Data Diversity Challenges in Genomics

Example 1: UCAN CAN-DU and CURE in Childhood Arthritis
Example 2: SOLVE Whole Exome Sequencing in Rare Disease

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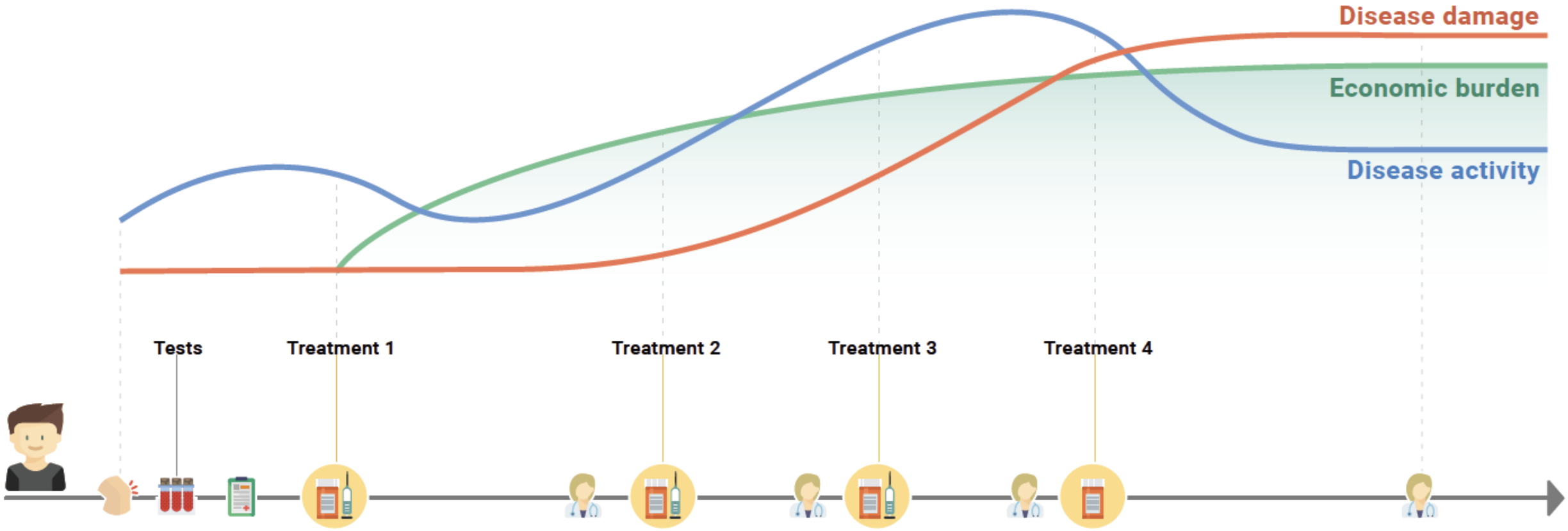
Moving from Trial and Error to Precision Decisions in Childhood Arthritis (JIA)

UCAN CAN-DU: Understanding Childhood Arthritis Canada-Netherlands Personalized Medicine Network in Childhood Arthritis and Rheumatic Disease

CURE (Precision Decisions for Childhood Arthritis):

