gross-Goupil et al 2018	13	**Axitinib versus placebo as an adjuvant treatment of renal cell carcinoma: results from the phase III, randomized ATLAS trial.**

Interactive Extractor

Renal Cell Carcinoma | Adjuvant Renal Cell Carcinoma | Extract by paper

9 studies (included in SR) — PMID, short #, first author name

Naomi B Haas et al 2016 is selected in 7 outcomes

Save | Toggle | Outcome na

Interactive Table

Network MA

Primary Analysis
- Class
- All cause AEs (all grades)
- All cause AEs (grade ≥ 3)
- Disease free survival
- Overall survival
- Treatment related AEs (all grades)
- Treatment related AEs (grade ≥ 3)
- default
- All cause AEs (all grades)
- All cause AEs (grade ≥ 3)
- Disease free survival
- Overall survival
- Treatment related AEs (all grades)
- Treatment related AEs (grade ≥ 3)

Pairwise MA

Primary Analysis
- default
- All cause AEs (all grades)
- All cause AEs (grade ≥ 3)
- Disease free survival
- Overall survival
- Treatment related AEs (all grades)
- Treatment related AEs (grade ≥ 3)

primary
default | Disease free survival

Save | Fill | 3

Comp 1 | Comp 2

Result

TE: 1.02

Lower CI: 0.85

Upper CI: 1.23

Detail

Survival in Control: 6.6

Ec: 287

Et: 647

Abstract | PDFs

2016-03-09 - Lancet

Adjuvant sunitinib or sorafenib for high-risk, non-metastatic renal-cell carcinoma (ECOG-ACRIN E2805): a double-blind, placebo-controlled, randomised, phase 3 trial.

Naomi B Haas, Judith Manola, Robert G Uzzo, Keith T Flaherty, Christopher G Wood, Christopher Kane, Michael Jewett, Janice P Dutcher, Michael B Atkins, Michael Pins, George Wilding, David Cella, Lynne Wagner, Surena Matin, Timothy M Kuzel, Wade J Sexton, Yu-Ning Wong, Toni K Choueiri, Roberto Pili, Igor Puzanov, Manish Kohli, Walter Stadler, Michael Carducci, Robert Coomes, Robert S DiPaola

Clinical Trial ID: NCT00326898 | PMID: 26969090

Abstract

Renal-cell carcinoma is highly vascular, and proliferates primarily through dysregulation of the vascular endothelial growth factor (VEGF) pathway. We tested sunitinib and sorafenib, two oral anti-angiogenic agents that are effective in advanced renal-cell carcinoma, in patients with resected local disease at high risk for recurrence. In this double-blind, placebo-controlled, randomised, phase 3 trial, we enrolled patients at 226 study centres in the USA and Canada. Eligible patients had pathological stage high-grade T1b or greater with completely resected non-metastatic renal-cell carcinoma and adequate cardiac, renal, and hepatic function. Patients were stratified by recurrence risk, histology, Eastern Cooperative Oncology Group (ECOG) performance status, and surgical approach, and computerised double-blind randomisation was done centrally with permuted blocks. Patients were randomly assigned (1:1:1) to receive 54 weeks of sunitinib 50 mg per day orally throughout the first 4 weeks of each 6 week cycle, sorafenib 400 mg twice per day orally throughout each cycle, or placebo. Placebo could be sunitinib placebo given continuously for 4 weeks of every 6 week cycle or sorafenib placebo given twice per day throughout the study. The primary objective was to compare disease-free survival between each experimental group and placebo in the intention-to-treat population. All treated patients with at least one follow-up assessment were included in the safety analysis. This trial is registered with ClinicalTrials.gov, number NCT00326898. Between April 24, 2006, and Sept 1, 2010, 1943 patients from the National Clinical Trials Network were randomly assigned to sunitinib (n=647), sorafenib (n=649), or placebo (n=647). Following high rates of toxicity-related discontinuation after 1323 patients had enrolled (treatment discontinued by 193 [44%] of 438 patients on sunitinib, 199 [45%] of 441 patients on sorafenib), the starting dose of each drug was reduced and then individually titrated up to the original full doses. On Oct 16, 2014, because of low conditional power for the primary endpoint, the ECOG-ACRIN Data Safety Monitoring Committee recommended that blinded follow-up cease and the results be released. The primary analysis showed no significant differences in disease-free survival. Median disease-free survival was 5·8 years (IQR 1·6-8·2) for sunitinib (hazard ratio [HR] 1·02, 97·5% CI 0·85-1·23, p=0·8038), 6·1 years (IQR 1·7-not estimable [NE]) for sorafenib (HR 0·97, 97·5% CI 0·80-1·17, p=0·7184), and 6·6 years (IQR 1·5-NE) for placebo. The

× Highlighted **1·02**

Result

TE

Lower CI

Upper CI

Detail

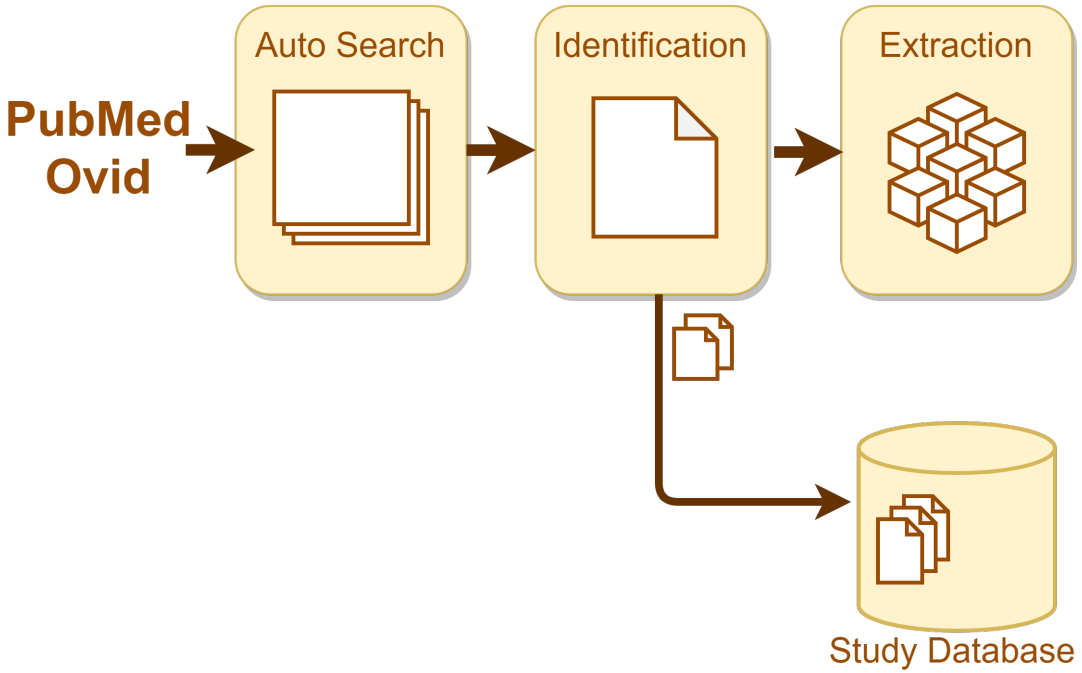
Survival in Control

Ec

Et

sunitinib and 102 [16%] patients on sorafenib), hand-foot syndrome (94 [ ]atients on sorafenib), rash (15 [2%] patients on sunitinib and 95 [15%] patients on sorafenib), and fatigue 110 [18%] patie[ ]e deaths related to treatment or occurring within 30 days of the end of treatment; one patient receiving sorafenib died from in[ ]r patients receiving sunitinib died, with one death due to each of neurological sequelae, sequelae of gastric perforation, pul[ ]. Revised dosing still resulted in high toxicity. Adjuvant treatment with the VEGF receptor tyrosine kinase inhibitors sor[ ]efit relative to placebo in a definitive phase 3 study. Furthermore, substantial treatment discontinuation occurred because of[ ]. These results provide a strong rationale against the use of these drugs for high-risk kidney cancer in the adjuvant setting and[ ]ce might be independent of angiogenesis. US National Cancer Institute and ECOG-ACRIN Cancer Research Group, Pfize[ ]

LIVING EVIDENCE WORKFLOW



Study list panel

Renal Cell Carcinoma | Adjuvant Renal Cell Carcinoma | Extract by paper

9 studies (included in SR) — PMID, short #, first author name

#	PID	9 studies	Outcomes	
503	34407342	Toni K Choueiri et al 2021	7	**Adjuvant Pembrolizumab after Nephrectomy in Renal-Cell Carcinoma.**
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Interactive Extractor

Renal Cell Carcinoma | Adjuvant Renal Cell Carcinoma | Extract by paper

9 studies (included in SR) — PMID, short #, first author name

Naomi B Haas et al 2016 is selected in 7 outcomes

Outcomes list

Abstract | PDFs

2016-03-09 - Lancet

Adjuvant sunitinib or sorafenib for high-risk, non-metastatic renal-cell carcinoma (ECOG-ACRIN E2805): a double-blind, placebo-controlled, randomised, phase 3 trial.

Naomi B Haas, Judith Manola, Robert G Uzzo, Keith T Flaherty, Christopher G Wood, Christopher Kane, Michael Jewett, Janice P Dutcher, Michael B Atkins, Michael Pins, George Wilding, David Cella, Lynne Wagner, Surena Matin, Timothy M Kuzel, Wade J Sexton, Yu-Ning Wong, Toni K Choueiri, Roberto Pili, Igor Puzanov, Manish Kohli, Walter Stadler, Michael Carducci, Robert Coomes, Robert S DiPaola

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× Highlighted **1·02**

Result

TE

Lower CI

Upper CI

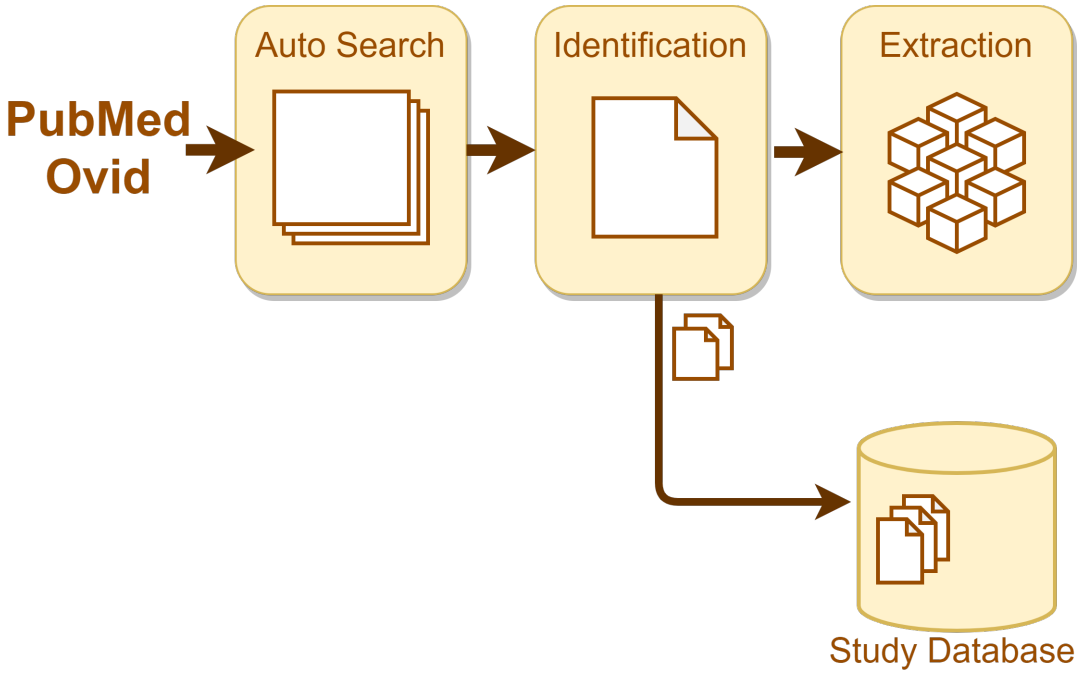
Detail

Survival in Control

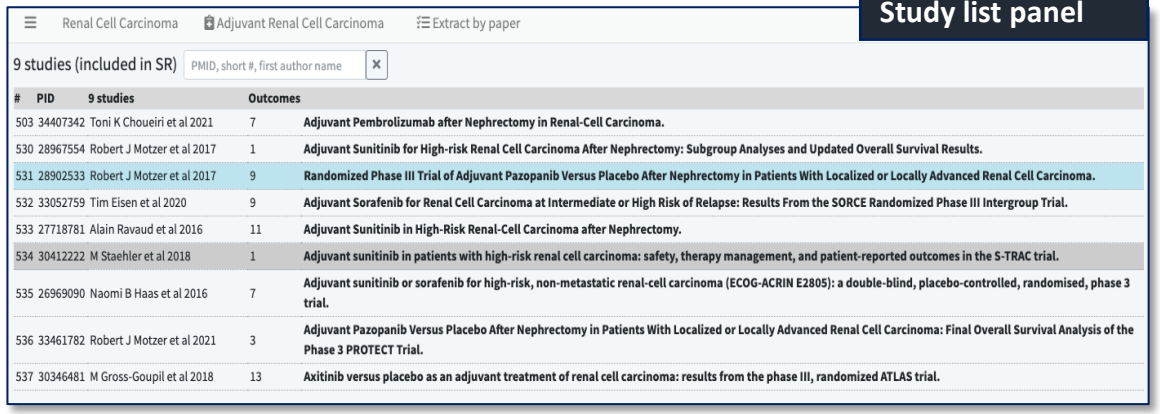
Ec

Et

LIVING EVIDENCE WORKFLOW



Study list panel



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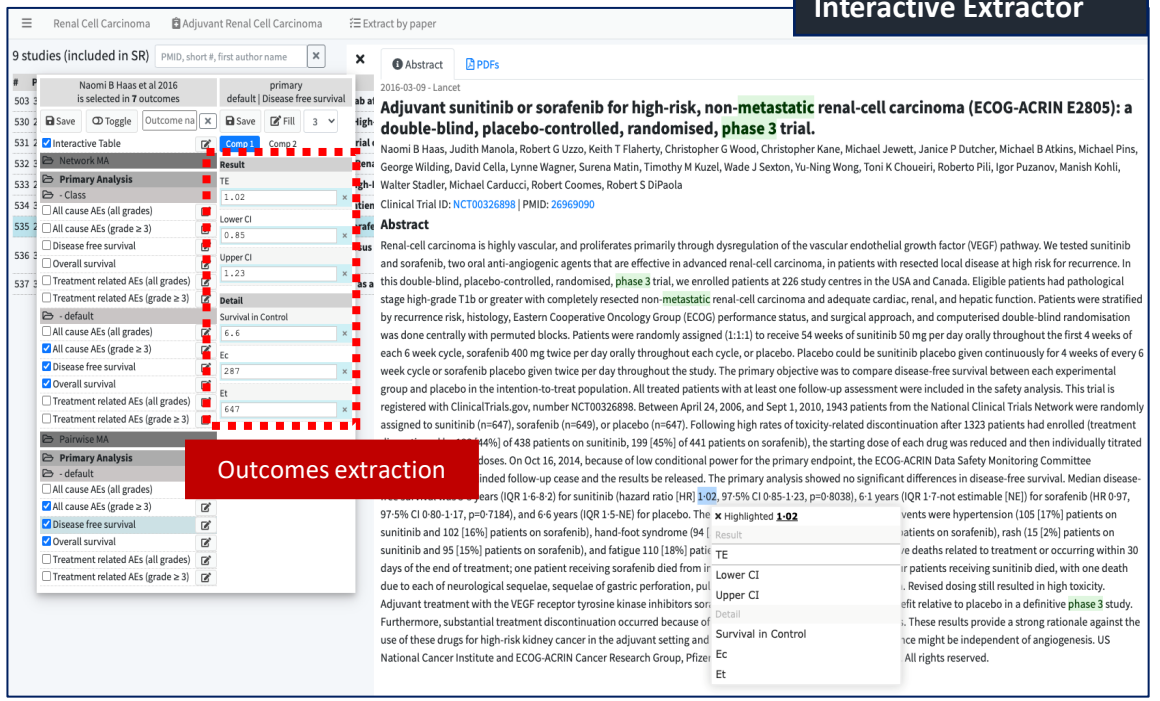
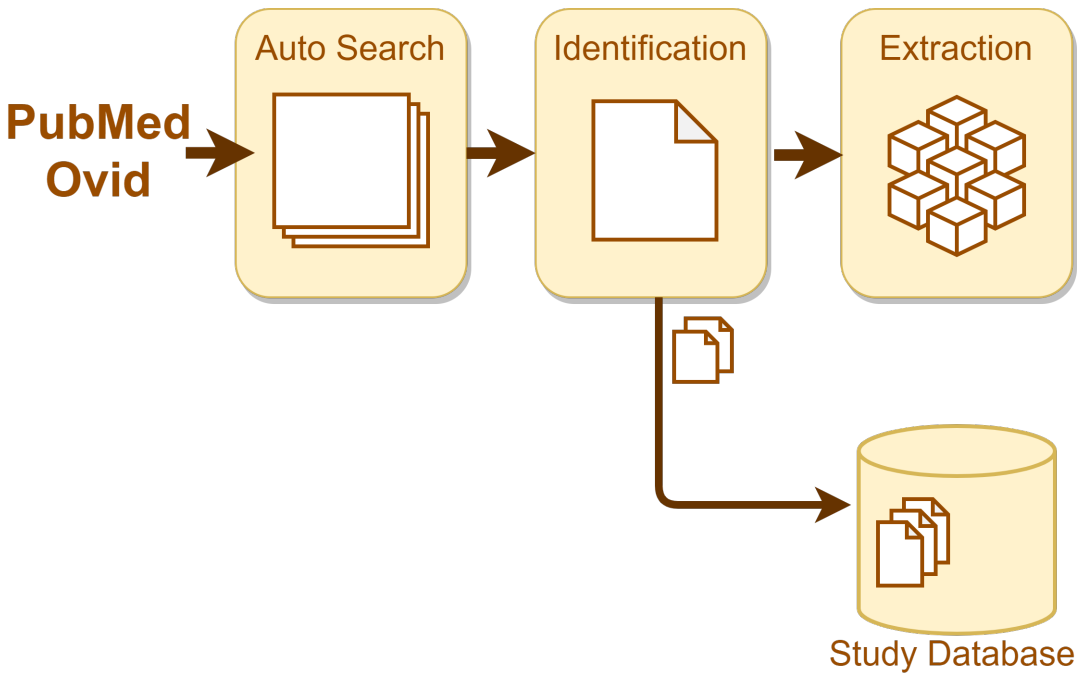
Interactive Extractor



LIVING EVIDENCE WORKFLOW



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Interactive Extractor

Text panel

Renal Cell Carcinoma | Adjuvant Renal Cell Carcinoma | Extract by paper

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Naomi B Haas et al 2016 is selected in 7 outcomes

Save | Toggle | Outcome na

Interactive Table

Network MA

Primary Analysis

- Class

All cause AEs (all grades)
All cause AEs (grade ≥ 3)
Disease free survival
Overall survival
Treatment related AEs (all grades)
Treatment related AEs (grade ≥ 3)

- default

All cause AEs (all grades)
All cause AEs (grade ≥ 3)
Disease free survival
Overall survival
Treatment related AEs (all grades)
Treatment related AEs (grade ≥ 3)

Pairwise MA

Primary Analysis

- default

All cause AEs (all grades)
All cause AEs (grade ≥ 3)
Disease free survival
Overall survival
Treatment related AEs (all grades)
Treatment related AEs (grade ≥ 3)

primary
default | Disease free survival

Save | Fill | 3

Comp 1 | Comp 2

Result

TE: 1.02

Lower CI: 0.85

Upper CI: 1.23

Detail

Survival in Control: 6.6

Ec: 287

Et: 647

Abstract | PDFs

2016-05-09 - Lancet

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× Highlighted **1-02**

Result

TE

Lower CI

Upper CI

Detail

Survival in Control

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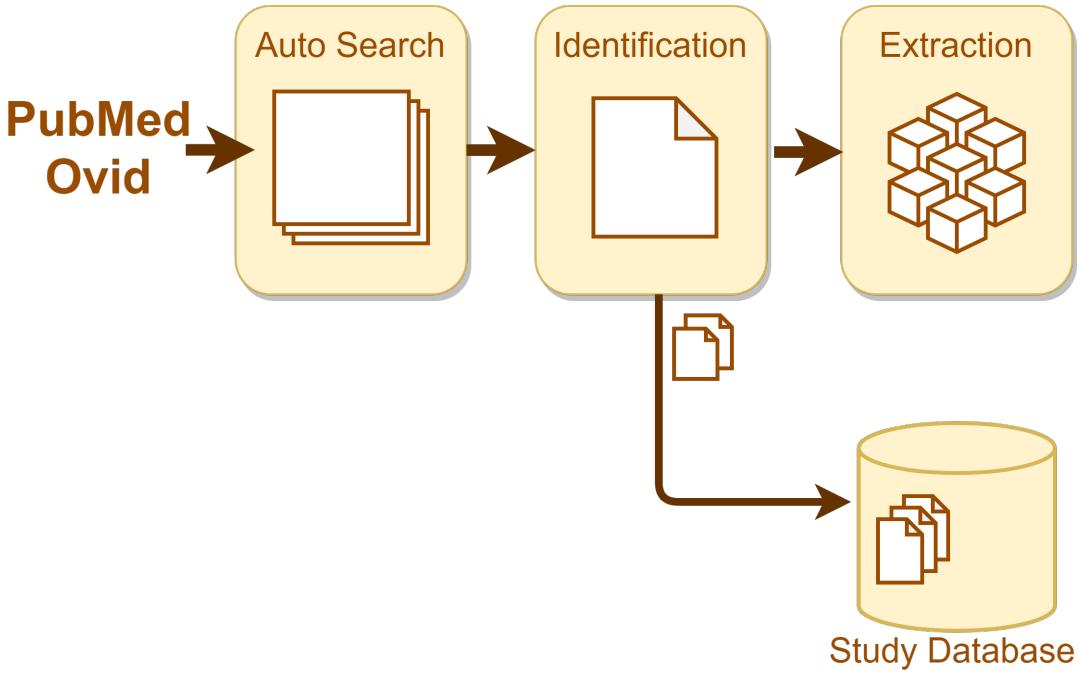
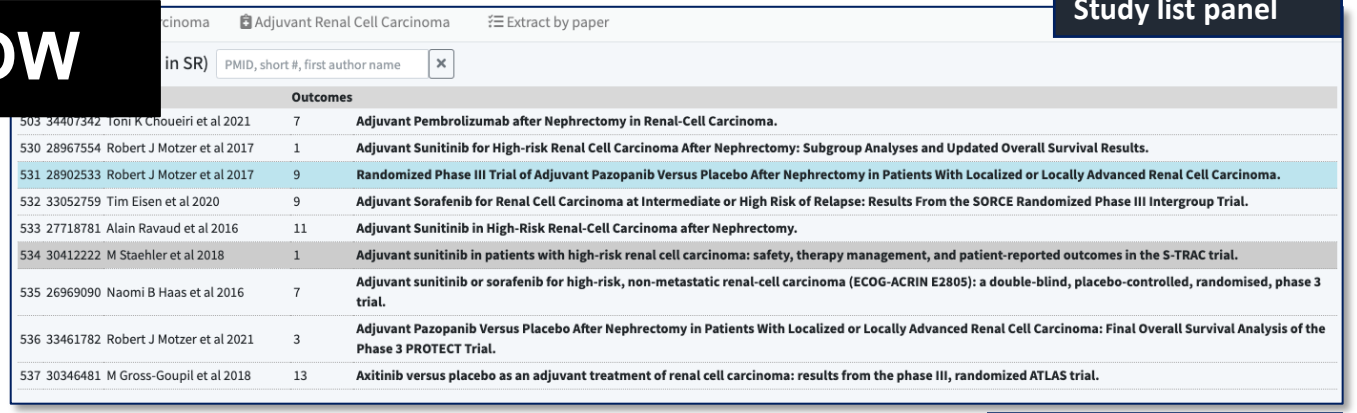
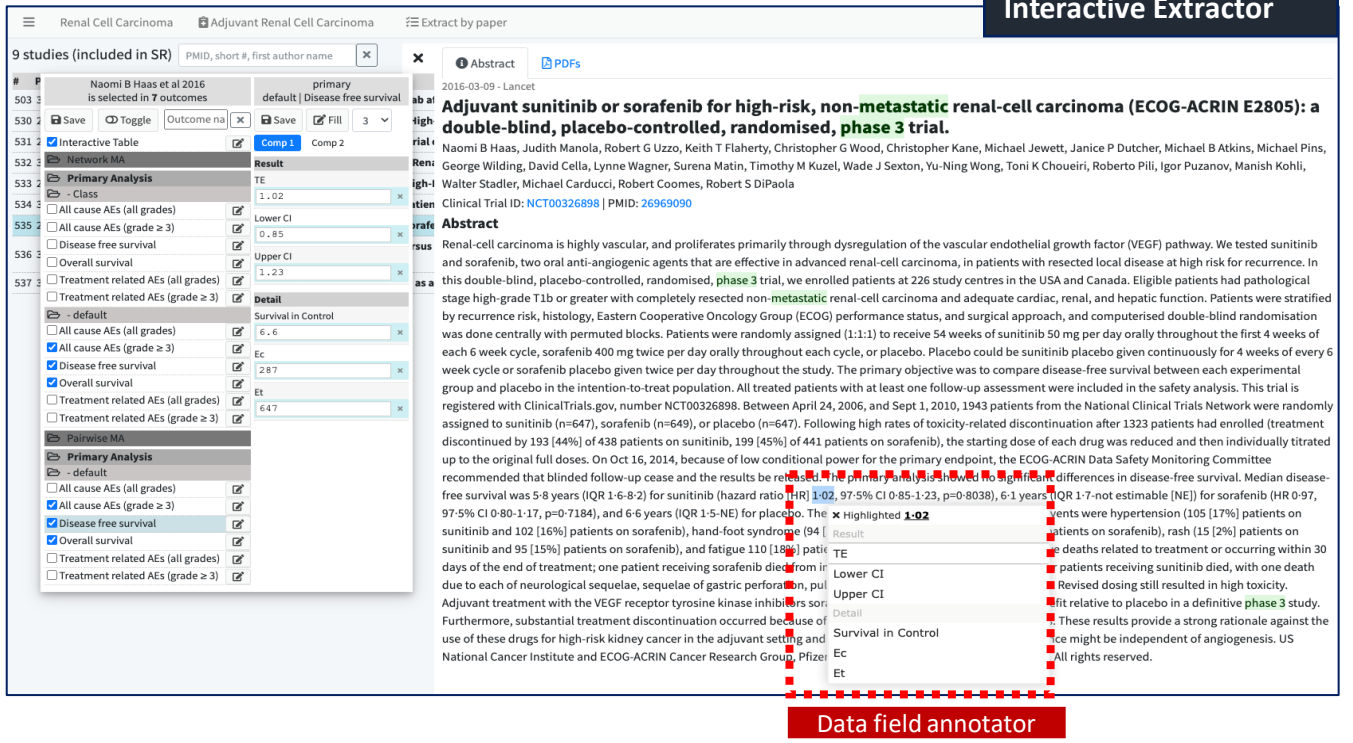
LIVING EVIDENCE WORKFLOW



