

ThinkRare

Harnessing AI for the Early Identification of Patients with Undiagnosed Rare Genetic Diseases

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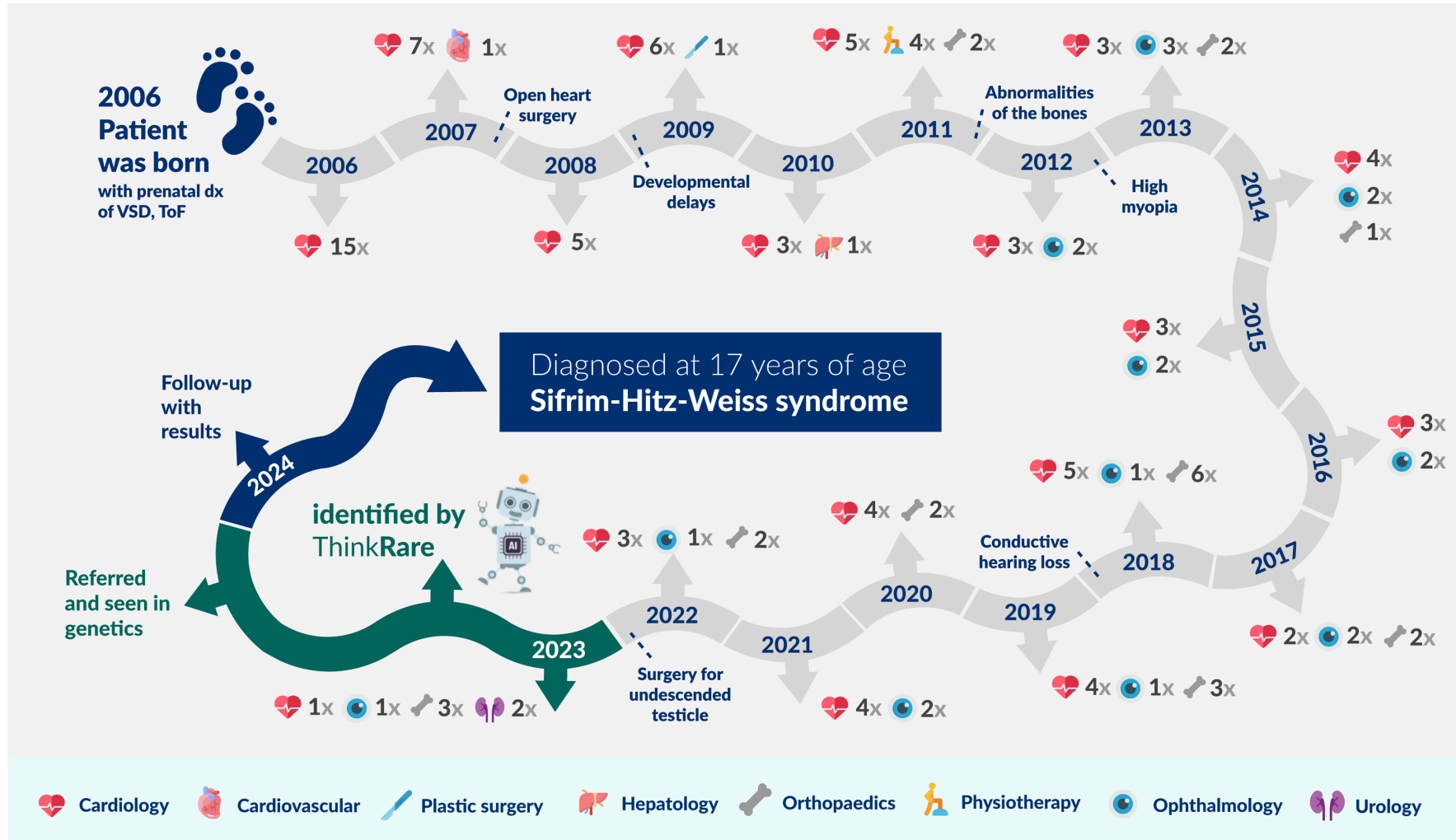
Clinical Geneticist, CHEO