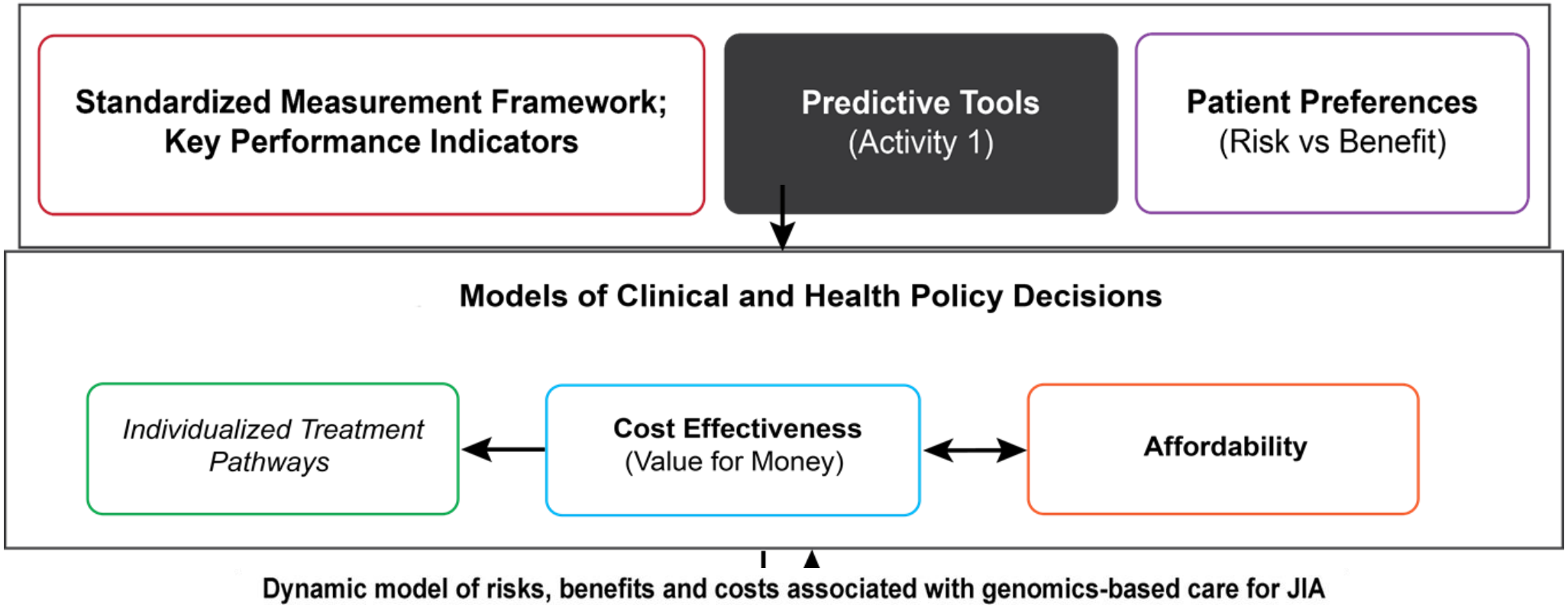
CIHR and Genome Canada funded Large Scale Applied Research

