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The Professional Society for Health Economics and Outcomes Research (ISPOR NA)

13–16 May 2025 | Montreal, Quebec, Canada

Posters

A Real-World Perspective of Quadruple Treatment Patterns for 1L Multiple Myeloma Patients Across North and South America, Europe, and Asia

Post-DCE Qualitative Interviews: A Novel Method to Understand the Rationale for Stated Preferences – An Example Among Patients and Physicians in Severe Asthma

Mind the Gap: Delays between Vaccine Licensure and NITAG Recommendation in the US vs. Europe

Exploring Treatment Preferences for Rare Diseases: A Systematic Review of Quantitative Preference Studies

Stability of a Large Language Model for Data Extraction in Systematic Literature Reviews

Leveraging Real-world Data vs. External Trials to Inform Comparative Efficacy within Single-arm Trial-based NICE Submissions

ISPOR (NA) 2025

13–16 May 2025 | Montreal, Quebec, Canada

Poster Title

A Real-World Perspective of Quadruple Treatment Patterns for 1L Multiple Myeloma Patients Across North and South America, Europe, and Asia

Objective

- The objective of this study is to identify and examine QD treatment patterns among 1L MM patients across different countries in the top 10 markets (Brazil, Mexico, US, France, Germany, Italy, Spain, UK, China, and Japan).

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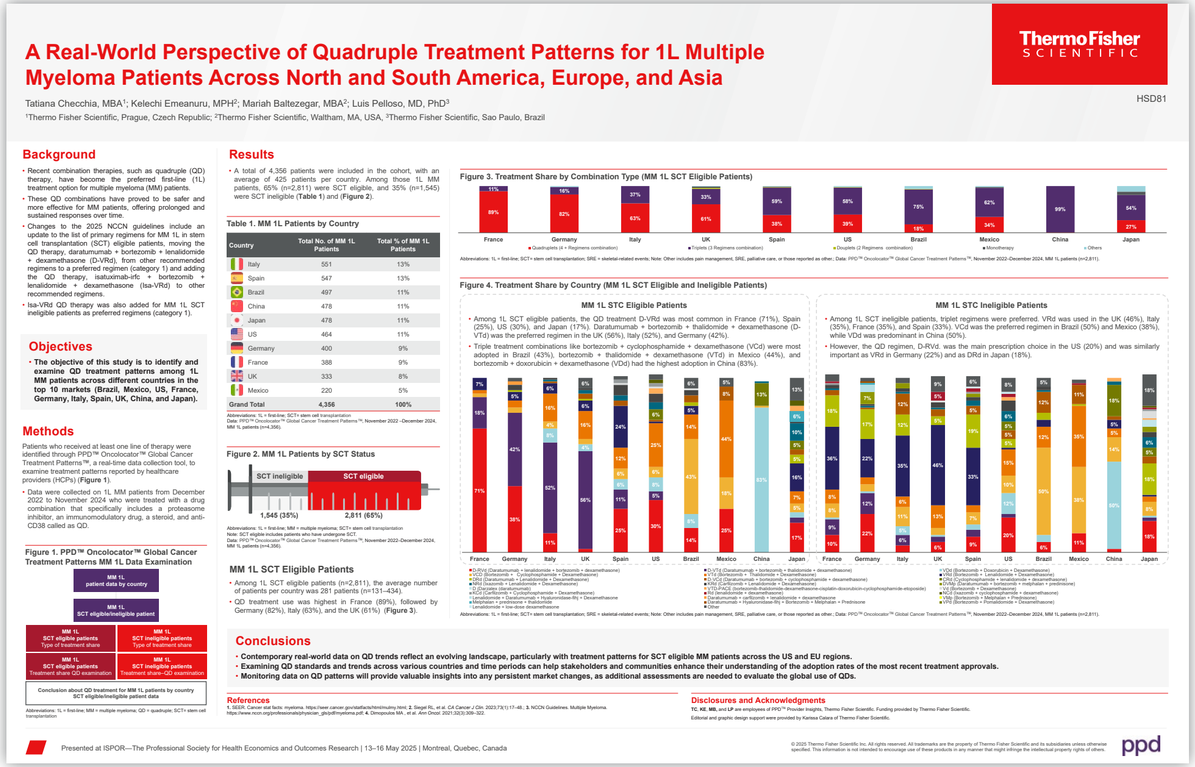

A Real-World Perspective of Quadruple Treatment Patterns for 1L Multiple Myeloma Patients Across North and South America, Europe, and Asia

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Background

- Recent combination therapies, such as quadruple (QD) therapy, have become the preferred first-line (1L) treatment option for multiple myeloma (MM) patients.
- These QD combinations have proved to be safer and more effective for MM patients, offering prolonged and sustained responses over time.
- Changes to the 2025 NCCN guidelines include an update to the list of primary regimens for MM 1L in stem cell transplantation (SCT) eligible patients, moving the QD therapy, daratumumab + bortezomib + lenalidomide + dexamethasone (D-VRd), from other recommended regimens to a preferred regimen (category 1) and adding the QD therapy, isatuximab-irfc + bortezomib + lenalidomide + dexamethasone (Isa-VRd) to other recommended regimens.
- Isa-VRd QD therapy was also added for MM 1L SCT ineligible patients as preferred regimens (category 1).

Objectives

- **The objective of this study is to identify and examine QD treatment patterns among 1L MM patients across different countries in the top 10 markets (Brazil, Mexico, US, France, Germany, Italy, Spain, UK, China, and Japan).**

Methods

Patients who received at least one line of therapy were identified through PPD™ Oncolocator™ Global Cancer Treatment Patterns™, a real-time data collection tool, to examine treatment patterns reported by healthcare providers (HCPs) (**Figure 1**).

- Data were collected on 1L MM patients from December 2022 to November 2024 who were treated with a drug combination that specifically includes a proteasome inhibitor, an immunomodulatory drug, a steroid, and anti-CD38 called as QD.

Figure 1. PPD™ Oncolocator™ Global Cancer Treatment Patterns MM 1L Data Examination

Abbreviations: 1L = first-line; MM = multiple myeloma; QD = quadruple; SCT= stem cell transplantation

Results

- A total of 4,356 patients were included in the cohort, with an average of 425 patients per country. Among those 1L MM patients, 65% (n=2,811) were SCT eligible, and 35% (n=1,545) were SCT ineligible (**Table 1**) and (**Figure 2**).

Table 1. MM 1L Patients by Country

Country	Total No. of MM 1L Patients	Total % of MM 1L Patients
Italy	551	13%
Spain	547	13%
Brazil	497	11%
China	478	11%
Japan	478	11%
US	464	11%
Germany	400	9%
France	388	9%
UK	333	8%
Mexico	220	5%
Grand Total	**4,356**	**100%**

Abbreviations: 1L = first-line; SCT= stem cell transplantation
Data: PPD™ Oncolocator™ Global Cancer Treatment Patterns™, November 2022 –December 2024, MM 1L patients (n=4,356).

Figure 2. MM 1L Patients by SCT Status

Abbreviations: 1L = first-line; MM = multiple myeloma; SCT= stem cell transplantation
Note: SCT eligible includes patients who have undergone SCT.
Data: PPD™ Oncolocator™ Global Cancer Treatment Patterns™, November 2022–December 2024, MM 1L patients (n=4,356).

MM 1L SCT Eligible Patients

- Among 1L SCT eligible patients (n=2,811), the average number of patients per country was 281 patients (n=131–434).
- QD treatment use was highest in France (89%), followed by Germany (82%), Italy (63%), and the UK (61%) (**Figure 3**).

Figure 3. Treatment Share by Combination Type (MM 1L SCT Eligible Patients)

Abbreviations: 1L = first-line; SCT= stem cell transplantation; SRE = skeletal-related events; Note: Other includes pain management, SRE, palliative care, or those reported as other.; Data: PPD™ Oncolocator™ Global Cancer Treatment Patterns™, November 2022–December 2024, MM 1L patients (n=2,811).

Figure 4. Treatment Share by Country (MM 1L SCT Eligible and Ineligible Patients)

MM 1L STC Eligible Patients

- Among 1L SCT eligible patients, the QD treatment D-VRd was most common in France (71%), Spain (25%), US (30%), and Japan (17%). Daratumumab + bortezomib + thalidomide + dexamethasone (D-VTd) was the preferred regimen in the UK (56%), Italy (52%), and Germany (42%).
- Triple treatment combinations like bortezomib + cyclophosphamide + dexamethasone (VCd) were most adopted in Brazil (43%), bortezomib + thalidomide + dexamethasone (VTd) in Mexico (44%), and bortezomib + doxorubicin + dexamethasone (VDd) had the highest adoption in China (83%).

MM 1L STC Ineligible Patients

- Among 1L SCT ineligible patients, triplet regimens were preferred. VRd was used in the UK (46%), Italy (35%), France (35%), and Spain (33%). VCd was the preferred regimen in Brazil (50%) and Mexico (38%), while VDd was predominant in China (50%).
- However, the QD regimen, D-RVd, was the main prescription choice in the US (20%) and was similarly important as VRd in Germany (22%) and as DRd in Japan (18%).

Abbreviations: 1L = first-line; SCT= stem cell transplantation; SRE = skeletal-related events; Note: Other includes pain management, SRE, palliative care, or those reported as other.; Data: PPD™ Oncolocator™ Global Cancer Treatment Patterns™, November 2022–December 2024, MM 1L patients (n=2,811).

Conclusions

- **Contemporary real-world data on QD trends reflect an evolving landscape, particularly with treatment patterns for SCT eligible MM patients across the US and EU regions.**
- **Examining QD standards and trends across various countries and time periods can help stakeholders and communities enhance their understanding of the adoption rates of the most recent treatment approvals.**
- **Monitoring data on QD patterns will provide valuable insights into any persistent market changes, as additional assessments are needed to evaluate the global use of QDs.**

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Poster Title

Post-DCE Qualitative Interviews: A Novel Method to Understand the Rationale for Stated Preferences – An Example Among Patients and Physicians in Severe Asthma

Objective

- We present a novel qualitative post-DCE interview method helpful in elucidating individuals' rationale for stated preferences and deriving rich insights into the drivers of the heterogeneity often observed in stated preference studies.

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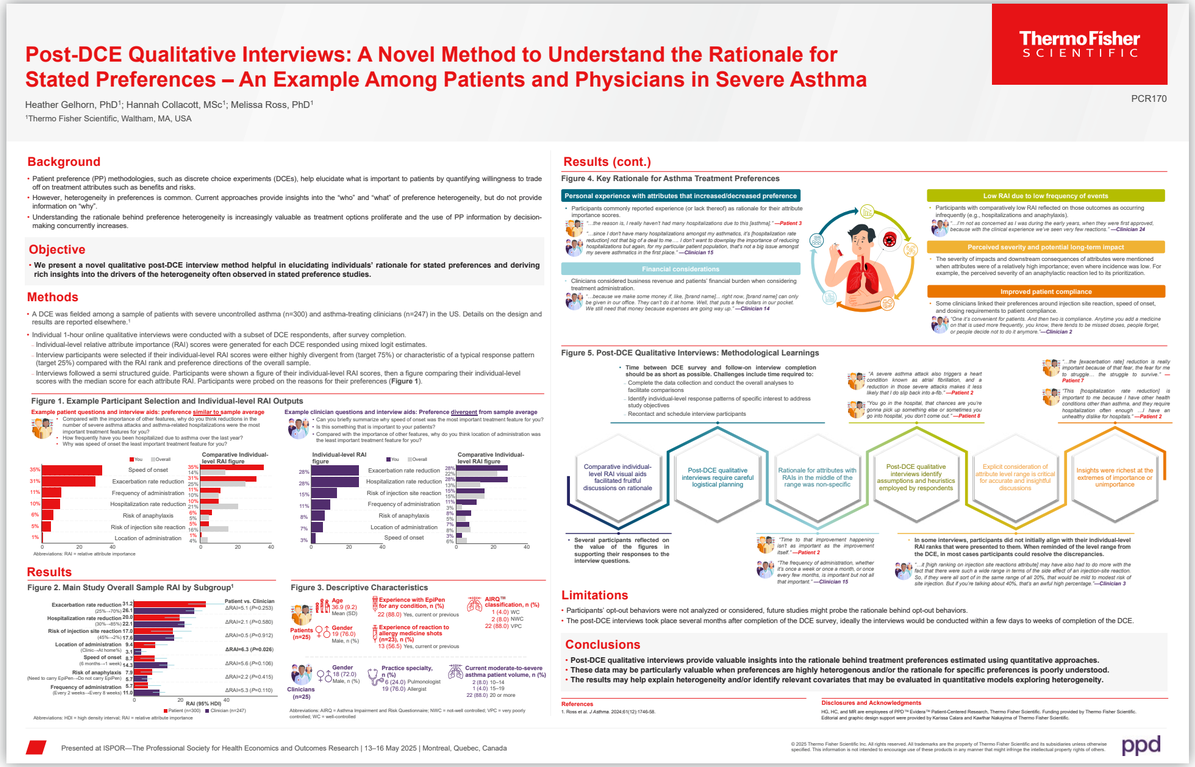

Post-DCE Qualitative Interviews: A Novel Method to Understand the Rationale for Stated Preferences – An Example Among Patients and Physicians in Severe Asthma

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Background

- Patient preference (PP) methodologies, such as discrete choice experiments (DCEs), help elucidate what is important to patients by quantifying willingness to trade off on treatment attributes such as benefits and risks.
- However, heterogeneity in preferences is common. Current approaches provide insights into the "who" and "what" of preference heterogeneity, but do not provide information on "why".
- Understanding the rationale behind preference heterogeneity is increasingly valuable as treatment options proliferate and the use of PP information by decision-making concurrently increases.

Objective

- **We present a novel qualitative post-DCE interview method helpful in elucidating individuals' rationale for stated preferences and deriving rich insights into the drivers of the heterogeneity often observed in stated preference studies.**

Methods

- A DCE was fielded among a sample of patients with severe uncontrolled asthma (n=300) and asthma-treating clinicians (n=247) in the US. Details on the design and results are reported elsewhere.[1]
- Individual 1-hour online qualitative interviews were conducted with a subset of DCE respondents, after survey completion.
  - Individual-level relative attribute importance (RAI) scores were generated for each DCE responded using mixed logit estimates.
  - Interview participants were selected if their individual-level RAI scores were either highly divergent from (target 75%) or characteristic of a typical response pattern (target 25%) compared with the RAI rank and preference directions of the overall sample.
  - Interviews followed a semi structured guide. Participants were shown a figure of their individual-level RAI scores, then a figure comparing their individual-level scores with the median score for each attribute RAI. Participants were probed on the reasons for their preferences (**Figure 1**).

Figure 1. Example Participant Selection and Individual-level RAI Outputs

Results

Figure 2. Main Study Overall Sample RAI by Subgroup[1]

Figure 3. Descriptive Characteristics

Results (cont.)

Figure 4. Key Rationale for Asthma Treatment Preferences

Figure 5. Post-DCE Qualitative Interviews: Methodological Learnings

Limitations

- Participants' opt-out behaviors were not analyzed or considered, future studies might probe the rationale behind opt-out behaviors.
- The post-DCE interviews took place several months after completion of the DCE survey, ideally the interviews would be conducted within a few days to weeks of completion of the DCE.

Conclusions

- **Post-DCE qualitative interviews provide valuable insights into the rationale behind treatment preferences estimated using quantitative approaches.**
- **These data may be particularly valuable when preferences are highly heterogenous and/or the rationale for specific preferences is poorly understood.**
- **The results may help explain heterogeneity and/or identify relevant covariates that may be evaluated in quantitative models exploring heterogeneity.**

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Poster Title

Mind the Gap: Delays between Vaccine Licensure and NITAG Recommendation in the US vs. Europe

Objective

- Given the importance of vaccine uptake for the prevention of communicable diseases, the goal of this project was to compare the delay between vaccine licensure and NITAG evaluation in the US vs. Europe.

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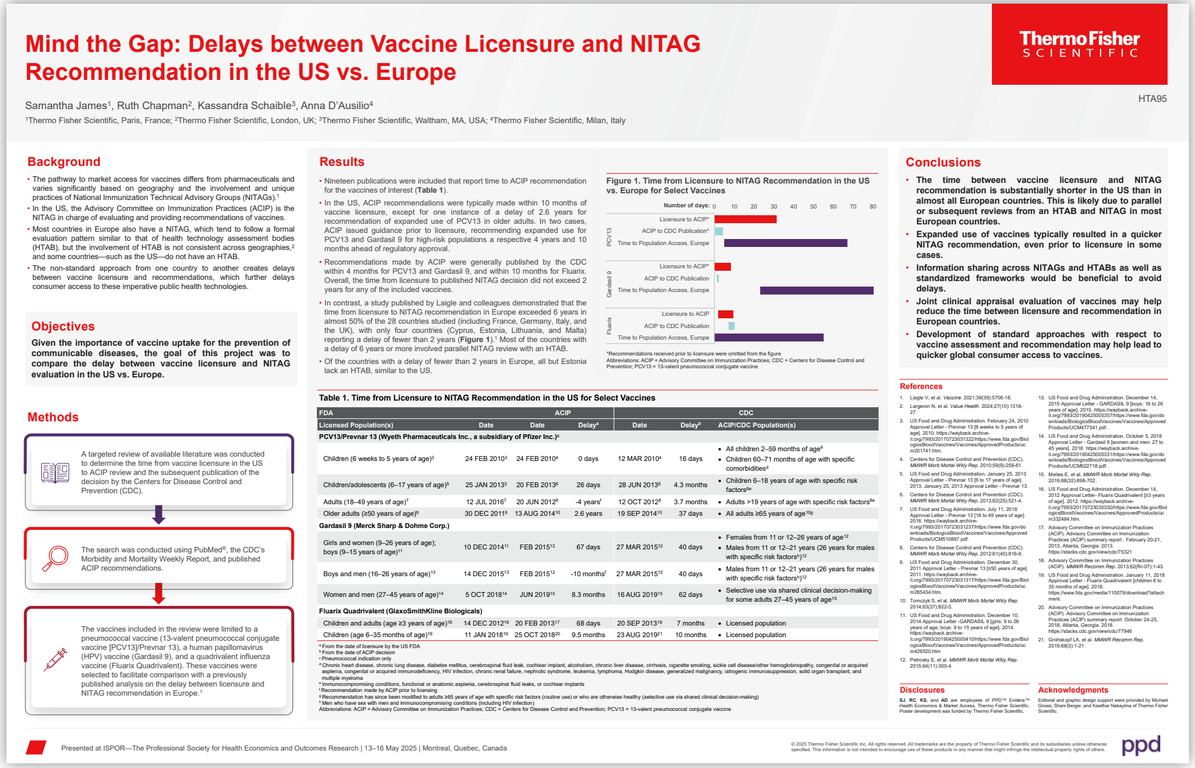

Mind the Gap: Delays between Vaccine Licensure and NITAG Recommendation in the US vs. Europe

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Background

- The pathway to market access for vaccines differs from pharmaceuticals and varies significantly based on geography and the involvement and unique practices of National Immunization Technical Advisory Groups (NITAGs).[1]
- In the US, the Advisory Committee on Immunization Practices (ACIP) is the NITAG in charge of evaluating and providing recommendations of vaccines.
- Most countries in Europe also have a NITAG, which tend to follow a formal evaluation pattern similar to that of health technology assessment bodies (HTAB), but the involvement of HTAB is not consistent across geographies,[2] and some countries—such as the US—do not have an HTAB.
- The non-standard approach from one country to another creates delays between vaccine licensure and recommendations, which further delays consumer access to these imperative public health technologies.

Objectives

Given the importance of vaccine uptake for the prevention of communicable diseases, the goal of this project was to compare the delay between vaccine licensure and NITAG evaluation in the US vs. Europe.

Methods

A targeted review of available literature was conducted to determine the time from vaccine licensure in the US to ACIP review and the subsequent publication of the decision by the Centers for Disease Control and Prevention (CDC).

The search was conducted using PubMed®, the CDC's Morbidity and Mortality Weekly Report, and published ACIP recommendations.

The vaccines included in the review were limited to a pneumococcal vaccine (13-valent pneumococcal conjugate vaccine [PCV13]/Prevnar 13), a human papillomavirus (HPV) vaccine (Gardasil 9), and a quadrivalent influenza vaccine (Fluarix Quadrivalent). These vaccines were selected to facilitate comparison with a previously published analysis on the delay between licensure and NITAG recommendation in Europe.[3]

Results

- Nineteen publications were included that report time to ACIP recommendation for the vaccines of interest (**Table 1**).
- In the US, ACIP recommendations were typically made within 10 months of vaccine licensure, except for one instance of a delay of 2.6 years for recommendation of expanded use of PCV13 in older adults. In two cases, ACIP issued guidance prior to licensure, recommending expanded use for PCV13 and Gardasil 9 for high-risk populations a respective 4 years and 10 months ahead of regulatory approval.
- Recommendations made by ACIP were generally published by the CDC within 4 months for PCV13 and Gardasil 9, and within 10 months for Fluarix. Overall, the time from licensure to published NITAG decision did not exceed 2 years for any of the included vaccines.
- In contrast, a study published by Laigle and colleagues demonstrated that the time from licensure to NITAG recommendation in Europe exceeded 6 years in almost 50% of the 28 countries studied (including France, Germany, Italy, and the UK), with only four countries (Cyprus, Estonia, Lithuania, and Malta) reporting a delay of fewer than 2 years (**Figure 1**).[1] Most of the countries with a delay of 6 years or more involved parallel NITAG review with an HTAB.
- Of the countries with a delay of fewer than 2 years in Europe, all but Estonia lack an HTAB, similar to the US.

