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Developing and Implementing an Indirect Treatment Comparison Program to Support Global HTA and Reimbursement Submissions

ISPOR 2020 Workshop

Wednesday, May 20, 2020; 10:00 AM - 11:00 AM EST

Workshop Introduction

- Thank you everyone for joining the workshop on ***"Developing and Implementing an Indirect Treatment Comparison Program to Support Global HTA and Reimbursement Submissions"***
- We will answer audience **questions** at the end of the workshop.

Today's Presenters

CHRIS CAMERON

Senior Vice President of Data Analytics and Evidence Synthesis at EVERSANA

STEVE PETERSON

Director, Janssen Global Market Access – Rheumatology

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Manager, Janssen Health Economics Design & Analytics

AGATA SCHUBERT

Compound Market Access Leader for Dermatology & Rheumatology at Janssen Europe, Middle East & Africa (EMEA)

Conflicts of Interest

- Chris Cameron is an employee and shareholder for EVERSANA. EVERSANA provides commercialization services to life science industry.
- Steve Peterson, Sandhya Nair, and Agata Schubert are employees of Janssen, the Pharmaceutical Companies of Johnson & Johnson.
- Steve Peterson and Agata Schubert are shareholders of Johnson & Johnson.

Agenda

Developing and Implementing an Indirect Treatment Comparison Program to Support Global HTA and Reimbursement Submissions

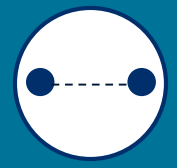
1. Introduction to Indirect Treatment Comparisons (ITCs)
2. Guidance on Selecting the Most Appropriate ITC Methods for a Global ITC Program
3. Developing a global ITC Program, including early feasibility assessment with timelines
4. Building a Global ITC Program – Guidance from a Global HEOR Lead
5. Global ITC Program – A European Perspective
6. Application of a Global ITC Program – Interactive Case Studies

Introduction to Indirect Treatment Comparisons (ITCs)

> ***Indirect treatment comparison refers to a comparison of different healthcare interventions using data from separate studies, in contrast to a direct comparison within randomized controlled trials. Indirect comparison is often used because of a lack of, or insufficient, evidence from head-to-head comparative trials.***

Types of indirect treatment comparisons

Summary Level Data Only



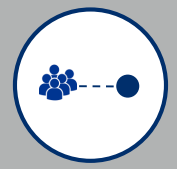
Naïve Indirect Comparison

Anchored Indirect Comparison

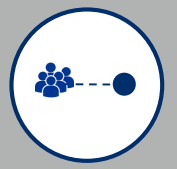
Network Meta-Analysis (NMA)

NMA Involving Meta-Regression

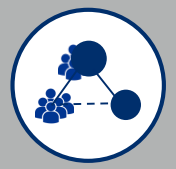
Mix of IPD and Summary Level Data



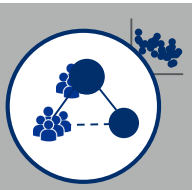
Unanchored MAIC



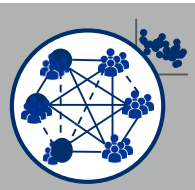
Unanchored STC



Anchored MAIC

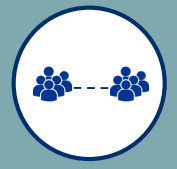


Anchored STC

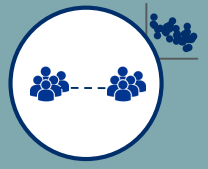


NMA Leveraging IPD

IPD Only



Propensity Score Reweighing and Matching



Multivariable Regression Using IPD

NMA:	Network meta-analysis
IPD:	Individual patient data
MAIC:	Matching-adjusted indirect comparison
STC:	Simulated treatment comparison

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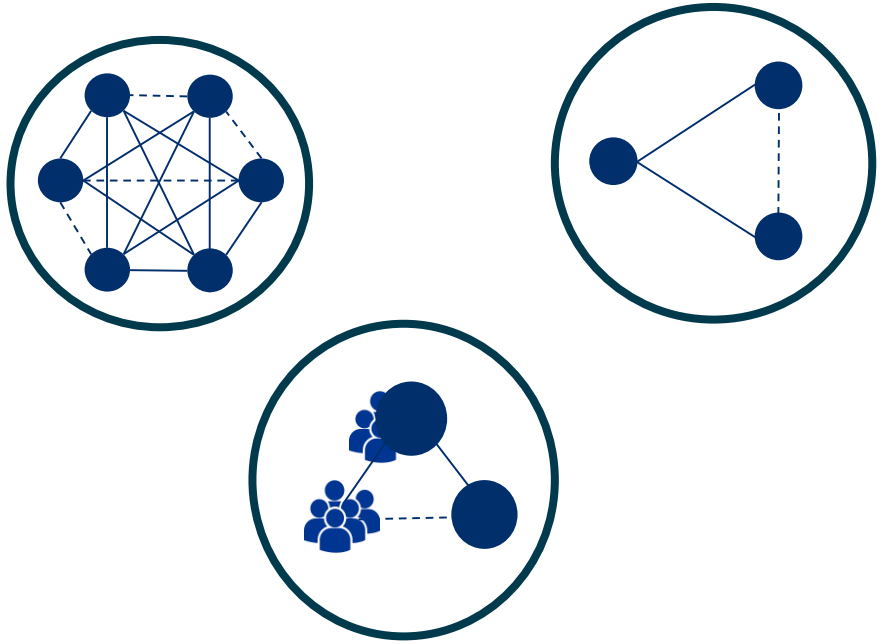
Guidance on Selecting the Most Appropriate ITC Methods for a Global ITC Program