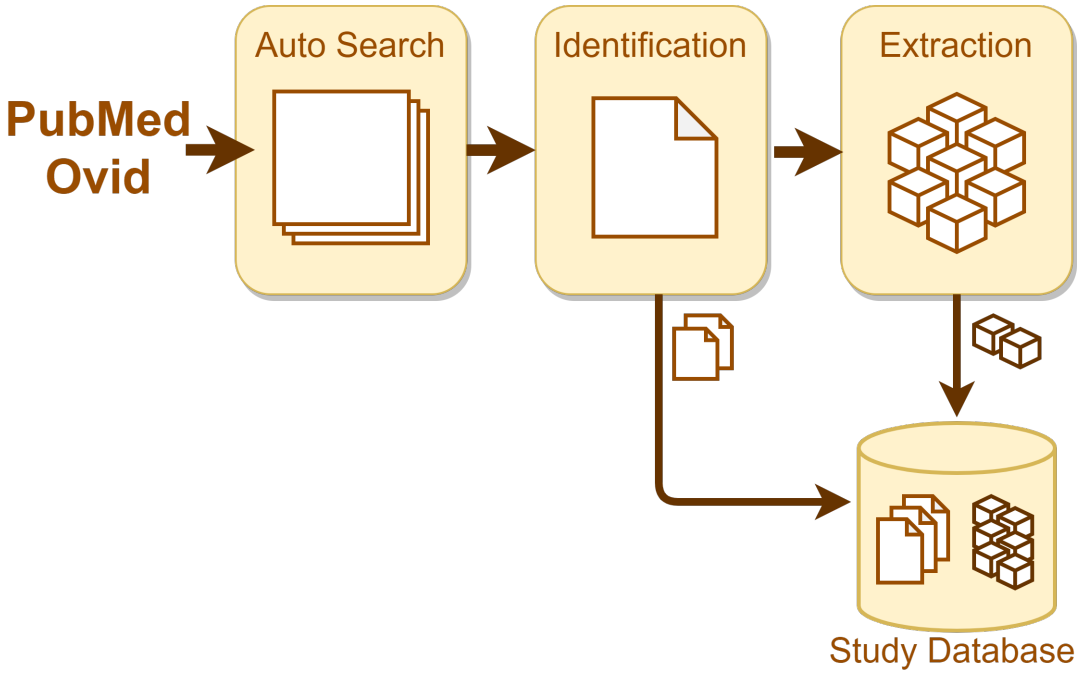
Study list panel



Interactive Extractor



LIVING EVIDENCE WORKFLOW



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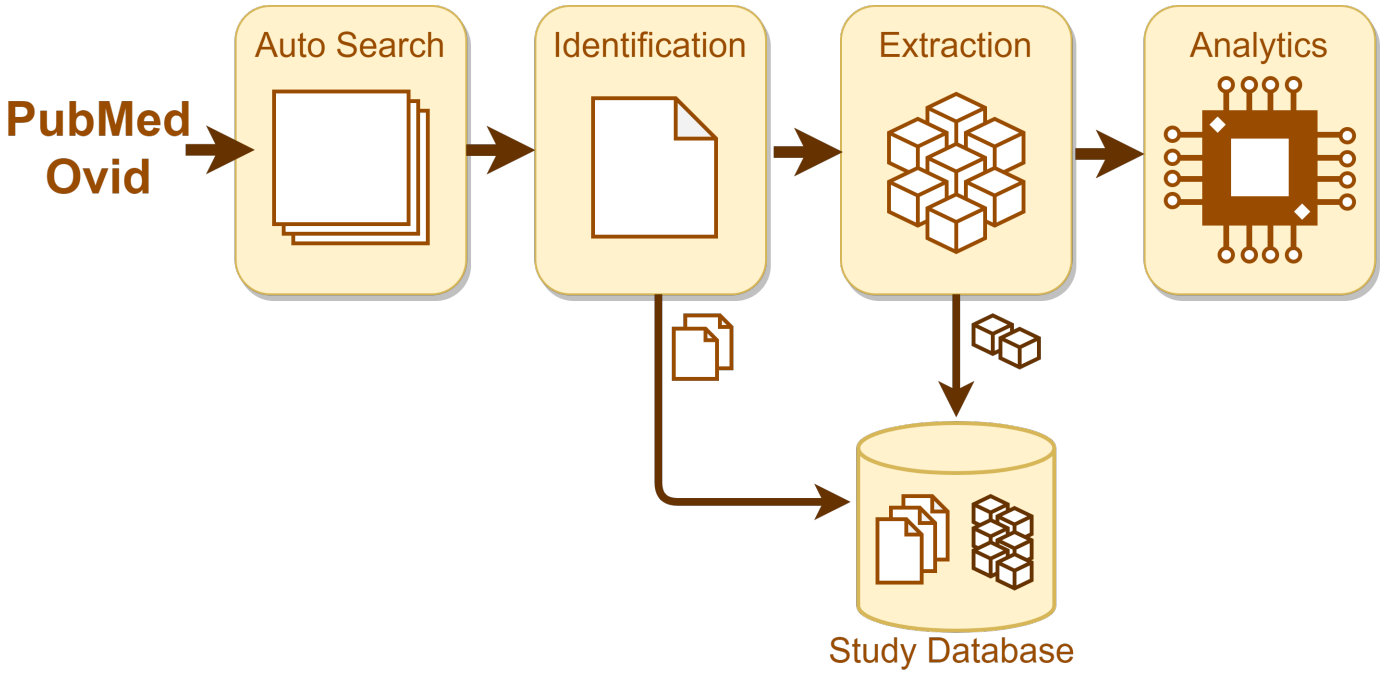

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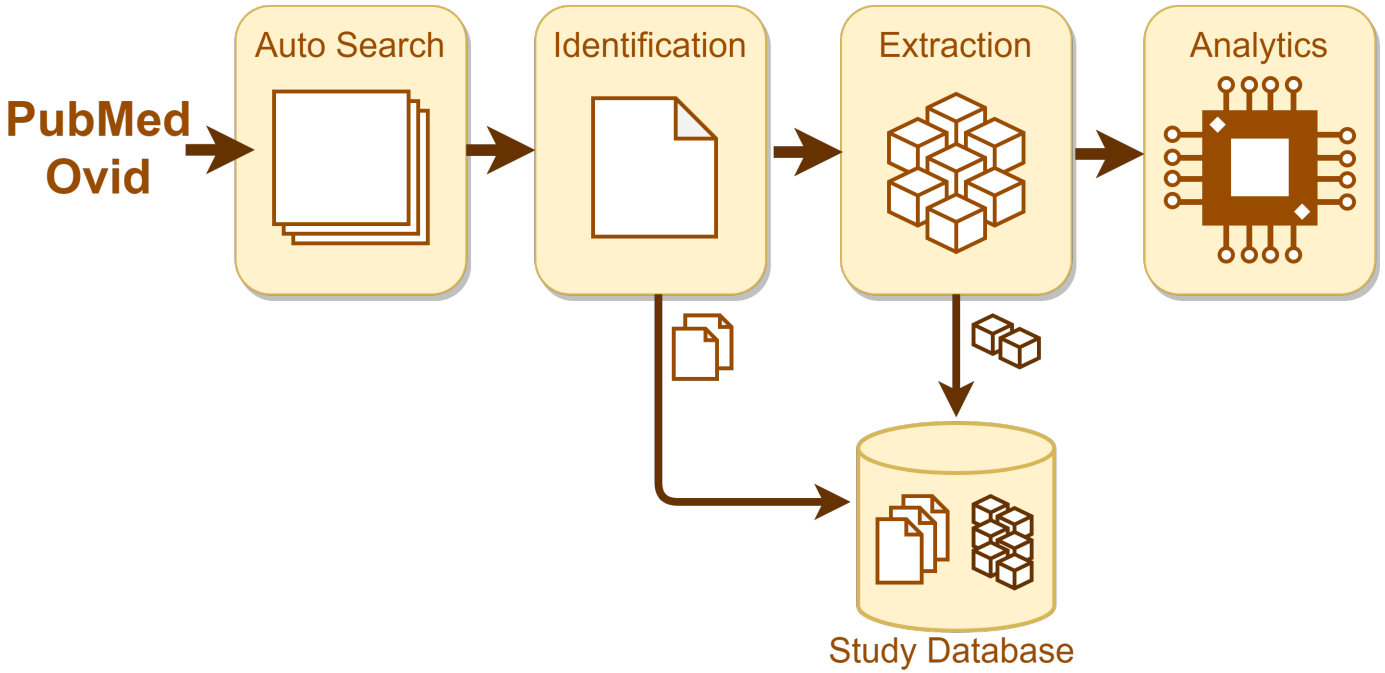

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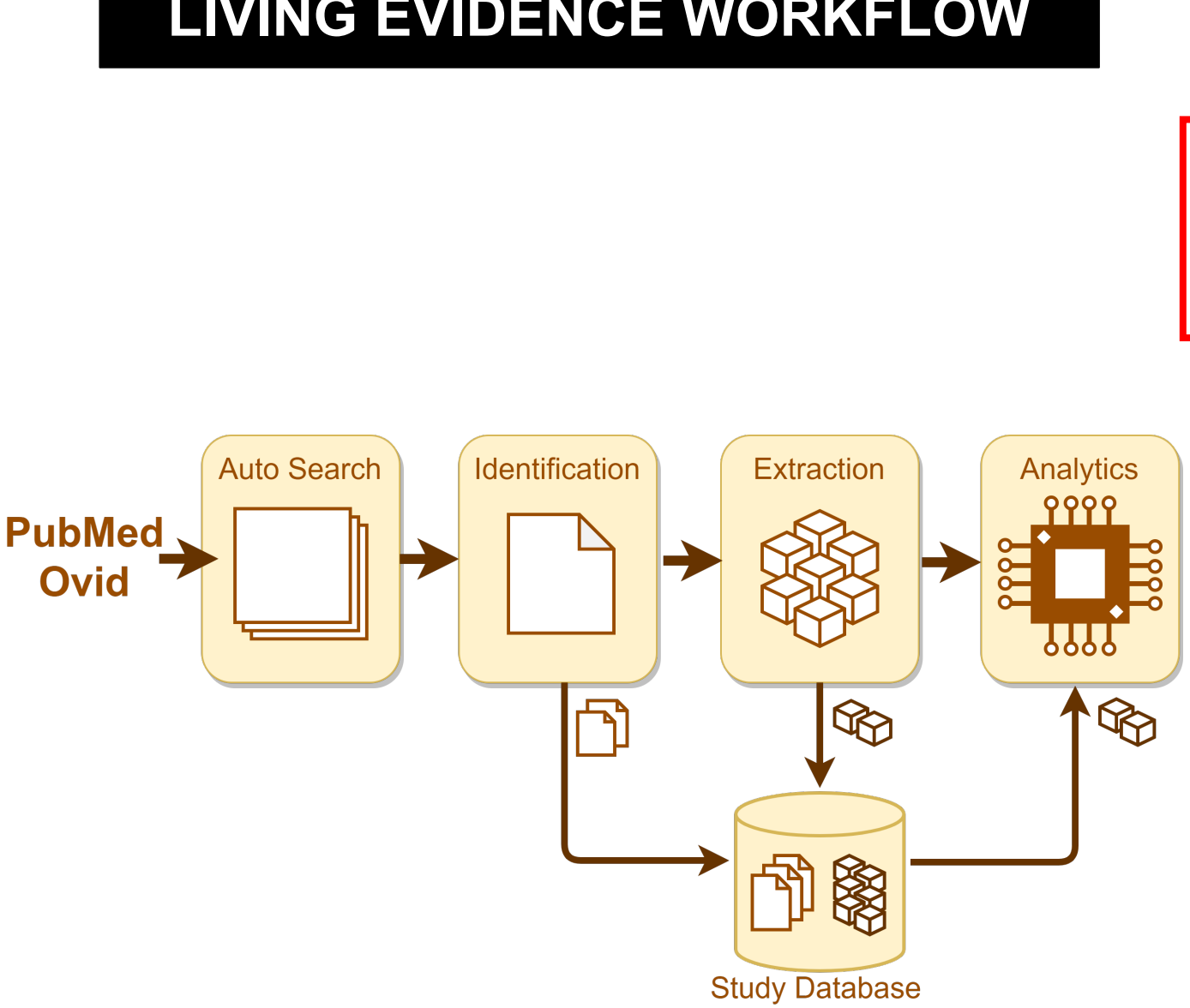
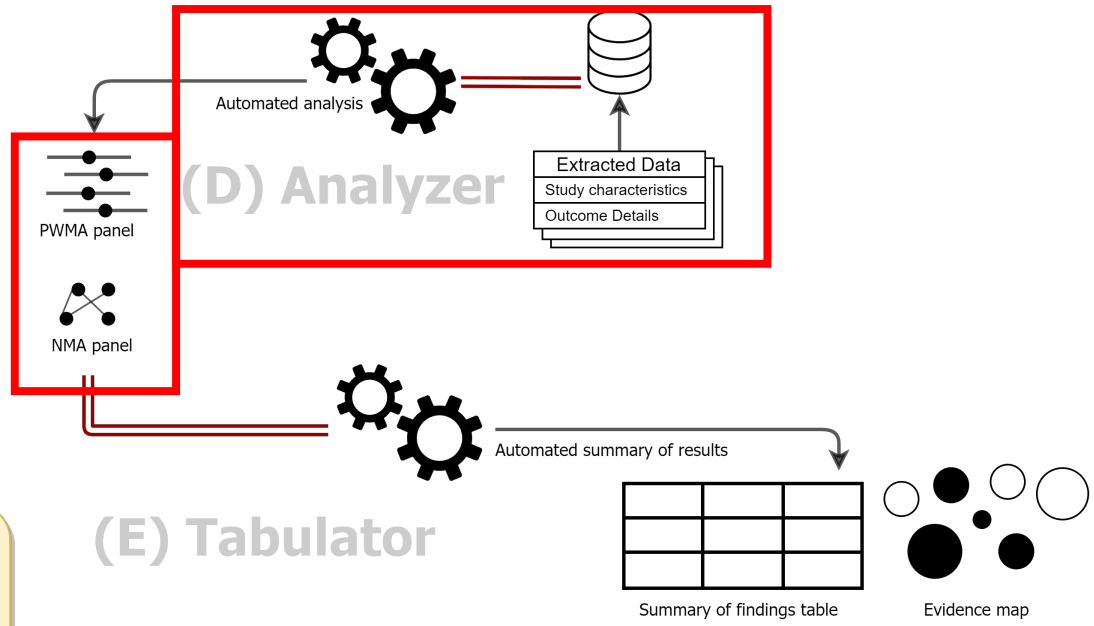




LIVING EVIDENCE WORKFLOW

DATASET

Select Data File Choose File ORR.xlsx

Upload & Read Data File

Input Data Summary

Filename: ORR.xlsx

Input Format: **PRIM_CAT_RAW** format

Studies: **3** studies of 3 lines

Treatment: **Axi-cel**

Control: **SOC**

SETTINGS

Pairwise Analysis Method:	Primary Analysis
Model:	Random-Effect
Measure of Effect:	Relative Risk
Pooling Method:	Mantel-Haenszel
Tau Estimation Method:	DerSimonian-Laird
Hartung-Knapp Adjustment:	Yes
Prediction Interval:	No
Sensitivity Analysis:	○ Yes ◉ No
Cumulative Meta-Analysis:	○ Yes ◉ No

Analyze

Analysis parameters

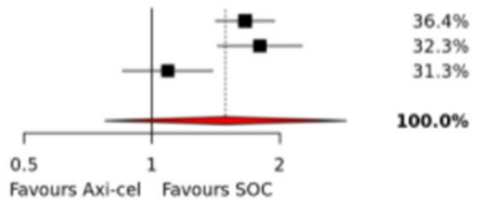
PAIRWISE META-ANALYSIS RESULTS

Analysis Result | Download Figure

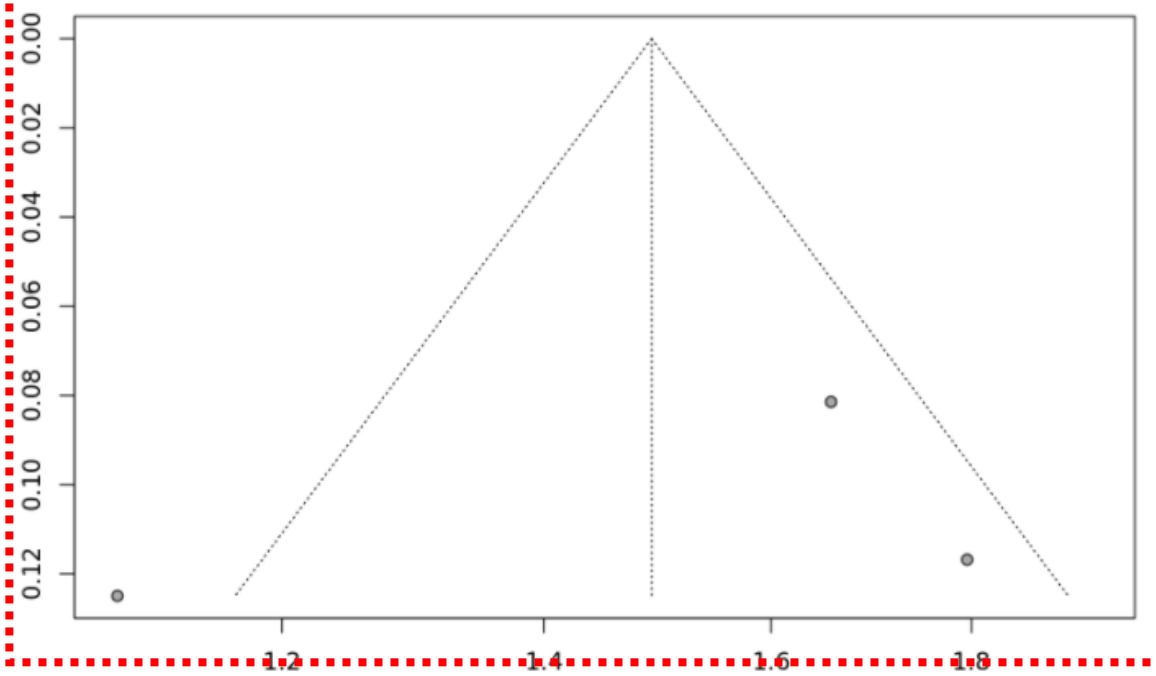
Results pane

Study	Axi-cel Events	Axi-cel Total	SOC Events	SOC Total	RR	95%-CI	Relative weight
ZUMA 7	150	180	90	179	1.66	[1.41; 1.94]	36.4%
TRANSFORM	79	92	44	92	1.80	[1.43; 2.26]	32.3%
BELINDA	75	162	68	160	1.09	[0.85; 1.39]	31.3%
Random effects model	**304**	**434**	**202**	**431**	**1.49**	**[0.78; 2.87]**	**100.0%**

Heterogeneity: $I^2 = 81\%$, $\tau^2 = 0.0481$, $p < 0.01$



Analysis Result Funnel Plot | Download Figure



LIVING EVIDENCE WORKFLOW

DATASET

Select Data File

Choose File | SOFTABL...LIZED.xlsx

Upload & Read Data File

Input Data Summary

SOFTABLE_NMA_DATA_FINALIZED.xlsx

HRLU format

8 treats: ADT, E+D+ADT, DARO+D+ADT, APA+D+ADT, API+ADT, D+ADT, AAP+D+ADT, E+AAP+ADT

17 studies of 17 lines

SETTINGS

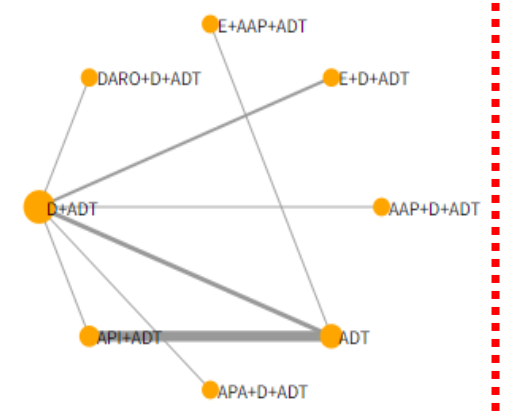
Input Format:	HR, Lower, L
Analysis Method:	Frequentist
Measure of Effect:	Hazard Ratio
Ref. Treatment:	D+ADT
Fixed / Random:	Fixed Effect
Which is Better:	Lower is Bet