Current Standard of Care Trial and Error Approach

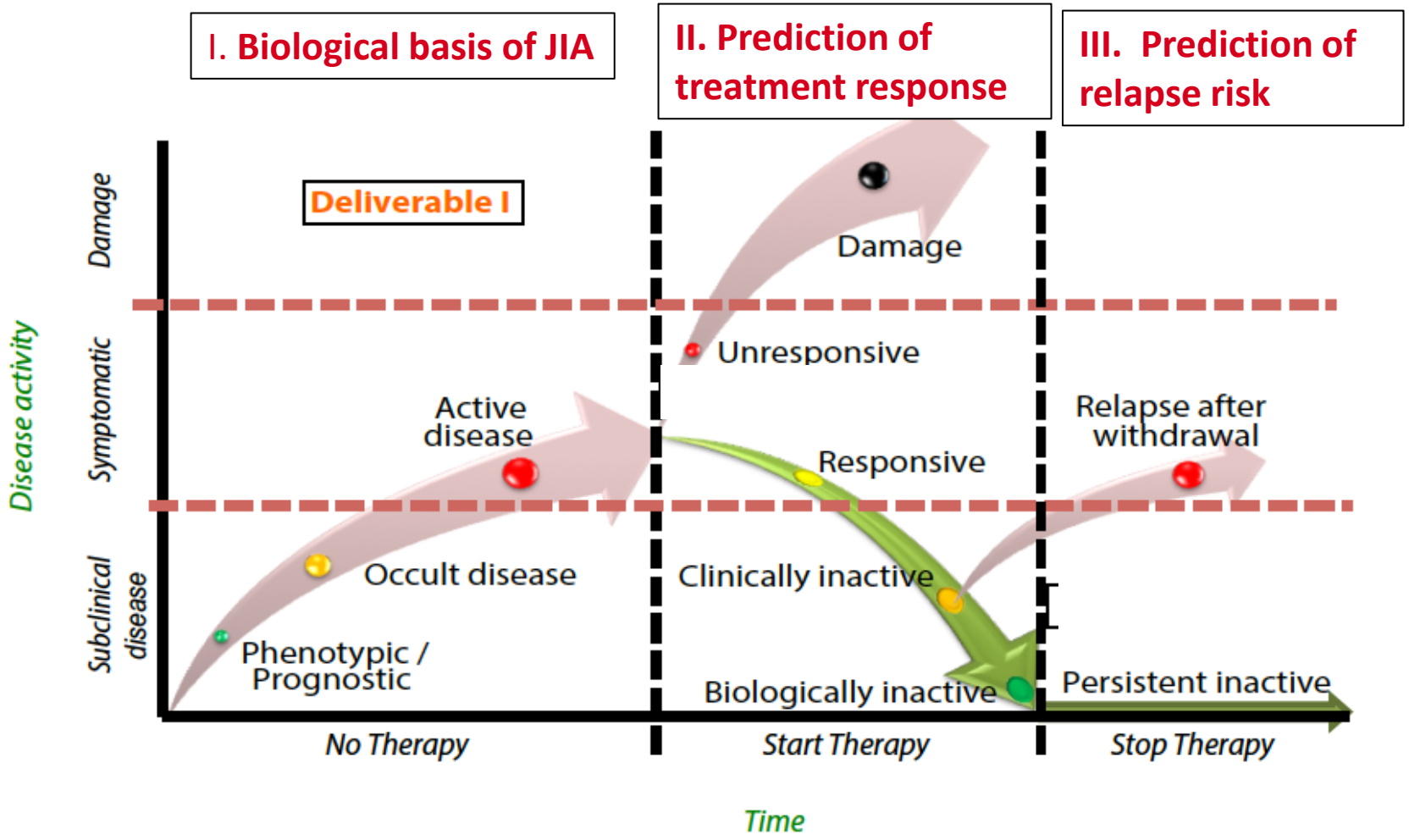


Need Evidence-based tools to Guide Therapy

Assessing Health Economic and Socioeconomic Benefits from Optimizing Clinical Management



Predictive Tools to Guide Clinical Decisions



Precision Health Approach to Childhood Arthritis (JIA)

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1. Communicating the right knowledge to the right people
2. Recognizing and diagnosing JIA early
3. Eliminating the trial-and-error approach to treatment
4. Enabling treat-to-target
5. Enabling appropriate treatment stopping protocols

Approach built on a foundation of integrated, standardized, longitudinal data from patients, providers and the health system.

Complexity of Treatment Patterns in JIA

- First study to assess treatment sequences for different drug classes in current routine practice “real world”
- 112 unique treatment sequences in cohort of 325 patients over 5 years
- To what extent is this equity-driven given limited access to biologics?