Figure 1. Time from Licensure to NITAG Recommendation in the US vs. Europe for Select Vaccines

*Recommendations received prior to licensure were omitted from the figure.
Abbreviations: ACIP = Advisory Committee on Immunization Practices; CDC = Centers for Disease Control and Prevention; PCV13 = 13-valent pneumococcal conjugate vaccine

Table 1. Time from Licensure to NITAG Recommendation in the US for Select Vaccines

FDA	ACIP			CDC		
Licensed Population(s)	**Date**	**Date**	**Delay[a]**	**Date**	**Delay[b]**	**ACIP/CDC Population(s)**
PCV13/Prevnar 13 (Wyeth Pharmaceuticals Inc., a subsidiary of Pfizer Inc.)[c]						
Children (6 weeks to 5 years of age)[3]	24 FEB 2010[3]	24 FEB 2010[4]	0 days	12 MAR 2010[4]	16 days	• All children 2–59 months of age[d] • Children 60–71 months of age with specific comorbidities[d]
Children/adolescents (6–17 years of age)[5]	25 JAN 2013[5]	20 FEB 2013[6]	26 days	28 JUN 2013[6]	4.3 months	• Children 6–18 years of age with specific risk factors[de]
Adults (18–49 years of age)[7]	12 JUL 2016[7]	20 JUN 2012[8]	-4 years[f]	12 OCT 2012[8]	3.7 months	• Adults >19 years of age with specific risk factors[de]
Older adults (≥50 years of age)[9]	30 DEC 2011[9]	13 AUG 2014[10]	2.6 years	19 SEP 2014[10]	37 days	• All adults ≥65 years of age[dg]
Gardasil 9 (Merck Sharp & Dohme Corp.)						
Girls and women (9–26 years of age); boys (9–15 years of age)[11]	10 DEC 2014[11]	FEB 2015[12]	67 days	27 MAR 2015[12]	40 days	• Females from 11 or 12–26 years of age[12] • Males from 11 or 12–21 years (26 years for males with specific risk factors)[9,12]
Boys and men (16–26 years of age)[13]	14 DEC 2015[13]	FEB 2015[12]	-10 months[f]	27 MAR 2015[12]	40 days	• Males from 11 or 12–21 years (26 years for males with specific risk factors)[9,12]
Women and men (27–45 years of age)[14]	5 OCT 2018[14]	JUN 2019[15]	8.3 months	16 AUG 2019[15]	62 days	• Selective use via shared clinical decision-making for some adults 27–45 years of age[16]
Fluarix Quadrivalent (GlaxoSmithKline Biologicals)						
Children and adults (age ≥3 years of age)[18]	14 DEC 2012[18]	20 FEB 2013[17]	68 days	20 SEP 2013[18]	7 months	• Licensed population
Children (age 6–35 months of age)[19]	11 JAN 2018[19]	25 OCT 2018[20]	9.5 months	23 AUG 2019[21]	10 months	• Licensed population

[a] From the date of licensure by the US FDA
[b] From the date of ACIP decision
[c] Pneumococcal indication only
[d] Chronic heart disease, chronic lung disease, diabetes mellitus, cerebrospinal fluid leak, cochlear implant, alcoholism, chronic liver disease, cirrhosis, cigarette smoking, sickle cell disease/other hemoglobinopathy, congenital or acquired asplenia, congenital or acquired immunodeficiency, HIV infection, chronic renal failure, nephrotic syndrome, leukemia, lymphoma, Hodgkin disease, generalized malignancy, iatrogenic immunosuppression, solid organ transplant, and multiple myeloma
[e] Immunocompromising conditions, functional or anatomic asplenia, cerebrospinal fluid leaks, or cochlear implants
[f] Recommendation made by ACIP prior to licensing
[g] Recommendation has since been modified to adults ≥65 years of age with specific risk factors (routine use) or who are otherwise healthy (selective use via shared clinical decision-making)
[h] Men who have sex with men and immunocompromising conditions (including HIV infection)
Abbreviations: ACIP = Advisory Committee on Immunization Practices; CDC = Centers for Disease Control and Prevention; PCV13 = 13-valent pneumococcal conjugate vaccine

Conclusions

- **The time between vaccine licensure and NITAG recommendation is substantially shorter in the US than in almost all European countries. This is likely due to parallel or subsequent reviews from an HTAB and NITAG in most European countries.**
- **Expanded use of vaccines typically resulted in a quicker NITAG recommendation, even prior to licensure in some cases.**
- **Information sharing across NITAGs and HTABs as well as standardized frameworks would be beneficial to avoid delays.**
- **Joint clinical appraisal evaluation of vaccines may help reduce the time between licensure and recommendation in European countries.**
- **Development of standard approaches with respect to vaccine assessment and recommendation may help lead to quicker global consumer access to vaccines.**

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Poster Title

Exploring Treatment Preferences for Rare Diseases: A Systematic Review of Quantitative Preference Studies

Objective

- Patient preference information (PPI) is increasingly important throughout the medical product lifecycle. PPI can provide valuable insights into the relative importance that patients and their families place on benefits and risks associated with novel treatments, which can inform regulatory and clinical decision-making.
- Using standard quantitative preference elicitation methods to generate robust PPI can be challenging with small patient populations, particularly when there are few existing treatments and uncertainty around clinical evidence.
- To understand the state of practice, systematic review of the literature was conducted to identify studies using quantitative preference elicitation methods.

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Exploring Treatment Preferences for Rare Diseases: A Systematic Review of Quantitative Preference Studies

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Objectives

- **Patient preference information (PPI) is increasingly important throughout the medical product lifecycle. PPI can provide valuable insights into the relative importance that patients and their families place on benefits and risks associated with novel treatments, which can inform regulatory and clinical decision-making.**
- **Using standard quantitative preference elicitation methods to generate robust PPI can be challenging with small patient populations, particularly when there are few existing treatments and uncertainty around clinical evidence.**
- **To understand the state of practice, systematic review of the literature was conducted to identify studies using quantitative preference elicitation methods to assess preferences for treatments for rare diseases.**

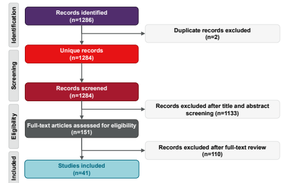
Methods

- A systematic search of EMBASE and MEDLINE was conducted in March 2023 to identify English-language articles reporting results of primary research. Studies were double-screened, and extraction was completed following a prespecified template.

Results

- A total of 1,286 citations were identified and screened based on title and abstract. Following full-text review of 151 studies, 41 met inclusion criteria and were included in the review (**Figure 1**).

Figure 1. PRISMA Diagram

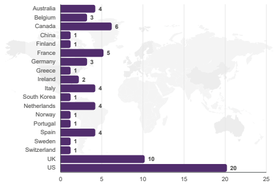


Abbreviations: PRISMA = preferred reporting items for systematic reviews and meta-analyses

Results (cont.)

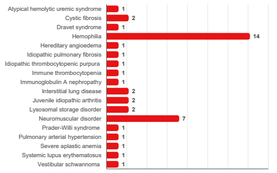
- Studies were published between 2005 and 2023, with 54% (n=22) published in 2020 or later. The majority of studies (n=32, 78%) were conducted in a single country; nine studies (22%) were conducted in two or more countries (**Figure 2**).

Figure 2. Study Countries



- A variety of health conditions were represented in the included preference studies (**Figure 3**). Overall, 30 studies (73%) assessed preferences for treatment of genetic disorders. Of these, treatment for hemophilia was the subject of 14 studies (47%). Seven studies (23%) assessed preferences for the treatment of neuromuscular disorders, such as muscular dystrophy and spinal muscular atrophy.

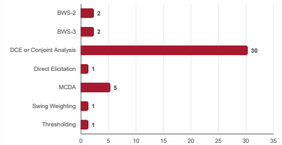
Figure 3. Number of Studies by Disease Area



Lysosomal storage disorders included Fabry disease and Neuronal Ceroid Lipofuscinosis type 2.
Neuromuscular disorders included muscular dystrophy and spinal muscular atrophy.

- Discrete choice experiments (DCEs) were the most frequently used method of preference elicitation (n=31, 75%), followed by multicriteria decision analysis (MCDA; n=5, 12%) and best-worst scaling (BWS; n=4, 10%). Swing weighting, direct elicitation, and thresholding were used in one study each (**Figure 4**).

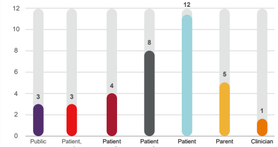
Figure 4. Preference Elicitation Methods[a]



Abbreviations: BWS = best-worst scaling; DCE = discrete choice experiment; MCDA = multicriteria decision analysis
[a]More than one method used in one study

- Instrument design was informed by a review of published literature or clinical data in half of included studies (n=20, 49%).
- One quarter of studies engaged with community stakeholders (patients or caregivers) (n=5, 12%) or conducted qualitative research with patients (n=4, 10%) or parents (n=1, 2%).
- Respondent populations included patients (n=28, 68%), parents/caregivers (n=14, 34%), clinicians (n=10, 24%), and the general population (n=3, 7%) (**Figure 5**).

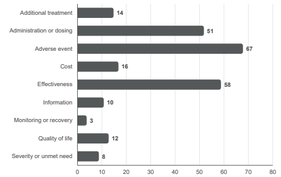
Figure 5. Respondent Populations in Choice-based Preference Studies[a]



[a] Excludes studies using MCDA (multicriteria decision analysis)

- Across choice-based preference studies, studies with respondent populations that included patients had a mean of 164 patients (range: 9–1,542, median: 94). Studies that included parent/caregiver respondents a mean of 104 parents/caregivers (range: 19–468, median: 84).
- The number of attributes included in each preference study ranged from 1–13 (mean=6). Across all studies, 239 attributes were included. Of these, the most frequent types of attributes were adverse events (n=67), treatment efficacy or effectiveness (n=58), and items related to treatment administration or dosing (n=51) (**Figure 6**).

Figure 6. Typology of Included Attributes



Conclusions

- **DCEs are the most frequently used method of elicitation when assessing preferences for treatment for rare diseases.**
- **Preference studies are often designed without patient or parent/caregiver input and therefore may not include attributes of treatment that are most meaningful to patients and families affected by rare diseases.**
- **Exploration and adoption of individual-level preference elicitation methodologies that are suitable for implementation with smaller sample sizes can support increasing adoption and utilization of PPI among rare disease populations.**

Disclosures

CMI, MV, KM, and **EV** are employees of PPD™ Evidera™ Patient-Centered Research, Thermo Fisher Scientific. **ZB** was an employee of Thermo Fisher Scientific at the time this study was conducted. Poster development was funded by Thermo Fisher Scientific.

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Presented at ISPOR—The Professional Society for Health Economics and Outcomes Research | 13–16 May 2025 | Montreal, Quebec, Canada

ISPOR (NA) 2025

13–16 May 2025 | Montreal, Quebec, Canada

Poster Title

Stability of a Large Language Model for Data Extraction in Systematic Literature Reviews

Objective

- This study aimed to evaluate the reproducibility and reliability of LLM-extracted data when considering variations with the same user or different users from two geographic locations. Additionally, the accuracy of LLM-extracted data was compared with manual human extractions from a previously conducted traditional SLR.

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Stability of a Large Language Model for Data Extraction in Systematic Literature Reviews

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MSR105

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Background

- Artificial Intelligence (AI) has been extensively explored in systematic literature reviews (SLRs) to save time and reduce human error, including the ability of large language models (LLMs) to perform data extraction has been tested.[1,2]
- We previously reported the high accuracy (84%, range: 66% to 96%) of an LLM for data extraction in an SLR of randomized controlled trials (RCTs).[3] However, we noted variations in responses when the same prompts were used on different days.
- Recently, the UK's National Institute for Health and Care Excellence (NICE) released a position statement on the use of AI for evidence generation, raising concerns about the reproducibility of AI, particularly regarding automated data extraction.[4]
- To our knowledge, there is limited evidence on the reproducibility and reliability of LLMs for data extraction, particularly given that some response variability is expected with these models and the impact on the trustworthiness of LLM-extracted data has not yet been characterized.

Objectives

- **This study aimed to evaluate the reproducibility and reliability of LLM-extracted data when considering variations with the same user or different users from two geographic locations. Additionally, the accuracy of LLM-extracted data was compared with manual human extractions from a previously conducted traditional SLR.**

Methods

- Three previously developed[5] one-shot prompts were used to extract 29 variables from five RCTs on atopic dermatitis[6-10] (**Table 1**).

Table 1. Variables for data extraction

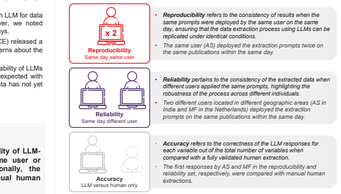
Category	Variable Type	Variables
Study characteristics	Free-text fields	Author, year, trial name, phase, population description, intervention, comparator, inclusion criteria, exclusion criteria, and overall sample size
Patient characteristics	Free-text fields	Author, year, treatment arm
	Numeric fields	Sample size, mean age, male sex (%), comorbidities (%), disease severity (%)
Outcomes	Free-text fields	Author, year, treatment arm, analysis population, time point
	Numeric fields	Sample size, mean CFB in DLQI score, EASI 75 (%), POEM (%), treatment discontinuation (%), serious adverse events (%)

Numeric fields included binary, categorical, and continuous variables.
Abbreviations: CFB = change from baseline; DLQI = Dermatology Life Quality Index; EASI = Eczema Area and Severity Index; POEM = Patient-Oriented Eczema Measure

- Two reviewers (AS and MF) used the same LLM prompts, with creativity set to 0, and the same publications to test data extraction by the LLM for reproducibility and reliability between responses (**Figure 1**) and accuracy compared with human extraction.
  - The first set of LLM responses obtained by AS in the reproducibility test served as the reference and was compared with the second LLM extraction by AS (reproducibility) and MF (reliability). Reproducibility and reliability were calculated as the proportion of variables where LLM-extracted content was the same between responses, considering both content and formatting.
  - Accuracy was calculated as the proportion of correctly extracted variables compared with the validated human extractions (conducted previously).[3]

Methods (cont.)

Figure 1. Methods to assess reproducibility, reliability, and accuracy



- ***Reproducibility** refers to the consistency of results when the same prompts were deployed by the same user on the same day, ensuring that the data extraction process using LLMs can be replicated under identical conditions.*
  - *The same user (AS) deployed the extraction prompts twice on the same publications within the same day.*
- ***Reliability** pertains to the consistency of the extracted data when different users applied the same prompts, highlighting the robustness of the process across different individuals.*
  - *Two different users located in different geographic areas (AS in India and MF in the Netherlands) deployed the extraction prompts on the same publications within the same day.*
- ***Accuracy** refers to the correctness of the LLM responses for each variable out of the total number of variables when compared with a fully validated human extraction.*
  - *The first responses by AS and MF in the reproducibility and reliability set, respectively, were compared with manual human extractions.*

Abbreviations: AS = Aiswarya Shree; LLM = large-language model; MF = Mariana Farraia

Results

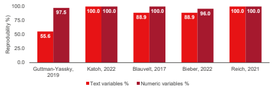
Reproducibility

- Reproducibility of LLM responses to the data extraction prompts ranged from 80.6% to 100% (**Figure 3**).
  - Reproducibility of responses for patient characteristics and outcome variables ranged from 88.5% to 100% and 72.7% to 100%, respectively.
  - Reproducibility of responses for study characteristics varied from 80% to 100%.
- Reproducibility of responses for text vs. numeric variables are displayed in **Figure 4**.
  - Reproducibility of responses for text variables was >85% in four studies, except for one study with 55.6%. Reproducibility for numeric variables was >95% in all studies.

Figure 3. Overall reproducibility and reliability; and by categories

Results (cont.)

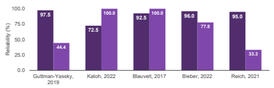
Figure 4. Reproducibility for text vs. numeric (binary, categorical, and continuous) variables



Reliability

- Reliability was lower than reproducibility, ranging from 65.7%–95.5% (**Figure 3**).
  - Reliability for patient characteristics and outcome variables ranged from 62.5% to 100% and 63.7% to 100%, respectively.
  - Reliability for study characteristics variables was the lowest, ranging from 50% to 90%.
- Reliability in text vs numeric variables.
  - None of the extractions were 100% reliable regarding text variables (range: 72.5% to 97.5%). Reliability of numeric variables varied considerably: responses for two studies had <50% reliability, while two others had 100% (**Figure 5**).

Figure 5. Reliability for text vs. numeric (binary, categorical, and continuous) variables



Accuracy

- Compared with validated human extractions, the LLM did not achieve an overall extraction accuracy of 100% for any publications in either test. The accuracy of LLM-extracted data was slightly higher with the reproducibility set of responses (79.1% to 98.5%) compared with the reliability set (74.6% to 97.7%).
  - Accuracy with text variables: Overall accuracy remained consistent between response sets as the LLM captured the same underlying information for text variables. Despite slight variations in syntax, style, or length of response, this did not impact the accuracy, as the content of the LLM-extracted data aligned with the manual human reference extraction.
  - Accuracy with numeric variables: Accuracy was adversely affected by the extraction of numeric fields, where discrepancies were observed between LLM responses and the human reference extraction.

Discussion

- This study highlights both the benefits and potential challenges of using LLMs for data extraction from RCTs. Our findings indicate high reproducibility rates, ranging from 80.6% to 100%, suggesting that LLMs can consistently replicate extraction of data under the same user conditions. However, reliability, which evaluates consistency between different users, was lower despite using identical prompts (range: 65.7% to 95.5%).

Discussion (cont.)

- Overall, the accuracy of LLMs for data extraction was high.
  - The observed variations in text responses did not negatively affect the overall accuracy of data extraction.
  - However, in addition to formatting inconsistencies, the extraction of numeric fields created discrepancies that led to errors that affected accuracy.
- SLRs require meticulous data extraction processes, often involving multiple extractors, followed by thorough data validation. This process may take several weeks (depending on study volume) and is susceptible to human error (up to 50%).[10,11] Using an LLM-based extraction approach may result in faster, more consistent and reliable results, particularly over time and across different users, and potentially reduce human error and increasing extraction quality.
- Additional research is needed to understand and mitigate the factors contributing to variation in LLM-extracted data, including developing techniques to improve the consistency of numeric data extraction and to reduce the impact of stochastic elements in LLMs.

Limitations

- Our findings may not be generalizable to other types of studies beyond RCTs, as different study designs and reporting of outcomes may introduce additional challenges.
- This study tested a small sample of publications. Larger volumes of data might exhibit higher variations in LLM responses, particularly if variables are reported more heterogeneously across publications.
- One-shot prompting was used; a more iterative prompting approach might achieve better accuracy, but could also introduce further variations between users, potentially impacting reproducibility and reliability.
- Testing was conducted at a specific time point (November 2024). Given how quickly LLMs are evolving, future testing may demonstrate different or improved results.
- Only one LLM was tested. Other LLMs may yield different results, and further research is needed to compare the performance of various models in data extraction tasks.

Conclusions

- **When using LLMs for data extraction in SLRs, reproducibility was generally high, but reliability was affected by user interaction, with variations between different users leading to discrepancies, particularly for numeric data. These findings highlight the need for human validation of LLM-extracted data to ensure data quality.**
- **While variations in text responses are expected with LLMs and the impact on overall accuracy was minimal, numerical discrepancies highlight the need for human oversight such that AI-driven extractions must still undergo human validation to ensure data accuracy.**
- **Transparent reporting of AI-assisted methods in SLRs is crucial to contextualize results and maintain scientific rigor. Our findings underscore the importance of addressing the concerns raised by NICE's AI position statement and are important for informing future Cochrane guidance on the applications of AI in SLRs.**

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Disclosures

AS, MF, CCC, and AC are employees of PPD™ Evidera™ Health Economics & Market Access, Thermo Fisher Scientific.

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ISPOR (NA) 2025

13–16 May 2025 | Montreal, Quebec, Canada

Poster Title

Leveraging Real-world Data vs. External Trials to Inform Comparative Efficacy within Single-arm Trial-based NICE Submissions

Objective

- This study reviewed the acceptance of RWD vs. external trials to inform comparative efficacy in SAT-based HTA submissions.

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Leveraging Real-world Data vs. External Trials to Inform Comparative Efficacy within Single-arm Trial-based NICE Submissions

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EE26

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Background

- Single-arm trials (SATs) have increasingly been used to support oncology appraisals by health technology assessment (HTA) bodies, driven by the ethical and practical challenges of conducting randomized controlled trials (RCTs) involving patients with specialized treatment needs.
- In the absence of direct comparative data in SATs, evidence may be obtained from external clinical trials and/or real-world data (RWD) to inform indirect treatment comparisons (ITCs).
- In consideration of the available external comparator data, statistical approaches including matching-adjusted indirect comparisons (MAIC), simulated treatment comparison (STC), or propensity score matching (PSM) may be employed.
- Currently, there are no explicit HTA guidelines for generating comparative evidence for SAT-based submissions.

Objectives

This study reviewed the acceptance of RWD vs. external trials to inform comparative efficacy in SAT-based HTA submissions.