Analyze

Analysis parameters

Network plot

NETWORK PLOT | Save PNG

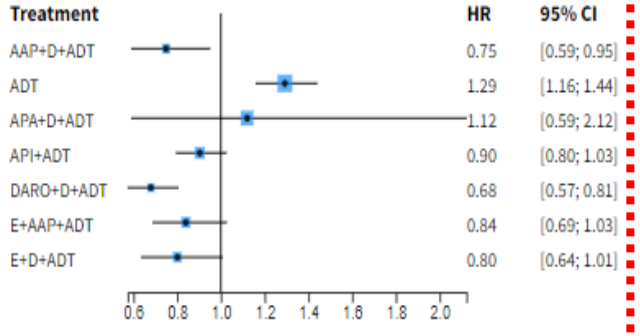


Forest plot

FOREST PLOT | Save PNG

Comparison vs 'D+ADT'

Fixed Effect Model



Rank table

RANK TABLE | Save CSV

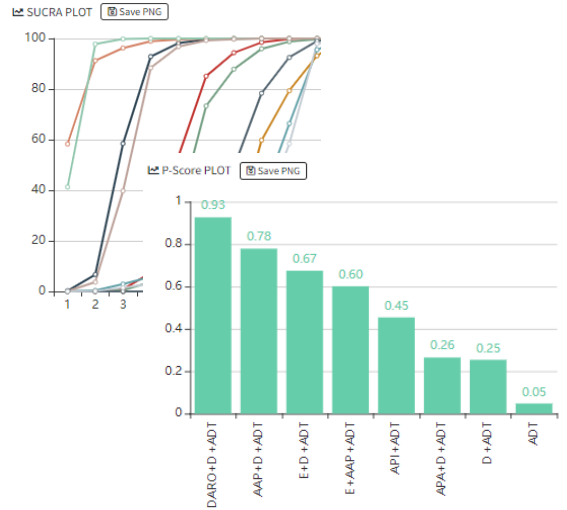
Treatment	P-Score	Rank
DARO+D+ADT	0.9263	1
AAP+D+ADT	0.7785	2
E+D+ADT	0.6743	3
E+AAP+ADT	0.6011	4
API+ADT	0.4539	5
APA+D+ADT	0.2647	6
D+ADT	0.2538	7
ADT	0.0475	8

League table

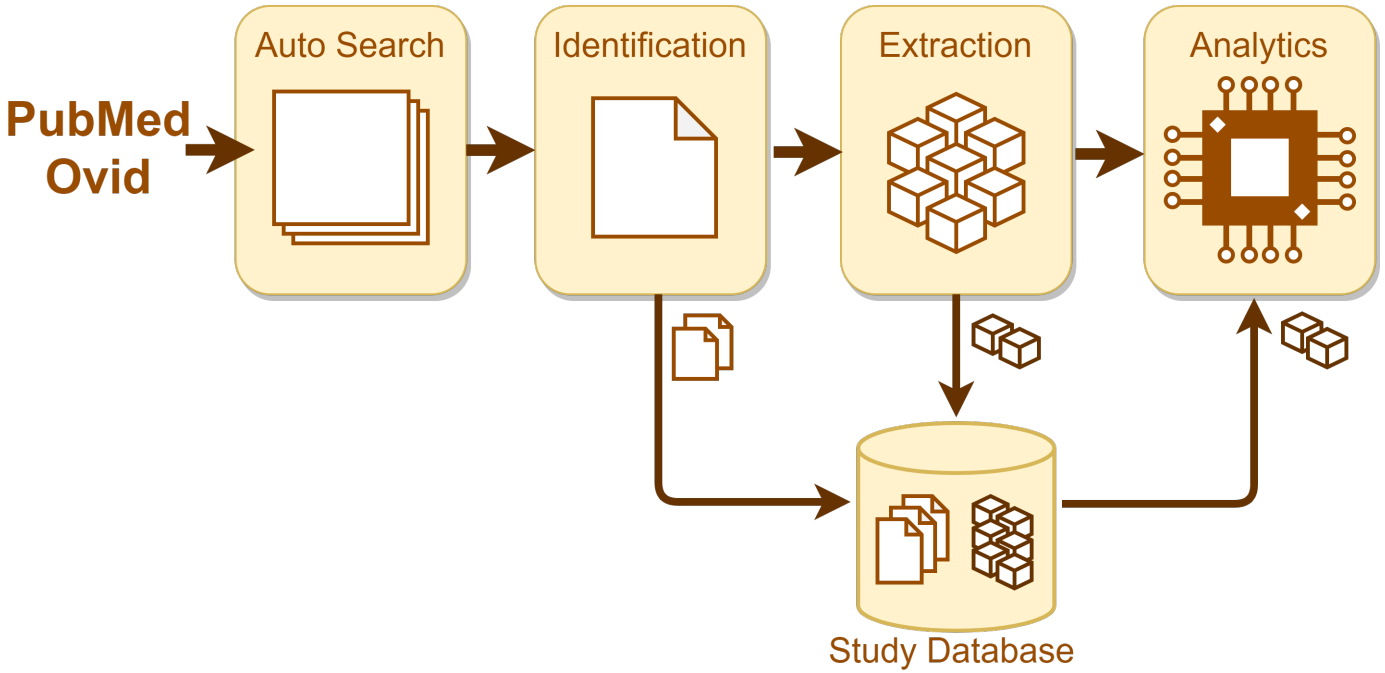
LEAGUE TABLE | Save PNG

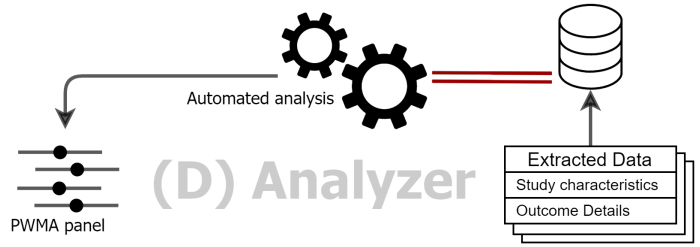
Comparator \ Treatments	AAP+D+ADT	ADT	APA+D+ADT	API+ADT	D+ADT	DARO+D+ADT	E+AAP+ADT	E+D+ADT
AAP+D+ADT		1.72 (1.33, 2.22)	1.49 (0.75, 2.94)	1.20 (0.92, 1.59)	1.33 (1.05, 1.69)	0.91 (0.68, 1.22)	1.12 (0.82, 1.54)	1.06 (0.77, 1.49)
ADT	0.58 (0.45, 0.75)		0.87 (0.45, 1.67)	0.70 (0.65, 0.75)	0.78 (0.69, 0.86)	0.53 (0.43, 0.65)	0.65 (0.55, 0.77)	0.62 (0.48, 0.80)
APA+D+ADT	0.67 (0.34, 1.33)	1.15 (0.60, 2.21)		0.81 (0.42, 1.54)	0.89 (0.47, 1.69)	0.61 (0.31, 1.18)	0.75 (0.38, 1.47)	0.71 (0.36, 1.41)
API+ADT	0.83 (0.63, 1.09)	1.43 (1.33, 1.54)	1.24 (0.65, 2.38)		1.11 (0.97, 1.25)	0.75 (0.61, 0.93)	0.93 (0.78, 1.12)	0.88 (0.68, 1.15)
D+ADT	0.75 (0.59, 0.95)	1.29 (1.16, 1.44)	1.12 (0.59, 2.12)	0.90 (0.80, 1.03)		0.68 (0.57, 0.81)	0.84 (0.69, 1.03)	0.80 (0.64, 1.01)
DARO+D+ADT	1.10 (0.82, 1.48)	1.90 (1.55, 2.32)	1.65 (0.85, 3.19)	1.33 (1.08, 1.64)	1.47 (1.24, 1.74)		1.23 (0.95, 1.61)	1.18 (0.88, 1.56)
E+AAP+ADT	0.89 (0.65, 1.22)	1.54 (1.30, 1.82)	1.33 (0.68, 2.60)	1.08 (0.89, 1.29)	1.19 (0.97, 1.45)	0.81 (0.62, 1.05)		0.95 (0.70, 1.30)
E+D+ADT	0.94 (0.67, 1.30)	1.61 (1.25, 2.08)	1.40 (0.71, 2.76)	1.13 (0.87, 1.47)	1.25 (0.99, 1.57)	0.85 (0.64, 1.13)	1.05 (0.77, 1.42)	

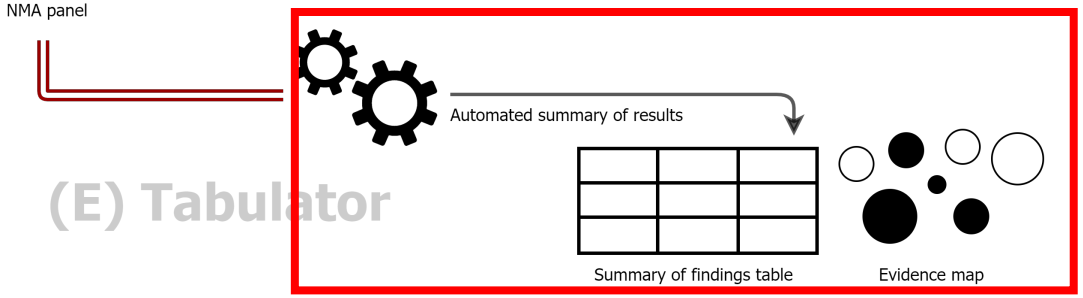
Rank plots



LIVING EVIDENCE WORKFLOW







LIVING EVIDENCE WORKFLOW

Interactive manager

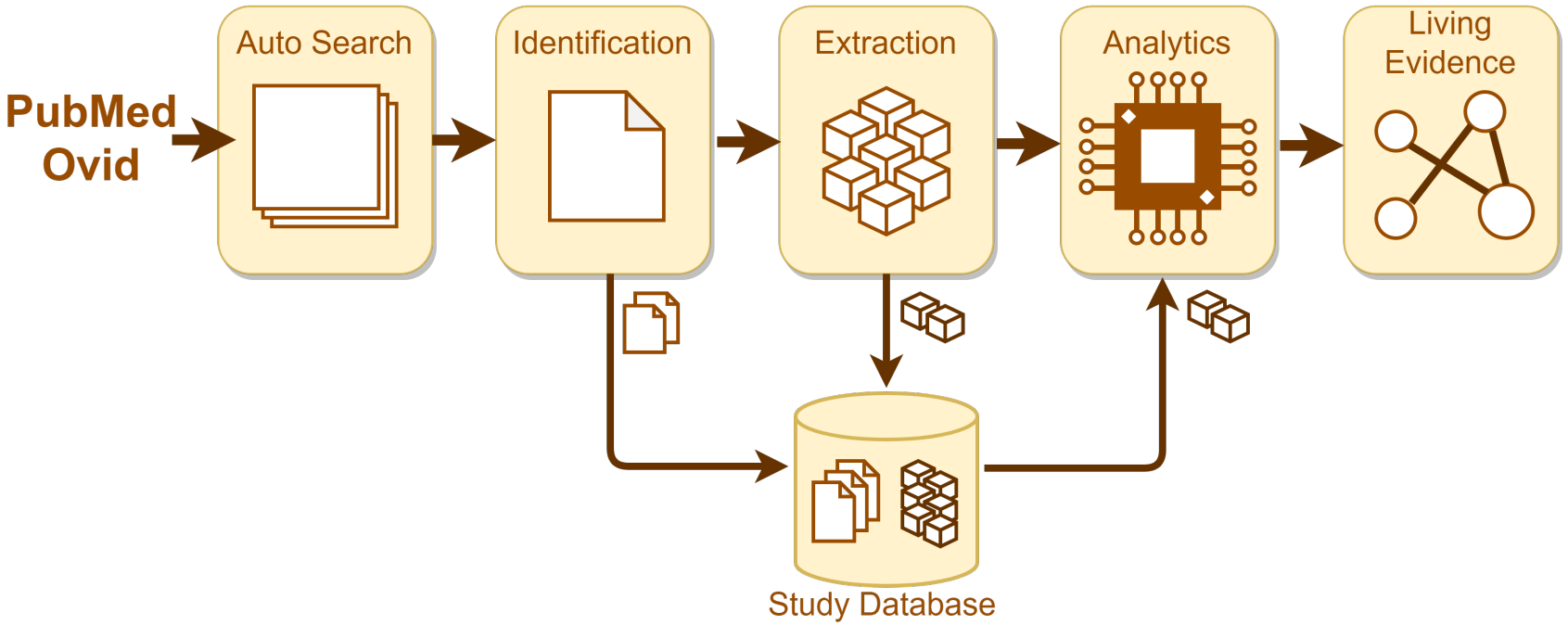
Choose reference treatment, measure of effect, and denominator for absolute effect.

Comparator: ADT | Show survival data: No | Display risks per: 1000 | Color guide

Evidence profile

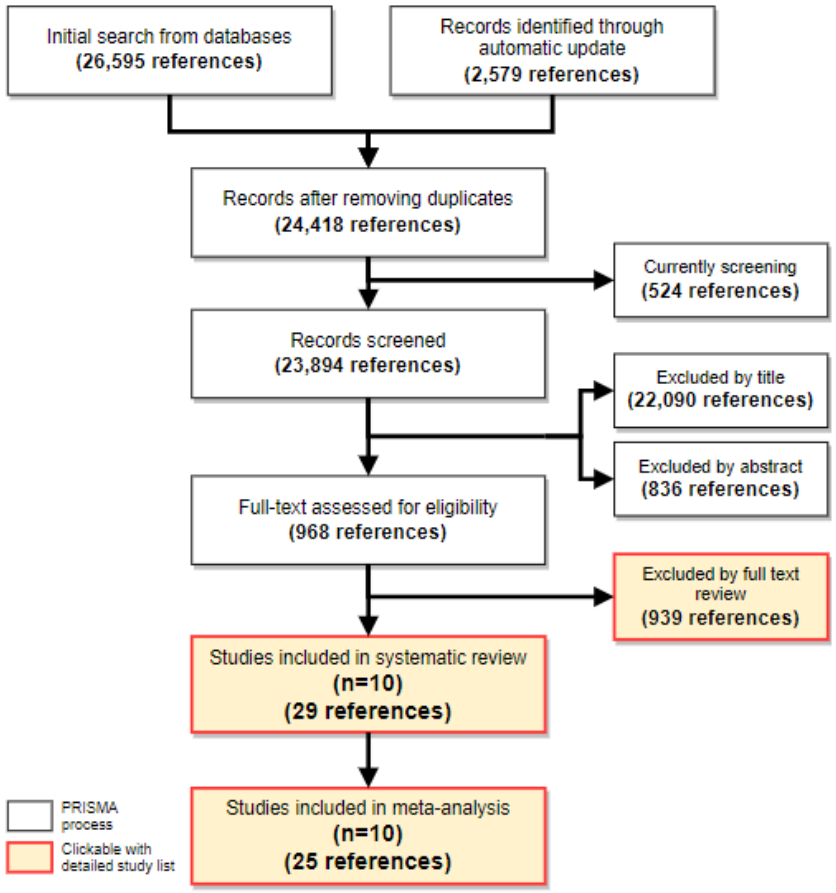
Outcome	Comparator: ADT	Darolutamide + Docetaxel	Abiraterone acetate + Docetaxel	Apalutamide	Enzalutamide	Abiraterone acetate	Docetaxel	TAK+ADT	NSAA+ADT
Overall survival (all patients) (HR)	549 per 1000 Rank 9	208 fewer Rank 1	179 fewer Rank 2	145 fewer Rank 3	141 fewer Rank 5	145 fewer Rank 4	91 fewer Rank 6	72 fewer Rank 7	21 fewer Rank 8
Progression free survival (all patients) (HR)	559 per 1000 Rank 8	NA NA	316 fewer Rank 1	228 fewer Rank 3	285 fewer Rank 2	191 fewer Rank 4	130 fewer Rank 6	189 fewer Rank 5	11 fewer Rank 7
Adverse events (grade ≥ 3) (RR)	366 per 1000 Rank 3	172 more Rank 7	256 more Rank 8	70 more Rank 4	17 fewer Rank 2	139 more Rank 5	150 more Rank 6	448 more Rank 9	103 fewer Rank 1
Overall survival (high volume disease) (HR)	586 per 1000 Rank 7	NA NA	218 fewer Rank 1	126 fewer Rank 4	146 fewer Rank 3	170 fewer Rank 2	114 fewer Rank 5	NA NA	66 fewer Rank 6
Overall survival (low volume disease) (HR)	378 per 1000 Rank 6	NA NA	78 fewer Rank 4	159 fewer Rank 1	110 fewer Rank 3	130 fewer Rank 2	27 fewer Rank 5	NA NA	62 more Rank 7
Progression free survival (high volume disease) (HR)	644 per 1000 Rank 7	NA NA	393 fewer Rank 1	223 fewer Rank 4	286 fewer Rank 2	266 fewer Rank 3	181 fewer Rank 5	NA NA	18 fewer Rank 6
Progression free survival (low volume disease) (HR)	429 per 1000 Rank 7	NA NA	215 fewer Rank 3	246 fewer Rank 2	298 fewer Rank 1	193 fewer Rank 4	89 fewer Rank 5	NA NA	56 fewer Rank 6
Overall survival (synchronous disease) (HR)	492 per 1000 Rank 8	185 fewer Rank 1	172 fewer Rank 2	123 fewer Rank 5	145 fewer Rank 3	145 fewer Rank 4	88 fewer Rank 6	NA NA	35 fewer Rank 7
Overall survival (metachronous disease) (HR)	357 per 1000 Rank 6	143 fewer Rank 2	NA NA	199 fewer Rank 1	88 fewer Rank 3	NA NA	29 fewer Rank 4	NA NA	0 fewer Rank 5
Progression-free survival (metachronous disease) (HR)	326 per 1000 Rank 4	NA NA	NA NA	177 fewer Rank 1	173 fewer Rank 2	NA NA	NA NA	NA NA	0 more Rank 3

LIVING EVIDENCE WORKFLOW



LIVING EVIDENCE WORKFLOW

Living Interactive PRISMA



Study List | Final number in quantitative synthesis (meta-analysis)

10 clinical trials, 25 references

1 Abiraterone plus Prednisone in Metastatic, Castration-Sensitive Prostate Cancer
Fizazi, Karim; Tran, NamPhuong; Fein, Luis; Matsubara, Nobuaki; Rodriguez-Antolin, Alfredo; Alekseev, Boris Y.; Ozguroglu, Mustafa; Ye, Dingwei; Feyerabend, Susan; Protheroe, Andrew; De Porre, Peter; Kheoh, Thian; Park, Youn C.; Todd, Mary B.; Chi, Kim N.; Latitude Investigators
2017 07 27 **New England Journal of Medicine; p. 352-360; vol. 377; (4)** . 28578607 NCT01715285

2 Apalutamide for Metastatic, Castration-Sensitive Prostate Cancer
Chi, Kim N.; Agarwal, Neeraj; Bjartell, Anders; Chung, Byung Ha; Pereira de Santana Gomes, Andrea J.; Given, Robert; Juarez Soto, Alvaro; Merseburger, Axel S.; Ozguroglu, Mustafa; Uemura, Hirotsugu; Ye, Dingwei; Deprince, Kris; Naini, Vahid; Li, Jinhui; Cheng, Shinta; Yu, Margaret K.; Zhang, Ke; Larsen, Julie S.; McCarthy, Sharon; Chowdhury, Simon; Titan Investigators
2019 07 04 **New England Journal of Medicine; p. 13-24; vol. 381; (1)** . 31150574 NCT02489318

3 Enzalutamide with Standard First-Line Therapy in Metastatic Prostate Cancer
Davis, Ian D.; Martin, Andrew J.; Stockler, Martin R.; Begbie, Stephen; Chi, Kim N.; Chowdhury, Simon; Coskinas, Xanthi; Frydenberg, Mark; Hague, Wendy E.; Horvath, Lisa G.; Joshua, Anthony M.; Lawrence, Nicola J.; Marx, Gavin; McCaffrey, John; McDermott, Ray; McJannett, Margaret; North, Scott A.; Parnis, Francis; Parulekar, Wendy; Pook, David W.; Reaume, M. Neil; Sandhu, Shahneen K.; Tan, Alvin; Tan, T. Hsiang; Thomson, Alastair; Tu, Emily; Vera-Badillo, Francisco; Williams, Scott G.; Yip, Sonia; Zhang, Alison Y.; Zielinski, Robert R.; Sweeney, Christopher J.; Enzamet Trial Investigators; the, Australian; New Zealand, Urogenital; Prostate Cancer Trials, Group
2019 07 11 **New England Journal of Medicine; p. 121-131; vol. 381; (2)** . 31157964 NCT02446405

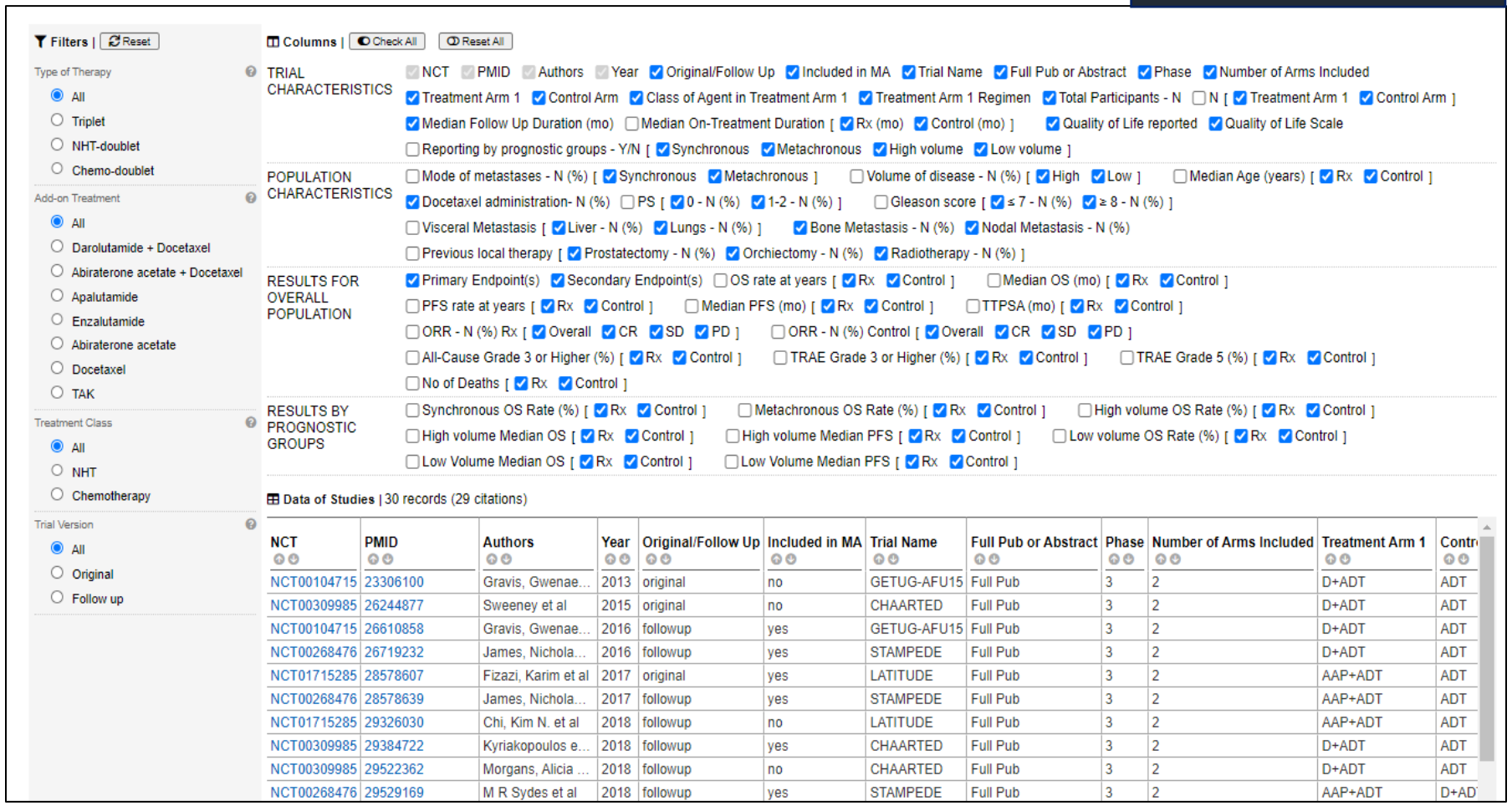
4 ARCHES: A Randomized, Phase III Study of Androgen Deprivation Therapy With Enzalutamide or Placebo in Men With Metastatic Hormone-Sensitive Prostate Cancer.
Andrew J Armstrong, Russell Z Szmulewitz, Daniel P Petrylak, Jeffrey Holzbeierlein, Arnauld Villers, Arun Azad, Antonio Alcaraz, Boris Alekseev, Taro Iguchi, Neal D Shore, Brad Rosbrook, Jennifer Sugg, Benoit Baron, Lucy Chen, Arnulf Stenzl
2019-07-22 **J Clin Oncol** . 31329516 NCT02677896