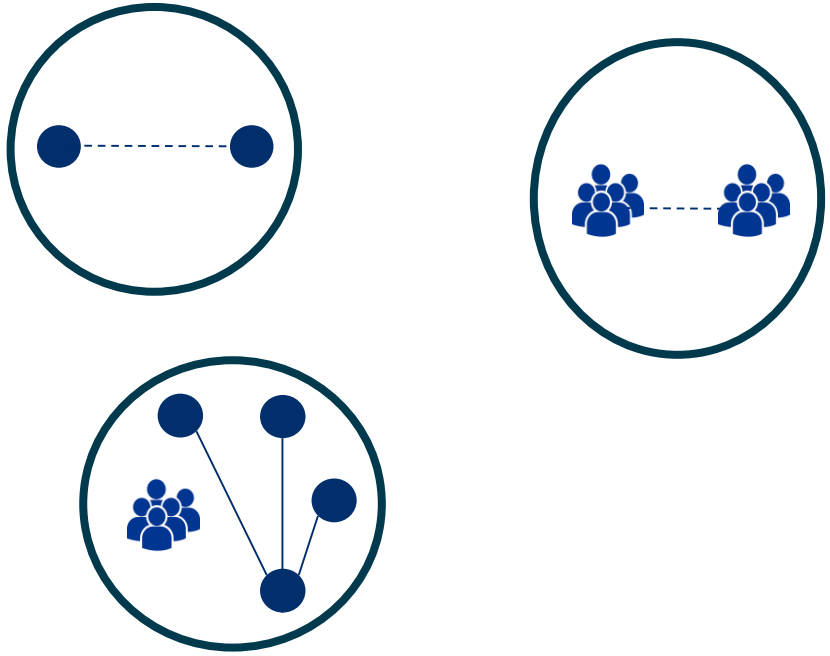
Connected Versus Disconnected Networks

Subhead can go here

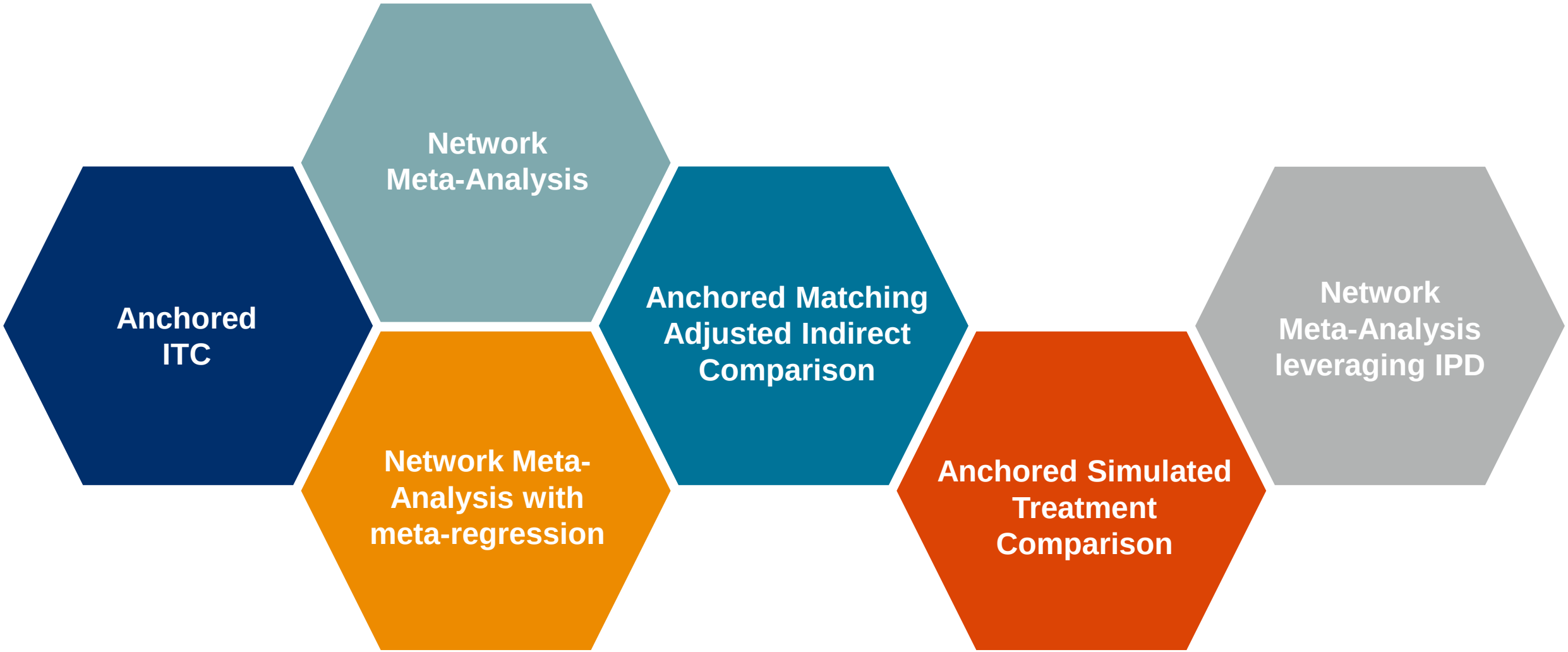
CONNECTED NETWORKS



DISCONNECTED NETWORKS



Most Common ITC Options when Comparative Data Can Connect with Network



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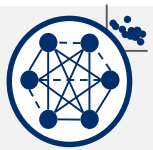
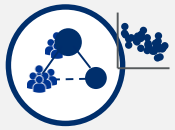
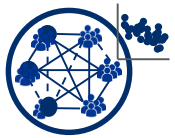
Choice of ITC when Comparative Data Can Connect with Network