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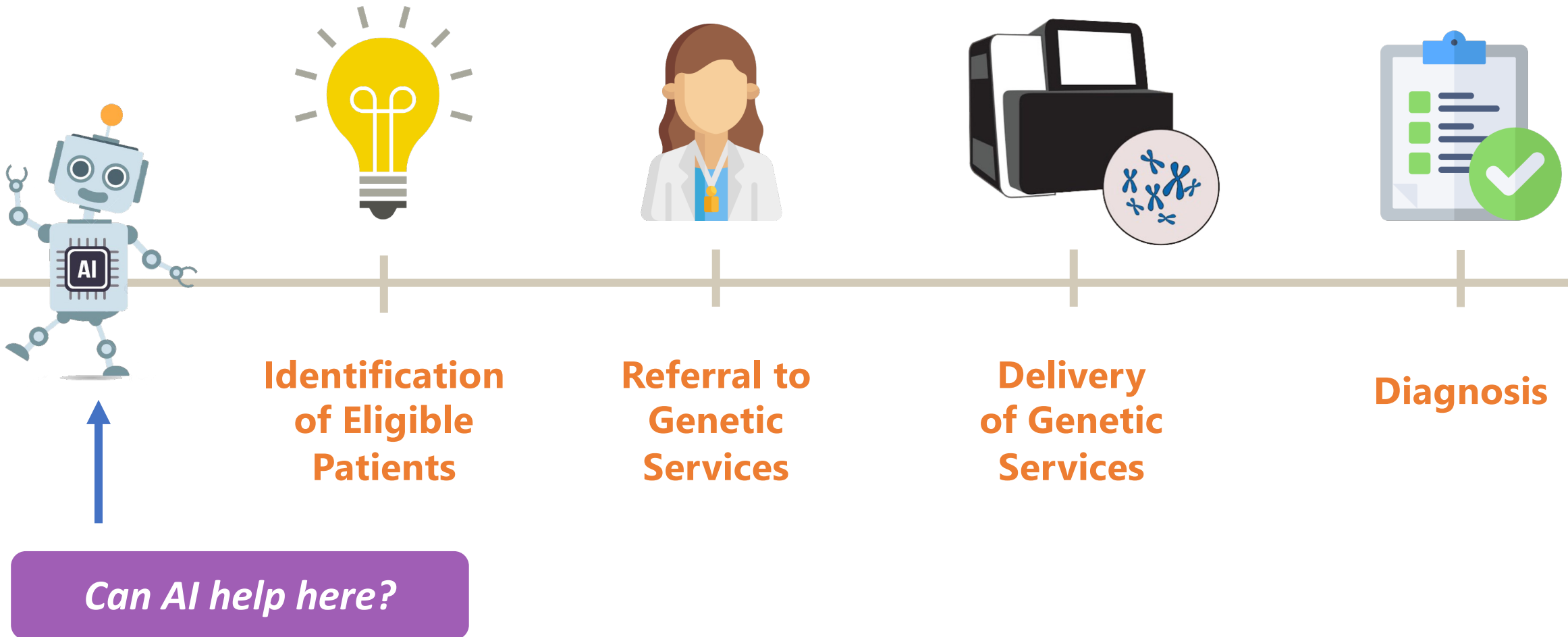
CORD Conference; April 30, 2025

Diagnostic Odyssey



150+ visits
9 departments

How Can Technology Assist in the Diagnostic Process?