5 Androgen Deprivation Therapy (ADT) Plus Docetaxel Versus ADT Alone in Metastatic Non castrate Prostate Cancer: Impact of Metastatic Burden and Long-term Survival Analysis of the Randomized Phase 3 GETUG-AFU15 Trial
Gravis, Gwenaelle; Boher, Jean-Marie; Joly, Florence; Soulie, Michel; Albiges, Laurence; Priou, Franck; Latorzeff, Igor; Delva, Remy; Krakowski, Ivan; Laguerre, Brigitte; Rolland, Frederic; Theodore, Christine; Deplanque, Gael; Ferrero, Jean-Marc; Culine, Stephane; Mourey, Loic; Beuzeboc, Philippe; Habibian, Muriel; Oudard, Stephane; Fizazi, Karim; Getug,
2016 08 **European Urology; p. 256-62; vol. 70; (2)** . 26610858 NCT00104715

6 Addition of docetaxel, zoledronic acid, or both to first-line long-term hormone therapy in prostate cancer (STAMPEDE): survival results from an adaptive, multiarm, multistage, platform randomised controlled trial

LIVING EVIDENCE WORKFLOW

Interactive Summary Table



Filters | Reset

Type of Therapy
- (•) All
- ( ) Triplet
- ( ) NHT-doublet
- ( ) Chemo-doublet

Add-on Treatment
- (•) All
- ( ) Darolutamide + Docetaxel
- ( ) Abiraterone acetate + Docetaxel
- ( ) Apalutamide
- ( ) Enzalutamide
- ( ) Abiraterone acetate
- ( ) Docetaxel
- ( ) TAK

Treatment Class
- (•) All
- ( ) NHT
- ( ) Chemotherapy

Trial Version
- (•) All
- ( ) Original
- ( ) Follow up

Columns | Check All | Reset All

TRIAL CHARACTERISTICS
[x] NCT [x] PMID [x] Authors [x] Year [x] Original/Follow Up [x] Included in MA [x] Trial Name [x] Full Pub or Abstract [x] Phase [x] Number of Arms Included
[x] Treatment Arm 1 [x] Control Arm [x] Class of Agent in Treatment Arm 1 [x] Treatment Arm 1 Regimen [x] Total Participants - N [ ] N [[x] Treatment Arm 1 [x] Control Arm]
[x] Median Follow Up Duration (mo) [ ] Median On-Treatment Duration [[x] Rx (mo) [x] Control (mo)] [x] Quality of Life reported [x] Quality of Life Scale
[ ] Reporting by prognostic groups - Y/N [[x] Synchronous [x] Metachronous [x] High volume [x] Low volume]

POPULATION CHARACTERISTICS
[ ] Mode of metastases - N (%) [[x] Synchronous [x] Metachronous] [ ] Volume of disease - N (%) [[x] High [x] Low] [ ] Median Age (years) [[x] Rx [x] Control]
[x] Docetaxel administration- N (%) [ ] PS [[x] 0 - N (%) [x] 1-2 - N (%)] [ ] Gleason score [[x] ≤ 7 - N (%) [x] ≥ 8 - N (%)]
[ ] Visceral Metastasis [[x] Liver - N (%) [x] Lungs - N (%)] [x] Bone Metastasis - N (%) [x] Nodal Metastasis - N (%)
[ ] Previous local therapy [[x] Prostatectomy - N (%) [x] Orchiectomy - N (%) [x] Radiotherapy - N (%)]

RESULTS FOR OVERALL POPULATION
[x] Primary Endpoint(s) [x] Secondary Endpoint(s) [ ] OS rate at years [[x] Rx [x] Control] [ ] Median OS (mo) [[x] Rx [x] Control]
[ ] PFS rate at years [[x] Rx [x] Control] [ ] Median PFS (mo) [[x] Rx [x] Control] [ ] TTPSA (mo) [[x] Rx [x] Control]
[ ] ORR - N (%) Rx [[x] Overall [x] CR [x] SD [x] PD] [ ] ORR - N (%) Control [[x] Overall [x] CR [x] SD [x] PD]
[ ] All-Cause Grade 3 or Higher (%) [[x] Rx [x] Control] [ ] TRAE Grade 3 or Higher (%) [[x] Rx [x] Control] [ ] TRAE Grade 5 (%) [[x] Rx [x] Control]
[ ] No of Deaths [[x] Rx [x] Control]

RESULTS BY PROGNOSTIC GROUPS
[ ] Synchronous OS Rate (%) [[x] Rx [x] Control] [ ] Metachronous OS Rate (%) [[x] Rx [x] Control] [ ] High volume OS Rate (%) [[x] Rx [x] Control]
[ ] High volume Median OS [[x] Rx [x] Control] [ ] High volume Median PFS [[x] Rx [x] Control] [ ] Low volume OS Rate (%) [[x] Rx [x] Control]
[ ] Low Volume Median OS [[x] Rx [x] Control] [ ] Low Volume Median PFS [[x] Rx [x] Control]

Data of Studies | 30 records (29 citations)

NCT	PMID	Authors	Year	Original/Follow Up	Included in MA	Trial Name	Full Pub or Abstract	Phase	Number of Arms Included	Treatment Arm 1	Contr
NCT00104715	23306100	Gravis, Gwenae...	2013	original	no	GETUG-AFU15	Full Pub	3	2	D+ADT	ADT
NCT00309985	26244877	Sweeney et al	2015	original	no	CHAARTED	Full Pub	3	2	D+ADT	ADT
NCT00104715	26610858	Gravis, Gwenae...	2016	followup	yes	GETUG-AFU15	Full Pub	3	2	D+ADT	ADT
NCT00268476	26719232	James, Nichola...	2016	followup	yes	STAMPEDE	Full Pub	3	2	D+ADT	ADT
NCT01715285	28578607	Fizazi, Karim et al	2017	original	yes	LATITUDE	Full Pub	3	2	AAP+ADT	ADT
NCT00268476	28578639	James, Nichola...	2017	followup	yes	STAMPEDE	Full Pub	3	2	AAP+ADT	ADT
NCT01715285	29326030	Chi, Kim N. et al	2018	followup	no	LATITUDE	Full Pub	3	2	AAP+ADT	ADT
NCT00309985	29384722	Kyriakopoulos e...	2018	followup	yes	CHAARTED	Full Pub	3	2	D+ADT	ADT
NCT00309985	29522362	Morgans, Alicia ...	2018	followup	no	CHAARTED	Full Pub	3	2	D+ADT	ADT
NCT00268476	29529169	M R Sydes et al	2018	followup	yes	STAMPEDE	Full Pub	3	2	AAP+ADT	D+AD

LIVING EVIDENCE WORKFLOW

Interactive PWMA Panel

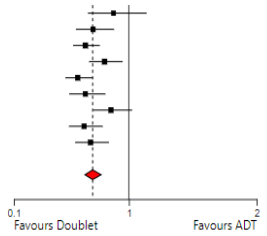
Primary Analysis

- **Overall survival (all patients)**
- Progression free survival (all patients)
- Adverse events (grade ≥ 3)

Forest Plot for Overall survival (all patients)

Study	HR	95% CI	Relative weight
Gravis, Gwenaelle et al 2016	0.88	[0.68; 1.14]	7.7%
Kyriakopoulos et al 2018	0.72	[0.59; 0.88]	10.2%
Fizazi, Karim et al 2019	0.66	[0.56; 0.77]	13.3%
Clarke, N. W. et al 2019	0.81	[0.69; 0.95]	13.1%
Nicholas D James et al 2022	0.60	[0.50; 0.71]	12.0%
Andrew J Armstrong et al 2022	0.66	[0.53; 0.82]	9.8%
Neeraj Agarwal et al 2022	0.86	[0.72; 1.02]	12.1%
Chi, Kim N. et al 2021	0.65	[0.53; 0.79]	10.5%
Davis, Ian D. et al 2022	0.70	[0.58; 0.84]	11.4%
Random effects model	**0.72**	**[0.66; 0.78]**	**100.0%**

Heterogeneity: I^2=48%, τ^2=0.0085, p=0.05



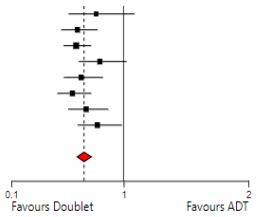
Sensitivity Analysis

- **Overall survival (high volume disease)**
- Overall survival (low volume disease)
- Progression free survival (high volume disease)
- Progression free survival (low volume disease)
- Overall survival (synchronous disease)
- Overall survival (metachronous disease)
- Progression-free survival (synchronous disease)
- Progression-free survival (metachronous disease)
- Overall survival (young)
- Overall survival (old)
- Progression free survival (young)
- Progression free survival (old)
- Overall survival (Gleason score ≥8)

Forest Plot for Overall survival (high volume disease)

Study	HR	95% CI	Relative weight
Gravis, Gwenaelle et al 2016	0.78	[0.56; 1.09]	6.1%
Kyriakopoulos et al 2018	0.63	[0.50; 0.79]	12.3%
Fizazi, Karim et al 2019	0.62	[0.52; 0.74]	19.5%
Clarke, N. W. et al 2019	0.81	[0.64; 1.02]	11.9%
Andrew J Armstrong et al 2022	0.66	[0.52; 0.83]	11.8%
James, N. et al 2020	0.59	[0.47; 0.74]	12.5%
Chi, Kim N. et al 2021	0.70	[0.56; 0.88]	12.6%
Davis, Ian D. et al 2022	0.79	[0.63; 0.98]	13.1%
Random effects model	**0.68**	**[0.63; 0.74]**	**100.0%**

Heterogeneity: I^2=9%, τ^2=0.0013, p=0.36

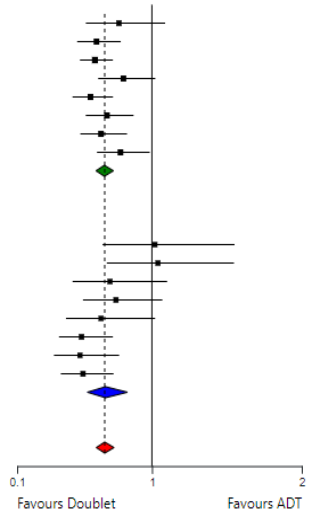


Subgroup Analysis

- Overall survival by choice of doublet therapy
- Progression free survival by choice of doublet therapy
- **Overall survival by volume of disease**
- Overall survival in high volume by choice of doublet therapy
- Overall survival in low volume by choice of doublet therapy
- Progression free survival by volume of disease
- Progression free survival in high volume by choice of doublet therapy
- Progression free survival in low volume by choice of doublet therapy
- Overall survival by mode of metastatic presentation
- Overall survival in synchronous metastases by choice of doublet therapy
- Overall survival in metachronous metastases by choice of doublet therapy

Forest Plot for Overall survival by volume of disease

Study	HR	95% CI	Relative weight
subgroup = High volume			
Gravis, Gwenaelle et al 2016	0.78	[0.56; 1.09]	5.1%
Kyriakopoulos et al 2018	0.63	[0.50; 0.79]	8.4%
Fizazi, Karim et al 2019	0.62	[0.52; 0.74]	11.1%
Clarke, N. W. et al 2019	0.81	[0.64; 1.02]	8.3%
James, N. et al 2020	0.59	[0.47; 0.74]	8.5%
Chi, Kim N. et al 2021	0.70	[0.56; 0.88]	8.6%
Armstrong, Andrew J. et al 202 ...	0.66	[0.52; 0.83]	8.2%
Davis, Ian D. et al 2022	0.79	[0.63; 0.99]	8.8%
Random effects model	**0.68**	**[0.63; 0.74]**	**66.9%**
Heterogeneity: I^2=9%, τ^2=0.0013, p=0.36			
subgroup = Low volume			
Gravis, Gwenaelle et al 2016	1.02	[0.67; 1.55]	3.5%
Kyriakopoulos et al 2018	1.04	[0.70; 1.55]	3.8%
Fizazi, Karim et al 2019	0.72	[0.47; 1.10]	3.4%
Clarke, N. W. et al 2019	0.76	[0.54; 1.07]	4.9%
Andrew J Armstrong et al 2022	0.66	[0.43; 1.02]	3.3%
James, N. et al 2020	0.53	[0.38; 0.74]	5.1%
Chi, Kim N. et al 2021	0.52	[0.35; 0.78]	3.7%
Davis, Ian D. et al 2022	0.54	[0.39; 0.74]	5.4%
Random effects model	**0.69**	**[0.57; 0.84]**	**33.1%**
Heterogeneity: I^2=51%, τ^2=0.0389, p=0.05			
Random effects model	**0.69**	**[0.63; 0.75]**	**100.0%**
Heterogeneity: I^2=32%, τ^2=0.0093, p=0.11			
Test for subgroup differences: χ^2_1=1%, df=1.0000, (p=0.92)			



LIVING EVIDENCE WORKFLOW

Interactive NMA Panel

Primary Analysis

Select outcome: Overall survival (all patients)

LEAGUE TABLE

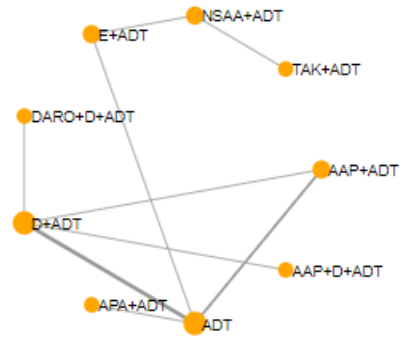
Comparator \ Treatments	AAP+ADT	AAP+D+ADT	ADT	APA+ADT	D+ADT	DARO+D+ADT	E+ADT	NSAA+ADT	TAK+ADT
AAP+ADT		0.88 (0.67, 1.16)	1.54 (1.37, 1.72)	0.99 (0.79, 1.25)	1.18 (1.01, 1.37)	0.80 (0.64, 1.00)	1.01 (0.79, 1.28)	1.45 (1.06, 1.96)	1.23 (0.87, 1.75)
AAP+D+ADT	1.14 (0.86, 1.50)		1.72 (1.33, 2.27)	1.12 (0.81, 1.56)	1.33 (1.05, 1.69)	0.91 (0.68, 1.22)	1.15 (0.82, 1.61)	1.64 (1.11, 2.38)	1.41 (0.93, 2.13)
ADT	0.65 (0.58, 0.73)	0.58 (0.44, 0.75)		0.65 (0.53, 0.79)	0.77 (0.69, 0.85)	0.52 (0.43, 0.64)	0.66 (0.53, 0.81)	0.94 (0.71, 1.25)	0.81 (0.58, 1.12)
APA+ADT	1.01 (0.80, 1.27)	0.89 (0.64, 1.23)	1.54 (1.26, 1.88)		1.18 (0.94, 1.49)	0.81 (0.61, 1.06)	1.02 (0.76, 1.35)	1.45 (1.03, 2.04)	1.25 (0.85, 1.85)
D+ADT	0.85 (0.73, 0.99)	0.75 (0.59, 0.95)	1.30 (1.17, 1.45)	0.85 (0.67, 1.06)		0.68 (0.57, 0.81)	0.86 (0.68, 1.09)	1.22 (0.91, 1.67)	1.05 (0.75, 1.49)
DARO+D+ADT	1.25 (1.00, 1.57)	1.10 (0.82, 1.48)	1.91 (1.56, 2.34)	1.24 (0.94, 1.65)	1.47 (1.24, 1.74)		1.27 (0.94, 1.69)	1.82 (1.28, 2.56)	1.56 (1.05, 2.27)
E+ADT	0.99 (0.78, 1.26)	0.87 (0.62, 1.22)	1.52 (1.23, 1.87)	0.98 (0.74, 1.32)	1.16 (0.92, 1.48)	0.79 (0.59, 1.06)		1.43 (1.19, 1.72)	1.23 (0.95, 1.59)
NSAA+ADT	0.69 (0.51, 0.94)	0.61 (0.42, 0.90)	1.06 (0.80, 1.41)	0.69 (0.49, 0.97)	0.82 (0.60, 1.10)	0.55 (0.39, 0.78)	0.70 (0.58, 0.84)		0.86 (0.72, 1.02)
TAK+ADT	0.81 (0.57, 1.15)	0.71 (0.47, 1.08)	1.23 (0.89, 1.72)	0.80 (0.54, 1.18)	0.95 (0.67, 1.34)	0.64 (0.44, 0.95)	0.81 (0.63, 1.05)	1.16 (0.98, 1.38)	

RANK TABLE

Treatment	P-Score	Rank
DARO+D+ADT	0.9476	1
AAP+D+ADT	0.8179	2
APA+ADT	0.6432	3
AAP+ADT	0.6343	4
E+ADT	0.6307	5
D+ADT	0.3414	6
TAK+ADT	0.3253	7
NSAA+ADT	0.1036	8
ADT	0.056	9

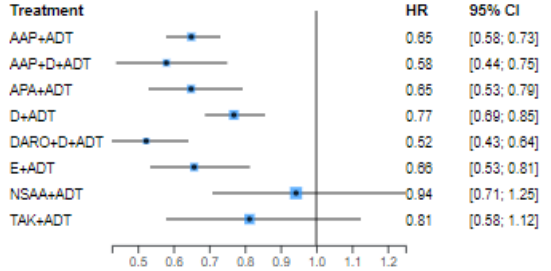
The values in each cell represent the relative treatment effect (and 95% CI) of the treatment on the top, compared to the treatment on the left. Green color suggests relative treatment benefit. Light green suggests non-significant benefit and dark green suggests significant benefit. Red color suggests relative treatment harm. Light red suggests non-significant harm and dark red suggests significant harm.

NETWORK PLOT



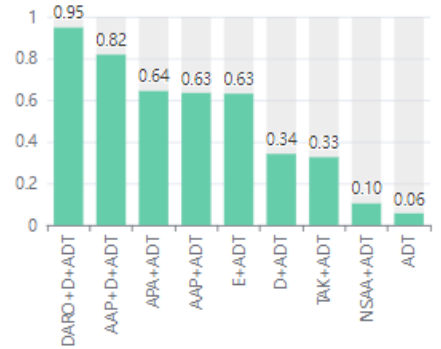
FOREST PLOT Select comparator: ADT

Comparison vs 'ADT'



Dynamic forest plots are generated by users input. Select reference treatment dynamically using the dropdown options at the top right corner of panel.

P-Score PLOT



LIVING EVIDENCE WORKFLOW

Interactive PWMA SoF

SUMMARY OF FINDINGS: PAIRWISE META-ANALYSIS

The Summary of Findings (SoF) table is designed to summarize the key results of pairwise meta-analysis and to evaluate confidence in the estimates of eff
This table summarizes results for patient-important outcomes for all treatment options investigated in included trials as compared to control, in adjuvant RCC. Users can select their outcome of interest from the left-hand panel by clicking on it and enter any baseline risk for that outcome, to visualize the absolute risk differences due to treatment.

Choose measure of effect and denominator for absolute effect.

Risks per: 1000 | Show raw data: No | Show CI: No | Show ARD: No | Show survival data: No | Color guide

Outcome	Relative	Absolute			Certainty in Evidence	Importance
		Intervention	Control	Risk Difference		
Overall survival (all patients) 9 Studies	HR 0.72 (0.66 to 0.78)	371 per 1000	476 per 1000	105 fewer per 1000	High	NA
Progression free survival (all patients) 9 Studies	HR 0.55 (0.49 to 0.63)	478 per 1000	692 per 1000	214 fewer per 1000	Moderate	NA
Adverse events (grade ≥ 3) 7 Studies	RR 1.42 (1.20 to 1.69)	491 per 1000	345 per 1000	146 more per 1000	Moderate	NA
Overall survival (high volume disease) 8 Studies	HR 0.68 (0.63 to 0.74)	436 per 1000	568 per 1000	132 fewer per 1000	Low	NA
Overall survival (low volume disease) 8 Studies	HR 0.69 (0.57 to 0.84)	274 per 1000	371 per 1000	97 fewer per 1000	Low	NA
Progression free survival (high volume disease) 8 Studies	HR 0.51 (0.46 to 0.57)	645 per 1000	869 per 1000	224 fewer per 1000	Low	NA
Progression free survival (low volume disease) 8 Studies	HR 0.49 (0.36 to 0.67)	353 per 1000	589 per 1000	236 fewer per 1000	Low	NA

LIVING EVIDENCE WORKFLOW

Interactive NMA SoF

SUMMARY OF FINDINGS: NETWORK META-ANALYSIS

The Summary of Findings (SoF) table is designed to display multiple comparisons in an interactive manner. All possible combinations in network meta-analysis can be compared using this framework. Users can interactively select or deselect SoF for a given clinical outcome by clicking the outcome of interest from the left-hand panel. Users can also enter any baseline risk for an outcome, to visualize the absolute risk differences due to treatment. Clicking on any of the colored boxes displays details of that effect estimate as well as its associated certainty of evidence assessment.

Choose reference treatment, measure of effect, and denominator for absolute effect.