Moderate to high Heterogeneity?	≥ 2 comparators?	Access to IPD?	Connections with ≥ 5 studies?	
✗	✗	✗	✗	Anchored (Bucher) ITC 
✗	✓	✗	✗	Network Meta-Analysis 
✓	✓	✗	✓	Network Meta-Analysis with Regression 
✓	✗	✓	✗	Anchored MAIC 
✓	✗	✓	✗	Anchored STC 
✓	✓	✓	✗	Network Meta-Analysis leveraging IPD 

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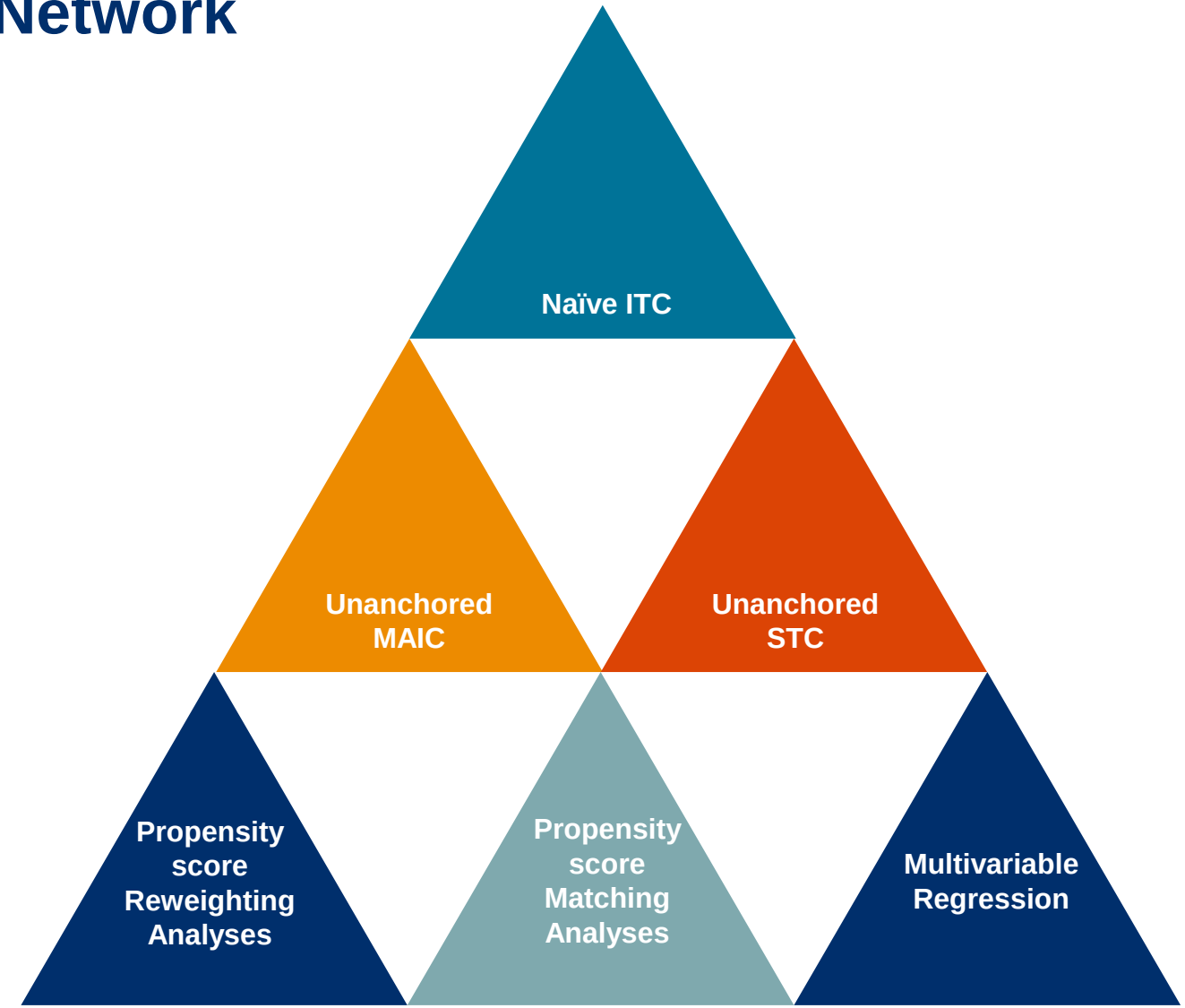
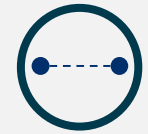
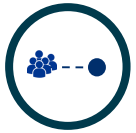
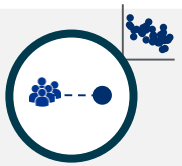
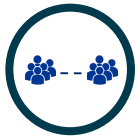
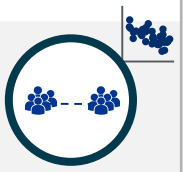
Most Common ITC Options when Lack of Comparative Data or Disconnected Network