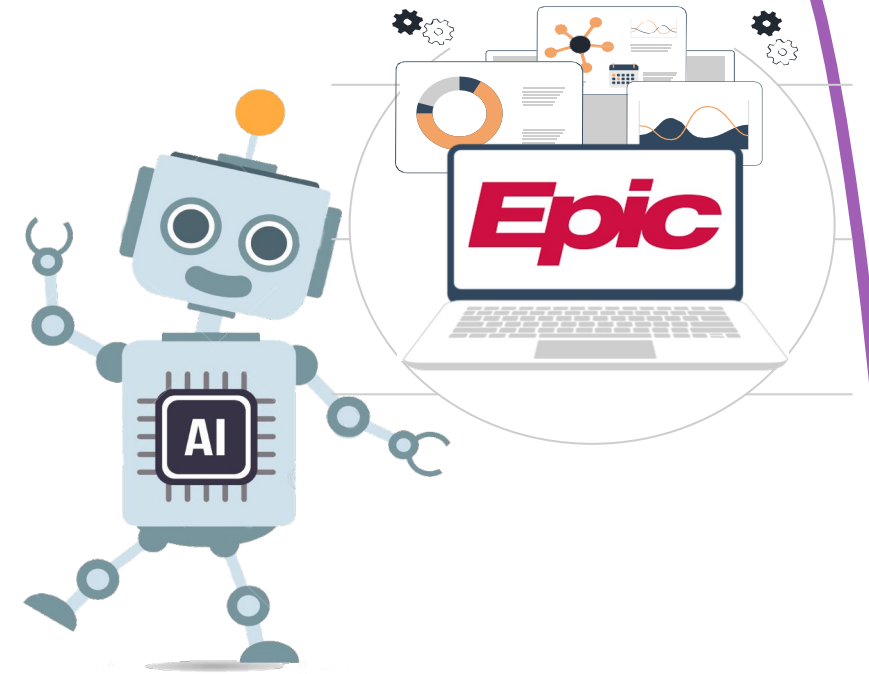


Background

'Think**Rare**' Search Algorithm

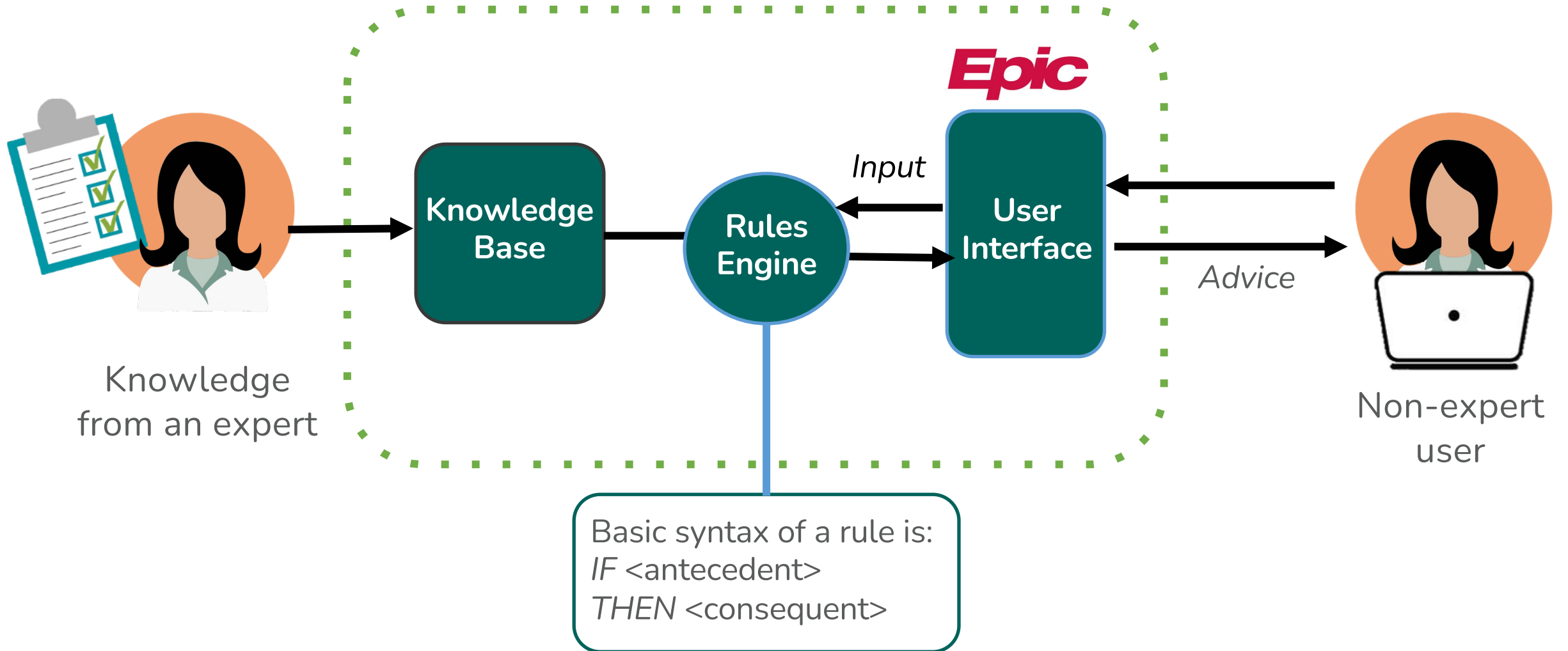
Recommendation:

Equipping frontline providers with tools for diagnosis and referral

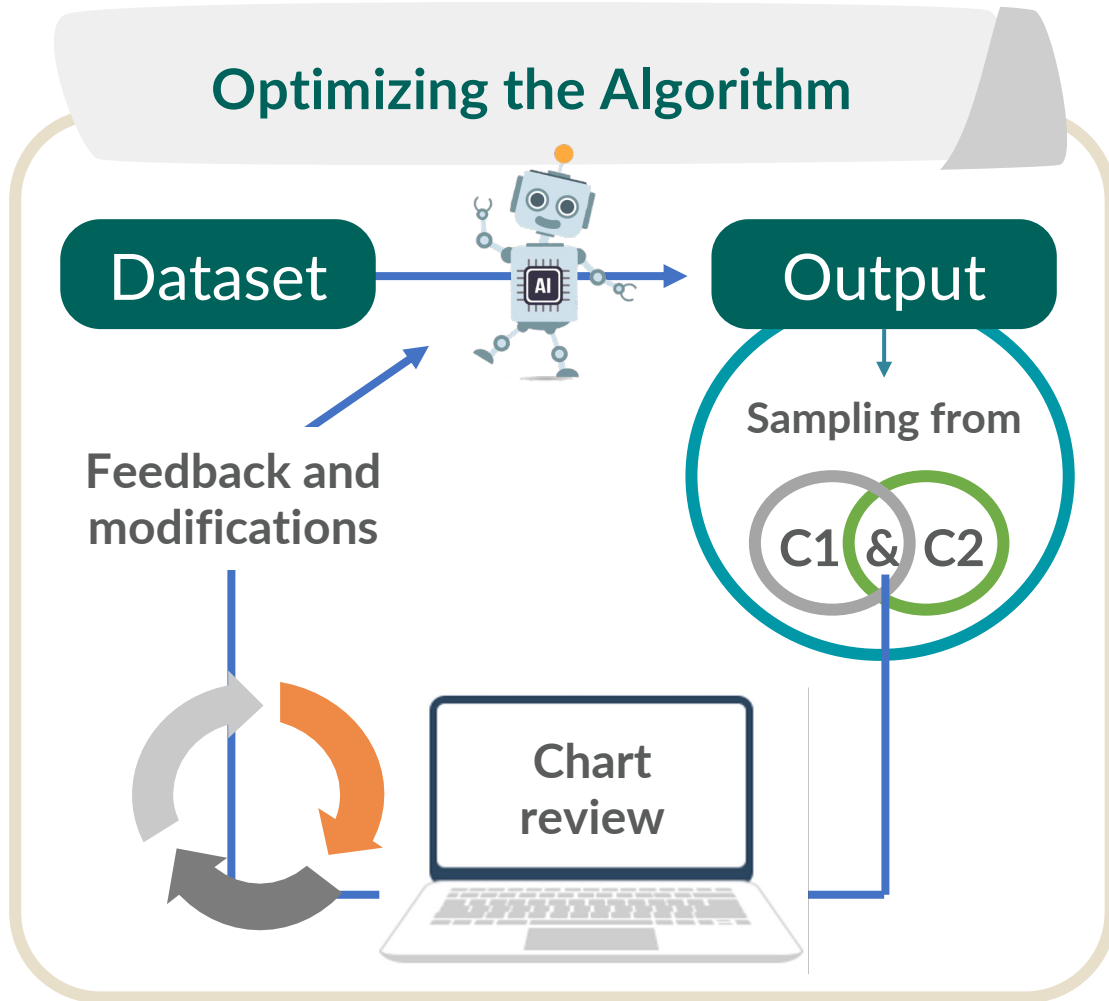


A rule-based expert system to retrospectively identify patients with a complex undiagnosed rare genetic disease

Baby AI



Project Lifecycle



Phase 1: Retrospective proof-of-concept study - 2018-2024

Phase 2: Silent prospective trial - 2024-2025

Phase 3: Clinical BPA implementation - March 2025

Final Algorithm (version 5 – 4 YEARS!!!!)