Comparator: Docetaxel | Show survival data: No | Display risks per: 1000 | Color guide

Outcome	Comparator: Docetaxel	Darolutamide + Docetaxel	Abiraterone acetate + Docetaxel	Apalutamide	Enzalutamide	Abiraterone acetate	TAK+ADT	NSAA+ADT	ADT
Overall survival (all patients) (HR)	458 per 1000 Rank 6	117 fewer Rank 1	90 fewer Rank 2	52 fewer Rank 3	48 fewer Rank 5	52 fewer Rank 4	17 more Rank 7	68 more Rank 8	91 more Rank 9
Progression free survival (all patients) (HR)	497 per 1000 Rank 6	NA NA	206 fewer Rank 1	111 fewer Rank 3	174 fewer Rank 2	66 fewer Rank 4	64 fewer Rank 5	128 more Rank 7	136 more Rank 8
Adverse events (grade ≥ 3) (RR)	557 per 1000 Rank 6	23 more Rank 7	117 more Rank 8	89 fewer Rank 4	181 fewer Rank 2	11 fewer Rank 5	313 more Rank 9	273 fewer Rank 1	162 fewer Rank 3
Overall survival (high volume disease) (HR)	566 per 1000 Rank 5	NA NA	114 fewer Rank 1	11 fewer Rank 4	34 fewer Rank 3	62 fewer Rank 2	NA NA	51 more Rank 6	118 more Rank 7
Overall survival (low volume disease) (HR)	344 per 1000 Rank 5	NA NA	49 fewer Rank 4	130 fewer Rank 1	81 fewer Rank 3	101 fewer Rank 2	NA NA	90 more Rank 7	27 more Rank 6
Progression free survival (high volume disease) (HR)	658 per 1000 Rank 5	NA NA	262 fewer Rank 1	47 fewer Rank 4	123 fewer Rank 2	100 fewer Rank 3	NA NA	160 more Rank 6	174 more Rank 7
Progression free survival (low volume disease) (HR)	426 per 1000 Rank 5	NA NA	151 fewer Rank 3	192 fewer Rank 2	256 fewer Rank 1	123 fewer Rank 4	NA NA	38 more Rank 6	101 more Rank 7

LIVING EVIDENCE WORKFLOW

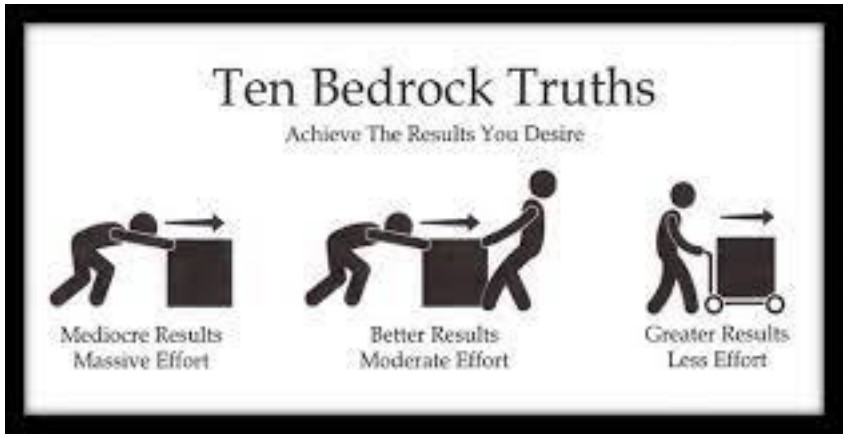
Interactive Evidence Map

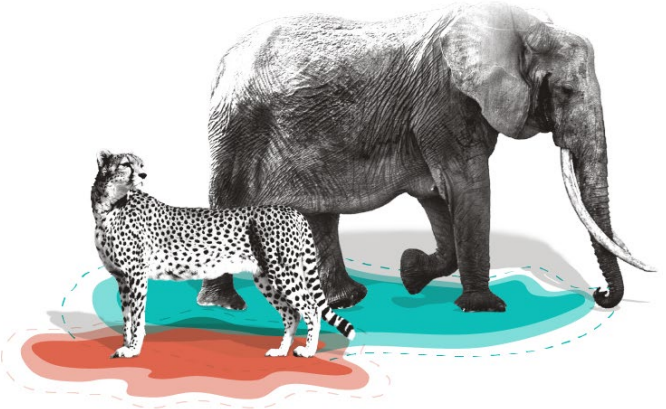
EVIDENCE MAP

The evidence map visually summarizes the evidence for available treatment comparisons and identifies evidence gaps that warrant future research. User can select a treatment option of interest from the dropdown to visualize whether it is comparable, beneficial or harmful (color), certainty of evidence (size of the circle) as compared to other treatment options in the network. Empty slots (no circles) denote the complete lack of evidence (either direct or indirect).

LIVING AND INTERACTIVE SYSTEMATIC REVIEWS!

- Truly living guidelines(real time updates, almost!)
- More with available resources(double output, same resources!)
- Rigor and Agility
- Standardization for EHR integration and downstream efforts(evidence summaries, shared decision-making aids, algorithms)





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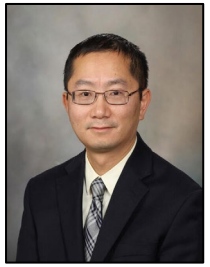
Chitta Baral


Zhen Wang


Huan He


Syed A.A. Naqvi

QUESTIONS & ANSWERS

Discussion

Break

Examples of CDS

Dr. Kensaku Kawamoto, University of Utah, and
Dr. Nathan Dean, Intermountain Health and University of Utah



AGENCY FOR HEALTHCARE RESEARCH AND QUALITY

AHRQ

Improving Lung Cancer Screening Through an EHR-Integrated Everyday Shared Decision-Making Tool and Clinician-Facing Prompts

Kensaku Kawamoto, M.D., Ph.D., M.H.S., F.A.C.M.I., F.A.M.I.A.

Professor of Biomedical Informatics
Associate Chief Medical Information Officer
Director, ReImagine EHR Initiative
Co-Senior Director, Digital Health Initiative
University of Utah

Disclosures

- Outside of this work, I report honoraria, consulting, sponsored research, writing assistance, licensing, or co-development with a number of organizations.
- I have no conflicts with direct relevance to this work.
- The Everyday shared decision-making tool described in this presentation (Decision Precision+) is available for free.
- This work was made possible by AHRQ R18HS026198.

Key Clinical Need: Improved Lung Cancer Screening

- Lung cancer: #1 cause of cancer deaths in United States for both men and women.[1]
- Lung cancer screening (LCS) with annual low-dose CT scans can reduce lung cancer deaths by ~20%.[2,3]
- The US Preventive Services Task Force (USPSTF) has recommended offering screening to high-risk patients (older patients with a history of heavy smoking) since 2013.[4,5]
- The vast majority of eligible patients in the United States are not screened.
  - 2020: 6.5% screening rate nationwide; < 2% in Utah.[6]

1. https://www.cancer.org/cancer/types/lung-cancer/about/key-statistics.html
2. Aberle DR et al. *N Engl J Med.* 2011;365(5):395-409.
3. De Koning HJ et al. *N Engl J Med*. 2020;382(6):503-513.
4. https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/lung-cancer-screening-december-2013
5. https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/lung-cancer-screening
6. Fedewa SA et al. *Chest*. 2022;161(2):586-589.

Provider Barriers to Screening[1]

- Lack of familiarity with eligibility criteria and insurance coverage.
- Difficulty identifying eligible patients.
- Need for guidance on management of screening results.
- Skepticism about benefits of screening.
- Insufficient time or knowledge to conduct shared decision making (SDM).
  - Important due to potential downsides (e.g., biopsy complications) and wide individual variation in expected benefit (e.g., reduction in lung cancer deaths was ~60x higher in patients at the highest vs. lowest quintile of risk in the National Lung Screening Trial[2]).
  - Recommended by clinical guidelines.[3,4]
  - Required by CMS prior to initiating screening; includes need to use a decision aid.[5]

1. Wang GX et al. *Radiology.* 2019;290(2):278-287.
2. Kovalchik SA et al. *N Engl J Med.* 2013;369(3):245-254.
3. https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/lung-cancer-screening
4. https://info.chestnet.org/screening-for-lung-cancer-chest-guideline-and-expert-panel-report
5. https://www.cms.gov/medicare-coverage-database/view/ncacal-decision-memo.aspx?proposed=N&ncaid=304

Project Objective

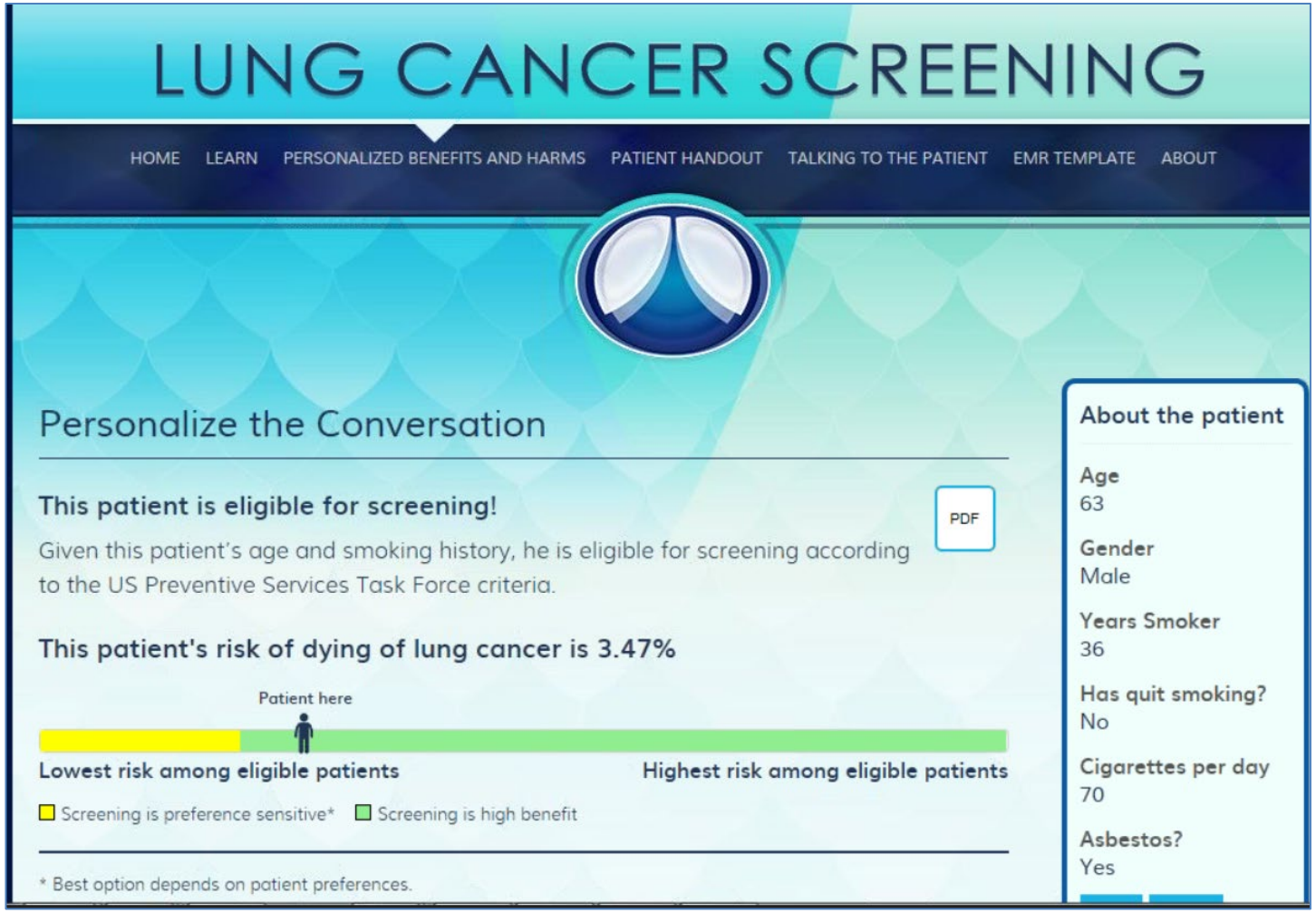
- Design, develop, and evaluate a widely scalable approach to enabling LCS that addresses key barriers to screening.

Intervention Goals

- Integrate with routine primary care workflows.
- Make it easy for providers to identify patients who are eligible for LCS.
- Make it easy and fast for providers to conduct SDM.
  - Support an Everyday SDM model that can be completed within 1-2 minutes, while supporting Full SDM when the time is available.[1,2]
- Use an approach that can be widely scaled.

1. Caverly TJ et al. *J Gen Intern Med*. 2020;35(10):3045-3049.
2. Caverly TJ et al. *MDM Policy Pract*. 2021;6(2):23814683211055120.

Key Starting Resource: Decision Precision



Web-based LCS SDM tool developed with VA funding by Drs. Tanner Caverly and Angie Fagerlin at Univ. of Michigan and Ann Arbor VA

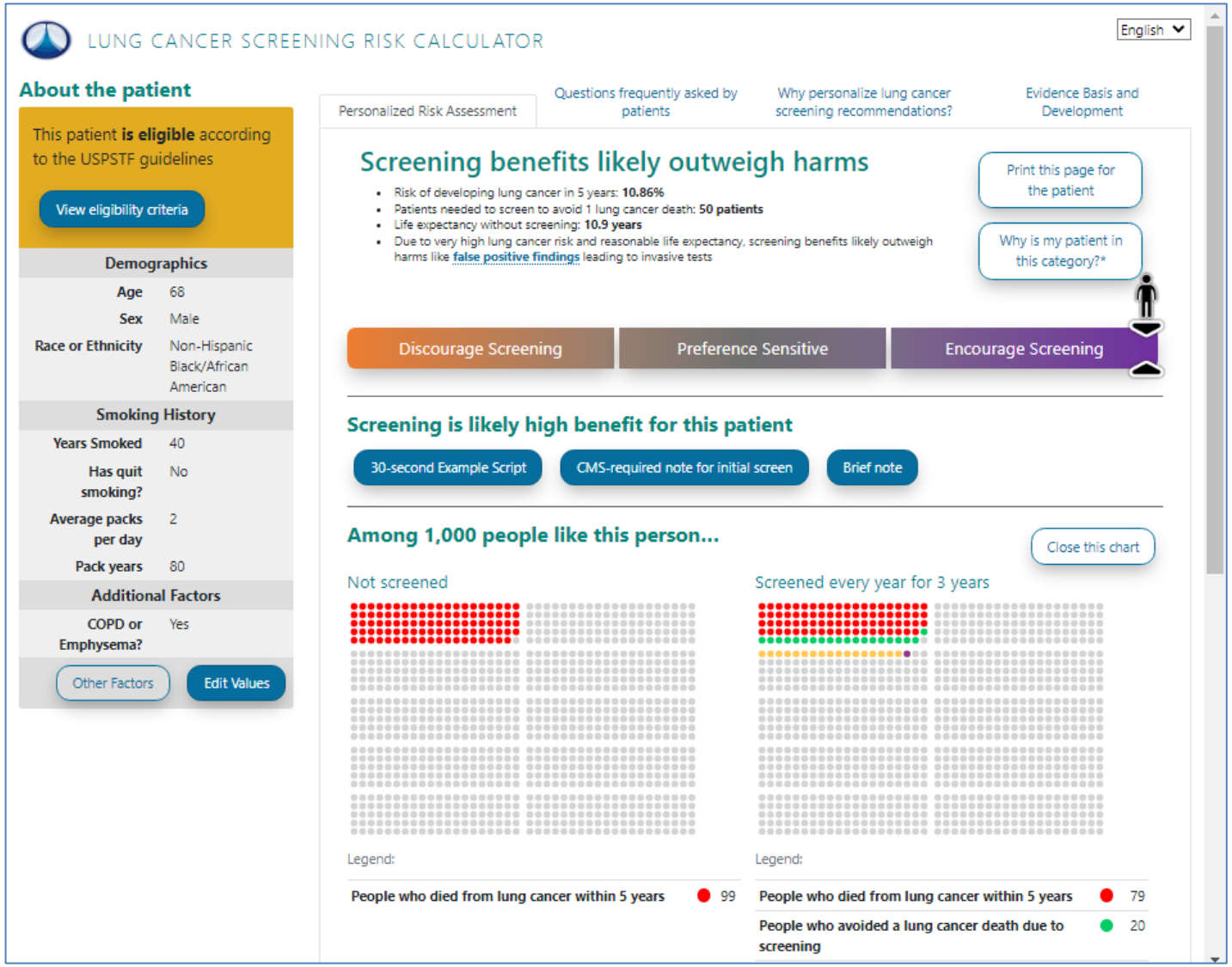
Originally designed to support Full SDM

Worked well when used by full-time LCS coordinators in the context of dedicated LCS SDM sessions at the VA[1]

Too time-consuming to use routinely in primary care settings

1. Lowery J et al. *JMIR Hum Factors*. 2022;9(2):e32399.

Enhancement of Decision Precision to Support Everyday SDM



Only elements needed for Everyday SDM kept on main Web page

Content relevant to Full SDM moved to supplemental tabs

Replete with numerous time-saving features

Available for free at https://screenlc.com

Incorporated in the Foundation (default recommended) LCS module of Epic electronic health record (EHR) system

Decision Precision+: EHR Integration with SMART on FHIR

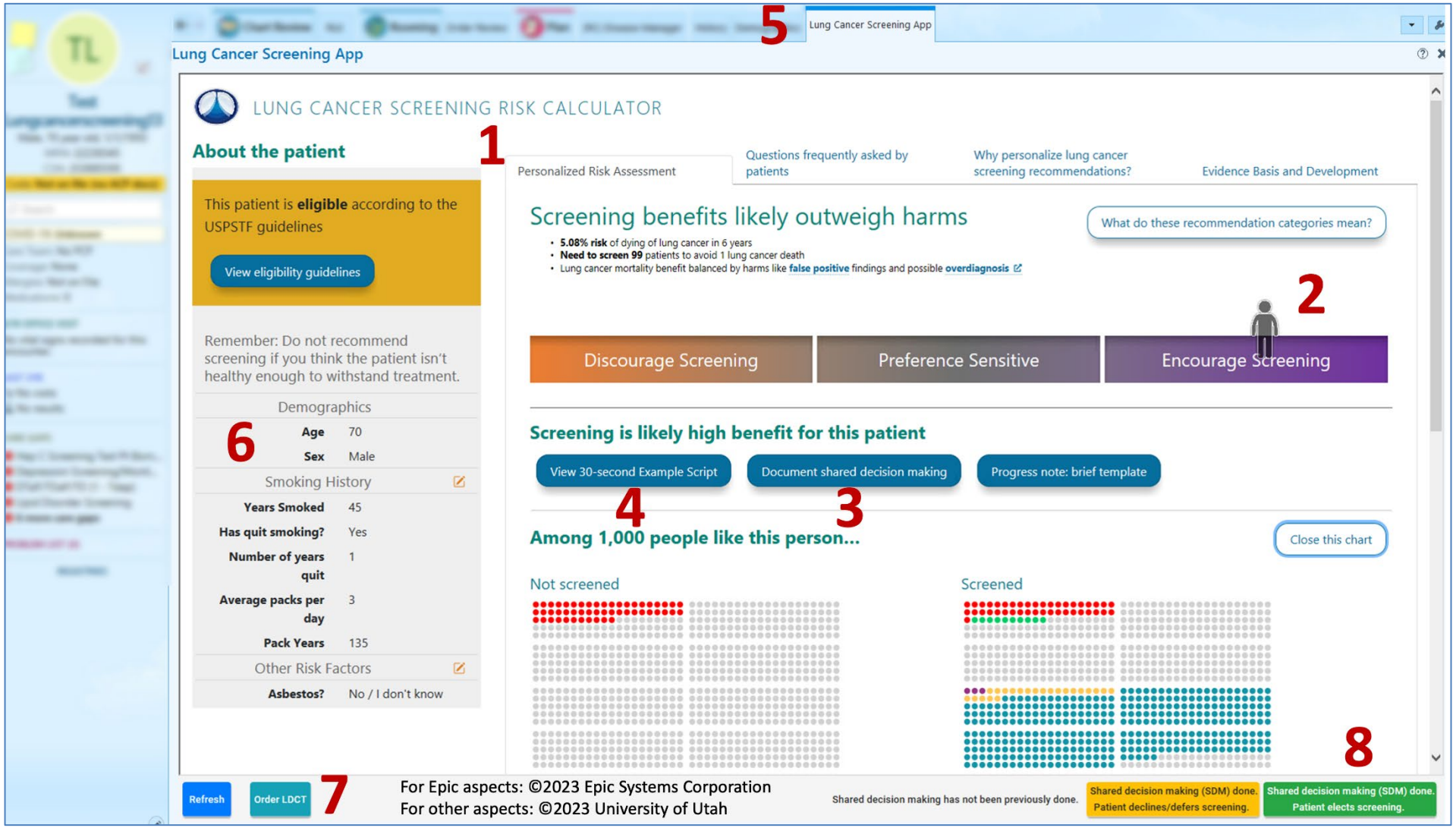


Figure 3 from Kukhareva PV et al. *Chest*. 2023 May 2;S0012-3692(23)00641-4. doi: 10.1016/j.chest.2023.04.040.

EHR Prompts for LCS and LCS Discussion

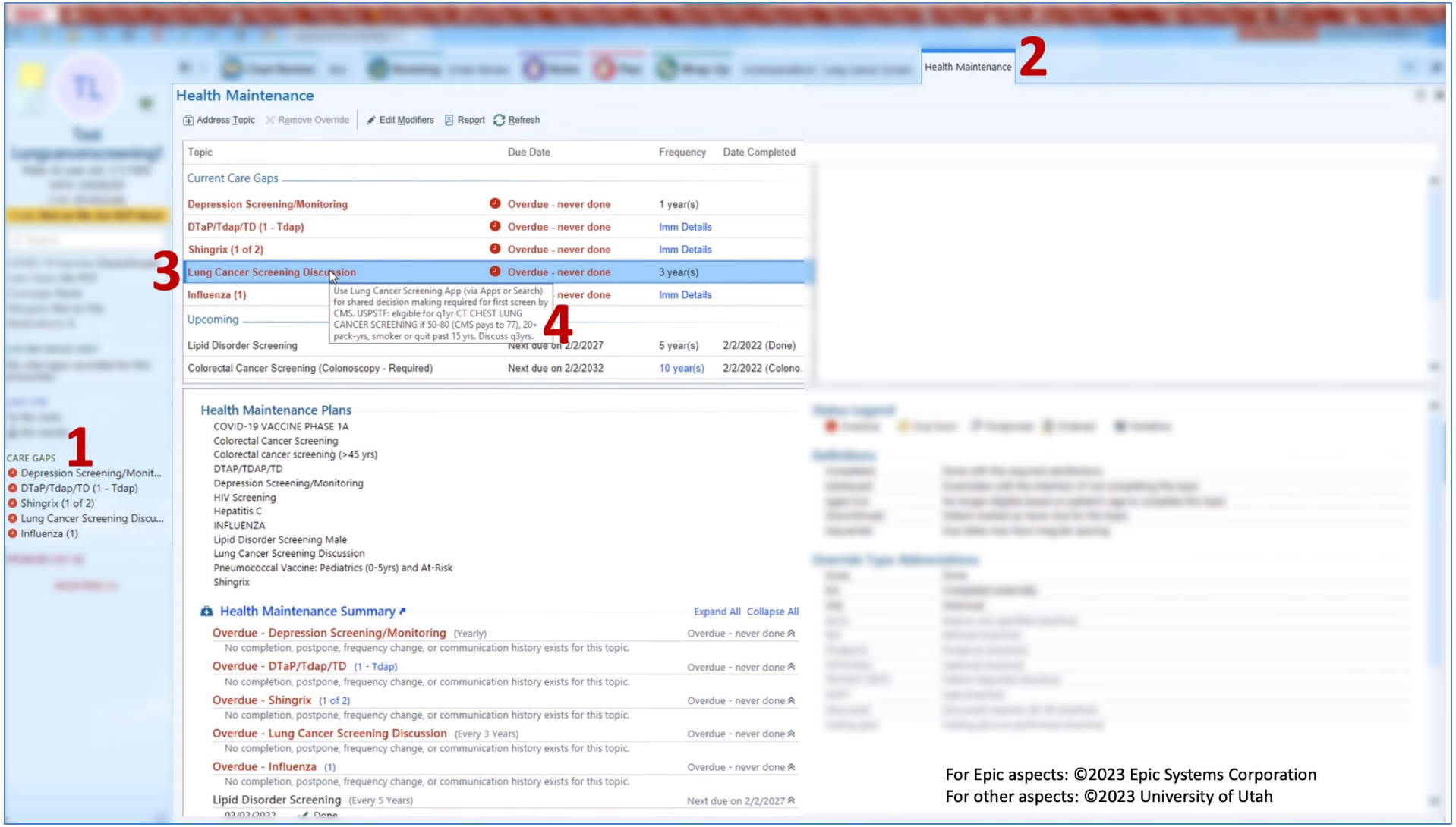


Figure 1 from Kukhareva PV et al. *Chest*. 2023 May 2;S0012-3692(23)00641-4. doi: 10.1016/j.chest.2023.04.040.