Methods

- Oncology SAT-based appraisals from the National Institute for Health and Care Excellence (NICE) between May 2017 and May 2022 were reviewed.
- Full-text screening of committee papers and technology appraisal guidance was conducted by a single investigator, and the extracted data were validated by a second investigator.
- The review focused on identification of the ITC approach used to derive comparative efficacy and the related committee commentaries.

Results

- Of the 31 submissions reviewed, 58% (18/31) used external trials only to derive comparative efficacy, 29% (9/31) used RWD only, and 13% (4/31) used both, with the variance driven by external data availability, limitations, and relevance (**Figure 1**). Half of these sources were deemed fit-for-purpose by the committee.

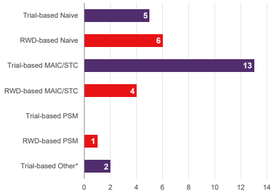
Results (cont.)

Figure 1. Type of Evidence Used in NICE Submissions

Abbreviation: NICE = National Institute for Health and Care Excellence; RWD = real-world data

- Of all submissions, around one-third (11 of 31) obtained individual patient-level data for the external control arm. MAIC/STC was the most commonly used method (13 of 20) when external trial data was the primary source, while naive analysis was most frequently applied to RWD (six of 11) (**Figure 2**).

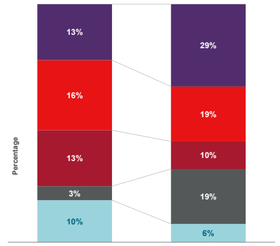
Figure 2. ITC Methods—RWD vs. External Trials for Comparators



Abbreviation: MAIC = matching-adjusted indirect comparison; PSM = propensity-score matching; RWD = real-world data; STC = simulated treatment comparison
*Note: Both submissions with other ITC approaches used single-arm trials as the primary source, with one constructing the comparator arm from its own trial and the other submission from landmark analysis.

- Among the 13 submissions leveraging RWD, more than 60% (n=8) were accepted as valid evidence,[1-8] benefiting from the ability to mitigate uncertainty due to lack of direct comparison by allowing precise matching and covariate adjustment.
- Overall, criticisms of SAT-based submissions were primarily due to data limitations (42%) and insufficient comparability (35%). Other concerns included limited generalizability of the results (23%), inadequate covariate adjustments (23%), and inappropriate statistical methods (16%) (**Figure 3**).

Figure 3. Criticism on Quality of Evidence: RWD vs. External Trials



Abbreviations: ITC = indirect treatment comparison; RWD = real-world data

- In particular, the committee emphasized that unanchored MAIC does not effectively reduce uncertainty or bias, often favoring supplementation with naive analyses as benchmarks (52%, 16/31).
- Submissions using external trials as primary evidence were mainly criticized for lack of comparability with trial population and insufficient adjustments of population difference, followed by concerns about result generalizability to the market-authorized population.
- In contrast, RWD-based submissions were criticized for high uncertainty due to data limitations (e.g., small sample size, immaturity, short follow-up), followed by insufficient covariate adjustments in ITC analyses and lack of comparability to trial populations.

Conclusions

RWD has been increasingly used as an alternative to suboptimal trials for external control in SAT-based HTA submissions, offering more granularity and flexibility. HTA consensus on its appropriateness for external control remains low, with key discussions on whether the data are fit-for-purpose and the adequacy of covariate adjustments.

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Disclosures

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Biostatistics & Health Analytics

7–9 July 2025 | Aegina, Greece

Posters

Extrapolating Overall Survival Data: A Practical Guide to Methods and Model Selection for Long-term Predictions

Biostatistics & Health Analytics 2025

7–9 July 2025 | Aegina, Greece

Poster Title

Extrapolating Overall Survival Data: A Practical Guide to Methods and Model Selection for Long-term Predictions

Objective

- This poster offers a summary of prevalent techniques for extrapolating OS, describes their foundational assumptions, and emphasizes practical aspects for choosing and validating these models.

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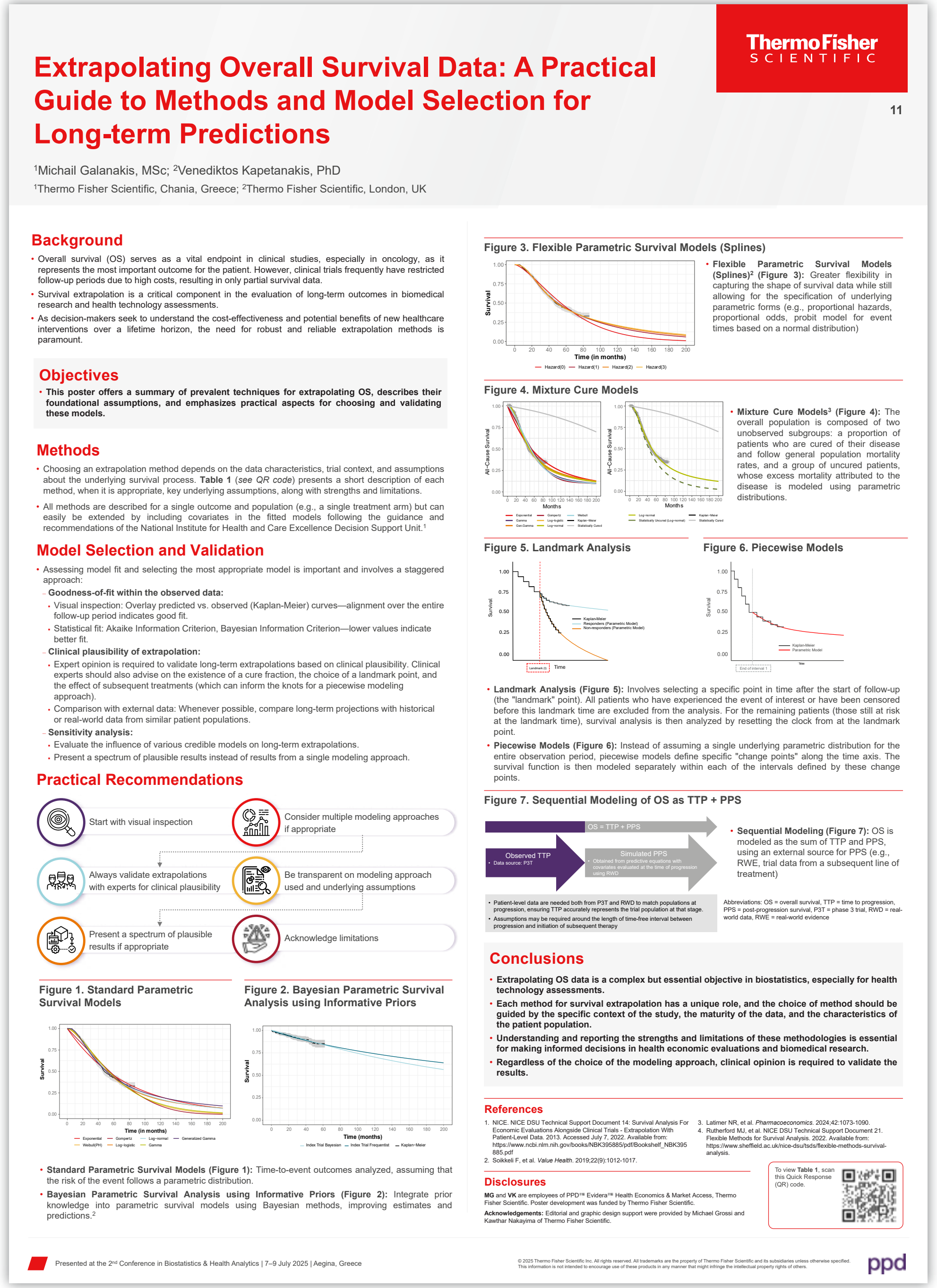

International Society for Pharmacoepidemiology (ISPE)

22–26 August 2025 | Washington, DC, USA

Posters

Interpretable Machine Learning Models: Describing Treatment Patterns of Healthcare Providers Selecting Rheumatoid Arthritis Therapies to Evaluate Treatment Policies

Post-Approval Real-World Studies of RNA Therapies in the EU: What Can We Learn From Study Characteristics?

Beyond Comparison: Target Trial Emulation (TTE) Principles Strengthen Observational Single-arm (SA) Effectiveness Studies

Longitudinal, Regulatory-grade Registry Data Can Be Used to Emulate a Target Trial: An Application on Evaluating Treatments for Plaque Psoriasis

Policy Impact on Pregnancy Registry Participation and Reporting of Maternal/Infant Outcomes

Nuances of Risk Window Selection for Evaluation of Acute Adverse Events

Evolving Landscape of Post-marketing Surveillance (PMS) Studies in Japan Utilising Secondary Real-world Data (RWD)

Mandated Long-Term Follow-Up Studies of Patients Treated With Gene and Cell Therapies Approved in the European Union (EU): An Analysis of Commonalities and Variations

Review of Ongoing PASS Submitted to the HMA-EMA Catalogue of RWD Studies Evaluating Cancer as an Outcome

Vaccine-related Studies Listed in the Heads of Medicines Agencies-European Medicines Agency (HMA-EMA) Catalogue of Real-world Data Studies: What Can We Learn from Study Characteristics?

Methodological Considerations about Policy Impact on Studies of Pregnancy Registries and Maternal/Infant Outcomes

An Alternative to Non-responder Imputation for Study Participants with Missing Outcomes in Single-arm Drug-effectiveness Studies: A Case Study in the PPD CorEvitas Psoriasis Registry

Landscape and Study Design Characteristics of Prospective Observational Cohort Studies on Pregnant Women in China

ISPE 2025

22–26 August 2025 | Washington, DC, USA

Poster Title

Interpretable Machine Learning Models: Describing Treatment Patterns of Healthcare Providers Selecting Rheumatoid Arthritis Therapies to Evaluate Treatment Policies

Objective

- Demonstrate the strengths of interpretable ML models compared to black-box models for predicting treatment selection in rheumatoid arthritis (RA).

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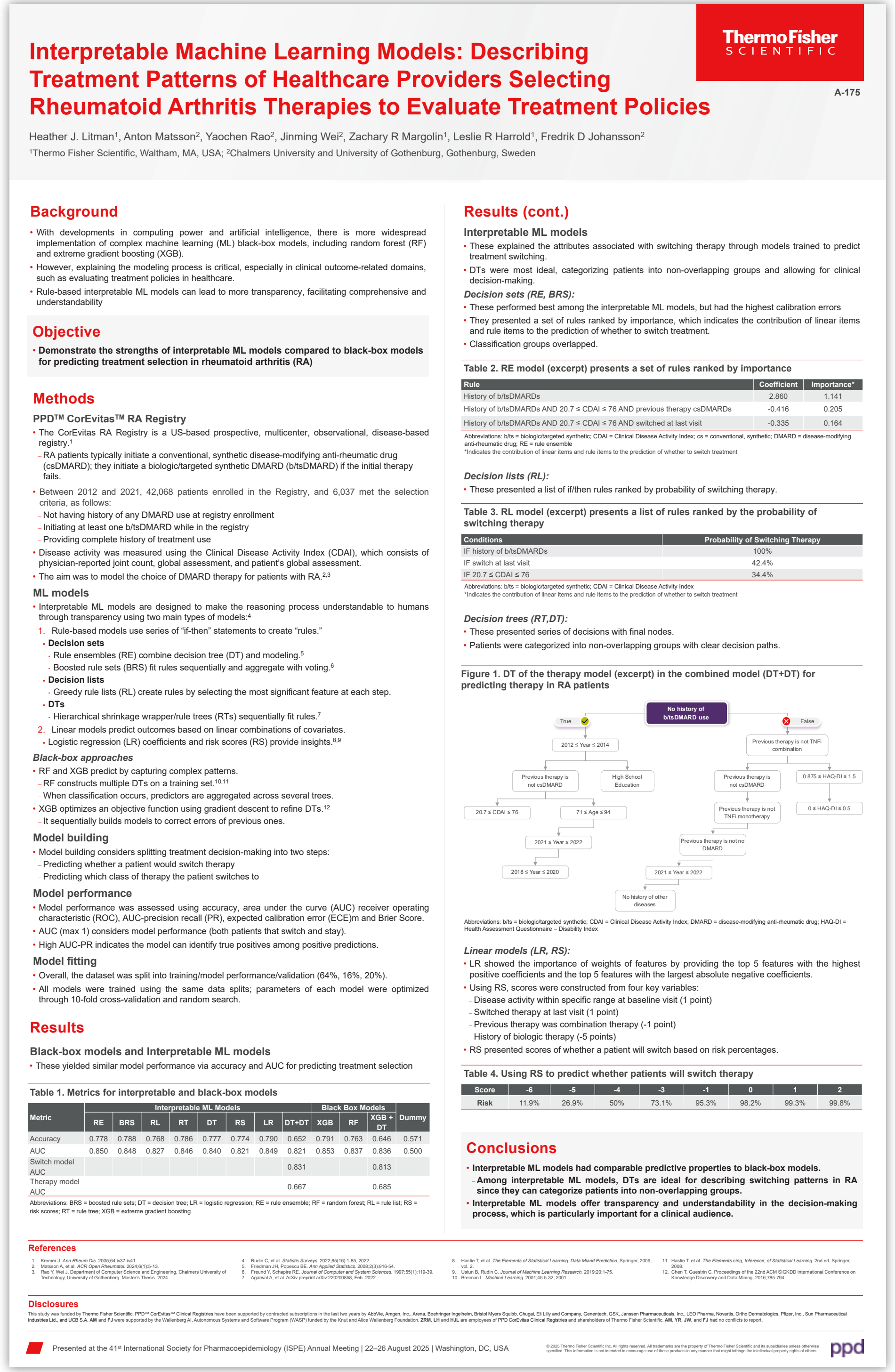

ISPE 2025

22–26 August 2025 | Washington, DC, USA

Poster Title

Post-Approval Real-World Studies of RNA Therapies in the EU: What Can We Learn From Study Characteristics?

Objective

- To provide an overview of key design characteristics of studies that are registered in the Heads of Medicines Agencies (HMA)-EMA Catalogues (HMA-EMA)[4] and ClinicalTrials.gov (CTgov)[5] of real-world data (RWD) studies on RNA therapies approved in the EU.

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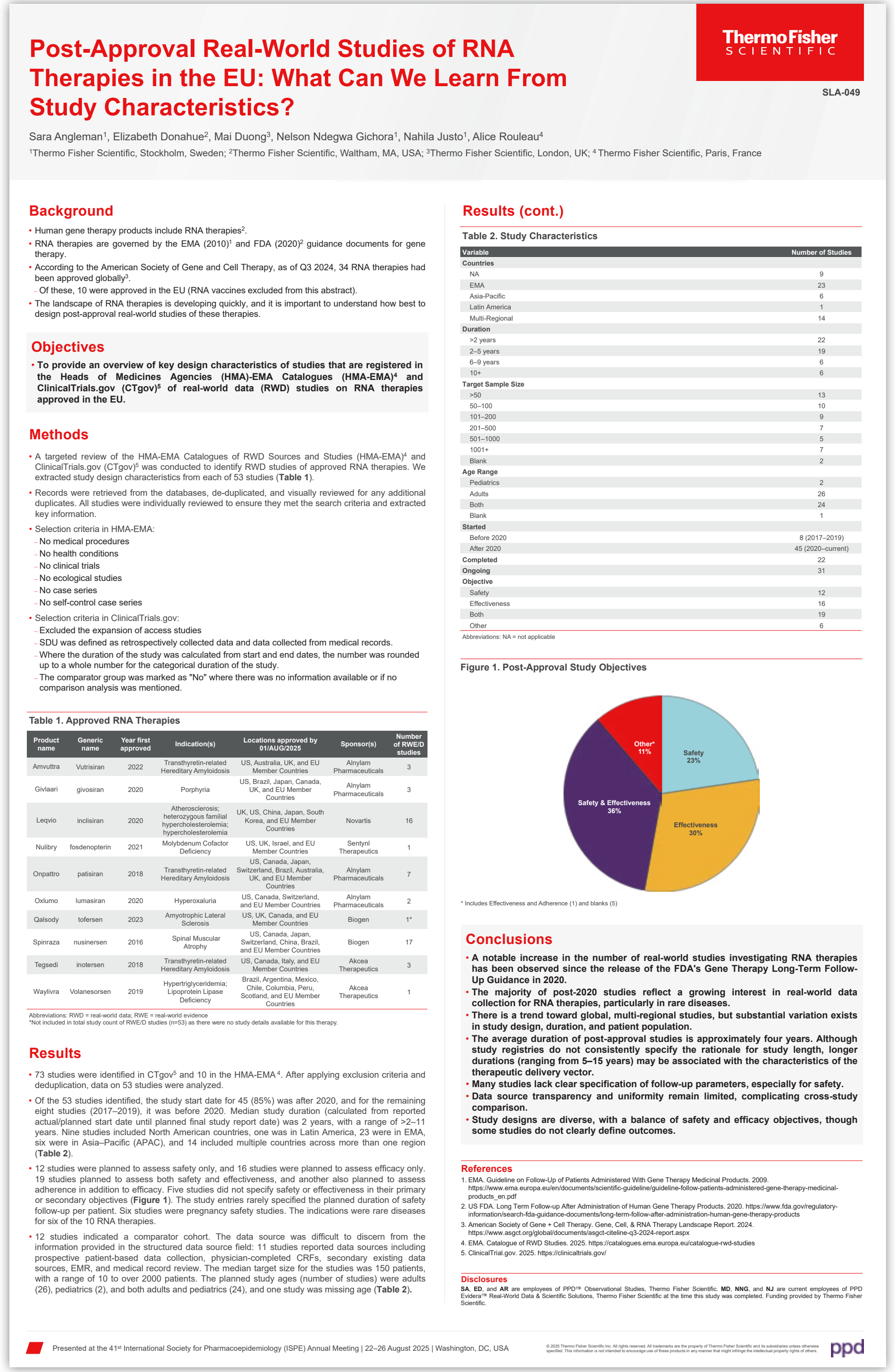

Post-Approval Real-World Studies of RNA Therapies in the EU: What Can We Learn From Study Characteristics?

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SLA-049

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Background

- Human gene therapy products include RNA therapies[2].
- RNA therapies are governed by the EMA (2010)[1] and FDA (2020)[2] guidance documents for gene therapy.
- According to the American Society of Gene and Cell Therapy, as of Q3 2024, 34 RNA therapies had been approved globally[3].
  - Of these, 10 were approved in the EU (RNA vaccines excluded from this abstract).
- The landscape of RNA therapies is developing quickly, and it is important to understand how best to design post-approval real-world studies of these therapies.

Objectives

- **To provide an overview of key design characteristics of studies that are registered in the Heads of Medicines Agencies (HMA)-EMA Catalogues (HMA-EMA)[4] and ClinicalTrials.gov (CTgov)[5] of real-world data (RWD) studies on RNA therapies approved in the EU.**

Methods

- A targeted review of the HMA-EMA Catalogues of RWD Sources and Studies (HMA-EMA)[4] and ClinicalTrials.gov (CTgov)[5] was conducted to identify RWD studies of approved RNA therapies. We extracted study design characteristics from each of 53 studies (**Table 1**).
- Records were retrieved from the databases, de-duplicated, and visually reviewed for any additional duplicates. All studies were individually reviewed to ensure they met the search criteria and extracted key information.
- Selection criteria in HMA-EMA:
  - No medical procedures
  - No health conditions
  - No clinical trials
  - No ecological studies
  - No case series
  - No self-control case series
- Selection criteria in ClinicalTrials.gov:
  - Excluded the expansion of access studies
  - SDU was defined as retrospectively collected data and data collected from medical records.
  - Where the duration of the study was calculated from start and end dates, the number was rounded up to a whole number for the categorical duration of the study.
  - The comparator group was marked as "No" where there was no information available or if no comparison analysis was mentioned.

Table 1. Approved RNA Therapies

Product name	Generic name	Year first approved	Indication(s)	Locations approved by 01/AUG/2025	Sponsor(s)	Number of RWE/D studies
Amvuttra	Vutrisiran	2022	Transthyretin-related Hereditary Amyloidosis	US, Australia, UK, and EU Member Countries	Alnylam Pharmaceuticals	3
Givlaari	givosiran	2020	Porphyria	US, Brazil, Japan, Canada, UK, and EU Member Countries	Alnylam Pharmaceuticals	3
Leqvio	inclisiran	2020	Atherosclerosis; heterozygous familial hypercholesterolemia; hypercholesterolemia	UK, US, China, Japan, South Korea, and EU Member Countries	Novartis	16
Nulibry	fosdenopterin	2021	Molybdenum Cofactor Deficiency	US, UK, Israel, and EU Member Countries	Sentynl Therapeutics	1
Onpattro	patisiran	2018	Transthyretin-related Hereditary Amyloidosis	US, Canada, Japan, Switzerland, Brazil, Australia, UK, and EU Member Countries	Alnylam Pharmaceuticals	7
Oxlumo	lumasiran	2020	Hyperoxaluria	US, Canada, Switzerland, and EU Member Countries	Alnylam Pharmaceuticals	2
Qalsody	tofersen	2023	Amyotrophic Lateral Sclerosis	US, UK, Canada, and EU Member Countries	Biogen	1*
Spinraza	nusinersen	2016	Spinal Muscular Atrophy	US, Canada, Japan, Switzerland, China, Brazil, and EU Member Countries	Biogen	17
Tegsedi	inotersen	2018	Transthyretin-related Hereditary Amyloidosis	US, Canada, Italy, and EU Member Countries	Akcea Therapeutics	3
Waylivra	Volanesorsen	2019	Hypertriglyceridemia; Lipoprotein Lipase Deficiency	Brazil, Argentina, Mexico, Chile, Columbia, Peru, Scotland, and EU Member Countries	Akcea Therapeutics	1

Abbreviations: RWD = real-world data; RWE = real-world evidence
*Not included in total study count of RWE/D studies (n=53) as there were no study details available for this therapy.