Input: Dataset

Algorithm: Exclusion criteria

>18yo

Seen exclusively in oncology, rheumatology and/or hematology,

Abnormal genetic test result

Seen in metabolics and/or genetics

Diagnosis code in our exclusion list

Algorithm: Inclusion criteria

Criteria 1 – Two or more specific diagnosis codes (ICD-10 codes)

AND

Criteria 2 – Encounters (visits) in two or more departments

Output:
“Selected Patients”

Outcomes of Phase 1 and 2

Input: 2018-2024: **376,728 patients**

35patients referred

Rapid Genomics Clinic

75% diagnostic yield

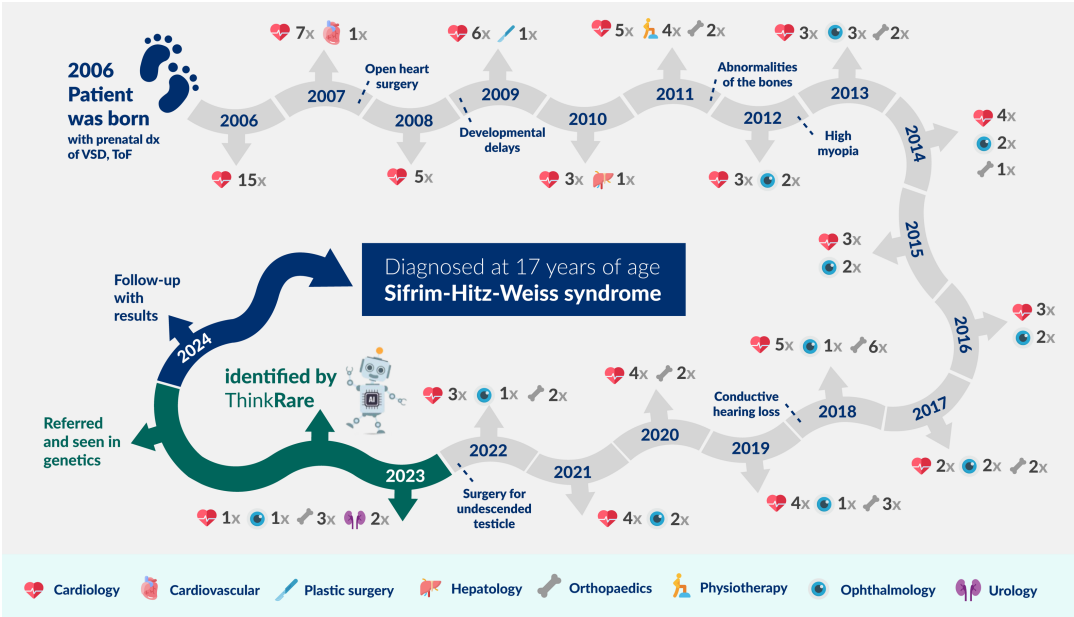


“ It seems this would have been good information to have after he was born. **Why weren’t we referred to you then?** ”



“Less questions, less stress, less blaming ourselves” – Antony’s father

“This investigation definitely gave us peace of mind” – Eddy’s mother



Lessons Learned

Lesson #1

Multidisciplinary team is required to support developing an algorithm/tool



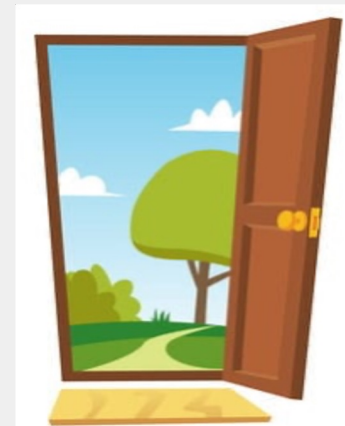
Lesson #2

Algorithm is only as good as your data



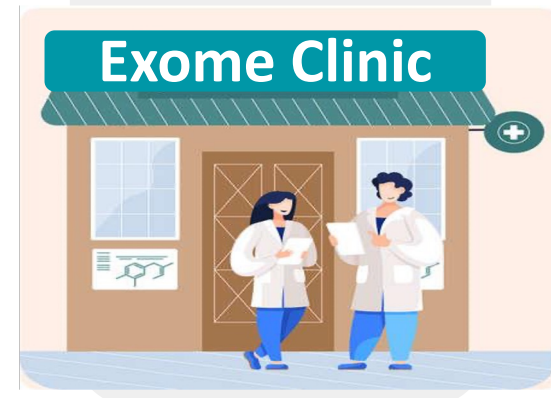
Lesson #3

Optimize the specificity over the sensitivity



Lesson #4

A well-resourced clinic is essential



Phase 3: ThinkRare Best Practise Advisory (BPA)