EHR Prompts on Need to Conduct SDM Prior to Initiating Screening

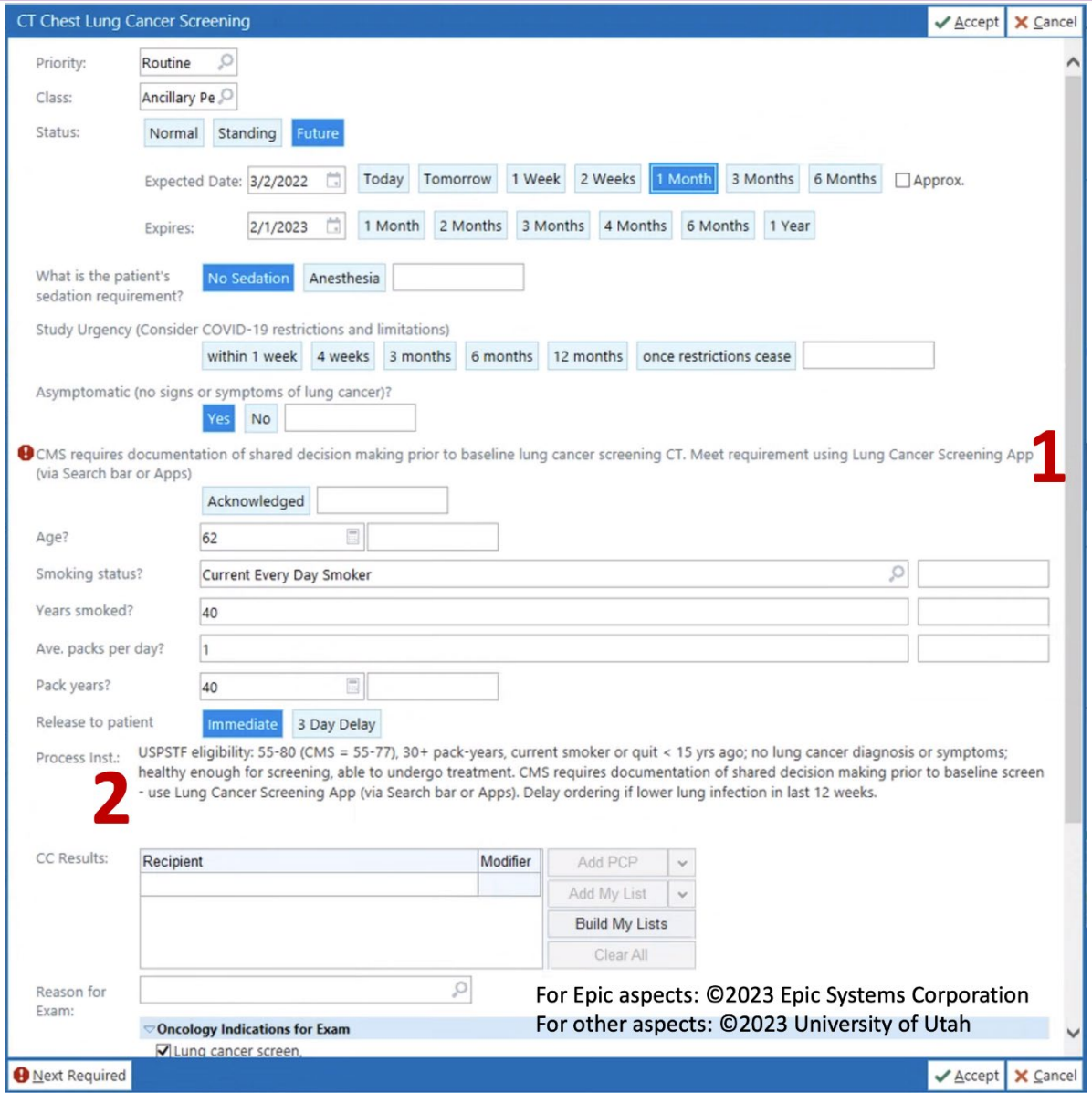


Figure 2 from Kukhareva PV et al. *Chest*. 2023 May 2;S0012-3692(23)00641-4. doi: 10.1016/j.chest.2023.04.040.

Pragmatic Clinical Trial

- Setting:
  - 30 primary care & 4 pulmonary clinics at Univ. of Utah Health (UHealth).
- Intervention:
  - EHR prompts and EHR-integrated Everyday SDM tool.
- Design:
  - Pre-post intervention analysis with 12-month pre-intervention phase (8/24/19 – 8/23/20) and 9-month intervention phase (8/24/20 – 5/23/21).
- Statistical Methods:
  - Population: primary care patients meeting 2013 USPSTF criteria with no chest CT in past year who had not declined screening in last 3 years.
  - Primary outcomes: LCS ordering and completion
  - Logistic regression with mixed-effect models and covariate adjustment.

Results

- 1,435 patients included
- Low-dose CT ordering: 7.1% → 27.3% (adjusted OR 4.9, p < .001)
- Low-dose CT completion: 4.4% → 17.7% (adjusted OR 4.7, p < .001)
- SDM tool used prior to low-dose CT ordering for 25.2% of patients.

LCS Ordering and Completion Stratified by Screening Benefit Level

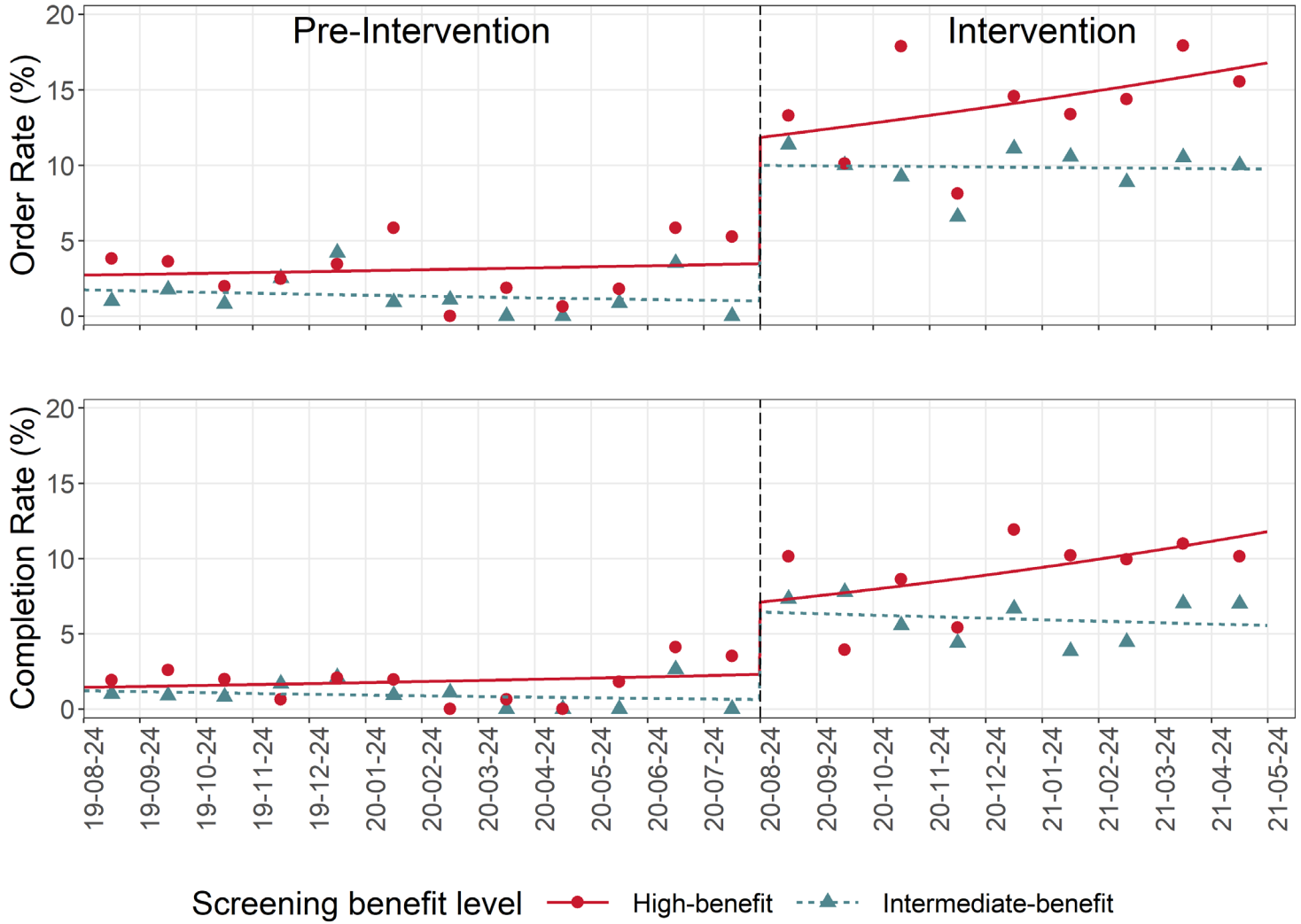


Figure 4 from Kukhareva PV et al. *Chest*. 2023 May 2;S0012-3692(23)00641-4. doi: 10.1016/j.chest.2023.04.040.

Summary

- Introduction of an EHR-integrated Everyday SDM tool and provider prompts was associated with significantly increased LCS ordering and completion at a single health system (adjusted OR of ~5).
- SDM tool use was ~25% prior to initiating screening.
  - Sub-optimal, but still higher than many previously reported SDM and SDM tool use rates in primary care settings.
  - Even a few minutes may be too much to add to busy primary care workflows for patients with many conditions requiring attention.

For More Information…

- Decision Precision: https://screenlc.com
- Decision Precision+: ReImagineEHR@utah.edu
- Clinical Trial:

Kukhareva PV et al. Implementation of lung cancer screening in primary care and pulmonary clinics: pragmatic clinical trial of electronic health record-integrated Everyday shared decision making tool and clinician-facing prompts. *Chest*. 2023 May 2:S0012-3692(23)00641-4.

- ReImagine EHR initiative:

Kawamoto K et al. Establishing a multidisciplinary initiative for interoperable electronic health record innovations at an academic medical center. *JAMIA Open*. 2021 Jul 31;4(3):ooab041.

Thank You!

Kensaku Kawamoto, M.D., Ph.D., M.H.S., F.A.C.M.I., F.A.M.I.A.

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ePneumonia

Electronic Clinical Decision Support

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Pulmonary and Critical Care Medicine, Intermountain Health

Professor of Medicine University of Utah

November 8th 2023

No conflicts of interest

Supported by AHRQ grants #5R18HS02688 and #1R18HS028955

Key functions of ePneumonia

Screens Emergency Department patients in real time

CheXED AI for Chest X-Ray images plus Bayesian probabilistic algorithm using 40 data elements to estimate likelihood of pneumonia

Diagnosis and prompt for enrollment triggers at 40% likelihood

Severity of illness stratification to recommend site of care

Inpatient versus outpatient, ward versus ICU

eCURB, PaO2/FiO2, sCAP criteria, presence of parapneumonic effusion

Identifies risk factors for resistant pathogens – DRIP score

ED administration of antibiotics tailored to site of care and likely pathogens

Recommends appropriate microbiology studies

Allows for clinician judgment – room to opt out/disagree and provide reasoning

Treatment Assessment

Severe Hypoxemia? (PaO2/FiO2 Ratio <= 120 mmHg)	Y	N
PaO2/FiO2 Ratio: 137 mmHg		

How many of the following Severe CAP Criteria exist?

More than 3	✓

Vitals ----------

Age: 65 Years

Confusion *(patient not oriented to person, place, or time)*: **No**

Temperature *(<= 36 C)*: **36 C**

Respiratory Rate *(>= 30 BPM)*: **30 BPM**

Systolic Blood Pressure *(< 90 mmHg)*: **105 mmHg**

Labs ----------

BUN *(>=20)*: **30**

WBC *(< 4 K/mcL)*: **10 K/mcL**

Platelet Count *(< 100 K/mcL)*: No Data Found

PaO2/FiO2 Ratio *(<=213)*: **137 mmHg**

Radiology ----------

Infiltrates *(Multilobar)*: No Data Found

ICU Admission is recommended. This patient has Severe Pneumonia based on 81% likelihood of needing ICU treatment and 4 Severe CAP Criteria.

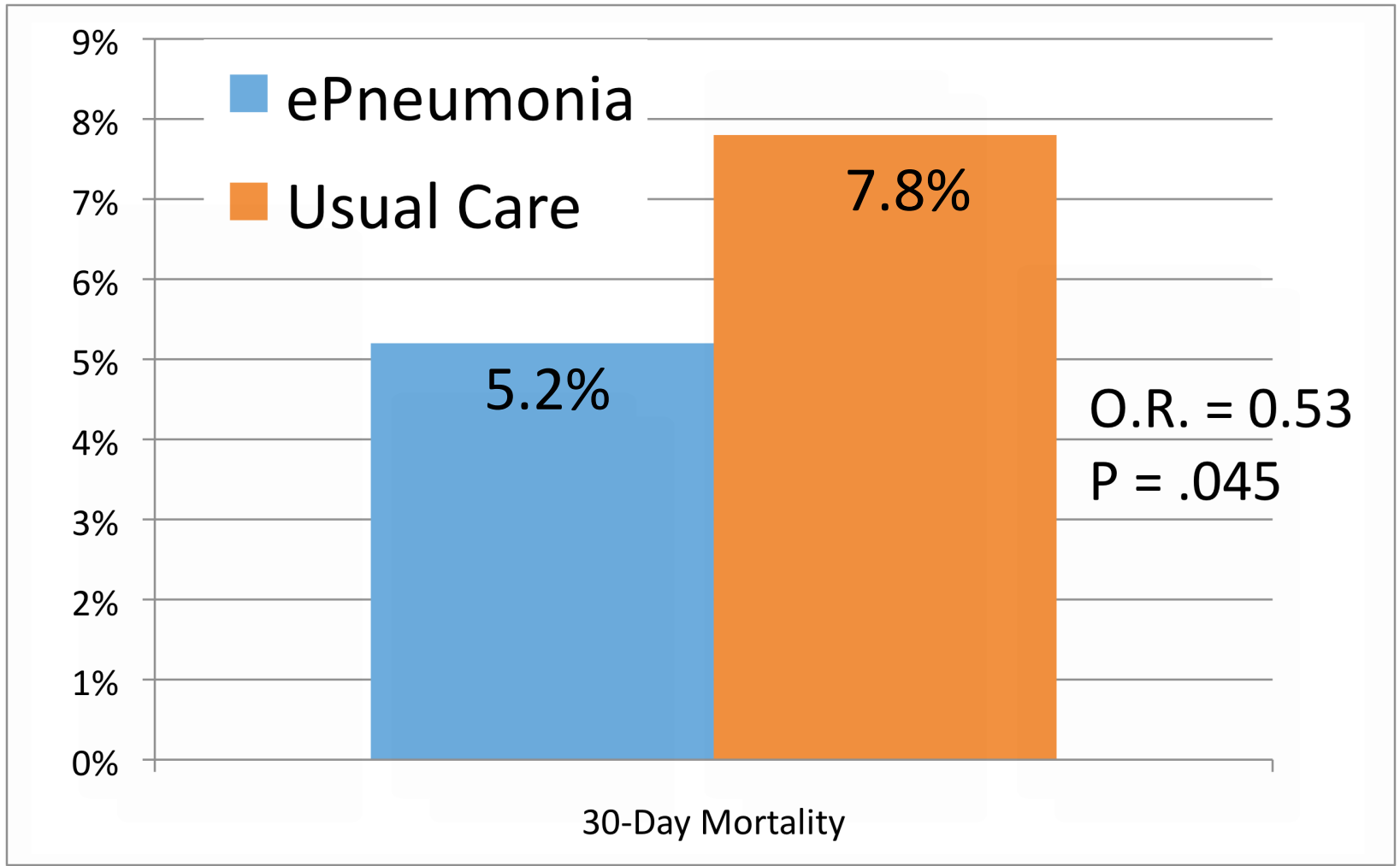
Do you agree with ICU Admission Recommendation?

Agree with Recommendation	√
Disagree with Recommendation	

Save

Odds ratios for community-acquired pneumonia mortality associated with implementation of ePneumonia

Dean Annals Emergency Medicine 2015



Intermountain® Healthcare

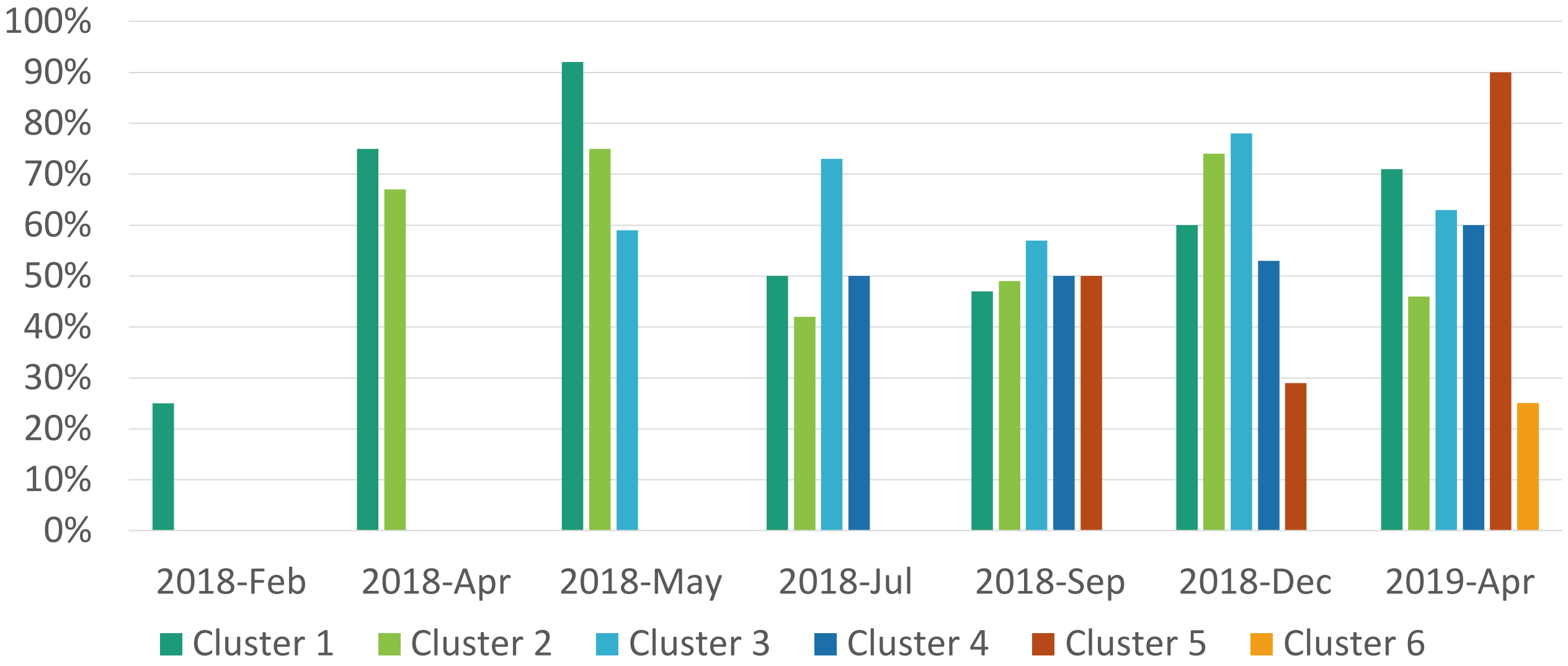
Deployment of ePneumonia across Intermountain Health

- ED leadership support systemwide and at each study site
- ED clinician engagement in tool development and deployment
- Interactive educational meetings
- Local champions taught and encouraged use of ePneumonia
- Nurse educator visited clinicians during their shifts to teach and encourage use
- Audit and feedback at regular intervals
- Familiarized hospital admitting physicians with ePneumonia to smooth transitions of care

Dean AMIA Annual Symposium Proceedings 2020

Carr Journal of Rural Health 2020

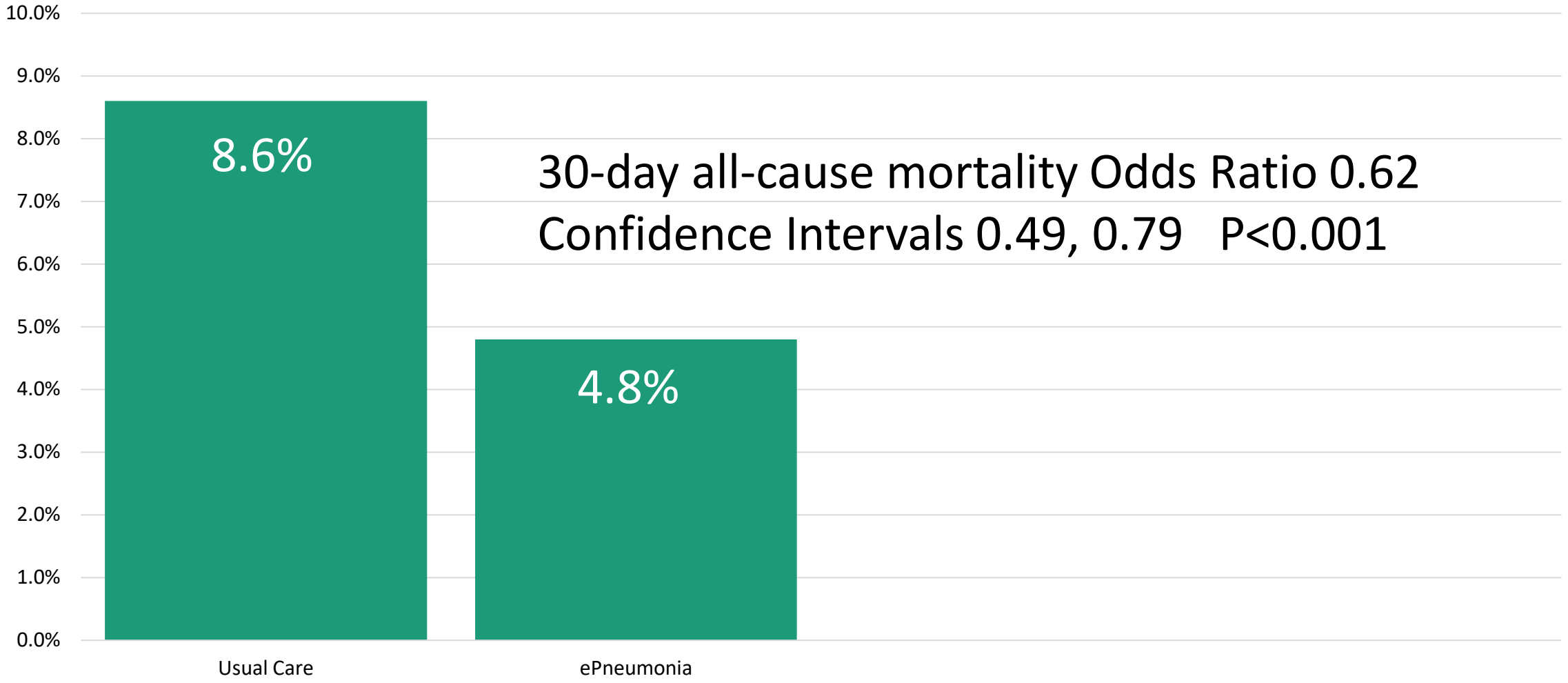
ePneumonia utilization after deployment



Overall ePneumonia utilization averaged 67% of ED patients with pneumonia

A pragmatic stepped-wedge, cluster-controlled trial of real-time pneumonia clinical decision support