Results

- 73 studies were identified in CTgov[5] and 10 in the HMA-EMA[4]. After applying exclusion criteria and deduplication, data on 53 studies were analyzed.
- Of the 53 studies identified, the study start date for 45 (85%) was after 2020, and for the remaining eight studies (2017–2019), it was before 2020. Median study duration (calculated from reported actual/planned start date until planned final study report date) was 2 years, with a range of >2–11 years. Nine studies included North American countries, one was in Latin America, 23 were in EMA, six were in Asia–Pacific (APAC), and 14 included multiple countries across more than one region (**Table 2**).
- 12 studies were planned to assess safety only, and 16 studies were planned to assess efficacy only. 19 studies planned to assess both safety and effectiveness, and another also planned to assess adherence in addition to efficacy. Five studies did not specify safety or effectiveness in their primary or secondary objectives (**Figure 1**). The study entries rarely specified the planned duration of safety follow-up per patient. Six studies were pregnancy safety studies. The indications were rare diseases for six of the 10 RNA therapies.
- 12 studies indicated a comparator cohort. The data source was difficult to discern from the information provided in the structured data source field: 11 studies reported data sources including prospective patient-based data collection, physician-completed CRFs, secondary existing data sources, EMR, and medical record review. The median target size for the studies was 150 patients, with a range of 10 to over 2000 patients. The planned study ages (number of studies) were adults (26), pediatrics (2), and both adults and pediatrics (24), and one study was missing age (**Table 2**).

Results (cont.)

Table 2. Study Characteristics

Variable	Number of Studies
Countries	
NA	9
EMA	23
Asia-Pacific	6
Latin America	1
Multi-Regional	14
Duration	
>2 years	22
2–5 years	19
6–9 years	6
10+	6
Target Sample Size	
>50	13
50–100	10
101–200	9
201–500	7
501–1000	5
1001+	7
Blank	2
Age Range	
Pediatrics	2
Adults	26
Both	24
Blank	1
Started	
Before 2020	8 (2017–2019)
After 2020	45 (2020–current)
Completed	22
Ongoing	31
Objective	
Safety	12
Effectiveness	16
Both	19
Other	6

Abbreviations: NA = not applicable

Figure 1. Post-Approval Study Objectives

* Includes Effectiveness and Adherence (1) and blanks (5)

Conclusions

- **A notable increase in the number of real-world studies investigating RNA therapies has been observed since the release of the FDA's Gene Therapy Long-Term Follow-Up Guidance in 2020.**
- **The majority of post-2020 studies reflect a growing interest in real-world data collection for RNA therapies, particularly in rare diseases.**
- **There is a trend toward global, multi-regional studies, but substantial variation exists in study design, duration, and patient population.**
- **The average duration of post-approval studies is approximately four years. Although study registries do not consistently specify the rationale for study length, longer durations (ranging from 5–15 years) may be associated with the characteristics of the therapeutic delivery vector.**
- **Many studies lack clear specification of follow-up parameters, especially for safety.**
- **Data source transparency and uniformity remain limited, complicating cross-study comparison.**
- **Study designs are diverse, with a balance of safety and efficacy objectives, though some studies do not clearly define outcomes.**

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Disclosures

SA, **ED**, and **AR** are employees of PPD™ Observational Studies, Thermo Fisher Scientific. **MD**, **NNG**, and **NJ** are current employees of PPD Evidera™ Real-World Data & Scientific Solutions, Thermo Fisher Scientific at the time this study was completed. Funding provided by Thermo Fisher Scientific.

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ISPE 2025

22–26 August 2025 | Washington, DC, USA

Poster Title

Beyond Comparison: Target Trial Emulation (TTE) Principles Strengthen Observational Single-arm (SA) Effectiveness Studies

Objective

- Describe implementation of TTE principles for SA effectiveness studies based on registry data.

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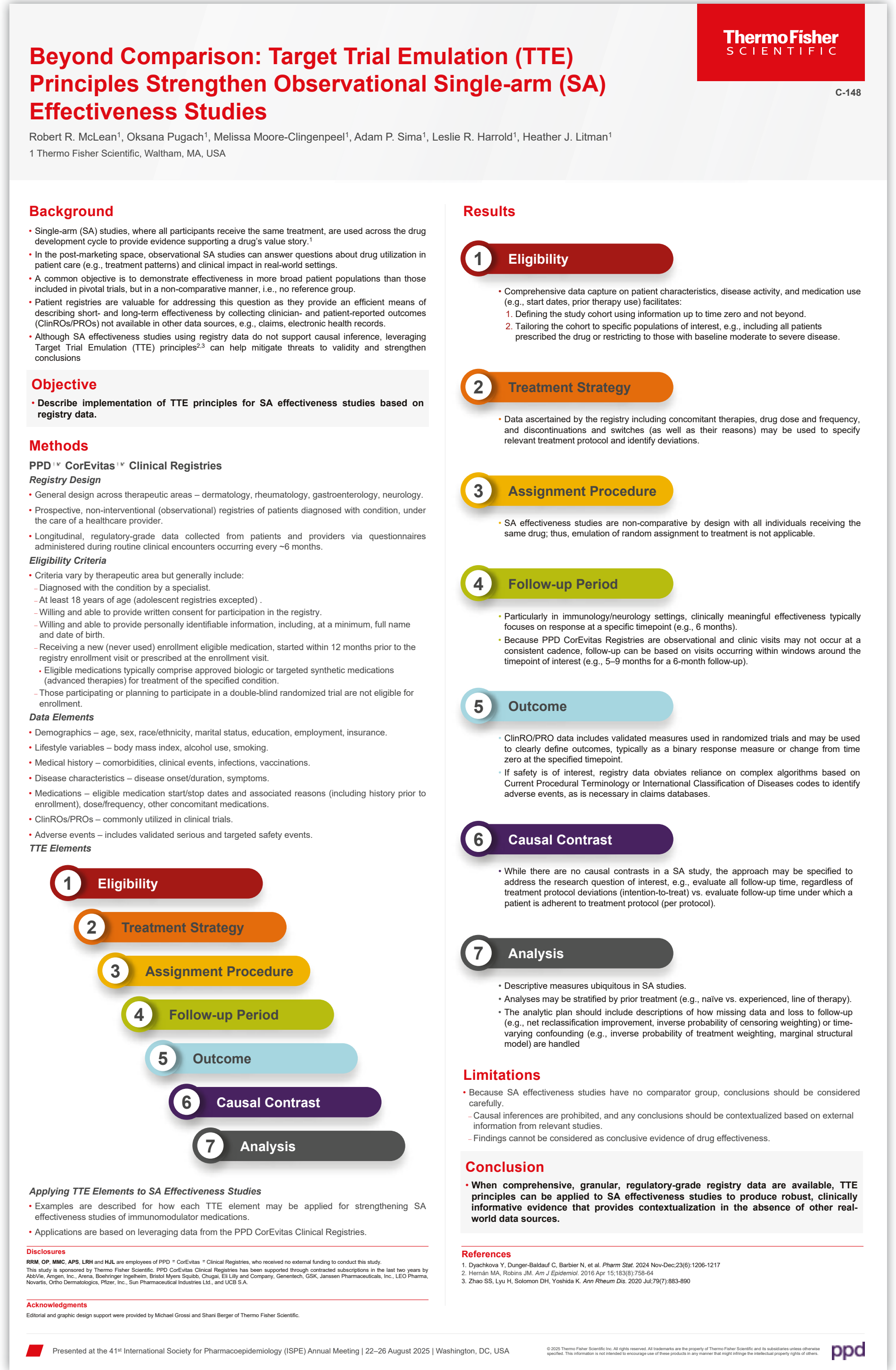

ISPE 2025

22–26 August 2025 | Washington, DC, USA

Poster Title

Longitudinal, Regulatory-grade Registry Data Can Be Used to Emulate a Target Trial: An Application on Evaluating Treatments for Plaque Psoriasis

Objective

- To demonstrate how registry data can fit a TTE framework to answer comparative effectiveness and safety questions about real-world medication use.

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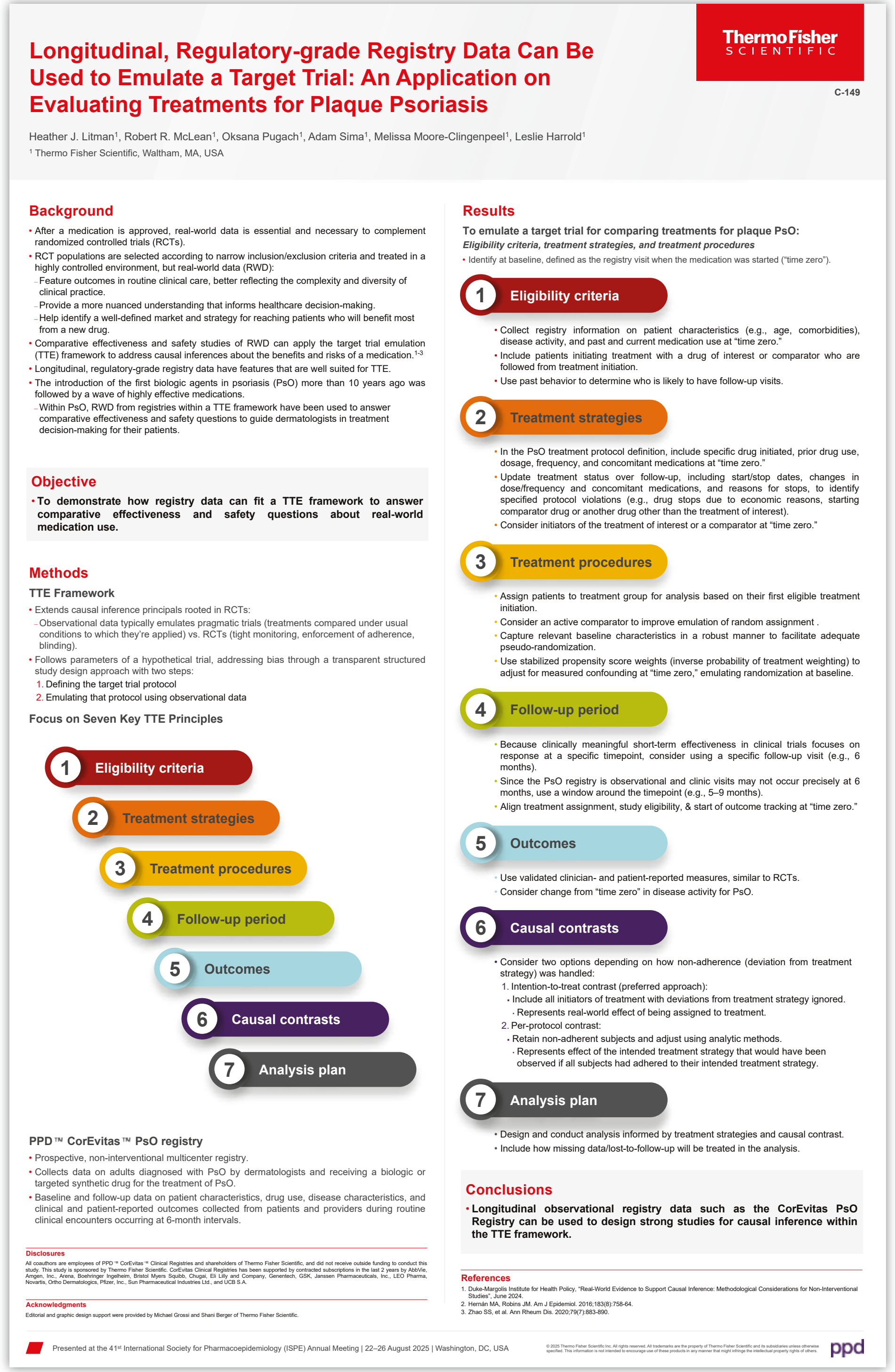

ISPE 2025

22–26 August 2025 | Washington, DC, USA

Poster Title

Policy Impact on Pregnancy Registry Participation and Reporting of Maternal/Infant Outcomes

Objective

- To review published and/or gray literature, defined as information produced outside of academic or commercial publishing pathways (e.g., technical reports, white papers) to assess the potential impact of the Dobbs ruling on:
  - Objective 1: Pregnancy registry enrollment, loss to follow-up, and missing data.
  - Objective 2: Maternal and infant outcomes, particularly in congenital anomalies, which is a critical outcome studied in pregnancy registries.

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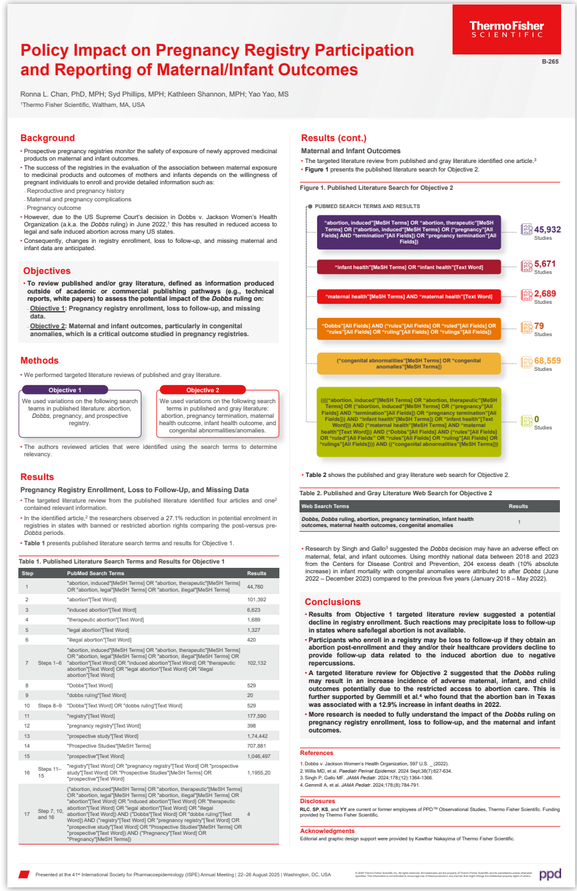

Policy Impact on Pregnancy Registry Participation and Reporting of Maternal/Infant Outcomes

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B-265

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Background

- Prospective pregnancy registries monitor the safety of exposure of newly approved medicinal products on maternal and infant outcomes.
- The success of the registries in the evaluation of the association between maternal exposure to medicinal products and outcomes of mothers and infants depends on the willingness of pregnant individuals to enroll and provide detailed information such as:
  - Reproductive and pregnancy history
  - Maternal and pregnancy complications
  - Pregnancy outcome
- However, due to the US Supreme Court's decision in Dobbs v. Jackson Women's Health Organization (a.k.a. the *Dobbs* ruling) in June 2022,[1] this has resulted in reduced access to legal and safe induced abortion across many US states.
- Consequently, changes in registry enrollment, loss to follow-up, and missing maternal and infant data are anticipated.

Objectives

- **To review published and/or gray literature, defined as information produced outside of academic or commercial publishing pathways (e.g., technical reports, white papers) to assess the potential impact of the *Dobbs* ruling on:**

  Objective 1: Pregnancy registry enrollment, loss to follow-up, and missing data.

  Objective 2: Maternal and infant outcomes, particularly in congenital anomalies, which is a critical outcome studied in pregnancy registries.

Methods

- We performed targeted literature reviews of published and gray literature.

Objective 1
We used variations on the following search teams in published literature: abortion, *Dobbs*, pregnancy, and prospective registry.

Objective 2
We used variations on the following search terms in published and gray literature: abortion, pregnancy termination, maternal health outcome, infant health outcome, and congenital abnormalities/anomalies.

- The authors reviewed articles that were identified using the search terms to determine relevancy.

Results

Pregnancy Registry Enrollment, Loss to Follow-Up, and Missing Data

- The targeted literature review from the published literature identified four articles and one[2] contained relevant information.
- In the identified article,[2] the researchers observed a 27.1% reduction in potential enrollment in registries in states with banned or restricted abortion rights comparing the post-versus pre-*Dobbs* periods.
- **Table 1** presents published literature search terms and results for Objective 1.

Table 1. Published Literature Search Terms and Results for Objective 1

Step	PubMed Search Terms	Results
1	"abortion, induced"[MeSH Terms] OR "abortion, therapeutic"[MeSH Terms] OR "abortion, legal"[MeSH Terms] OR "abortion, illegal"[MeSH Terms]	44,760
2	"abortion"[Text Word]	101,392
3	"induced abortion"[Text Word]	6,623
4	"therapeutic abortion"[Text Word]	1,689
5	"legal abortion"[Text Word]	1,327
6	"illegal abortion"[Text Word]	420
7	Steps 1–6	"abortion, induced"[MeSH Terms] OR "abortion, therapeutic"[MeSH Terms] OR "abortion, legal"[MeSH Terms] OR "abortion, illegal"[MeSH Terms] OR "abortion"[Text Word] OR "induced abortion"[Text Word] OR "therapeutic abortion"[Text Word] OR "legal abortion"[Text Word] OR "illegal abortion"[Text Word]	102,132
8		"Dobbs"[Text Word]	529
9		"dobbs ruling"[Text Word]	20
10	Steps 8–9	"Dobbs"[Text Word] OR "dobbs ruling"[Text Word]	529
11		"registry"[Text Word]	177,592
12		"pregnancy registry"[Text Word]	398
13		"prospective study"[Text Word]	1,74,442
14		"Prospective Studies"[MeSH Terms]	707,881
15		"prospective"[Text Word]	1,046,497
16	Steps 11–15	"registry"[Text Word] OR "pregnancy registry"[Text Word] OR "prospective study"[Text Word] OR "Prospective Studies"[MeSH Terms] OR "prospective"[Text Word]	1,1955,20
17	Step 7, 10, and 16	("abortion, induced"[MeSH Terms] OR "abortion, therapeutic"[MeSH Terms] OR "abortion, legal"[MeSH Terms] OR "abortion, illegal"[MeSH Terms] OR "abortion"[Text Word] OR "induced abortion"[Text Word] OR "therapeutic abortion"[Text Word] OR "legal abortion"[Text Word] OR "illegal abortion"[Text Word]) AND ("Dobbs"[Text Word] OR "dobbs ruling"[Text Word]) AND ("registry"[Text Word] OR "pregnancy registry"[Text Word] OR "prospective study"[Text Word] OR "Prospective Studies"[MeSH Terms] OR "prospective"[Text Word]) AND ("Pregnancy"[Text Word] OR "Pregnancy"[MeSH Terms])	4

Results (cont.)

Maternal and Infant Outcomes

- The targeted literature review from published and gray literature identified one article.[3]
- **Figure 1** presents the published literature search for Objective 2.

Figure 1. Published Literature Search for Objective 2

- **Table 2** shows the published and gray literature web search for Objective 2.

Table 2. Published and Gray Literature Web Search for Objective 2

Web Search Terms	Results
***Dobbs*, *Dobbs* ruling, abortion, pregnancy termination, infant health outcomes, maternal health outcomes, congenital anomalies**	1

- Research by Singh and Gallo[3] suggested the *Dobbs* decision may have an adverse effect on maternal, fetal, and infant outcomes. Using monthly national data between 2018 and 2023 from the Centers for Disease Control and Prevention, 204 excess death (10% absolute increase) in infant mortality with congenital anomalies were attributed to after *Dobbs* (June 2022 – December 2023) compared to the previous five years (January 2018 – May 2022).

Conclusions

- **Results from Objective 1 targeted literature review suggested a potential decline in registry enrollment. Such reactions may precipitate loss to follow-up in states where safe/legal abortion is not available.**
- **Participants who enroll in a registry may be loss to follow-up if they obtain an abortion post-enrollment and they and/or their healthcare providers decline to provide follow-up data related to the induced abortion due to negative repercussions.**
- **A targeted literature review for Objective 2 suggested that the *Dobbs* ruling may result in an increase incidence of adverse maternal, infant, and child outcomes potentially due to the restricted access to abortion care. This is further supported by Gemmill et al.[4] who found that the abortion ban in Texas was associated with a 12.9% increase in infant deaths in 2022.**
- **More research is needed to fully understand the impact of the *Dobbs* ruling on pregnancy registry enrollment, loss to follow-up, and the maternal and infant outcomes.**

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Disclosures

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ISPE 2025

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Poster Title

Nuances of Risk Window Selection for Evaluation of Acute Adverse Events

Objective

- To examine the implications of using multiple RCWs, with emphasis on eligibility of exposure episodes and indexing of events.