Choice of ITC when Lack of Comparative Data or Disconnected Network

Moderate to high Heterogeneity?	≥ 2 comparators?	Access to IPD?	Connections with ≥ 5 studies?	
✗	✗	✗	✗	Naïve ITC 
✓	✗	✓	✗	Unanchored MAIC 
✓	✗	✓	✗	Unanchored STC 
✓	✗	✓	✓	Propensity Score Matching/Reweighting 
✓	✗	✓	✓	Multivariable regression 

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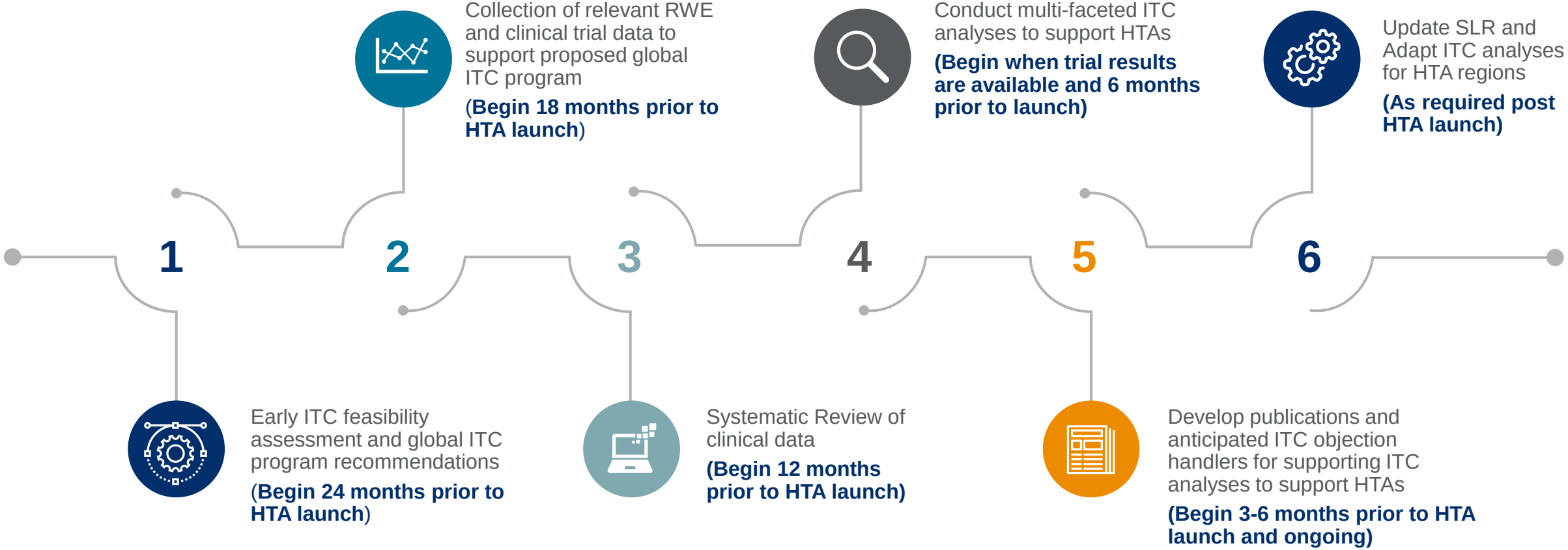
Developing a Global ITC Program, Including Early Feasibility Assessment and Timelines

Steps in Developing a Global ITC Program for HTA submissions

Timelines to implement Global ITC Program for New Product



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Results from Early Feasibility Assessment for Sample Global ITC Program in 2020 with Comparative Data and Connected Network

EARLY ITC FEASIBILITY ASSESSMENT

- Key studies for indication were compared for similarities and differences across: study design, inclusion/exclusion criteria, baseline patient characteristics, outcome definitions, and placebo response
- Evidence Networks Developed and availability of data for comparators assessed

RECOMMENDATION #1

Develop a multi-faceted indirect treatment comparison program to support many HTA regions

RECOMMENDATION #2

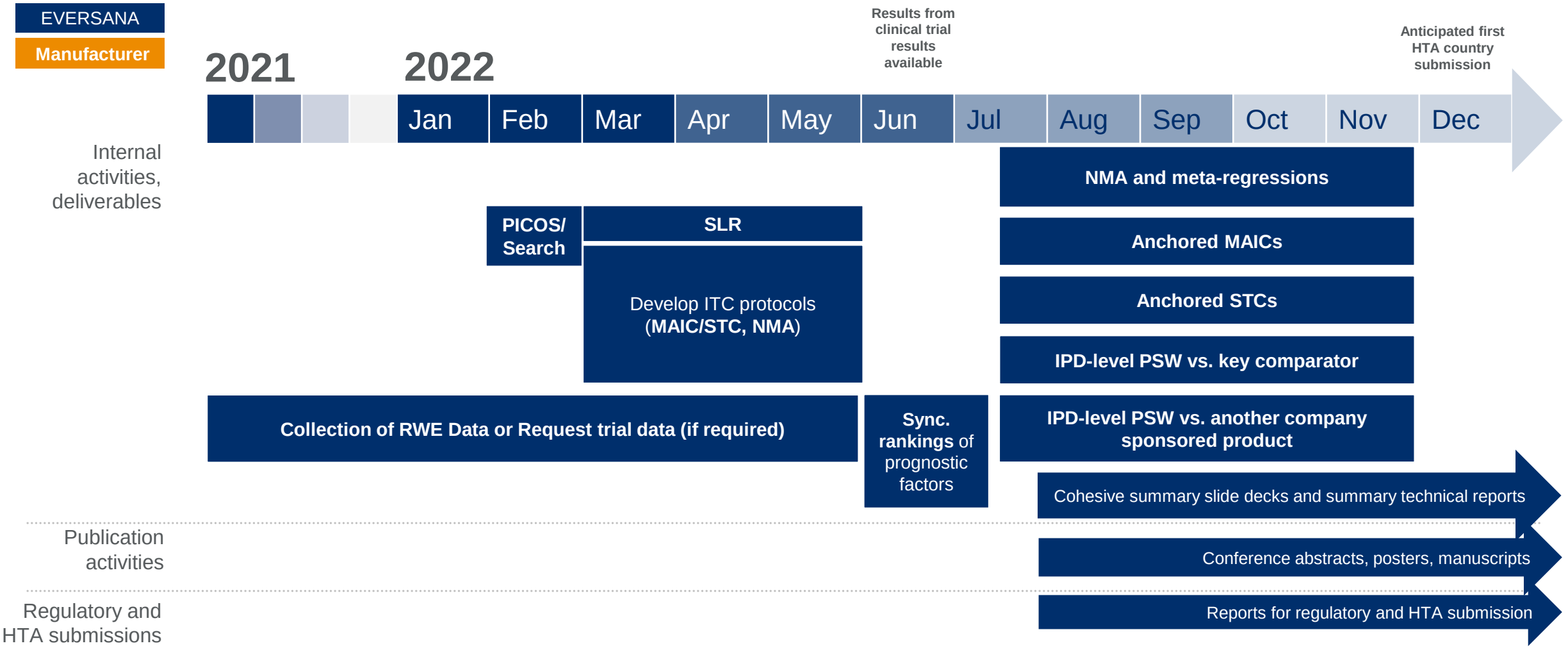
Systematically collect and summarize applicable data to be prepared for launch; initiate SLR at least 12-months prior to launch