Dean Am J Resp Crit Care Med 2022



Disposition home among patients recommended by ePneumonia for outpatient care

	ePNa → Home Pre-deployment	ePNa → Home Post-deployment
Home	49%	66.6%

Seven-day secondary hospital admission rate unchanged

Antibiotics initiated 9 minutes earlier and were more guideline consistent/narrow spectrum

Median length of hospital stay decreased from 3.2 to 2.6 days

Intermountain® Healthcare

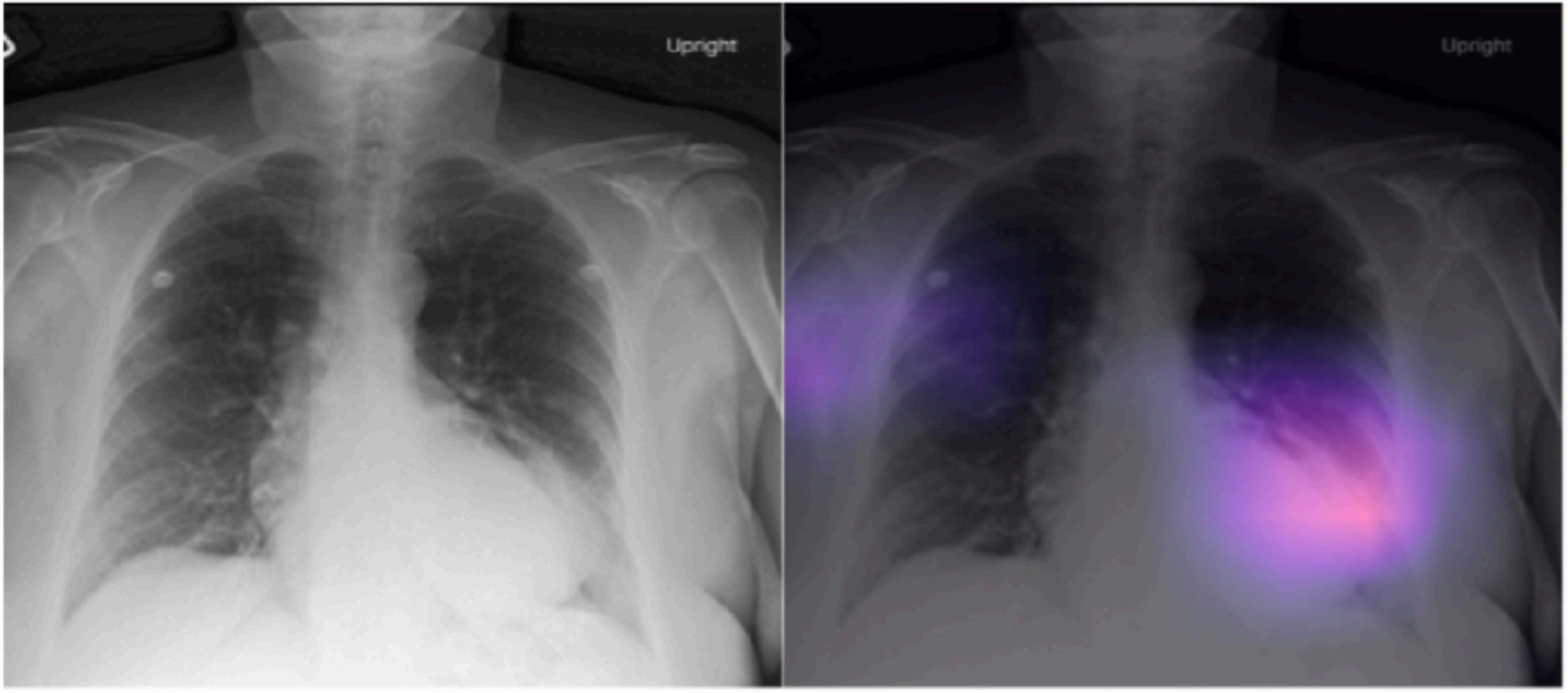
Limitations of Radiology – Natural Language Processing

Artificial Intelligence Imaging Analysis

Time delay	**1 second**	Patient and provider dissatisfaction
Free text	**Source Image - CheXED**	Errors in critical element extraction
Physician variability	**Consistent**	Disagreement and inconsistency in radiologist interpretation

Irvin J Thoracic Imaging 2022 37:162

CheXED Artificial Intelligence

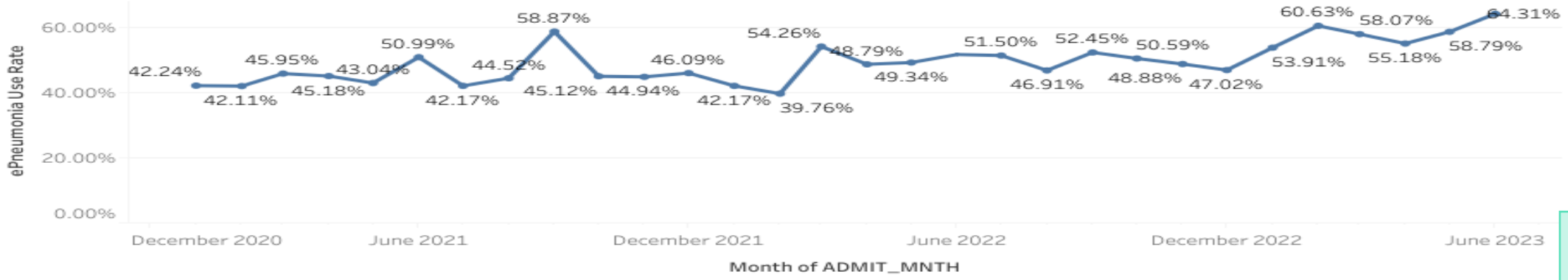


- **Ongoing monitoring of ePneumonia use by Office of Patient Experience:**

  https://tab.intermountain.net/t/intab/views/ePneumoniaDashboard/OverallSummary?:showAppBanner=false&:n&:origin=viz_share_link

- Driven by Department of Emergency Medicine leadership
- Automated – ICD-10 J18.X discharge code plus CheXED evidence for radiographic pneumonia

Trend-(Filters on Right Or Select Hospital From Table Below)



Hospital
All

Physician Group
All

Affinity Group
All

ADMIT_MNTH
1/1/2021 12:00:00 AM to..

Summary By Year

Affinity Group	Hospital	Opportunities 2021	Opportunities 2022	Opportunities 2023	Used Tool 2021	Used Tool 2022	Used Tool 2023	ePneumonia Use Rate 2021	ePneumonia Use Rate 2022	ePneumonia Use Rate 2023
Large		532	610	466	320	352	320	60.15%	57.70%	68.67%
		488	583	428	224	244	222	45.90%	41.85%	51.87%
		343	363	242	182	148	127	53.06%	40.77%	52.48%
		240	274	216	63	111	102	26.25%	40.51%	47.22%
		1,603	**1,830**	**1,352**	**789**	**855**	**771**	**49.22%**	**46.72%**	**57.03%**
Community		252	266	212	60	127	131	23.81%	47.74%	61.79%
		176	188	150	96	108	95	54.55%	57.45%	63.33%
		172	175	115	34	57	47	19.77%	32.57%	40.87%
		131	161	158	78	91	99	59.54%	56.52%	62.66%
		116	152	116	62	71	75	53.45%	46.71%	64.66%
		115	132	111	78	94	77	67.83%	71.21%	69.37%
		92	150	81	68	97	60	73.91%	64.67%	74.07%
		60	90	75	21	45	41	35.00%	50.00%	54.67%
		47	46	45	26	27	34	55.32%	58.70%	75.56%
		18	25	24	1	7	10	5.56%	28.00%	41.67%
		1,179	**1,385**	**1,087**	**524**	**724**	**669**	**44.44%**	**52.27%**	**61.55%**
Rural		95	96	49	38	42	23	40.00%	43.75%	46.94%
		86	82	58	27	34	45	31.40%	41.46%	77.59%
		65	50	42	40	29	22	61.54%	58.00%	52.38%
		31	42	33	16	27	24	51.61%	64.29%	72.73%
		21	36	40	2	14	18	9.52%	38.89%	45.00%
		30	30	20	12	15	16	40.00%	50.00%	80.00%
		26	31	21	1	5	2	3.85%	16.13%	9.52%
		23	35	12	7	12	4	30.43%	34.29%	33.33%
		377	**402**	**275**	**143**	**178**	**154**	**37.93%**	**44.28%**	**56.00%**
		4	4	5	1	1	2	25.00%	25.00%	40.00%
		4	**4**	**5**	**1**	**1**	**2**	**25.00%**	**25.00%**	**40.00%**
Grand Total		**3,163**	**3,621**	**2,719**	**1,457**	**1,758**	**1,596**	**46.06%**	**48.55%**	**58.70%**

Extending ePneumonia

ePneumonia adaptation for Intermountain Urgent Care Clinics

AHRQ R-18 grant $1.35M for adaptation and pilot trial, currently year 4 (extension)

Development of SMART on FHIR ePneumonia

Interoperable with different Electronic Health Records

New User Interface for Epic, new patient centered feature to support shared decision making

AHRQ R-18 grant $3M over 3 years in conjunction with Stanford and Vanderbilt

ePneumonia for Urgent Care Clinics

Developed new user interfaces and Bayesian probabilistic models

1) Initial alert/interface recommending Chest X-Ray ordering in selected patients (reason for visit, respiratory symptoms, vital signs, physician/nurse practitioner chest exam)
2) Displays CheXED findings combined with additional data elements for % likelihood of pneumonia
3) Alert displays if clinician enters pneumonia diagnostic code without radiographic confirmation

Presented at American Thoracic Society International Conference May 2023

Site of Care

Recommends hospital admission for patients with radiographically confirmed pneumonia and:

1) SpO2 < 90% (5% of patients)
2) **Or** significant parapneumonic effusion(s) (2% of patients)
3) **Or** patients with high severity of illness by Bayesian Probabilistic Model including age, gender, comorbid illness, shock index, respiratory rate, multi-lobar disease, temperature, SpO2, reason for visit, influenza/SARS-coV-2

Thanks to the ePneumonia team

Colleagues at Intermountain Health– Emergency Medicine, Pulmonary/CCM, Infectious Disease, Hospital Medicine, Urgent Care Clinics, Pharmacy, Nurses, and Respiratory Therapists

Informatics developers of ePneumonia: Kathryn Kuttler, Peter Haug, Herman Post, Darren Mann

Database and Statistical Analysts: Al Jephson, Jason Jacobs, Jackie Eve, and Allison Butler

Questions

Measuring and Evaluation Successes in CDS Development

Wes Sargent, CDC, Dr. Karen Nanji, Harvard Medical School, and Allison McCoy, Vanderbilt University

Creating Value by Modernizing and Measuring Electronic Clinical Decision Support Tools

Wesley Sargent, EdD, MA

Senior Health Scientist

11.8.2023

Division of Overdose Prevention

National Center for Injury Prevention and Control

Centers for Disease Control and Prevention

CDC's Strategic Priorities to address the Overdose Crisis

https://www.cdc.gov/drugoverdose/prevention/index.html

Health Systems Interventions

- Electronic health records (EHR) and PDMP (prescription drug monitoring program) data integration
- Clinical quality improvement and care coordination
- **Clinical decision support (CDS) tools embedded into EHRs**

Evaluating Clinical Decision Support (CDS) Tools

- **Implemented pilot CDS tools at four participating healthcare systems:**
  - Regional primary care health system based in Kansas
  - Large metropolitan hospital with outpatient clinics in Texas
  - Large hospital and outpatient care system in New York City
  - Regional hospital and primary care health system in Pennsylvania
- **Evaluated implementation process, use, and utility of CDS tools:**
  - Pre-/post- of EHR-generated measures using existing data
  - Conducted semi-structured interviews (n=8) with project champions and IT leads at participating healthcare systems

Evaluating CDS Tools

- **Each participating health system developed EHR-embedded CDS tools that align directly with the 2022 CDC Clinical Practice Guideline* recommendations and integrated directly into system clinical workflow. CDS tools developed included:**
  - Alerts
  - Access to prescription drug monitoring program (PDMP) data
  - Patient registries
  - Auto-population of prescription fields (e.g., quantity)
  - Order sets (e.g., SmartSet)
  - Morphine milligram equivalents (MMEs) calculators
  - Templates for clinical notes and referrals

* 2022 CDC Clinical Practice Guideline for Prescribing Opioids for Pain

Evaluation Results

- The number of patients with counseling on opioid risks and benefits increased from 5% to 7.5% (TX)
- Short-term follow-up increased slightly at (TX)
- Use of immediate release opioids when obtaining a new opioid prescription increased from 91% to 96% (TX)
- Urine drug testing increased by 50% (PA)
- Naloxone counseling increased by six-fold (PA)
- Use of PDMP information increased by 60% (KS)

Lessons Learned

- Development and implementation of CDS tools aligned with the CDC Guideline have the potential to promote safer opioid prescribing and improve patient care
- Design, validation, and implementation process for CDS tools can be highly variable
- Healthcare systems' capabilities and resources are critical in determining which CDS modules to implement and how
- Flexibility in creating CDS tools and data definitions is KEY to successful integration into clinical workflow

Lessons Learned Continued

- **Facilitators:**
  - In-house IT staff expertise and availability
  - Access to and relationship with EHR service advisor
  - EHR system-specific administrative regulations and clinical policies
  - Shared learning with other systems
  - Flexibility in creating CDS tools and data definitions is KEY to successful integration into clinical workflow
- **Barriers/Challenges:**
  - EHR system-specific limitations to how data are captured, or need to be built
  - Length of time to build, test, iterate, and implement
  - Limited resources available
  - Lacking internal expertise or IT experience with opioid-related data

Current Electronic CDS Projects

- **Health systems can help encourage the uptake and use of the 2022 CDC Clinical Practice Guideline for Prescribing Opioids for Pain**
- **CDC-funded effort to create electronic CDS tools that map to the 12 Guideline recommendations**
  - Contributors: ONC, Medical University of South Caroline, Yale, University of Washington, and Security Risk Solutions
- **Current work includes further refinement and development of electronic CDS to be used in EHRs, at the point-of-care**

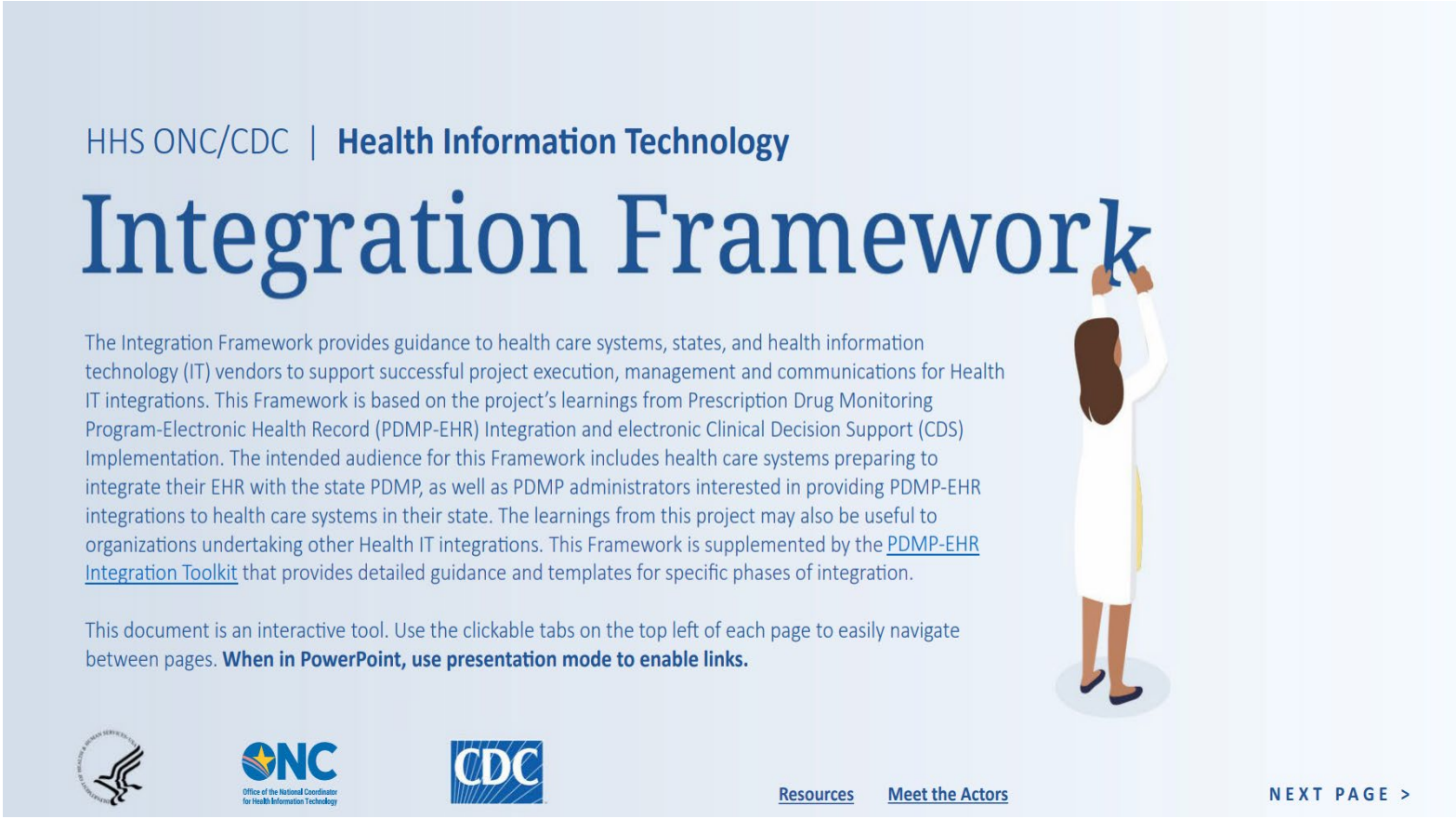
CDS Tools (Continued)

Health System Success

Print

Based on the pilot testing results, health systems have found great success in integrating the CDC Opioid Prescribing CDS Tools.

CDC Opioid Prescribing CDS Tools



- Electronic Clinical Decision Support Tools: Safer Patient Care for Opioid Prescribing | Opioids | CDC
- https://www.cdc.gov/opioids/pdf/Integration-Framework.pdf
- Integration Framework Toolkit
- Health System Success | Opioids | CDC

CDC Resources

CDC Overdose Prevention Website

- www.cdc.gov/drugoverdose

Resources for Clinicians

- https://www.cdc.gov/opioids/healthcare-professionals/index.html
- https://www.cdc.gov/drugoverdose/pdf/Pharmacists_Brochure-a.pdf
- https://www.cdc.gov/opioids/healthcare-admins/qi-cc-implementation.html
- https://www.cdc.gov/opioids/healthcare-admins/pdf/Quality-Improvement-Care-Coordination-508.pdf
- https://www.cdc.gov/opioids/healthcare-admins/pdf/Handbook-for-Healthcare-Executives.pdf

Clinical Decision Support Resources

- **CDC Clinical Decision Support EHR Website:** https://www.cdc.gov/opioids/healthcare-admins/ehr/index.html
- **Implementation Guide Output:** http://build.fhir.org/ig/cqframework/opioid-cds-r4/
- **Source for the implementation guide:** https://github.com/cqframework/opioid-cds
- **Supporting Java packages for the CQL-to-ELM translator and CQL Engine:** https://github.com/cqframework/opioid-cds-logic
- **Agency for Healthcare Research Quality's CDS Connect:** https://cds.ahrq.gov/cdsconnect/artifact/factors-consider-managing-chronic-pain-pain-management-summary

Thank you!

The findings and conclusions in this presentation are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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Clinical Decision Support Measurement

Allison B. McCoy, PhD, ACHIP, FAMIA

Assistant Professor, Biomedical Informatics

Director, Clinical Informatics Core

Measuring PC CDS

Scaling, Measurement, and Dissemination of CDS Workgroup Measurement Products

AHRQ
Agency for Healthcare Research and Quality

Clinical Decision Support Innovation Collaborative

PC CDS Performance Measurement Guide

Product Overview

Describes performance measures for PC CDS to help users understand *what they should measure* and *how they should measure it*, given their intervention-related aims (e.g., formative/summative evaluation) and who they are (e.g., researcher, health system leader, etc.).

Measures for evaluating PC CDS development and implementation processes

User scenarios to support inventory utility

Call to action, including identified gaps and recommendations

*Measures on clinical outcomes are described in the O&O measurement guide.

Types and Organization of Measures Included in the Guide

What did you design?

- **CDS Design**
  - User-based design
  - Organizational factors
  - Software performance
  - Information quality

What was used?

- **Users**
  - Adoption
  - Reach
- **Use Frequency**
  - Clinician workflow analysis
  - Patient life flow integration
  - Fidelity of implementation to design

What were the results?

- **Satisfaction with CDS Tool**
  - Intent to use
  - Alert fatigue
  - Usability
  - User satisfaction
  - Utility
- **Knowledge and Decision Making Quality**
  - Clinical guideline adherence
  - Policy and safety compliance
  - Patient engagement/participation
  - Clinician or patient knowledge
  - Patient decision-making processes
- **Collaboration & Workflow**
  - Shared Decision Making
  - Clinician attitudes & beliefs
  - Workflow integration
- **Cost of the CDS intervention**
  - Cost

Measurement Inventory

PC CDS Performance Measurement Guide					
Performance Areas of Measurement					
Implementation Phase	Intervention Component	Measurement Category	Measure Construct Assessed	Measure Constuct Description	Intervention Type
Design	CDS Design	User-based design	Usability flaws	Use error rating	Data integration display
Design	CDS Design	User-based design	Usability flaws	Potential clinical severity of usability is	Data integration display
Design	CDS Design	User-based design	Perceived usability	Assesses user perceptions of usability	Patient-saftey dashboard
Design	CDS Design	User-based design	Satisfaction with user-computer i	Users' subjective satisfaction with spec	Alerts (drug-lab interacti

Measure Properties				Measure Specifications		
Donabedian D	Assessment Type	Perspective Ass	Data Collection Approach	Tool/Approach	Items and Dimensions	Response Scale
Process	Formative	Care Team	Qualitative & Quantitative	Think aloud simula	Use Error Ratings (UERs) on a scale of 2–0 tc	
Process	Formative	Care Team	Qualitative & Quantitative	Think aloud simulation. Potential severity of the use error was c		
Process	Formative	Care Team & Patie	Quantitative	Health Information	Nielsen Heuristic Checkli	#1-5
Process	Formative	Care Team	Quantitative	Questionnaire for U	Six questions for an overall measure of sati	
Structure	Summative	System	Quantitative	Not Specified	Not Specified	Not Specitied

170+ measures

Covering a range of measurement areas assessing patient/caregiver and clinical care team perspectives.

Key Findings on Available Performance Measures

The most identified measure subdomains were CDS design, satisfaction with the CDS tool, use frequency, and users.

Commonly identified measure constructs included usability, alert fatigue, adoption, clinical guideline adherence.