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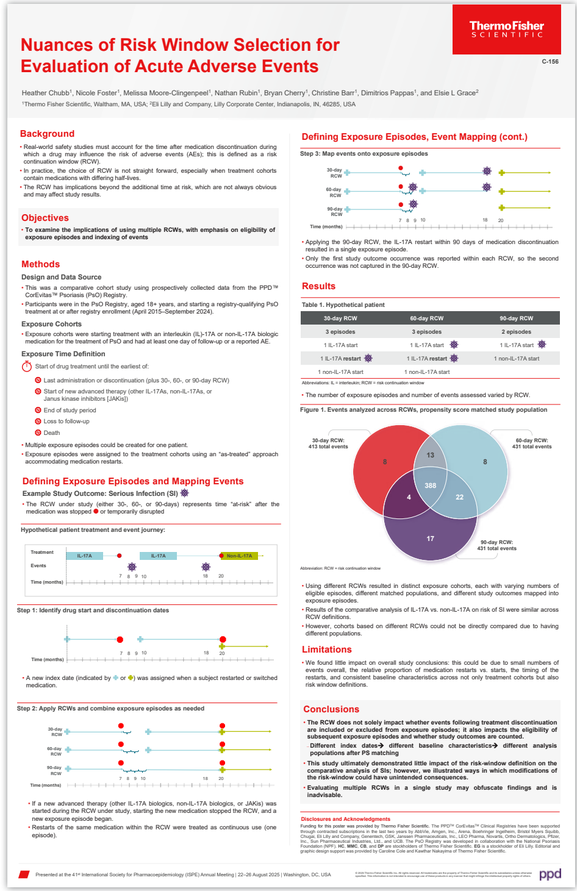

Nuances of Risk Window Selection for Evaluation of Acute Adverse Events

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Background

- Real-world safety studies must account for the time after medication discontinuation during which a drug may influence the risk of adverse events (AEs); this is defined as a risk continuation window (RCW).
- In practice, the choice of RCW is not straight forward, especially when treatment cohorts contain medications with differing half-lives.
- The RCW has implications beyond the additional time at risk, which are not always obvious and may affect study results.

Objectives

- **To examine the implications of using multiple RCWs, with emphasis on eligibility of exposure episodes and indexing of events**

Methods

Design and Data Source

- This was a comparative cohort study using prospectively collected data from the PPD™ CorEvitas™ Psoriasis (PsO) Registry.
- Participants were in the PsO Registry, aged 18+ years, and starting a registry-qualifying PsO treatment at or after registry enrollment (April 2015–September 2024).

Exposure Cohorts

- Exposure cohorts were starting treatment with an interleukin (IL)-17A or non-IL-17A biologic medication for the treatment of PsO and had at least one day of follow-up or a reported AE.

Exposure Time Definition

Start of drug treatment until the earliest of:

- Last administration or discontinuation (plus 30-, 60-, or 90-day RCW)
- Start of new advanced therapy (other IL-17As, non-IL-17As, or Janus kinase inhibitors [JAKis])
- End of study period
- Loss to follow-up
- Death

- Multiple exposure episodes could be created for one patient.
- Exposure episodes were assigned to the treatment cohorts using an "as-treated" approach accommodating medication restarts.

Defining Exposure Episodes and Mapping Events

Example Study Outcome: Serious Infection (SI)

- The RCW under study (either 30-, 60-, or 90-days) represents time "at-risk" after the medication was stopped or temporarily disrupted

Hypothetical patient treatment and event journey:

Step 1: Identify drug start and discontinuation dates

- A new index date (indicated by or) was assigned when a subject restarted or switched medication.

Step 2: Apply RCWs and combine exposure episodes as needed

- If a new advanced therapy (other IL-17A biologics, non-IL-17A biologics, or JAKis) was started during the RCW under study, starting the new medication stopped the RCW, and a new exposure episode began.
- Restarts of the same medication within the RCW were treated as continuous use (one episode).

Defining Exposure Episodes, Event Mapping (cont.)

Step 3: Map events onto exposure episodes

- Applying the 90-day RCW, the IL-17A restart within 90 days of medication discontinuation resulted in a single exposure episode.
- Only the first study outcome occurrence was reported within each RCW, so the second occurrence was not captured in the 90-day RCW.

Results

Table 1. Hypothetical patient

30-day RCW	60-day RCW	90-day RCW
3 episodes	3 episodes	2 episodes
1 IL-17A start	1 IL-17A start	1 IL-17A start
1 IL-17A **restart**	1 IL-17A **restart**	1 non-IL-17A start
1 non-IL-17A start	1 non-IL-17A start	

Abbreviations: IL-1 = interleukin; RCW = risk continuation window

- The number of exposure episodes and number of events assessed varied by RCW.

Figure 1. Events analyzed across RCWs, propensity score matched study population

Abbreviation: RCW = risk continuation window

- Using different RCWs resulted in distinct exposure cohorts, each with varying numbers of eligible episodes, different matched populations, and different study outcomes mapped into exposure episodes.
- Results of the comparative analysis of IL-17A vs. non-IL-17A on risk of SI were similar across RCW definitions.
- However, cohorts based on different RCWs could not be directly compared due to having different populations.

Limitations

- We found little impact on overall study conclusions: this could be due to small numbers of events overall, the relative proportion of medication restarts vs. starts, the timing of the restarts, and consistent baseline characteristics across not only treatment cohorts but also risk window definitions.

Conclusions

- **The RCW does not solely impact whether events following treatment discontinuation are included or excluded from exposure episodes; it also impacts the eligibility of subsequent exposure episodes and whether study outcomes are counted.**
  - **Different index dates→ different baseline characteristics→ different analysis populations after PS matching**
- **This study ultimately demonstrated little impact of the risk-window definition on the comparative analysis of SIs; however, we illustrated ways in which modifications of the risk-window could have unintended consequences.**
- **Evaluating multiple RCWs in a single study may obfuscate findings and is inadvisable.**

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Poster Title

Evolving Landscape of Post-marketing Surveillance (PMS) Studies in Japan Utilising Secondary Real-world Data (RWD)

Objective

- To describe the evolving landscape related to RWD use for PMS studies in Japan and discuss the implications compared to global practices.

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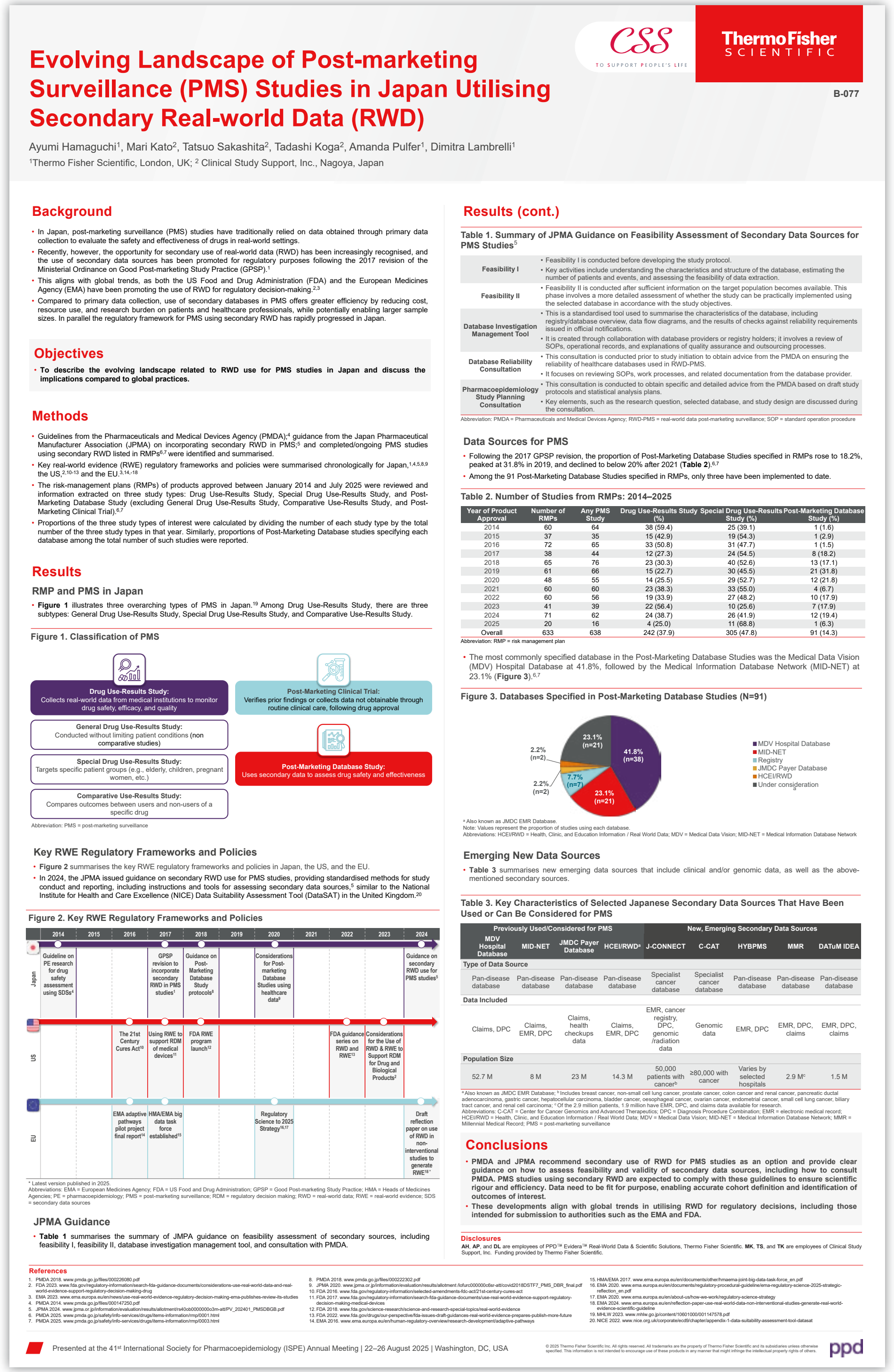

ISPE 2025

22–26 August 2025 | Washington, DC, USA

Poster Title

Mandated Long-Term Follow-Up Studies of Patients Treated With Gene and Cell Therapies Approved in the European Union (EU): An Analysis of Commonalities and Variations

Objective

- The aim of this study was to describe characteristics and identify commonalities and variations of LTFU studies for the 16 GCTs approved in the EU until 31/03/2025. Table 1 includes a list of therapies, the year of the first approval, indications, and other key information.

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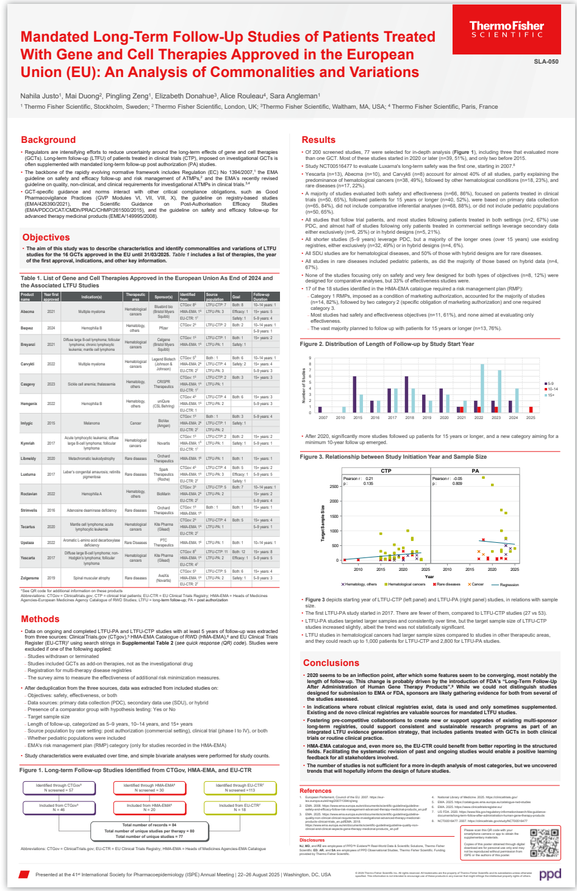

Mandated Long-Term Follow-Up Studies of Patients Treated With Gene and Cell Therapies Approved in the European Union (EU): An Analysis of Commonalities and Variations

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SLA-050

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Background

- Regulators are intensifying efforts to reduce uncertainty around the long-term effects of gene and cell therapies (GCTs). Long-term follow-up (LTFU) of patients treated in clinical trials (CTP), imposed on investigational GCTs is often supplemented with mandated long-term follow-up post authorization (PA) studies.
- The backbone of the rapidly evolving normative framework includes Regulation (EC) No 1394/2007,[1] the EMA guideline on safety and efficacy follow-up and risk management of ATMPs,[2] and the EMA's recently revised guideline on quality, non-clinical, and clinical requirements for investigational ATMPs in clinical trials.[3,4]
- GCT-specific guidance and norms interact with other critical compliance obligations, such as Good Pharmacovigilance Practices (GVP Modules VI, VIII, XI), the guideline on registry-based studies (EMA/426390/2021), the Scientific Guidance on Post-Authorisation Efficacy Studies (EMA/PDCO/CAT/CMDh/PRAC/CHMP/281505/2015), and the guideline on safety and efficacy follow-up for advanced therapy medicinal products (EMEA/149995/2008).

Objectives

- **The aim of this study was to describe characteristics and identify commonalities and variations of LTFU studies for the 16 GCTs approved in the EU until 31/03/2025.** ***Table 1*** **includes a list of therapies, the year of the first approval, indications, and other key information.**

Table 1. List of Gene and Cell Therapies Approved in the European Union As End of 2024 and the Associated LTFU Studies

Product Name	Year First Approved	Indication	Therapeutic Area	Sponsor(s)	Identified	Source	Year	Following
Abecma	2021	Multiple myeloma	Hematological cancers	Bristol-Myers Squibb	CTGov: 8[a] HMA-EMA: 1[b] EU-CTR: 0[c]	LTFU-CTP: 5 LTFU-PA: 3	Both: 5 Efficacy: 1 Safety: 1	15–16 years: 1 15+ years: 3 5–9 years: 4
Beqvez	2024	Hemophilia B	Hematology-others	Pfizer	CTGov: 2[a]	LTFU-CTP: 2	Both: 2	15–16 years: 1 5–9 years: 1
Breyanzi	2021	Diffuse large B-cell lymphoma; follicular lymphoma; chronic lymphocytic leukemia; mantle cell lymphoma	Hematological cancers	Celgene (Bristol-Myers Squibb)	CTGov: 11[a] HMA-EMA: 1[b]	LTFU-CTP: 1 LTFU-PA: 1	Both: 1 Safety: 1	15+ years: 2
Carvykti	2022	Multiple myeloma	Hematological cancers	Legend Biotech (Johnson & Johnson)	CTGov: 5[a] HMA-EMA: 2[b] EU-CTR: 2[c]	CTGov: 1 LTFU-CTP: 4 LTFU-PA: 1	Both: 1 Safety: 2	15–16 years: 1 15+ years: 4 5–9 years: 3
Casgevy	2023	Sickle cell anemia; thalassemia	Hemotology-others	CRISPR Therapeutics	CTGov: 11[a] HMA-EMA: 1[b] EU-CTR: 1[c]	LTFU-CTP: 3 LTFU-PA: 1	Both: 3	15+ years: 3
Hemgenix	2022	Hemophilia B	Hemotology-others	uniQure (CSL Behring)	CTGov: 5[a] HMA-EMA: 1[b] EU-CTR: 1[c]	LTFU-CTP: 4 LTFU-PA: 2	Both: 6	15+ years: 3 5–9 years: 3
Imlygic	2015	Melanoma	Cancer	BioVex (Amgen)	CTGov: 17[a] HMA-EMA: 2[b] EU-CTR: 2[c]	Both: 1 LTFU-CTP: 1 LTFU-PA: 2	Both: 3 Safety: 1	5–9 years: 4
Kymriah	2017	Acute lymphocytic leukemia; diffuse large B-cell lymphoma; follicular lymphoma	Hematological cancers	Novartis	CTGov: 11[a] HMA-EMA: 1[b] EU-CTR: 1[c]	LTFU-CTP: 2 LTFU-PA: 1	Both: 2 Safety: 1	15+ years: 2 5–9 years: 1
Libmeldy	2020	Metachromatic leukodystrophy	Rare diseases	Orchard Therapeutics	HMA-EMA: 3[b]	LTFU-PA: 1	Both: 1	15+ years: 1
Lumevoq	2017	Leber's congenital amaurosis; retinitis pigmentosa	Rare diseases	Spark Therapeutics (Roche)	CTGov: 4[a] HMA-EMA: 1[b] EU-CTR: 1[c]	LTFU-CTP: 4 LTFU-PA: 3	Both: 3 Efficacy: 1 Safety: 1	15+ years: 2 5–9 years: 3
Roctavian	2022	Hemophilia A	Hematology-others	BioMarin	CTGov: 37 HMA-EMA: 2[b] EU-CTR: 2[c]	LTFU-CTP: 3 LTFU-PA: 3	Both: 3	15–16 years: 1 15+ years: 2 5–9 years: 4
Strimvelis	2016	Adenosine deaminase deficiency	Rare diseases	Orchard Therapeutics	CTGov: 7 HMA-EMA: 1[b]	Both: 1	Both: 1	15+ years: 1
Tecartus	2020	Mantle cell lymphoma; acute lymphocytic leukemia	Hematological cancers	Kite Pharma (Gilead)	CTGov: 2[a] HMA-EMA: 1[b] EU-CTR: 2[c]	LTFU-CTP: 4 LTFU-PA: 1	Both: 3	15+ years: 4 5–9 years: 1
Upstaza	2022	Aromatic L-amino acid decarboxylase deficiency	Rare Diseases	PTC Therapeutics	HMA-EMA: 3[b]	LTFU-PA: 1	Both: 1	15–16 years: 1
Yescarta	2017	Diffuse large B-cell lymphoma; non-Hodgkin Lymphoma; follicular lymphoma	Hematological cancers	Kite Pharma (Gilead)	CTGov: 9[a] HMA-EMA: 1[b] EU-CTR: 2[c]	LTFU-CTP: 5 LTFU-PA: 2	Both: 12 Efficacy: 1	15+ years: 5 5–9 years: 5
Zolgensma	2019	Spinal muscular atrophy	Rare diseases	AveXis (Novartis)	CTGov: 37 HMA-EMA: 1[b] EU-CTR: 2[c]	LTFU-CTP: 5 LTFU-PA: 2	Both: 6 Safety: 1	15+ years: 4 5–9 years: 3

[a]See QR code for additional information on these products.
Abbreviations: CTGov = ClinicalTrials.gov; CTP = clinical trial patients; EU-CTR = EU Clinical Trials Registry; HMA-EMA = Heads of Medicines Agencies-European Medicines Agency Catalogue of RWD Studies; LTFU = long-term follow-up; PA = post authorization

Methods

- Data on ongoing and completed LTFU-PA and LTFU-CTP studies with at least 5 years of follow-up was extracted from three sources: ClinicalTrials.gov (CTgov),[5] HMA-EMA Catalogue of RWD (HMA-EMA),[6] and EU Clinical Trials Register (EU-CTR)[7] using search strings in **Supplemental Table 2** (see quick response (QR) code). Studies were excluded if one of the following applied:
  - Studies withdrawn or terminated
  - Studies included GCTs as add-on therapies, not as the investigational drug
  - Registration for multi-therapy disease registries
  - The survey aims to measure the effectiveness of additional risk minimization measures.
- After deduplication from the three sources, data was extracted from included studies on:
  - Objectives: safety, effectiveness, or both
  - Data sources: primary data collection (PDC), secondary data use (SDU), or hybrid
  - Presence of a comparator group with hypothesis testing: Yes or No
  - Target sample size
  - Length of follow-up, categorized as 5–9 years, 10–14 years, and 15+ years
  - Source population by care setting: post authorization (commercial setting), clinical trial (phase I to IV), or both
  - Whether pediatric populations were included
  - EMA's risk management plan (RMP) category (only for studies recorded in the HMA-EMA).
- Study characteristics were evaluated over time, and simple bivariate analyses were performed for study counts.

Figure 1. Long-term Follow-up Studies Identified from CTGov, HMA-EMA, and EU-CTR

Abbreviations: CTGov = ClinicalTrials.gov; EU-CTR = EU Clinical Trials Registry; HMA-EMA = Heads of Medicines Agencies-EMA Catalogue

Results

- Of 200 screened studies, 77 were selected for in-depth analysis (**Figure 1**), including three that evaluated more than one GCT. Most of these studies started in 2020 or later (n=39, 51%), and only two before 2010.
- Study NCT00516477 to evaluate Luxturna's long-term safety was the first one, starting in 2007.[7]
- Yescarta (n=12), Abecma (n=10), and Carvykti (n=8) account for almost 40% of all studies, partly explaining the high proportion of studies in hematological cancers (n=36, 49%), followed by other hematological conditions (n=18, 23%), and rare diseases (n=17, 22%).
- A majority of studies evaluated both safety and effectiveness (n=66, 86%), focused on patients treated in clinical trials (n=50, 65%), followed patients for 15 years or longer (n=42, 52%), were based on primary data collection (n=65, 84%), did not include comparative inferential analyses (n=68, 88%), or did not include pediatric populations (n=50, 65%).
- All studies that follow trial patients, and most studies following patients treated in both settings (n=2, 67%) use PDC, and almost half of studies following only patients treated in commercial settings leverage secondary data either exclusively (n=6, 25%) or in hybrid designs (n=5, 21%).
- All shorter studies (5–9 years) leverage PDC, but a majority of the longer ones (over 15 years) use existing registries, either exclusively (n=32, 49%) or in hybrid designs (n=4, 6%).
- All SDU studies are for hematological diseases, and 50% of those with hybrid designs are for rare diseases.
- All studies in rare diseases included pediatric patients, as did the majority of those based on hybrid data (n=4, 67%).
- None of the studies focusing only on safety and very few designed for both types of objectives (n=8, 12%) were designed for comparative analyses, but 33% of effectiveness studies were.
- 17 of the 18 studies identified in the HMA-EMA catalogue required a risk management plan (RMP):
  - Category 1 RMPs, imposed as a condition of marketing authorization, accounted for the majority of studies (n=14, 82%), followed by two category 2 (specific obligation of marketing authorization) and one required category 3.
  - Most studies had safety and effectiveness objectives (n=11, 61%), and none aimed at evaluating only effectiveness.
  - The vast majority planned to follow up with patients for 15 years or longer (n=13, 76%).