RECOMMENDATION #3

Develop publication program and data communication plan for ITCs

Abbreviations: IPD = individual patient data; ITC = indirect treatment comparison; MAIC = matching-adjusted indirect comparison; NMA = network meta-analysis; STC = simulated treatment comparison.

Timelines and Activities for sample Global ITC Program



Abbreviations: HTA = health technology assessment; IPD = individual patient data; ITC = indirect treatment comparison; MAIC = matching-adjusted indirect comparison, PSW = propensity score weighting; RWE = real-world evidence; SLR = systematic literature review; STC = simulated treatment comparison.

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Building a Global ITC Program – Guidance from a Global HEOR Lead

Global ITC Program: Grounding Principles, Team Requirements

Governing Principles: *Best Care of Patients, Best Information for all Stakeholders*

CORE PRINCIPLE	TEAM REQUIREMENTS
Most Robust Applicable Methods Chosen: *A Priori*	Methods approaches chosen according to HTA requirements, and data availability
Transparent and Documented Process	Internal medical alignment and protocol establishment, and external protocol declaration.
Adherence to Vetted / Accepted Practices	From SLR, to model designation, to production of results: Adherence to accepted, rigorous methods.
Balance and Conservatism in Interpretation	Careful articulation of defensible conclusions; Fair accounting of limitations of study where applicable.
Thorough Peer-Reviewed Reporting	Presentation of results in rigorous peer-reviewed congresses.

Global ITC Program Checklist for New Products

1. Begin early ITC Feasibility Assessment and global ITC Program at least two years before HTA launch
2. Find the right partner with ITC expertise and global HTA experience
3. Ensure medical team within company involved in co-production of Global ITC Program
4. Engage regional affiliates early in development of Global ITC Program
5. Develop various ITC analyses to support global HTA requirements
6. Develop technical ITC reports and explanatory materials before HTA launch and update as required
7. Develop ITC publication and communication program to support Global ITC Program
8. Ensure partner is available to adapt regional ITCs and respond to HTAs in timely manner