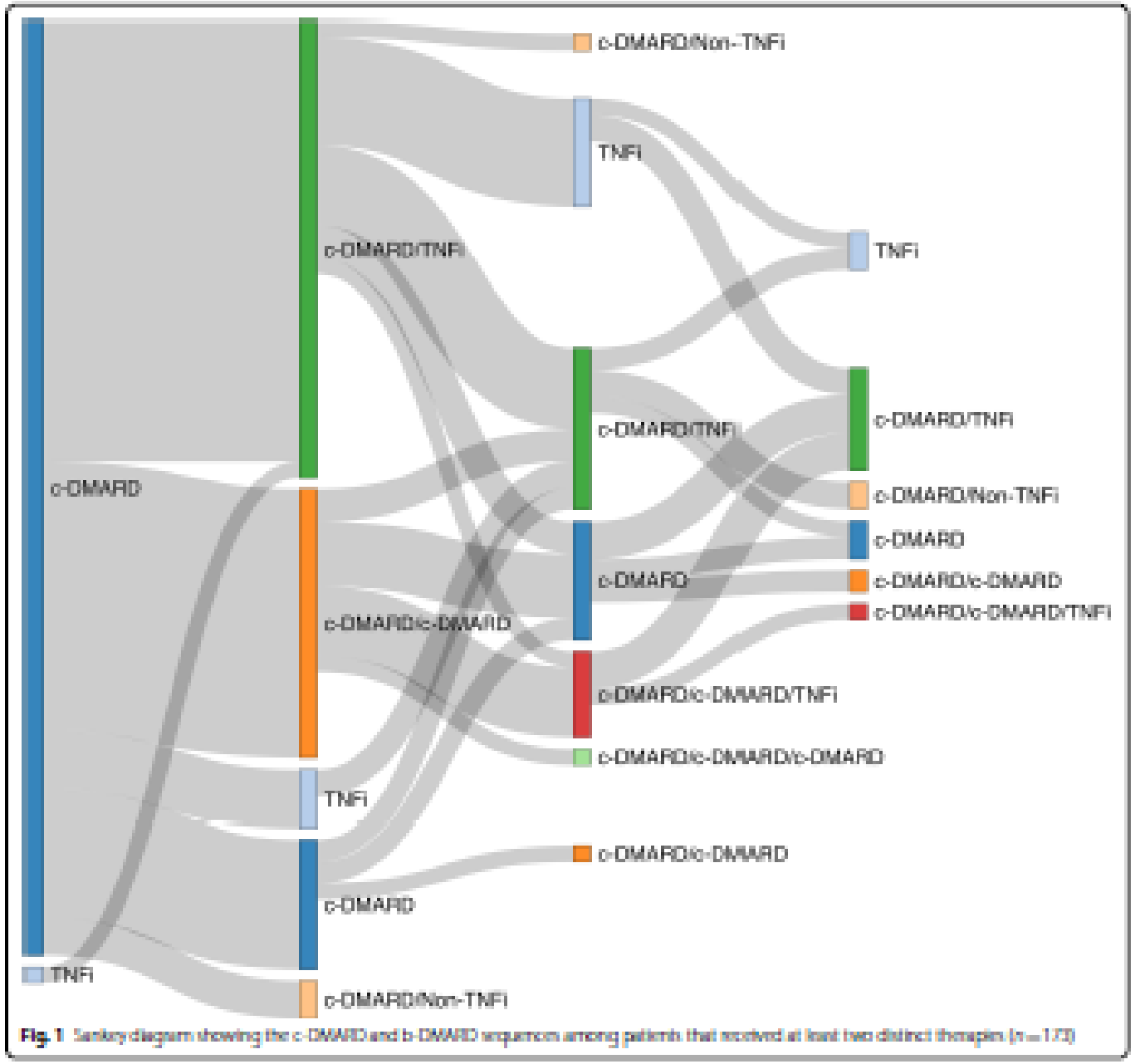

Fig. 1 Sankey diagram showing the c-DMARD and b-DMARD sequences among patients that received at least two distinct therapies (n = 173)

- Grazziotin LR, Currie G, Twilt M, Ijzerman MJ, Kip MMA, Koffijberg H, Benseler SM, Swart JF, Vastert SJ, Wulffraat NM, Yeung RSM, Marshall DA. Real-world data reveals the complexity of disease modifying anti-rheumatic drug treatment patterns in juvenile idiopathic arthritis: an observational study. Pediatr Rheumatol 2022 Apr 11;20(1):25. doi: 10.1186/s12969-022-00682-x