Figure 2. Distribution of Length of Follow-up by Study Start Year

- After 2020, significantly more studies followed up patients for 15 years or longer, and a new category aiming for a minimum 10-year follow-up emerged.

Figure 3. Relationship between Study Initiation Year and Sample Size

- **Figure 3** depicts starting year of LTFU-CTP (left-panel) and LTFU-PA (right panel) studies, in relations with sample sizes.
- The first LTFU-PA study started in 2017. There are fewer of them, compared to LTFU-CTP studies (27 vs 53).
- LTFU-PA studies targeted larger samples and consistently over time, but the target sample size of LTFU-CTP studies increased slightly, albeit the trend was not statistically significant.
- LTFU studies in hematological cancers had larger sample sizes compared to studies in other therapeutic areas, and they could reach up to 1,000 patients for LTFU-CTP and 2,800 for LTFU-PA studies.

Conclusions

- **2020 seems to be an inflection point, after which some features seem to be converging, most notably the length of follow-up. This change is probably driven by the introduction of FDA's "Long-Term Follow-Up After Administration of Human Gene Therapy Products".[8] While we could not distinguish studies designed for submission to EMA or FDA, sponsors are likely gathering evidence for both from several of the studies assessed.**
- **In indications where robust clinical registries exist, data is used and only sometimes supplemented. Existing and de novo clinical registries are valuable sources for mandated LTFU studies.**
- **Fostering pre-competitive collaborations to create new or support upgrades of existing multi-sponsor clinical registries, leveraging common protocols, could be a sustainable research pathway as part of an integrated LTFU evidence generation strategy, that includes patients treated with GCTs in both clinical trials or routine clinical practice.**
- **HMA-EMA catalogue and, even more so, the EU-CTR could benefit from better reporting in the structured fields. Facilitating the systematic revision of past and ongoing studies would enable a positive learning feedback for all stakeholders involved.**
- **The number of studies is not sufficient for a more in-depth analysis of most categories, but we uncovered trends that will hopefully inform the design of future studies.**

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Disclosures

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ISPE 2025

22–26 August 2025 | Washington, DC, USA

Poster Title

Review of Ongoing PASS Submitted to the HMA-EMA Catalogue of RWD Studies Evaluating Cancer as an Outcome

Objective

- Summarize the key characteristics and methodologic approaches of post-authorization safety studies (PASS) evaluating cancer as an outcome that have been submitted to the Heads of Medicines Agencies (HMA)-European Medicines Agency (EMA) Catalogue of RWD Studies.

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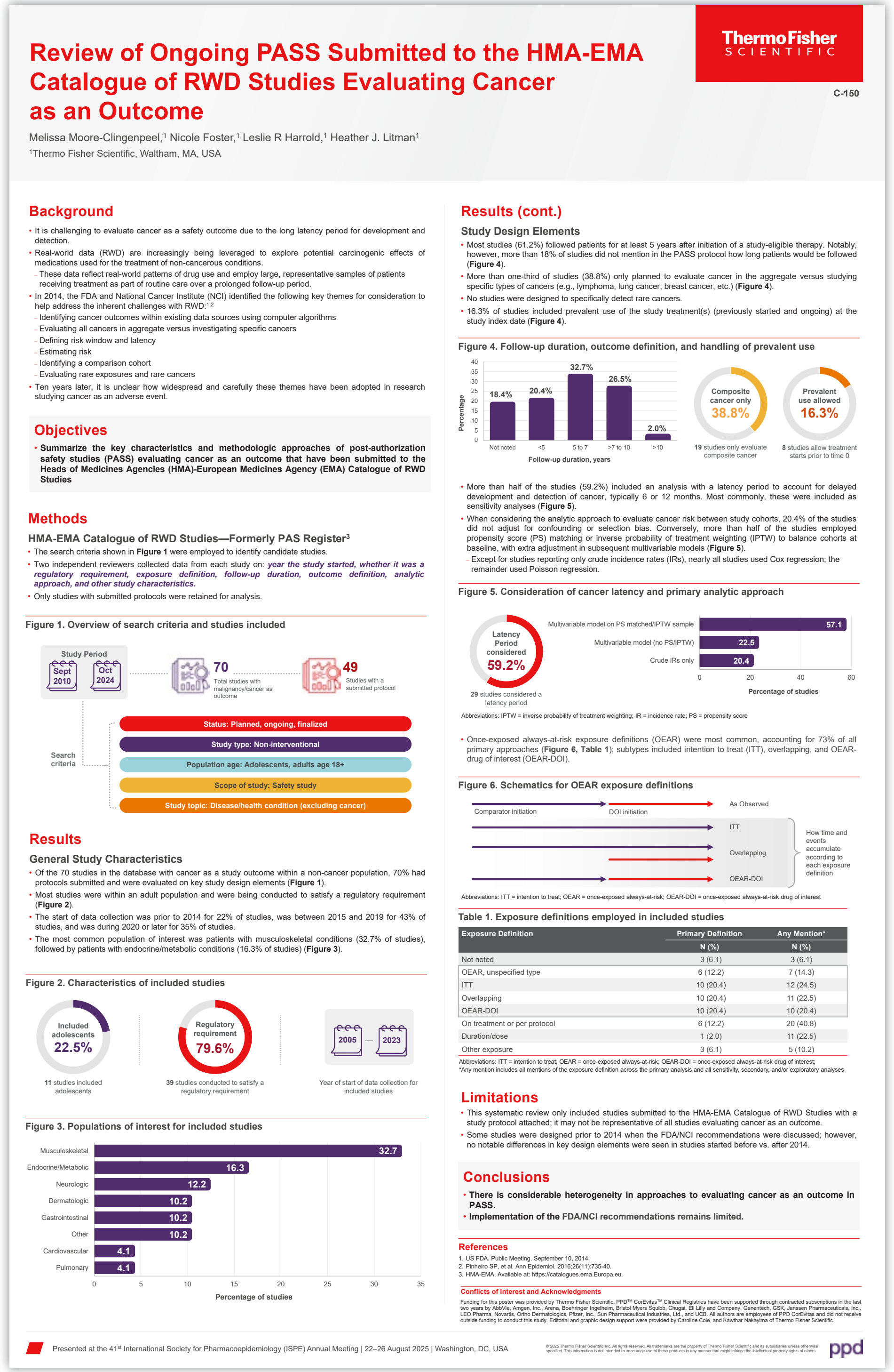

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Poster Title

Vaccine-related Studies Listed in the Heads of Medicines Agencies-European Medicines Agency (HMA-EMA) Catalogue of Real-world Data Studies: What Can We Learn from Study Characteristics?

Objective

- To provide an overview of key design characteristics of vaccine-related studies recorded in the Heads of Medicines Agencies-European Medicines Agency (HMA-EMA) Catalogue of RWD studies.

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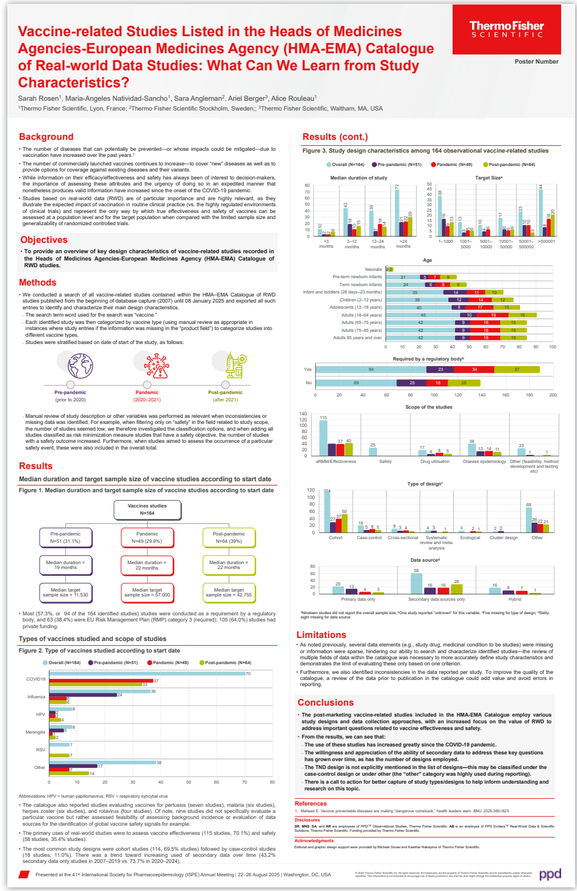

Vaccine-related Studies Listed in the Heads of Medicines Agencies-European Medicines Agency (HMA-EMA) Catalogue of Real-world Data Studies: What Can We Learn from Study Characteristics?

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Background

- The number of diseases that can potentially be prevented—or whose impacts could be mitigated—due to vaccination have increased over the past years.[1]
- The number of commercially launched vaccines continues to increase—to cover "new" diseases as well as to provide options for coverage against existing diseases and their variants.
- While information on their efficacy/effectiveness and safety has always been of interest to decision-makers, the importance of assessing these attributes and the urgency of doing so in an expedited manner that nonetheless produces valid information have increased since the onset of the COVID-19 pandemic.
- Studies based on real-world data (RWD) are of particular importance and are highly relevant, as they illustrate the expected impact of vaccination in routine clinical practice (vs. the highly regulated environments of clinical trials) and represent the only way by which true effectiveness and safety of vaccines can be assessed at a population level and for the target population when compared with the limited sample size and generalizability of randomized controlled trials.

Objectives

- **To provide an overview of key design characteristics of vaccine-related studies recorded in the Heads of Medicines Agencies-European Medicines Agency (HMA-EMA) Catalogue of RWD studies.**

Methods

- We conducted a search of all vaccine-related studies contained within the HMA–EMA Catalogue of RWD studies published from the beginning of database capture (2007) until 08 January 2025 and exported all such entries to identify and characterize their main design characteristics.
  - The search term word used for the search was "vaccine."
  - Each identified study was then categorized by vaccine type (using manual review as appropriate in instances where study entries if the information was missing in the "product field") to categorize studies into different vaccine types.
  - Studies were stratified based on date of start of the study, as follows:

- Manual review of study description or other variables was performed as relevant when inconsistencies or missing data was identified. For example, when filtering only on "safety" in the field related to study scope, the number of studies seemed low; we therefore investigated the classification options, and when adding all studies classified as risk minimization measure studies that have a safety objective, the number of studies with a safety outcome increased. Furthermore, when studies aimed to assess the occurrence of a particular safety event, these were also included in the overall total.

Results

Median duration and target sample size of vaccine studies according to start date

Figure 1. Median duration and target sample size of vaccine studies according to start date

- Most (57.3%, or 94 of the 164 identified studies) studies were conducted as a requirement by a regulatory body, and 63 (38.4%) were EU Risk Management Plan (RMP) category 3 (required); 105 (64.0%) studies had private funding.

Types of vaccines studied and scope of studies

Figure 2. Type of vaccines studied according to start date

Abbreviations: HPV = human papillomavirus; RSV = respiratory syncytial virus

- The catalogue also reported studies evaluating vaccines for pertussis (seven studies), malaria (six studies), herpes zoster (six studies), and rotavirus (four studies). Of note, nine studies did not specifically evaluate a particular vaccine but rather assessed feasibility of assessing background incidence or evaluation of data sources for the identification of global vaccine safety signals for example.
- The primary uses of real-world studies were to assess vaccine effectiveness (115 studies, 70.1%) and safety (39 studies, 23.4% studies).
- The most common study designs were cohort studies (114, 69.5% studies) followed by case-control studies (18 studies, 11.0%). There was a trend toward increasing used of secondary data over time (43.2% secondary data only studies in 2007–2019 vs. 73.7% in 2020–2024).

Results (cont.)

Figure 3. Study design characteristics among 164 observational vaccine-related studies

*Nineteen studies did not report the overall sample size; †One study reported "unknown" for this variable; ‡Five missing for type of design; §Sixty-eight missing for data source

Limitations

- As noted previously, several data elements (e.g., study drug, medicinal condition to be studies) were missing or information were sparse, hindering our ability to search and characterize identified studies—the review of multiple fields of data within the catalogue was necessary to more accurately define study characteristics and demonstrates the limit of evaluating these only based on one criterion.
- Furthermore, we also identified inconsistencies in the data reported per study. To improve the quality of the catalogue, a review of the data prior to publication in the catalogue could add value and avoid errors in reporting.

Conclusions

- **The post-marketing vaccine-related studies included in the HMA-EMA Catalogue employ various study designs and data collection approaches, with an increased focus on the value of RWD to address important questions related to vaccine effectiveness and safety.**
- **From the results, we can see that:**
  - **The use of these studies has increased greatly since the COVID-19 pandemic.**
  - **The willingness and appreciation of the ability of secondary data to address these key questions has grown over time, as has the number of designs employed.**
  - **The TND design is not explicitly mentioned in the list of designs—this may be classified under the case-control design or under other (the "other" category was highly used during reporting).**
  - **There is a call to action for better capture of study types/designs to help inform understanding and research on this topic.**

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Disclosures

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ISPE 2025

22–26 August 2025 | Washington, DC, USA

Poster Title

Methodological Considerations about Policy Impact on Studies of Pregnancy Registries and Maternal/Infant Outcomes

Objective

Objective 1

- Identify potential types of bias resulting from the Dobbs decision in the collection and/or analysis of pregnancy data in the US (Table 1 and Table 2).

Objective 2

- Determine which methods have been used to adjust for those sources of bias and assess their appropriateness (Table 3).

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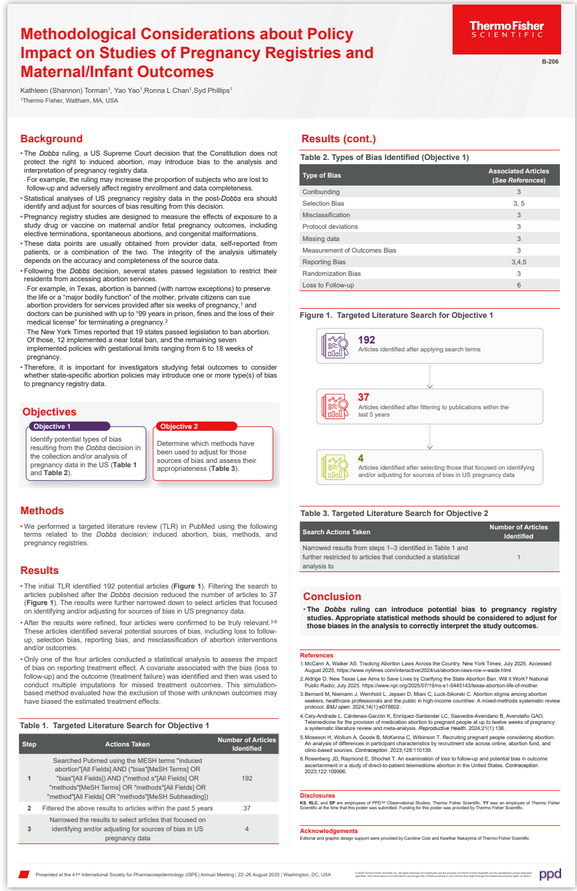

Methodological Considerations about Policy Impact on Studies of Pregnancy Registries and Maternal/Infant Outcomes

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B-206

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Background

- The *Dobbs* ruling, a US Supreme Court decision that the Constitution does not protect the right to induced abortion, may introduce bias to the analysis and interpretation of pregnancy registry data.
  - For example, the ruling may increase the proportion of subjects who are lost to follow-up and adversely affect registry enrollment and data completeness.
- Statistical analyses of US pregnancy registry data in the post-*Dobbs* era should identify and adjust for sources of bias resulting from this decision.
- Pregnancy registry studies are designed to measure the effects of exposure to a study drug or vaccine on maternal and/or fetal pregnancy outcomes, including elective terminations, spontaneous abortions, and congenital malformations.
- These data points are usually obtained from provider data, self-reported from patients, or a combination of the two. The integrity of the analysis ultimately depends on the accuracy and completeness of the source data.
- Following the *Dobbs* decision, several states passed legislation to restrict their residents from accessing abortion services.
  - For example, in Texas, abortion is banned (with narrow exceptions) to preserve the life or a "major bodily function" of the mother, private citizens can sue abortion providers for services provided after six weeks of pregnancy,[1] and doctors can be punished with up to "99 years in prison, fines and the loss of their medical license" for terminating a pregnancy.[2]
  - The New York Times reported that 19 states passed legislation to ban abortion. Of those, 12 implemented a near total ban, and the remaining seven implemented policies with gestational limits ranging from 6 to 18 weeks of pregnancy.
- Therefore, it is important for investigators studying fetal outcomes to consider whether state-specific abortion policies may introduce one or more type(s) of bias to pregnancy registry data.

Objectives

Objective 1

Identify potential types of bias resulting from the *Dobbs* decision in the collection and/or analysis of pregnancy data in the US (**Table 1** and **Table 2**).

Objective 2

Determine which methods have been used to adjust for those sources of bias and assess their appropriateness (**Table 3**).

Methods

- We performed a targeted literature review (TLR) in PubMed using the following terms related to the *Dobbs* decision: induced abortion, bias, methods, and pregnancy registries.

Results

- The initial TLR identified 192 potential articles (**Figure 1**). Filtering the search to articles published after the *Dobbs* decision reduced the number of articles to 37 (**Figure 1**). The results were further narrowed down to select articles that focused on identifying and/or adjusting for sources of bias in US pregnancy data.
- After the results were refined, four articles were confirmed to be truly relevant.[3-6] These articles identified several potential sources of bias, including loss to follow-up, selection bias, reporting bias, and misclassification of abortion interventions and/or outcomes.
- Only one of the four articles conducted a statistical analysis to assess the impact of bias on reporting treatment effect. A covariate associated with the bias (loss to follow-up) and the outcome (treatment failure) was identified and then was used to conduct multiple imputations for missed treatment outcomes. This simulation-based method evaluated how the exclusion of those with unknown outcomes may have biased the estimated treatment effects.

Table 1. Targeted Literature Search for Objective 1

Step	Actions Taken	Number of Articles Identified
1	Searched Pubmed using the MESH terms "induced abortion"[All Fields] AND ("bias"[MeSH Terms] OR "bias"[All Fields]) AND ("method s"[All Fields] OR "methods"[MeSH Terms] OR "methods"[All Fields] OR "method"[All Fields] OR "methods"[MeSH Subheading])	192
2	Filtered the above results to articles within the past 5 years	37
3	Narrowed the results to select articles that focused on identifying and/or adjusting for sources of bias in US pregnancy data	4

Results (cont.)

Table 2. Types of Bias Identified (Objective 1)

Type of Bias	Associated Articles (*See References*)
Confounding	3
Selection Bias	3, 5
Misclassification	3
Protocol deviations	3
Missing data	3
Measurement of Outcomes Bias	3
Reporting Bias	3,4,5
Randomization Bias	3
Loss to Follow-up	6

Figure 1. Targeted Literature Search for Objective 1

Table 3. Targeted Literature Search for Objective 2

Search Actions Taken	Number of Articles Identified
Narrowed results from steps 1–3 identified in Table 1 and further restricted to articles that conducted a statistical analysis to	1

Conclusion

- **The *Dobbs* ruling can introduce potential bias to pregnancy registry studies. Appropriate statistical methods should be considered to adjust for those biases in the analysis to correctly interpret the study outcomes.**

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ISPE 2025

22–26 August 2025 | Washington, DC, USA

Poster Title

An Alternative to Non-responder Imputation for Study Participants with Missing Outcomes in Single-arm Drug-effectiveness Studies: A Case Study in the PPD™ CorEvitas™ Psoriasis Registry

Objective

- To demonstrate an alternative to NRI for binary outcomes in a single-arm study that allows evaluation of more clinically informed assumptions about true response rates for patients with missing outcomes.