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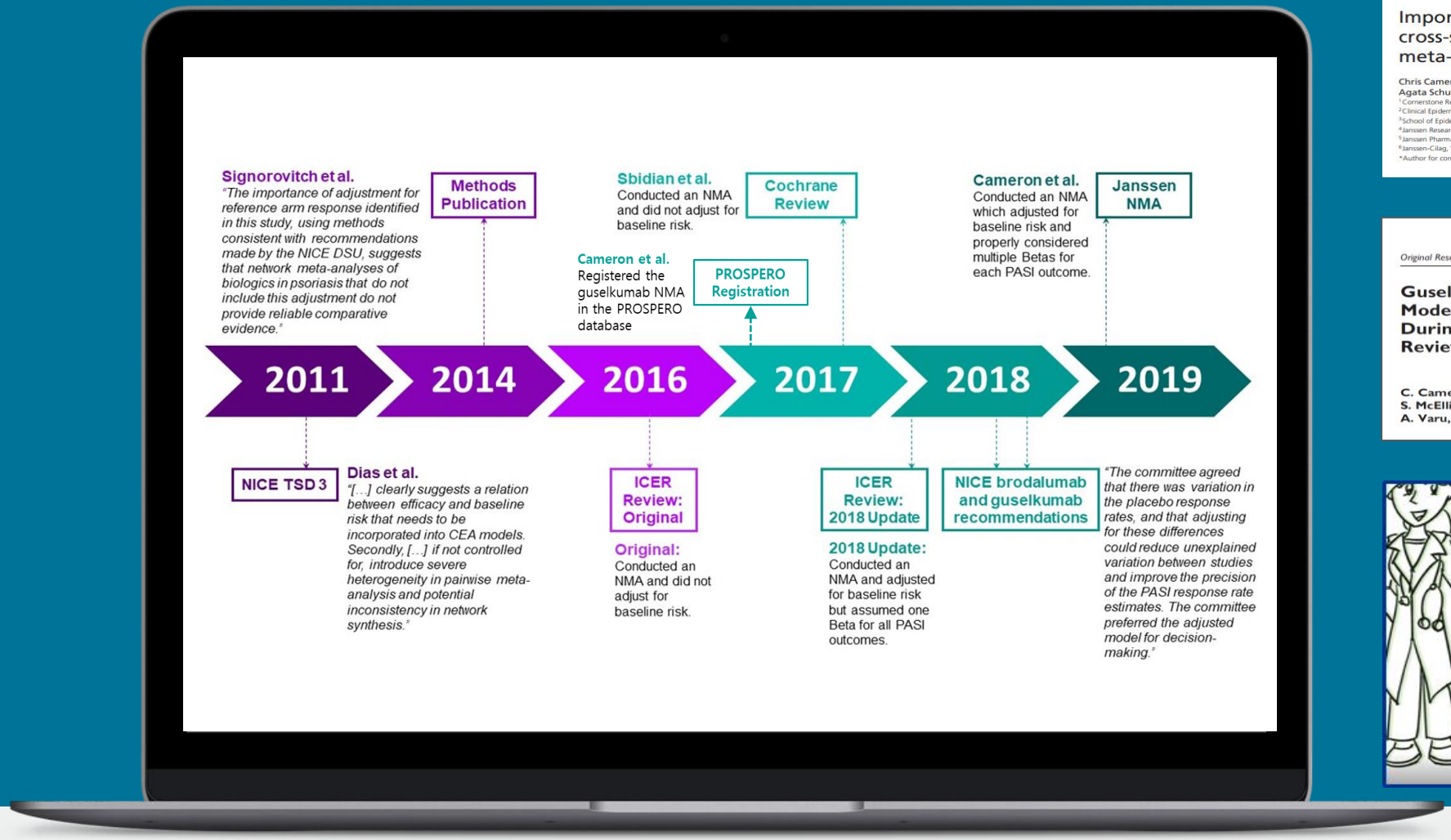
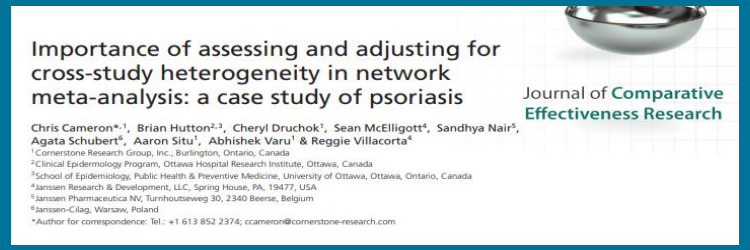
Global ITC Program in Action – Guselkumab for Psoriasis**




Importance of assessing and adjusting for cross-study heterogeneity in network meta-analysis: a case study of psoriasis

Journal of Comparative Effectiveness Research

Chris Cameron*[1], Brian Hutton[2,3], Cheryl Druchok[1], Sean McElligott[4], Sandhya Nair[5], Agata Schubert[6], Aaron Situ[1], Abhishek Varu[1] & Reggie Villacorta[4]

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[2]Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ottawa, Canada
[3]School of Epidemiology, Public Health & Preventive Medicine, University of Ottawa, Ottawa, Ontario, Canada
[4]Janssen Research & Development, LLC, Spring House, PA, 19477, USA
[5]Janssen Pharmaceutica NV, Turnhoutseweg 30, 2340 Beerse, Belgium
[6]Janssen-Cilag, Warsaw, Poland
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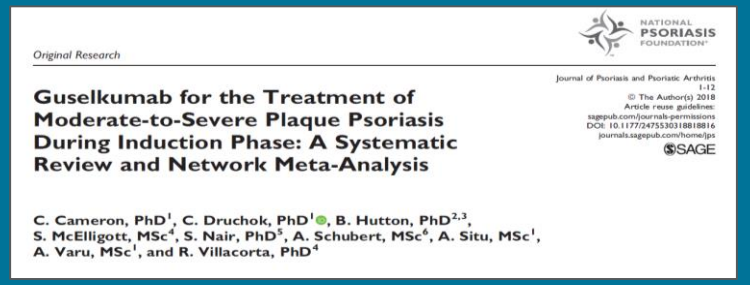
Original Research

Guselkumab for the Treatment of Moderate-to-Severe Plaque Psoriasis During Induction Phase: A Systematic Review and Network Meta-Analysis

C. Cameron, PhD[1], C. Druchok, PhD[1], B. Hutton, PhD[2,3], S. McElligott, MSc[4], S. Nair, PhD[5], A. Schubert, MSc[6], A. Situ, MSc[1], A. Varu, MSc[1], and R. Villacorta, PhD[4]

Journal of Psoriasis and Psoriatic Arthritis 1-12
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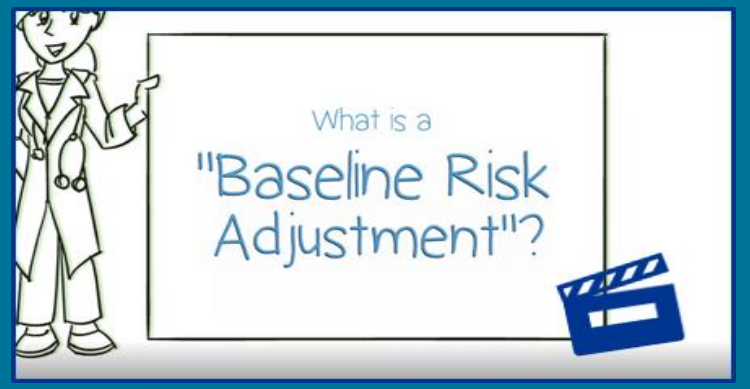