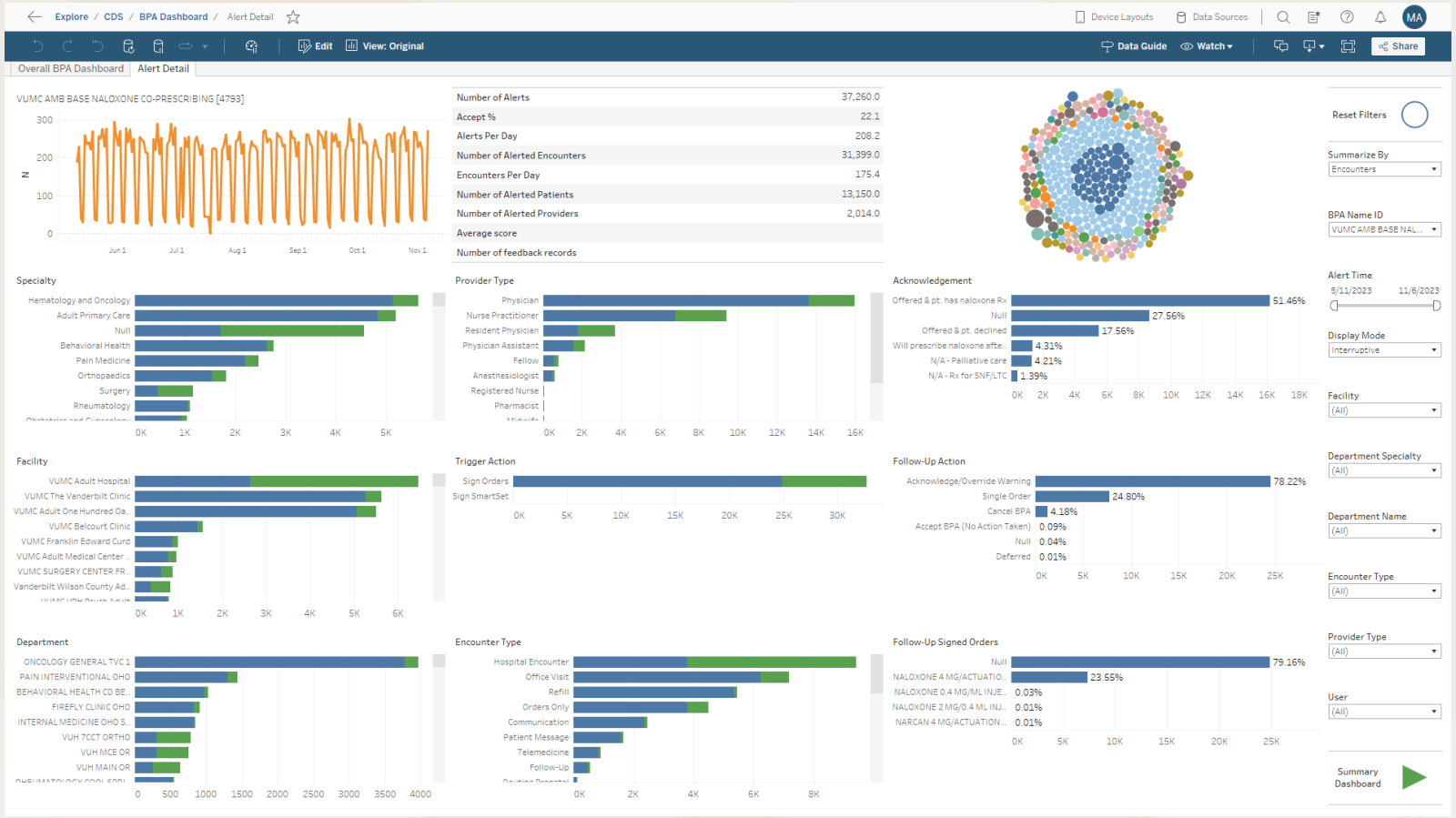
Common implementation settings include primary care, inpatient settings, and emergency departments.

Measurement Gaps

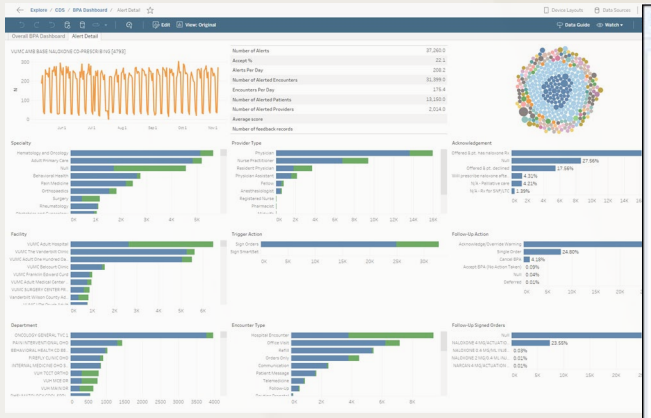
Patient-centered Measures	Measure Availability	Evidence Scope or Quality	Study Design
• Much less attention paid to patient-centered measures for assessing the development and implementation of PC CDS interventions in the literature, compared to measures focused on the clinical care team perspective.	• Few/no measures captured for measurement categories identified important by the Workgroup in feasibility, fairness and equity, and standards conformity. • Standardized measures needed for patient knowledge, patient informed choice, cognitive workload, alert fatigue, and tool acceptance to be able to compare effects across studies.	• The majority of evidence related to CDS performance was rated as “low quality” or at “high risk of bias” by systematic reviews and meta-analyses. • Primary focus on technical feasibility with less emphasis on socio-technical aspects of intervention.	• Limited direct assessment of workflow/life flow changes; reliance on proxy measures as indicator of quality, completeness, or accuracy of a workflow. • Lacking robust analytic approaches and methods that demonstrate evidence-based improvements and to build the case for wider implementation.

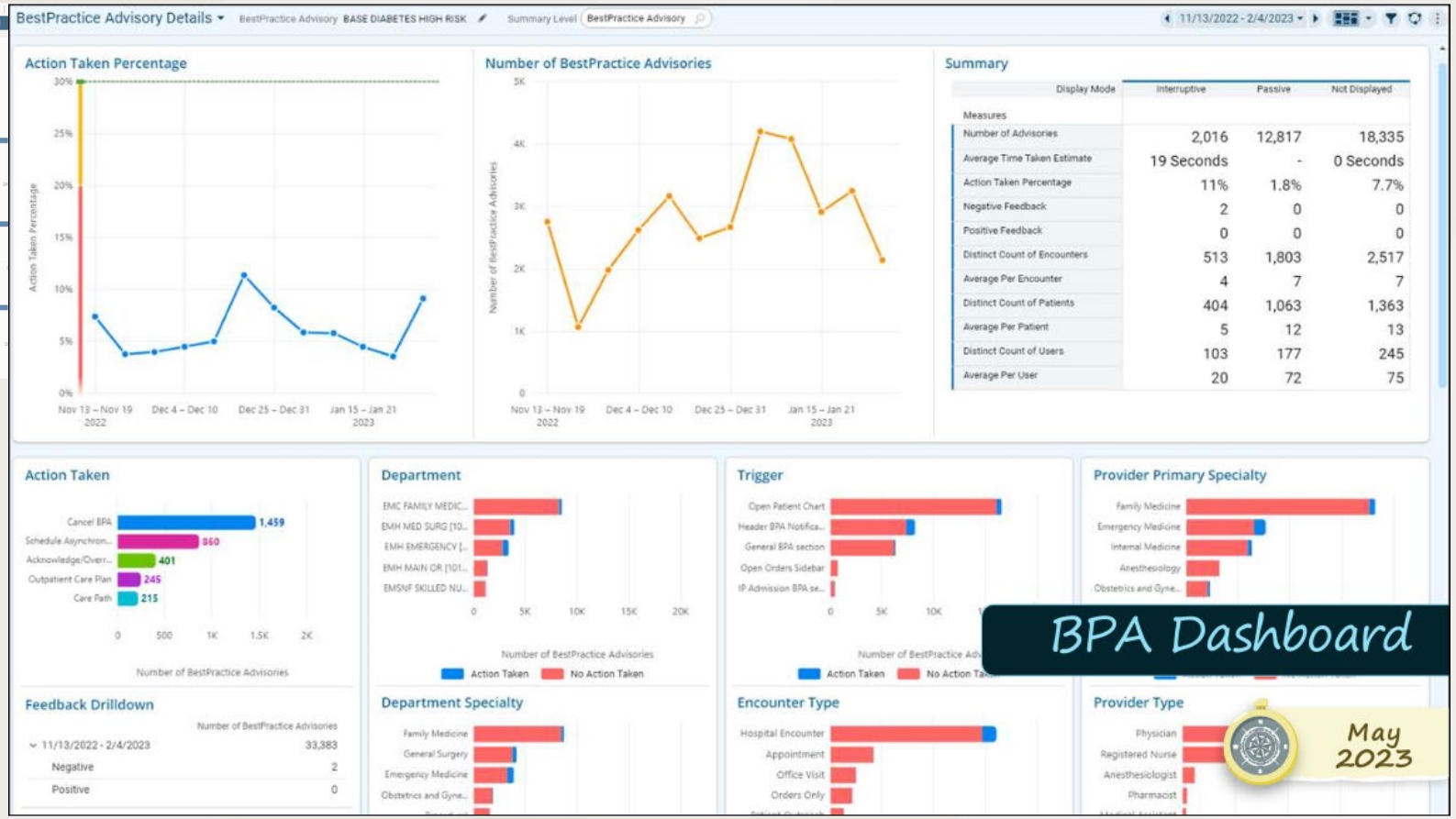
CDS Measurement at Vanderbilt University Medical Center

Locally Developed and Vendor-Provided Tools



Locally Developed and Vendor-Provided Tools





Advanced AI Approaches

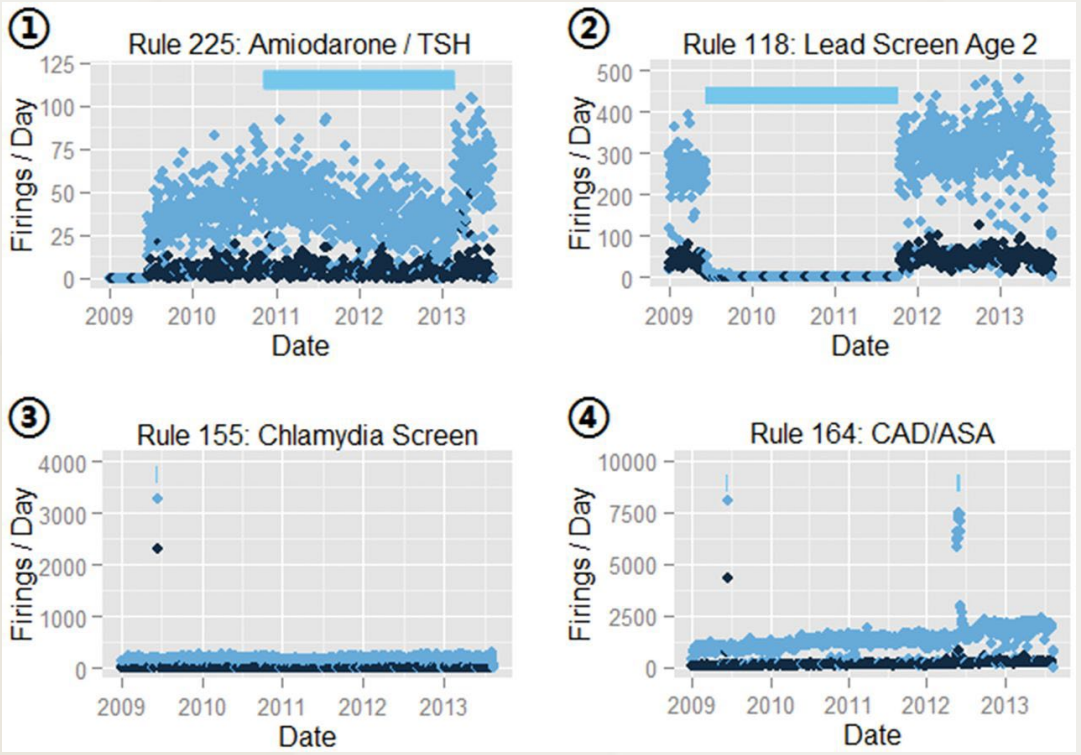
Analysis of clinical decision support system malfunctions: a case series and survey

RECEIVED 6 November 2
REVISED 7 January 2
ACCEPTED 12 January 2
PUBLISHED ONLINE FIRST 28 March 2

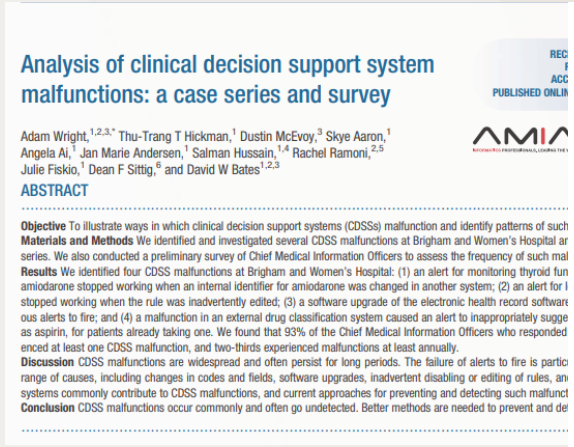
Adam Wright,[1,2,3,*] Thu-Trang T Hickman,[1] Dustin McEvoy,[3] Skye Aaron,[1] Angela Ai,[1] Jan Marie Andersen,[1] Salman Hussain,[1,4] Rachel Ramoni,[2,5] Julie Fiskio,[1] Dean F Sittig,[6] and David W Bates[1,2,3]

ABSTRACT

Objective To illustrate ways in which clinical decision support systems (CDSSs) malfunction and identify patterns of such malfunctions.
Materials and Methods We identified and investigated several CDSS malfunctions at Brigham and Women's Hospital and present them as series. We also conducted a preliminary survey of Chief Medical Information Officers to assess the frequency of such malfunctions.
Results We identified four CDSS malfunctions at Brigham and Women's Hospital: (1) an alert for monitoring thyroid function in patients r amiodarone stopped working when an internal identifier for amiodarone was changed in another system; (2) an alert for lead screening for stopped working when the rule was inadvertently edited; (3) a software upgrade of the electronic health record software caused numerou ous alerts to fire; and (4) a malfunction in an external drug classification system caused an alert to inappropriately suggest antiplatelet drug as aspirin, for patients already taking one. We found that 93% of the Chief Medical Information Officers who responded to our survey had enced at least one CDSS malfunction, and two-thirds experienced malfunctions at least annually.
Discussion CDSS malfunctions are widespread and often persist for long periods. The failure of alerts to fire is particularly difficult to d range of causes, including changes in codes and fields, software upgrades, inadvertent disabling or editing of rules, and malfunctions of systems commonly contribute to CDSS malfunctions, and current approaches for preventing and detecting such malfunctions are inadequat
Conclusion CDSS malfunctions occur commonly and often go undetected. Better methods are needed to prevent and detect these malfunc



Advanced AI Approaches



Analysis of clinical decision support system malfunctions: a case series and survey

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Research and Applications

Research and Applications

Cranky comments: detecting clinical decision support malfunctions through free-text override reasons

Skye Aaron,[1] Dustin S McEvoy,[2] Soumi Ray,[1,3] Thu-Trang T. Hickman,[4] and Adam Wright[1,2,3,5]

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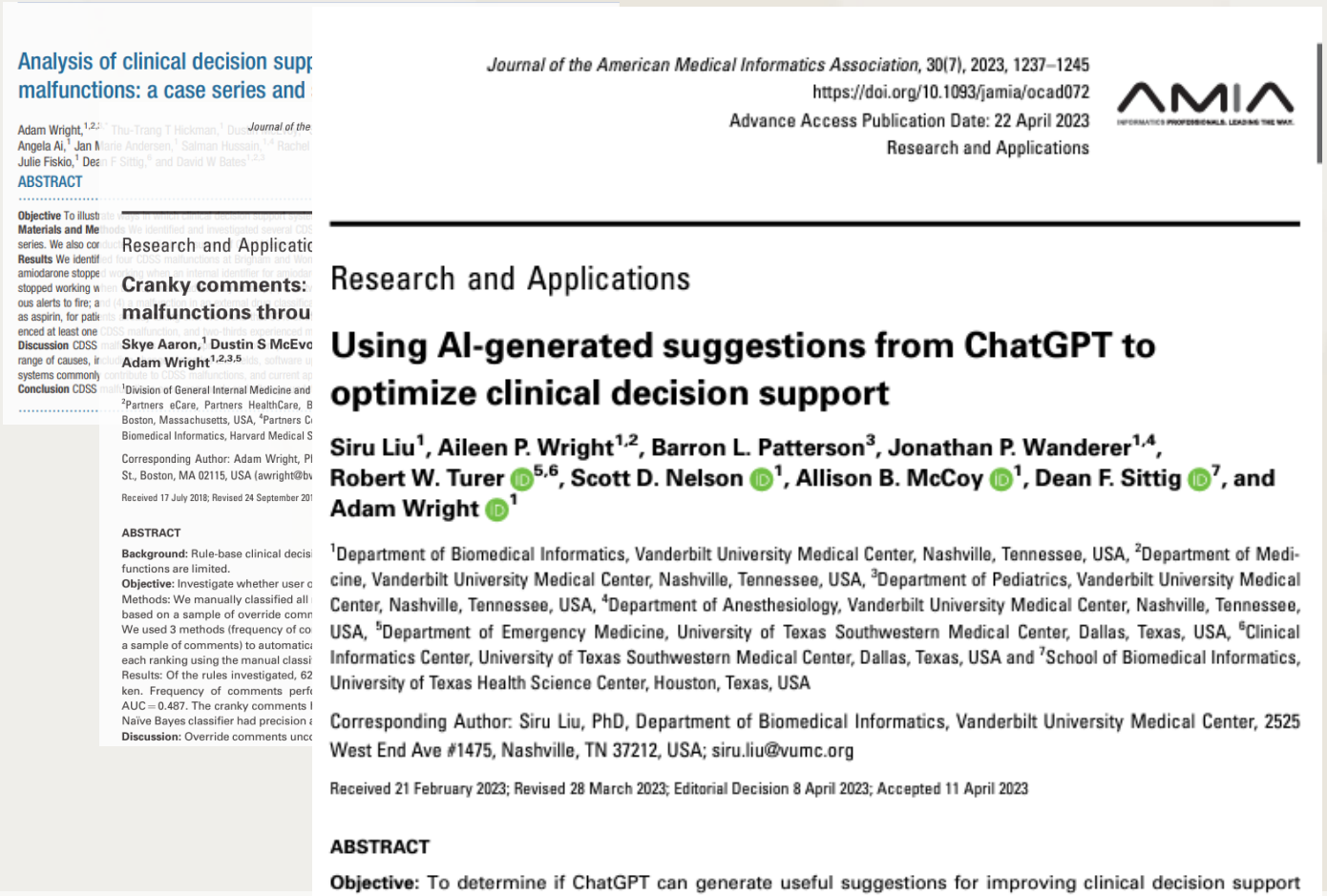
Received 17 July 2018; Revised 24 September 2018; Editorial Decision 2 October 2018; Accepted 8 October 2018

ABSTRACT

Background: Rule-base clinical decision support alerts are known to malfunction, but tools for discovering malfunctions are limited.
Objective: Investigate whether user override comments can be used to discover malfunctions.
Methods: We manually classified all rules in our database with at least 10 override comments into 3 categories

Advanced AI Approaches



Analysis of clinical decision supp
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Conclusion CDSS ...

Research and Applicatic

Cranky comments:
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Skye Aaron,[1] Dustin S McEvo
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[1]Division of General Internal Medicine and
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based on a sample of override comm
We used 3 methods (frequency of co
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each ranking using the manual classi
Results: Of the rules investigated, 62
ken. Frequency of comments perfo
AUC = 0.487. The cranky comments
Naïve Bayes classifier had precision a
Discussion: Override comments uncc

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Advance Access Publication Date: 22 April 2023
Research and Applications

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Research and Applications

Using AI-generated suggestions from ChatGPT to optimize clinical decision support

Siru Liu[1], Aileen P. Wright[1,2], Barron L. Patterson[3], Jonathan P. Wanderer[1,4], Robert W. Turer[5,6], Scott D. Nelson[1], Allison B. McCoy[1], Dean F. Sittig[7], and Adam Wright[1]

[1]Department of Biomedical Informatics, Vanderbilt University Medical Center, Nashville, Tennessee, USA, [2]Department of Medicine, Vanderbilt University Medical Center, Nashville, Tennessee, USA, [3]Department of Pediatrics, Vanderbilt University Medical Center, Nashville, Tennessee, USA, [4]Department of Anesthesiology, Vanderbilt University Medical Center, Nashville, Tennessee, USA, [5]Department of Emergency Medicine, University of Texas Southwestern Medical Center, Dallas, Texas, USA, [6]Clinical Informatics Center, University of Texas Southwestern Medical Center, Dallas, Texas, USA and [7]School of Biomedical Informatics, University of Texas Health Science Center, Houston, Texas, USA

Corresponding Author: Siru Liu, PhD, Department of Biomedical Informatics, Vanderbilt University Medical Center, 2525 West End Ave #1475, Nashville, TN 37212, USA; siru.liu@vumc.org

Received 21 February 2023; Revised 28 March 2023; Editorial Decision 8 April 2023; Accepted 11 April 2023

ABSTRACT

Objective: To determine if ChatGPT can generate useful suggestions for improving clinical decision support (CDS) logic and to assess noninferiority compared to human-generated suggestions.
Methods: We supplied summaries of CDS logic to ChatGPT, an artificial intelligence (AI) tool for question answering that uses a large language model, and asked it to generate suggestions. We asked human clinician reviewers to review the AI-generated suggestions as well as human-generated suggestions for improving the same CDS alerts, and rate the suggestions for their usefulness, acceptance, relevance, understanding, work-

A

I have a clinical decision support alert to identify potentially inappropriate use of albuterol or chest x-rays (CXR) in children with bronchiolitis. — Alert description

In AAP guideline, it states, “Clinicians should not administer albuterol (or salbutamol) to infants and children with a diagnosis of bronchiolitis (Evidence Quality: B; Recommendation Strength: Strong Recommendation)” and “When clinicians diagnose bronchiolitis on the basis of history and physical examination, radiographic or laboratory studies should not be obtained routinely (Evidence Quality: B; Recommendation Strength: Moderate Recommendation).” — Statement of guideline or standard, if available

The current inclusion and exclusion criteria are listed below. Are there any other exclusions should be added?
if INPATIENT bronchiolitis order set was used or bronchiolitis was added to problem list in last 14 days
AND
Either CXR ordered or albuterol ordered
Age inclusion is “to 2 years” — Inclusion and exclusion criteria of the alert

Based on the information provided, it seems that the current inclusion and exclusion criteria for the clinical decision support alert are appropriate. However, it may be helpful to add additional exclusions to account for situations where chest radiography or albuterol may be indicated despite a diagnosis of bronchiolitis. Some possible exclusions to consider could include:

- Patients with other respiratory conditions, such as pneumonia or asthma, that may require chest radiography or albuterol treatment
- Patients who are experiencing respiratory distress or other symptoms that may indicate the need for chest radiography or albuterol treatment
- Patients who are receiving other medications, such as corticosteroids or antibiotics, that may affect their respiratory status and warrant chest radiography or albuterol treatment

It's important to carefully consider the inclusion and exclusion criteria for clinical decision support alerts, and to base these criteria on the latest evidence and guidelines. It may also be helpful to engage with healthcare providers and other stakeholders to gather their feedback and input, and to use this feedback to improve the performance and usability of the CDS system. Additionally, implementing a system for monitoring and evaluating the impact of the CDS alert can help ensure that it is having the desired effects on patient care and outcomes.

VANDERBILT UNIVERSITY MEDICAL CENTER

Critical Gaps in CDS Measurement

No standard set of measures exists for comprehensive, reproducible, accurate CDS measurement

Many EHRs do not provide appropriate access to data or tools for effective CDS measurement

Benchmarks for comparison across organizations are unavailable

Questions?

allison.b.mccoy@vumc.org

Questions

Office of the National Coordinator for Health Information Technology

Contact ONC

Alison Kemp alison.kemp@hhs.gov

Phone: 202-690-7151

Health IT Feedback Form: https://www.healthit.gov/form/healthit-feedback-form

Twitter: @onc_healthIT

LinkedIn: Office of the National Coordinator for Health Information Technology

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