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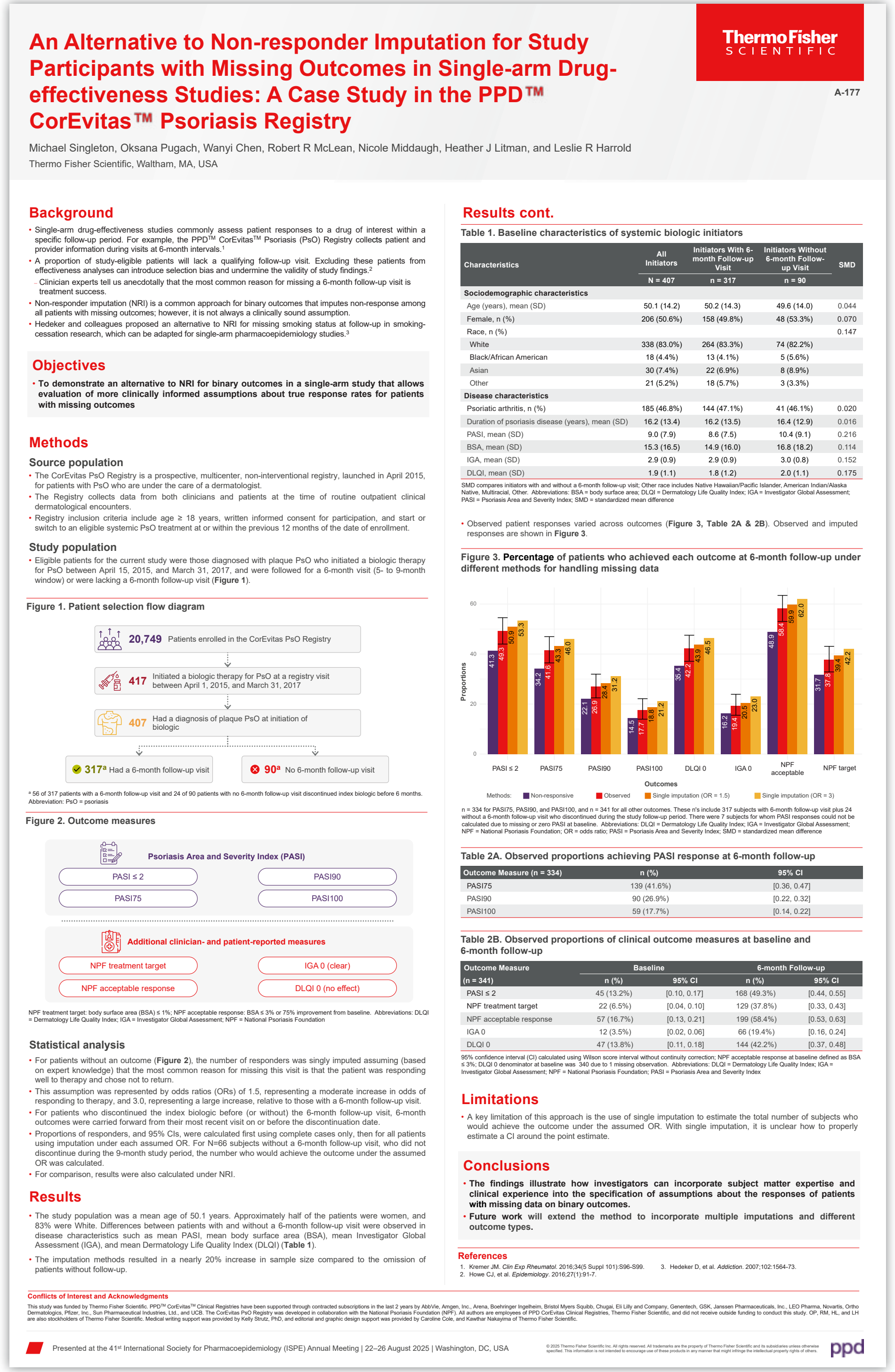

ISPE 2025

22–26 August 2025 | Washington, DC, USA

Poster Title

Landscape and Study Design Characteristics of Prospective Observational Cohort Studies on Pregnant Women in China

Objective

- To describe the landscape and key study design characteristics of prospective, observational, pregnancy cohort studies in China.

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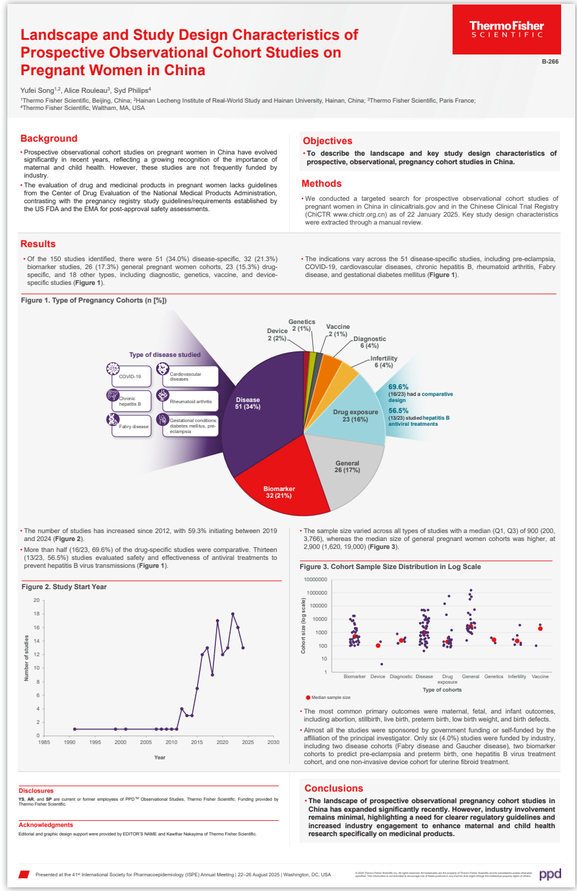

Landscape and Study Design Characteristics of Prospective Observational Cohort Studies on Pregnant Women in China

ThermoFisher SCIENTIFIC

B-266

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Background

- Prospective observational cohort studies on pregnant women in China have evolved significantly in recent years, reflecting a growing recognition of the importance of maternal and child health. However, these studies are not frequently funded by industry.
- The evaluation of drug and medicinal products in pregnant women lacks guidelines from the Center of Drug Evaluation of the National Medical Products Administration, contrasting with the pregnancy registry study guidelines/requirements established by the US FDA and the EMA for post-approval safety assessments.

Objectives

- **To describe the landscape and key study design characteristics of prospective, observational, pregnancy cohort studies in China.**

Methods

- We conducted a targeted search for prospective observational cohort studies of pregnant women in China in clinicaltrials.gov and in the Chinese Clinical Trial Registry (ChiCTR www.chictr.org.cn) as of 22 January 2025. Key study design characteristics were extracted through a manual review.

Results

- Of the 150 studies identified, there were 51 (34.0%) disease-specific, 32 (21.3%) biomarker studies, 26 (17.3%) general pregnant women cohorts, 23 (15.3%) drug-specific, and 18 other types, including diagnostic, genetics, vaccine, and device-specific studies (**Figure 1**).
- The indications vary across the 51 disease-specific studies, including pre-eclampsia, COVID-19, cardiovascular diseases, chronic hepatitis B, rheumatoid arthritis, Fabry disease, and gestational diabetes mellitus (**Figure 1**).

Figure 1. Type of Pregnancy Cohorts (n [%])

- The number of studies has increased since 2012, with 59.3% initiating between 2019 and 2024 (**Figure 2**).
- More than half (16/23, 69.6%) of the drug-specific studies were comparative. Thirteen (13/23, 56.5%) studies evaluated safety and effectiveness of antiviral treatments to prevent hepatitis B virus transmissions (**Figure 1**).

Figure 2. Study Start Year

- The sample size varied across all types of studies with a median (Q1, Q3) of 900 (200, 3,766), whereas the median size of general pregnant women cohorts was higher, at 2,900 (1,620, 19,000) (**Figure 3**).

Figure 3. Cohort Sample Size Distribution in Log Scale

- The most common primary outcomes were maternal, fetal, and infant outcomes, including abortion, stillbirth, live birth, preterm birth, low birth weight, and birth defects.
- Almost all the studies were sponsored by government funding or self-funded by the affiliation of the principal investigator. Only six (4.0%) studies were funded by industry, including two disease cohorts (Fabry disease and Gaucher disease), two biomarker cohorts to predict pre-eclampsia and preterm birth, one hepatitis B virus treatment cohort, and one non-invasive device cohort for uterine fibroid treatment.

Disclosures

YS, AR, and SP are current or former employees of PPD™ Observational Studies, Thermo Fisher Scientific. Funding provided by Thermo Fisher Scientific.

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Conclusions

- **The landscape of prospective observational pregnancy cohort studies in China has expanded significantly recently. However, industry involvement remains minimal, highlighting a need for clearer regulatory guidelines and increased industry engagement to enhance maternal and child health research specifically on medicinal products.**

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International Academy of Health Preference Research (IAHPR)

29 September–1 October 2025 | Enschede, Netherlands

Posters

Probabilistic Attribute Presentation in Discrete Choice Experiments: A Review of Current Practice

A Systematic Literature Review of Preference Studies in Migraine Treatments

IAHPR 2025

29 September–1 October 2025 | Enschede, Netherlands

Poster Title

Probabilistic Attribute Presentation in Discrete Choice Experiments: A Review of Current Practice

Objective

- This study aimed to synthesize current practice in presenting probabilities in DCEs, and report the nature of attributes, framing, and visual presentation.

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IAHPR 2025

29 September–1 October 2025 | Enschede, Netherlands

Poster Title

A Systematic Literature Review of Preference Studies in Migraine Treatments

Objective

- To identify, synthesize, and critically appraise stated-preference studies in migraine, with a focus on study design, treatment attributes and levels, analytical approaches, and the assessment of preference heterogeneity.

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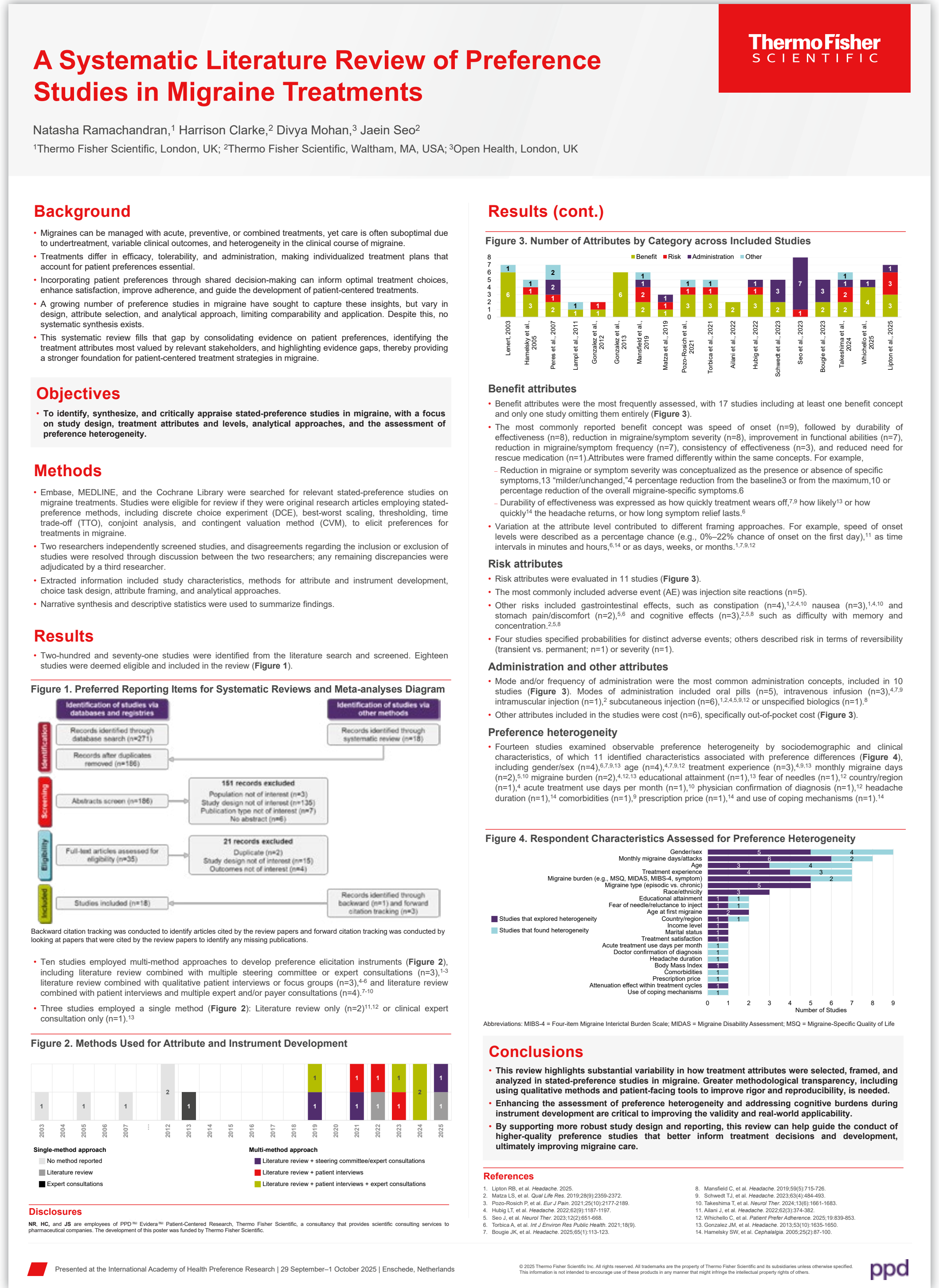

GetReal

1–2 October 2025 | Utrecht, The Netherlands

Posters

Low-left truncation mitigation rates in post marketing pregnancy exposure registries assessing the risk of spontaneous abortion (SAB)

Integrating Real-world Evidence for Advanced Therapies in Inflammatory Bowel Disease into Reimbursement Submissions: Insights and Considerations from the UK

Use of Real-world Evidence in Advice Reports Assessing Reimbursement in The Netherlands from 2023–2025

Is There a Lack of Dietary Data Collection in Real-world IBD Studies? Literature Review and Future Considerations

Are Cross-sectional Cohorts an Efficient Alternative to Prospective Cohort Design in Real-world Studies?

Data Reliability in Retrospective Chart Review Studies: Results and Considerations from a Novel Data Review Methodology

Cost-effectiveness of Radiotherapy in Uterine Serous Carcinoma (USC): A Real-world Study

A Real-world-derived Algorithm to Improve the Cost-effectiveness of External Beam Radiotherapy in Uterine Serous Carcinoma

Comparing Randomized Clinical Trials to Real-world Studies Evaluating the Effectiveness of a bDMARD in the Management of Crohn's Disease

Comparison of Randomized Controlled Trials (RCT) with Open-label, Single-cohort, Real-world Studies (RWS) in the evaluation of pharmacologic treatment of Non-small Cell Lung Cancer (NSCLC)

Utility of Real-world External Control Arm (ECA) in the Evaluation of Pharmacologic Treatment of Non-small Cell Lung Cancer (NSCLC)

GetReal 2025

1–2 October 2025 | Utrecht, The Netherlands

Poster Title

Low-left truncation mitigation rates in post-marketing pregnancy exposure registries assessing the risk of spontaneous abortion (SAB)

Objective

- To review the literature on approaches to the analysis of SAB risk in prospective observational studies, including pregnancy exposure registries.

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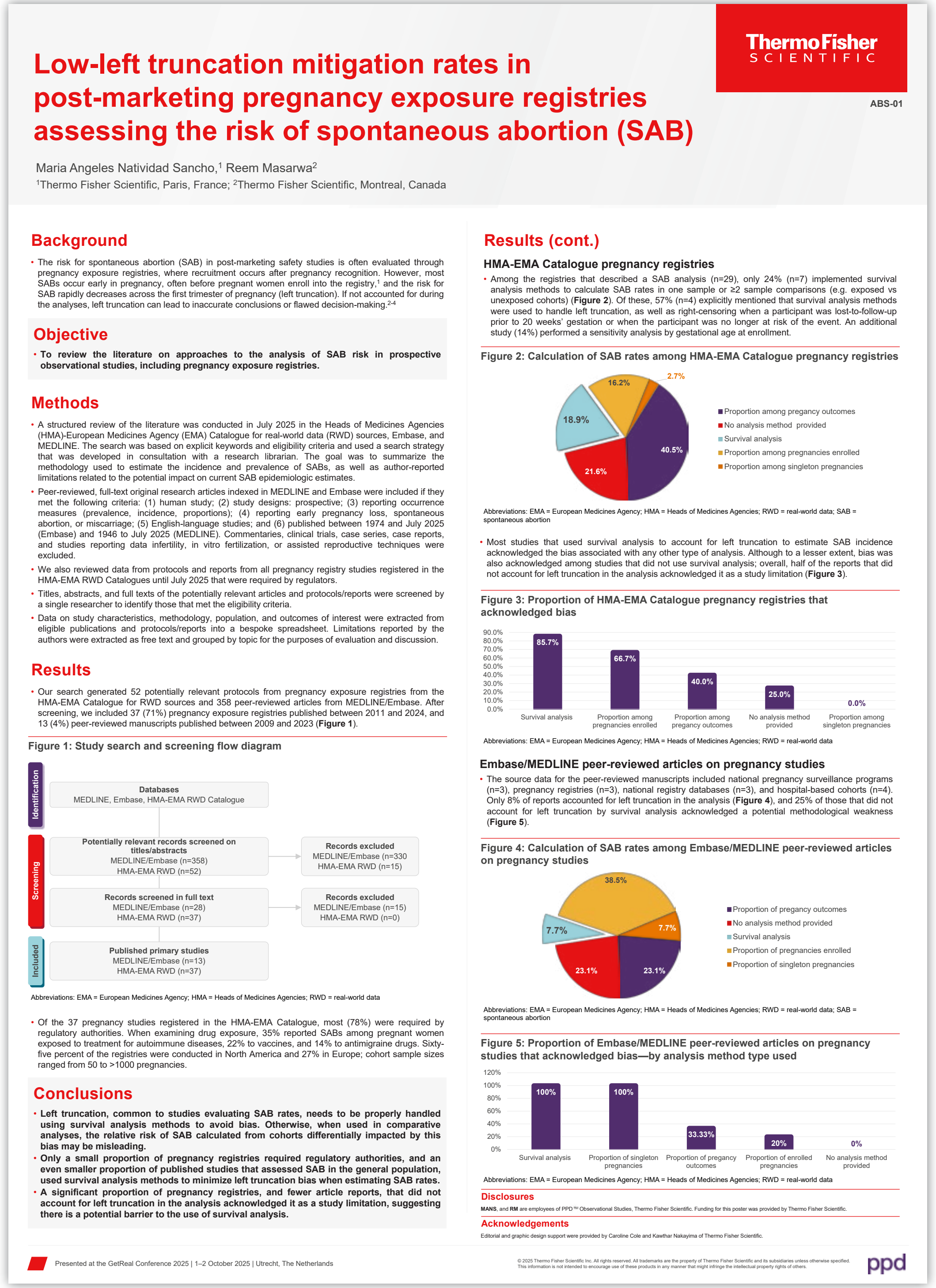

GetReal 2025

1–2 October 2025 | Utrecht, The Netherlands

Poster Title

Integrating Real-world Evidence for Advanced Therapies in Inflammatory Bowel Disease into Reimbursement Submissions: Insights and Considerations from the UK

Objective

- The objective was to evaluate RWE use in previous NICE HTA submissions for advanced IBD therapies for adults, including biologics and Janus kinase (JAK) inhibitors, and offer recommendations for incorporating real-world evidence (RWE) into future HTA submissions.

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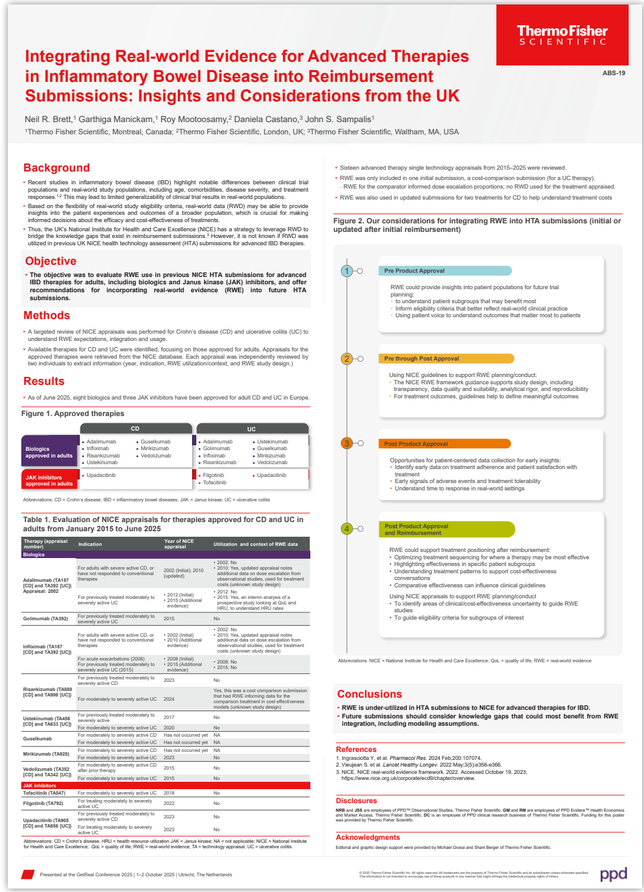

Integrating Real-world Evidence for Advanced Therapies in Inflammatory Bowel Disease into Reimbursement Submissions: Insights and Considerations from the UK

ABS-19

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Background

- Recent studies in inflammatory bowel disease (IBD) highlight notable differences between clinical trial populations and real-world study populations, including age, comorbidities, disease severity, and treatment responses.[1,2] This may lead to limited generalizability of clinical trial results in real-world populations.
- Based on the flexibility of real-world study eligibility criteria, real-world data (RWD) may be able to provide insights into the patient experiences and outcomes of a broader population, which is crucial for making informed decisions about the efficacy and cost-effectiveness of treatments.
- Thus, the UK's National Institute for Health and Care Excellence (NICE) has a strategy to leverage RWD to bridge the knowledge gaps that exist in reimbursement submissions.[3] However, it is not known if RWD was utilized in previous UK NICE health technology assessment (HTA) submissions for advanced IBD therapies.