How to get back to the BPA if you open the link

Reason for BPA

OurPractice Advisory - Cadence, Betty Ann

Suggestion (1)

⚠ This patient has been flagged as a potential candidate for a referral to CHEO Genetics.

ThinkRare

- Please review your patient's chart and consider a referral to Genetics if appropriate. The ThinkRare algorithm identifies patients that may have an undiagnosed rare genetic disease and could benefit from clinical genome-wide sequencing (click on the link below more information on genome-wide sequencing and the provincial criteria).
 - If you click on the link, you can come back to this advisory by clicking the 'This patient has been flagged as a potential candidate for a referral to CHEO Genetics.' flag found in the StoryBoard.
- The ThinkRare algorithm identifies patients with multi-system issues that have been seen in multiple departments at CHEO. The algorithm may identify patients who appear to have a genetic etiology, but may have a different explanation for their medical issues (I.e. prematurity, HIE, resolved issues, known diagnosis).
- If you have questions, please contact Alex White-Brown at awhitebrown@cheo.on.ca or 613-737-7600x4390

[Order](#) [Do Not Order](#) [Amb Referral to Genetics \(ThinkRare\)](#)

[Patient eligibility for clinical genome-wide sequencing](#)

Acknowledge Reason _____

[Does not meet criteria](#) [Family/Patient declines](#) [Other/Feedback](#)

[Accept](#) [Dismiss](#)

Explanation of the BPA and GSO criteria to help guide decision

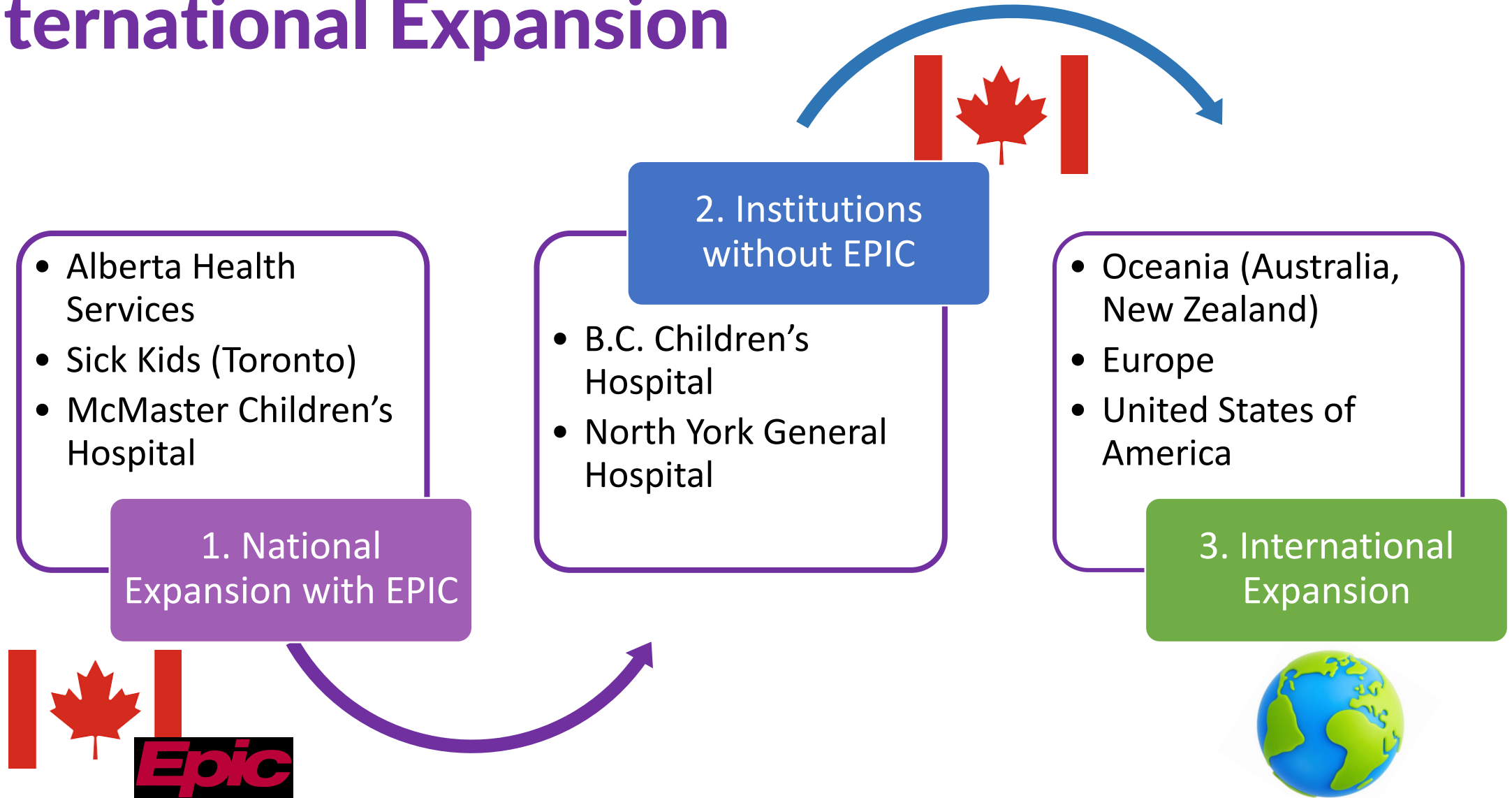
Explanation of why the patient was flagged and potential reasons for “false identification”