Variation in Clinical Practice Patterns for Tapering – Treatment Preferences and Access

- Approaches to tapering: Increase the interval between doses (59%); Stop immediately (8%); Reduce dose and increase interval (12%); Reduce dose and increase interval (8%); Increase the interval and maintain the longer interval (4%); Other (10%)
- Stopping immediately 10% Canadians; 0% in Netherlands
- Characteristics of patients/health systems:
  - history of complications and presence of co-morbidities
  - drug accessibility and continuity/availability of follow-up care related to health-care system and geography

Currie GR, Pham T, Twilt M, IJzerman MJ, Hull PM, Kip MMA, Benseler SM, Hazlewood GS, Yeung RSM, Wulffraat NM, Swart JF, Vastert SJ, Marshall DA. Perspectives of Pediatric Rheumatologists on Initiating and Tapering Biologics in Patients with Juvenile Idiopathic Arthritis: A Formative Qualitative Study. Patient. 2022 Sep;15(5):599-609. doi: 10.1007/s40271-022-00575-x

Economic Impact of Precision Medicine: Targeting interleukin-1 during 'window of opportunity' for systemic JIA

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- ✓ **Better outcomes for patients**
- ✓ **Long-term cost-savings for health system**
- ✓ **Validating clinical utility of biomarkers**

Current Practice

- Trial and error approach - fail conventional drugs prior to approval
- $15K – $416K/yr anti-IL-1
- Life-time drug costs = $1.2 to $33.3M for one child
- Budget Impact: Children with JIA on biologics in Canada (n~1000) = $16M to $445M per year

Personalized medicine

- Early start and Early stop
- $3,750 - $104,000 drug cost
- Avoid $1.2-33.2M over lifetime for one child
- Budget Impact – Avoid $10.7M to $298.2M per year in Canada

- Vastert SJ, de Jager W, Noordman BJ, Holzinger D, Kuis W, Prakken BJ, Wulffraat NM. Effectiveness of first-line treatment with recombinant interleukin-1 receptor antagonist in steroid-naive patients with new-onset systemic juvenile idiopathic arthritis: results of a prospective cohort study. Arthritis Rheumatol. 2014;66(4):1034-43. doi: 10.1002/art.38296

Value of Diagnostic Testing in Rare Genetic Diseases: Whole Exome Sequencing

- WES can rapidly identify disease-causing variants responsible for rare, single-gene diseases and potentially reduce duration of diagnostic odyssey
- **Care for Rare SOLVE Objective:** Cost-effectiveness of WES in the diagnostic pathway, and the value of a diagnosis in rare disease

Complexity of the Diagnostic Odyssey

- Among 228 patients mostly syndromic intellectual disability (n=155)
- average time spent seeking a diagnosis before sequencing was approximately **5.5 years**
- Included **16 diagnostic tests**

Duration of testing period, in days	
Mean, SD	1989 (2137)
Median, IQR	1136 (508-2923)
Range (min-max)	0-18,393
Number of diagnostic tests pursued (total)	
Mean, SD	16 (14)
Median, IQR	12 (7-21)
Range (min-max)	0-96

Hayeems R, Michaels Igbokwe C, Venkataramanan V, Hartley T, Acker M, Gillespie M, Ungar W, Mendoza-Londona R, Bernier FP, Boycott K, Marshall DA. The complexity of diagnosing rare disease: An organizing framework for outcomes research and health economics based on real-world evidence. Genet Med 2022; 24(3), 694–702

Summary: Making the Case for Value

Quality of evidence on effectiveness, outcomes and costs are affected by:

- Diversity of biologic profiles
- Access to testing, sequencing
- Access to health services and treatments
- Physician practice patterns
- Baseline socioeconomic status
- Preferences of patients, families and physicians