**All visuals and information below in public domain: ISPOR 2018 Cameron et al. Importance of properly adjusting for heterogeneity among network meta-analyses considering outcomes with multiple pre-defined levels: An illustrative example in psoriasis

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Acceptance of ITCs in North America and Asia

United States

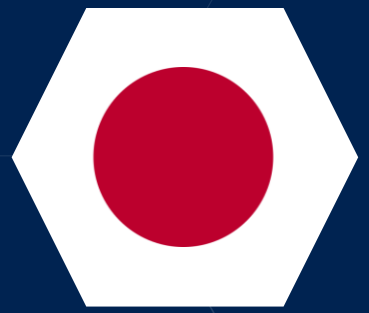
Preference for NMA; less acceptance of other ITC techniques but will accept if methods if rationale clearly described

Canada

Preference for NMA but accept all forms of ITC methods if rationale clearly described

Australia

Pairwise ITCs such as Bucher ITCs, MAICs and STCs accepted



Japan

Acceptance of NMAs; often include adaptations to Asian populations

Acceptance of ITCs by HTA Bodies – A European Perspective

Acceptance of ITCs by HTA bodies

United Kingdom

Preference for NMA but accept all forms of ITC methods if rationale clearly described

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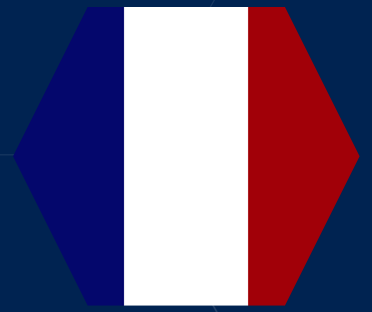
Preference for NMA but accept all forms of ITC methods if rationale clearly described

Germany

Strong preference for RCT; Acceptance of ITCs have been limited



France

Preference for NMA; less acceptance of other ITC techniques but will accept if methods if rationale clearly described

Available ITC Guidelines in Europe

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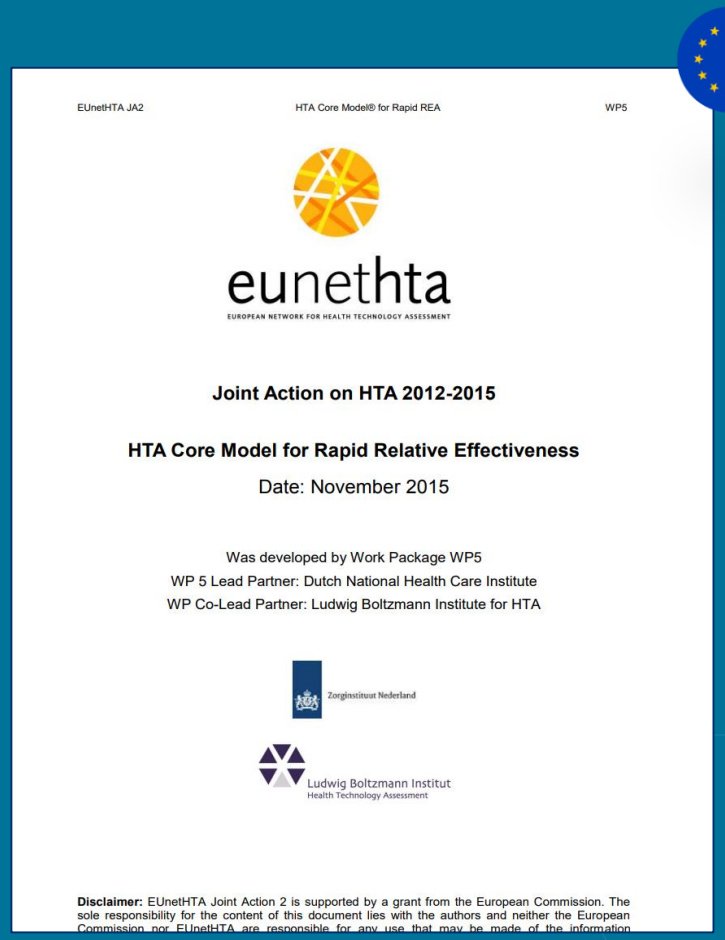
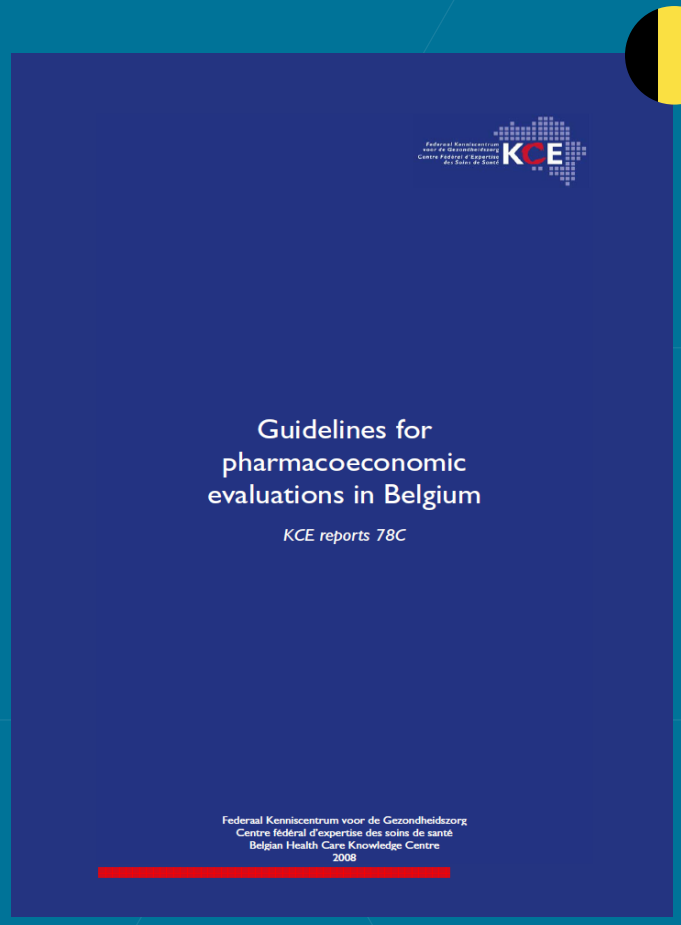
Available ITC Guidelines in Europe