Phase 4:
Improvements
to the
algorithm
and APP
development

Adding additional
machine learning models
on top of existing system

APP: more transportable
to other institutions

Phase 5: National and International Expansion



Acknowledgments

Alex White-Brown, M.Sc. - Genetic Counsellor

Sarah Sawyer, MD, PhD, FRCPC, FCCMG – Clinical Geneticist

Caitlin Chisholm, M.Sc., CGC - Genetic Counsellor

Grace Ediae, MS, CGC, CCGC - Genetic Counsellor

Ivan Terekhov, Technical Director - Research Informatics & Data Architect

Nicholas Mitsakakis, MSc, PhD, P. Stat. - Biostatistician and Associate Scientist

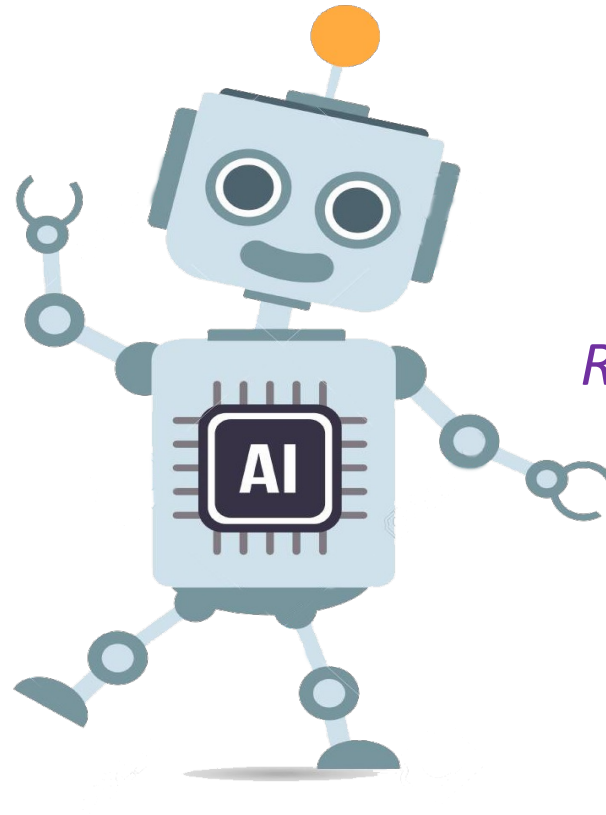
Jeff Guo, Data Warehouse Analyst

Jon Seymour, Senior Informatics Analyst



CHAMO
Innovation
Fund

QUESTIONS?



ThinkRare Retrospective study
Revision submitted to Genetics in Medicine