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Increasing Acceptance of ITCs by Major HTA Bodies in Europe and around the World

"The use of MAIC in the absence of direct comparisons between treatments has been increasing across different therapeutic areas, and so has its acceptability by HTA bodies"[1]

"An increased trend was found in the use of MAIC in published literature as well as NICE TA submissions. This methodology was also well received by NICE TAs. Overall, MAICs can provide comparative evidence to enable informed policy decisions."[2]

"ITC is generally accepted as a technique that allows demonstration of noninferiority to a comparator provided the chosen methodology and underlying assumptions are clear and justified."[3]

"Network meta-analyses and indirect comparisons are acknowledged methodologies by HTA agencies worldwide including the NICE, CADTH, HAS, and PBAC, as well as… Austria, Brazil, Colombia, Cuba, and Ireland.."[4]

[1]Thom et al. 2016; [2]Ndirangu et al. 2016; [3]Skali and Spoors. 2018; [4]Baston et al. 2016.
Abbreviations: CADTH = Canadian Agency for Drugs and Technologies in Health; HAS = French Haute Autorité de la Santé; HTA = health technology assessment; ITC = indirect treatment comparison; MAIC = matching-adjusted indirect comparison; NICE = National Institute for Health and Care Excellence; PBAC = Pharmaceutical Benefits Advisory Committee (in Australia); STA = single technology appraisal; STC = simulated treatment comparison TA = technology appraisal

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Adoption of ITCs by HTA bodies

NMA methods and guidelines developed

NMA methods accepted

MAIC/STC methods and guidelines developed

MAIC/STC methods accepted

Application of a Global ITC Program – Interactive Case Studies

Case Study (1): *Pipeline of candidate novel drugs for market access in mid-size biotech company*

A **mid-size biotech** company has **two novel drugs** in development across various therapeutic areas. The manufacturer has **limited HTA experience** and has not previously submitted ITCs, but plans to launch for market access for both drugs in **2022.**

The manufacturer of the mid-size biotech company should:

A. **Initiate global ITC program for each drug in pipeline years in advance of HTA launch**

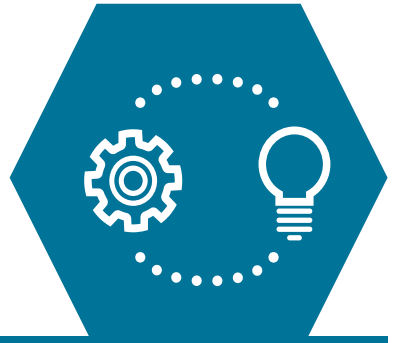
B. **Conduct multiple ITC analyses to meet various global HTA requirements**

C. **Engage regional affiliates within their company when developing the global ITC program for each product**

D. **Engage cross-functional teams within their company when developing global ITC program**

E. **All of the above**

Case Study (2): *Novel Drug for Treatment of Atrial Fibrillation*



A **new drug** is under development for **atrial fibrillation**. The manufacturer requires estimates of comparative efficacy versus **five key comparator drugs** in atrial fibrillation to support HTA submissions and market access. All drugs have been compared with **standard adjusted dose vitamin K antagonists**. Key comparators have also been approved largely based on **one large multi-national trial**, but they anticipate that there will be **cross-trial differences** between their drug and comparator drugs.

The Global ITC Program for a novel drug for atrial fibrillation with RCT data could consider:

A. Network Meta-Analysis

B. MAICs versus key comparator(s)

C. Anchored ITCs versus key comparator(s)

D. STCs versus key comparator(s)

E. All of the above

Case Study (3): *Novel Drug for Treatment in Oncology*

The Global ITC Program for a novel drug for oncology with single arm data could consider:

A. **Unanchored MAIC versus key comparator(s)**

B. **Unanchored STC versus key comparator(s)**

C. **Propensity score reweighting/matching versus RWD standard of care**

D. **Multivariable regression versus RWD standard of care**

E. **All of the above**

A **new drug** is under development for **oncology**. The manufacturer requires estimates of comparative efficacy versus **two key comparator drugs** in oncology to support HTA submissions and market access. The novel drug was approved based on a **single arm trial**. Key comparators have also been approved based on **single arm trials**, and manufacturer anticipates that there will be **cross-trial differences** between their drug and comparator drugs.

THANK YOU

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QUESTIONS?

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