Objective

- **The objective was to evaluate RWE use in previous NICE HTA submissions for advanced IBD therapies for adults, including biologics and Janus kinase (JAK) inhibitors, and offer recommendations for incorporating real-world evidence (RWE) into future HTA submissions.**

Methods

- A targeted review of NICE appraisals was performed for Crohn's disease (CD) and ulcerative colitis (UC) to understand RWE expectations, integration and usage.
- Available therapies for CD and UC were identified, focusing on those approved for adults. Appraisals for the approved therapies were retrieved from the NICE database. Each appraisal was independently reviewed by two individuals to extract information (year, indication, RWE utilization/context, and RWE study design.)

Results

- As of June 2025, eight biologics and three JAK inhibitors have been approved for adult CD and UC in Europe.

Figure 1. Approved therapies

	CD	UC
Biologics approved in adults	• Adalimumab • Infliximab • Risankizumab • Ustekinumab • Guselkumab • Mirikizumab • Vedolizumab	• Adalimumab • Golimumab • Infliximab • Risankizumab • Ustekinumab • Guselkumab • Mirikizumab • Vedolizumab
JAK inhibitors approved in adults	• Upadacitinib	• Filgotinib • Tofacitinib • Upadacitinib

Abbreviations: CD = Crohn's disease; IBD = inflammatory bowel diseases; JAK = Janus kinase; UC = ulcerative colitis

Table 1. Evaluation of NICE appraisals for therapies approved for CD and UC in adults from January 2015 to June 2025

Therapy (appraisal number)	Indication	Year of NICE appraisal	Utilization and context of RWE data
Biologics			
Adalimumab (TA187 [CD] and TA302 [UC]); Approval: 2002	For adults with severe active CD, or have not responded to conventional therapies	2002 (Initial); 2010 (updated)	• 2002: No • 2010: Yes, updated appraisal notes additional data on dose escalation from observational studies, used for treatment costs (unknown study design)
	For previously treated moderately to severely active UC	• 2012 (Initial) • 2015 (Additional evidence)	• 2012: No • 2015: Yes, an interim analysis of a prospective study looking at QoL and HRU, to understand HRU rates
Golimumab (TA262)	For previously treated moderately to severely active UC	2015	No
Infliximab (TA187 [CD] and TA392 [UC])	For adults with severe active CD, or have not responded to conventional therapies	• 2002 (Initial) • 2010 (Additional evidence)	• 2002: No • 2010: Yes, updated appraisal notes additional data on dose escalation from observational studies, used for treatment costs (unknown study design)
	For acute exacerbations (2008) For previously treated moderately to severely active UC (2015)	• 2008 (Initial) • 2015 (Additional evidence)	• 2008: No • 2015: No
Risankizumab (TA888 [CD] and TA896 [UC])	For previously treated moderately to severely active CD	2023	No
	For moderately to severely active UC	2024	Yes, this was a cost comparison submission that had RWE informing data for the comparison treatment in cost effectiveness models (unknown study design)
Ustekinumab (TA456 [CD] and TA633 [UC])	For previously treated moderately to severely active	2017	No
	For moderately to severely active UC	2020	No
Guselkumab	For moderately to severely active CD	Has not occurred yet	NA
	For moderately to severely active UC	Has not occurred yet	NA
Mirikizumab (TA925)	For moderately to severely active CD	Has not occurred yet	NA
	For moderately to severely active UC	2023	No
Vedolizumab (TA352 [CD] and TA342 [UC])	For moderately to severely active CD after prior therapy	2015	No
	For moderately to severely active UC	2015	No
JAK inhibitors			
Tofacitinib (TA547)	For moderately to severely active UC	2018	No
Filgotinib (TA792)	For treating moderately to severely active UC	2022	No
Upadacitinib (TA905 [CD] and TA896 [UC])	For previously treated moderately to severely active CD	2023	No
	For treating moderately to severely active UC	2023	No

Abbreviations: CD = Crohn's disease; HRU = health resource utilization; JAK = Janus kinase; NA = not applicable; NICE = National Institute for Health and Care Excellence; QoL = quality of life; RWE = real-world evidence; TA = technology appraisal; UC = ulcerative colitis

- Sixteen advanced therapy single technology appraisals from 2015–2025 were reviewed.
- RWE was only included in one initial submission, a cost-comparison submission (for a UC therapy).
  - RWE for the comparator informed dose-escalation proportions; no RWD used for the treatment appraised.
- RWE was also used in updated submissions for two treatments for CD to help understand treatment costs

Figure 2. Our considerations for integrating RWE into HTA submissions (initial or updated after initial reimbursement)

Abbreviations: NICE = National Institute for Health and Care Excellence; QoL = quality of life; RWE = real-world evidence

Conclusions

- **RWE is under-utilized in HTA submissions to NICE for advanced therapies for IBD.**
- **Future submissions should consider knowledge gaps that could most benefit from RWE integration, including modeling assumptions.**

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GetReal 2025

1–2 October 2025 | Utrecht, The Netherlands

Poster Title

Use of Real-world Evidence in Advice Reports Assessing Reimbursement in The Netherlands from 2023–2025

Objective

- This study aimed to assess the use of RWE in submissions that are reviewed by ZIN for reimbursement advice.
- The goal was to create an overview and look at trends of RWE use and reimbursement recommendations.

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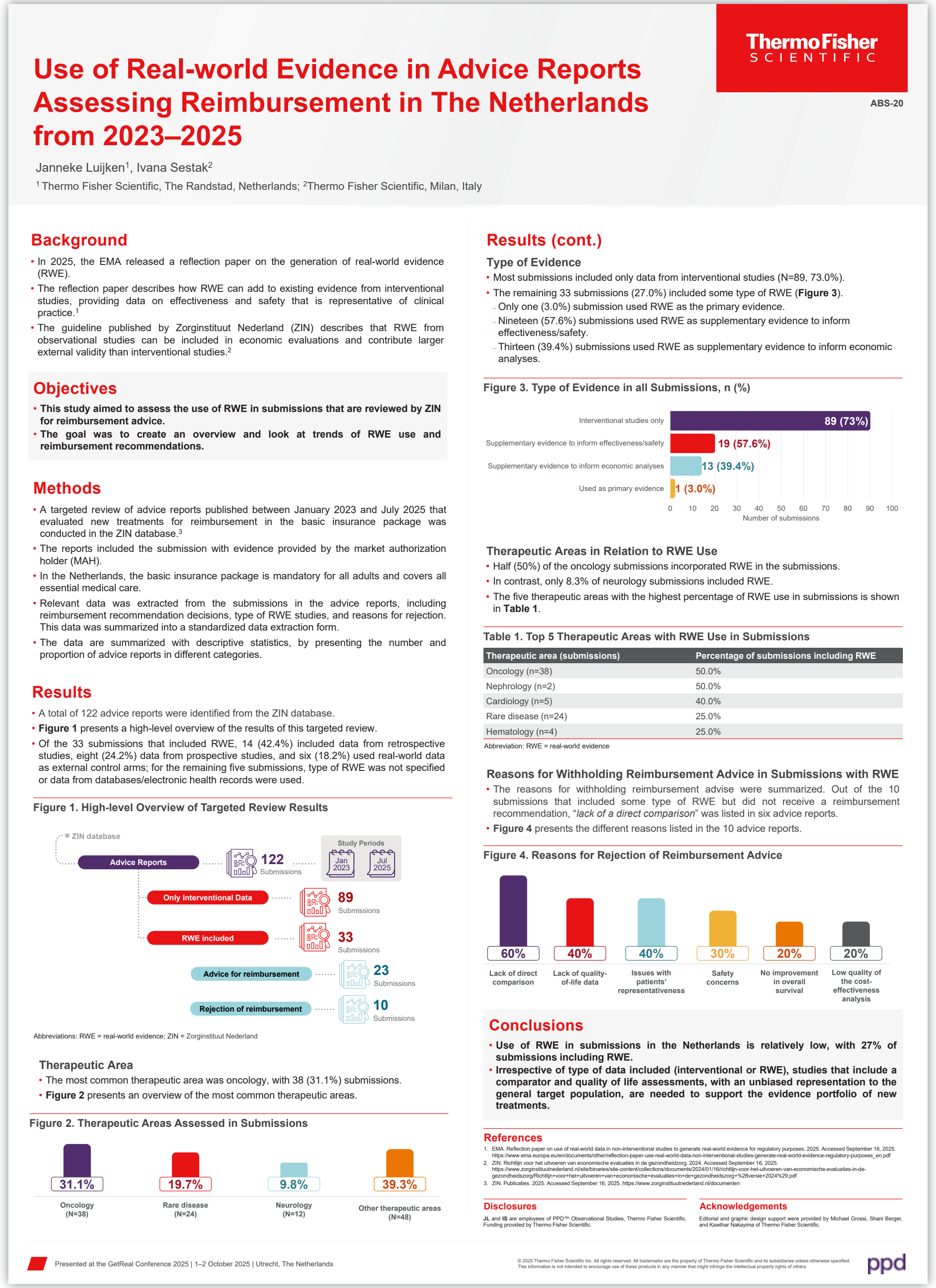

Use of Real-world Evidence in Advice Reports Assessing Reimbursement in The Netherlands from 2023–2025

ThermoFisher SCIENTIFIC

ABS-20

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Background

- In 2025, the EMA released a reflection paper on the generation of real-world evidence (RWE).
- The reflection paper describes how RWE can add to existing evidence from interventional studies, providing data on effectiveness and safety that is representative of clinical practice.[1]
- The guideline published by Zorginstituut Nederland (ZIN) describes that RWE from observational studies can be included in economic evaluations and contribute larger external validity than interventional studies.[2]

Objectives

- **This study aimed to assess the use of RWE in submissions that are reviewed by ZIN for reimbursement advice.**
- **The goal was to create an overview and look at trends of RWE use and reimbursement recommendations.**

Methods

- A targeted review of advice reports published between January 2023 and July 2025 that evaluated new treatments for reimbursement in the basic insurance package was conducted in the ZIN database.[3]
- The reports included the submission with evidence provided by the market authorization holder (MAH).
- In the Netherlands, the basic insurance package is mandatory for all adults and covers all essential medical care.
- Relevant data was extracted from the submissions in the advice reports, including reimbursement recommendation decisions, type of RWE studies, and reasons for rejection. This data was summarized into a standardized data extraction form.
- The data are summarized with descriptive statistics, by presenting the number and proportion of advice reports in different categories.

Results

- A total of 122 advice reports were identified from the ZIN database.
- **Figure 1** presents a high-level overview of the results of this targeted review.
- Of the 33 submissions that included RWE, 14 (42.4%) included data from retrospective studies, eight (24.2%) data from prospective studies, and six (18.2%) used real-world data as external control arms; for the remaining five submissions, type of RWE was not specified or data from databases/electronic health records were used.

Figure 1. High-level Overview of Targeted Review Results

ZIN database
Advice Reports — 122 Submissions
Study Periods: Jan 2023 – Jul 2025
Only Interventional Data — 89 Submissions
RWE included — 33 Submissions
Advice for reimbursement — 23 Submissions
Rejection of reimbursement — 10 Submissions

Abbreviations: RWE = real-world evidence; ZIN = Zorginstituut Nederland

Therapeutic Area

- The most common therapeutic area was oncology, with 38 (31.1%) submissions.
- **Figure 2** presents an overview of the most common therapeutic areas.

Figure 2. Therapeutic Areas Assessed in Submissions

31.1% Oncology (N=38)
19.7% Rare disease (N=24)
9.8% Neurology (N=12)
39.3% Other therapeutic areas (N=48)

Results (cont.)

Type of Evidence

- Most submissions included only data from interventional studies (N=89, 73.0%).
- The remaining 33 submissions (27.0%) included some type of RWE (**Figure 3**).
  - Only one (3.0%) submission used RWE as the primary evidence.
  - Nineteen (57.6%) submissions used RWE as supplementary evidence to inform effectiveness/safety.
  - Thirteen (39.4%) submissions used RWE as supplementary evidence to inform economic analyses.

Figure 3. Type of Evidence in all Submissions, n (%)

Interventional studies only — 89 (73%)
Supplementary evidence to inform effectiveness/safety — 19 (57.6%)
Supplementary evidence to inform economic analyses — 13 (39.4%)
Used as primary evidence — 1 (3.0%)
0 10 20 30 40 50 60 70 80 90 100
Number of submissions

Therapeutic Areas in Relation to RWE Use

- Half (50%) of the oncology submissions incorporated RWE in the submissions.
- In contrast, only 8.3% of neurology submissions included RWE.
- The five therapeutic areas with the highest percentage of RWE use in submissions is shown in **Table 1**.

Table 1. Top 5 Therapeutic Areas with RWE Use in Submissions

Therapeutic area (submissions)	Percentage of submissions including RWE
Oncology (n=38)	50.0%
Nephrology (n=2)	50.0%
Cardiology (n=5)	40.0%
Rare disease (n=24)	25.0%
Hematology (n=4)	25.0%

Abbreviation: RWE = real-world evidence

Reasons for Withholding Reimbursement Advice in Submissions with RWE

- The reasons for withholding reimbursement advise were summarized. Out of the 10 submissions that included some type of RWE but did not receive a reimbursement recommendation, "*lack of a direct comparison*" was listed in six advice reports.
- **Figure 4** presents the different reasons listed in the 10 advice reports.

Figure 4. Reasons for Rejection of Reimbursement Advice

60% Lack of direct comparison
40% Lack of quality-of-life data
40% Issues with patients' representativeness
30% Safety concerns
20% No improvement in overall survival
20% Low quality of the cost-effectiveness analysis

Conclusions

- **Use of RWE in submissions in the Netherlands is relatively low, with 27% of submissions including RWE.**
- **Irrespective of type of data included (interventional or RWE), studies that include a comparator and quality of life assessments, with an unbiased representation to the general target population, are needed to support the evidence portfolio of new treatments.**

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GetReal 2025

1–2 October 2025 | Utrecht, The Netherlands

Poster Title

Is There a Lack of Dietary Data Collection in Real-world IBD Studies? Literature Review and Future Considerations

Objective

- The objective was to describe dietary data collection methods and purposes in observational IBD studies and provide considerations to enhance future research.

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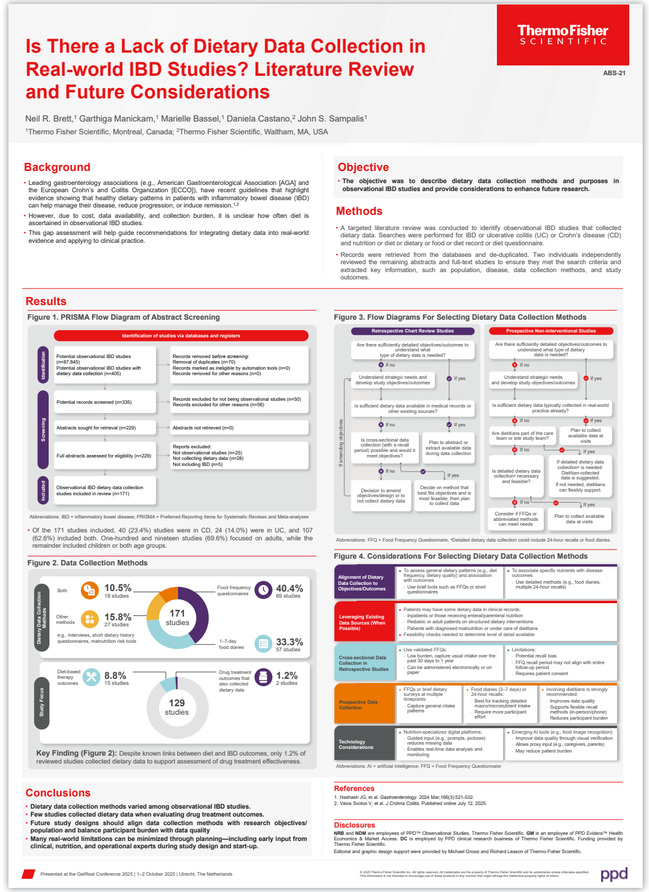

Is There a Lack of Dietary Data Collection in Real-world IBD Studies? Literature Review and Future Considerations

ThermoFisher SCIENTIFIC

ABS-21

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Background

- Leading gastroenterology associations (e.g., American Gastroenterological Association [AGA] and the European Crohn's and Colitis Organization [ECCO]), have recent guidelines that highlight evidence showing that healthy dietary patterns in patients with inflammatory bowel disease (IBD) can help manage their disease, reduce progression, or induce remission.[1,2]
- However, due to cost, data availability, and collection burden, it is unclear how often diet is ascertained in observational IBD studies.
- This gap assessment will help guide recommendations for integrating dietary data into real-world evidence and applying to clinical practice.

Objective

- **The objective was to describe dietary data collection methods and purposes in observational IBD studies and provide considerations to enhance future research.**

Methods

- A targeted literature review was conducted to identify observational IBD studies that collected dietary data. Searches were performed for IBD or ulcerative colitis (UC) or Crohn's disease (CD) and nutrition or diet or dietary or food or diet record or diet questionnaire.
- Records were retrieved from the databases and de-duplicated. Two individuals independently reviewed the remaining abstracts and full-text studies to ensure they met the search criteria and extracted key information, such as population, disease, data collection methods, and study outcomes.

Results

Figure 1. PRISMA Flow Diagram of Abstract Screening

Abbreviations: IBD = inflammatory bowel disease; PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-analyses

- Of the 171 studies included, 40 (23.4%) studies were in CD, 24 (14.0%) were in UC, and 107 (62.6%) included both. One-hundred and nineteen studies (69.6%) focused on adults, while the remainder included children or both age groups.

Figure 2. Data Collection Methods

Key Finding (Figure 2): Despite known links between diet and IBD outcomes, only 1.2% of reviewed studies collected dietary data to support assessment of drug treatment effectiveness.

Figure 3. Flow Diagrams For Selecting Dietary Data Collection Methods

Abbreviations: FFQ = Food Frequency Questionnaire. *Detailed dietary data collection could include 24-hour recalls or food diaries.

Figure 4. Considerations For Selecting Dietary Data Collection Methods

Abbreviations: AI = artificial intelligence; FFQ = Food Frequency Questionnaire

Conclusions

- **Dietary data collection methods varied among observational IBD studies.**
- **Few studies collected dietary data when evaluating drug treatment outcomes.**
- **Future study designs should align data collection methods with research objectives/ population and balance participant burden with data quality**
- **Many real-world limitations can be minimized through planning—including early input from clinical, nutrition, and operational experts during study design and start-up.**

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Disclosures

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Poster Title

Are Cross-sectional Cohorts an Efficient Alternative to Prospective Cohort Design in Real-world Studies?

Objective

- The objective was to compare CSC study design with LPC study design in a cohort of patients with rheumatoid arthritis (RA).

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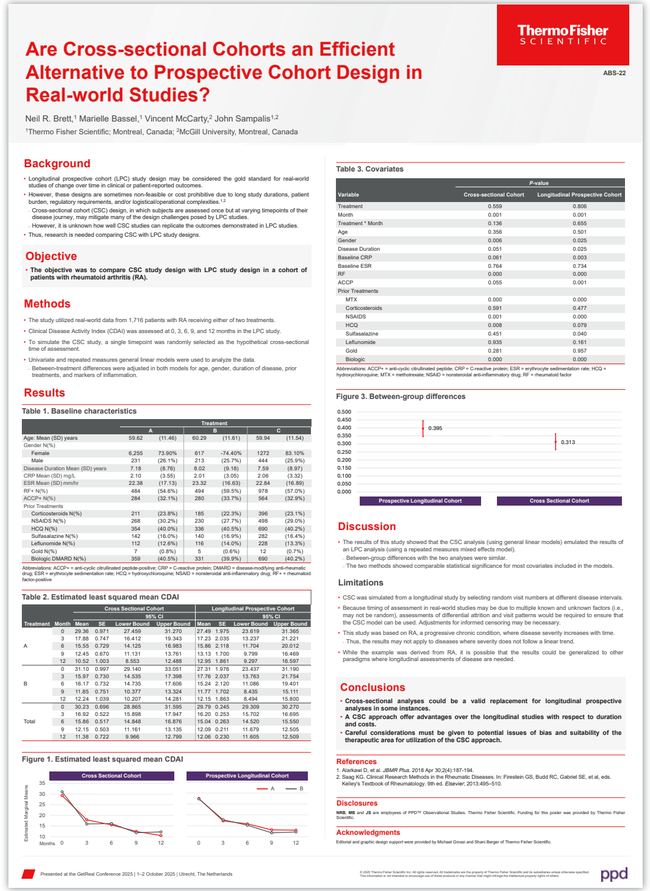

Are Cross-sectional Cohorts an Efficient Alternative to Prospective Cohort Design in Real-world Studies?

ABS-22

Neil R. Brett,[1] Marielle Bassel,[1] Vincent McCarty,[2] John Sampalis[1,2]
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Background

- Longitudinal prospective cohort (LPC) study design may be considered the gold standard for real-world studies of change over time in clinical or patient-reported outcomes.
- However, these designs are sometimes non-feasible or cost prohibitive due to long study durations, patient burden, regulatory requirements, and/or logistical/operational complexities.[1,2]
  - Cross-sectional cohort (CSC) design, in which subjects are assessed once but at varying timepoints of their disease journey, may mitigate many of the design challenges posed by LPC studies.
  - However, it is unknown how well CSC studies can replicate the outcomes demonstrated in LPC studies.
- Thus, research is needed comparing CSC with LPC study designs.

Objective

- **The objective was to compare CSC study design with LPC study design in a cohort of patients with rheumatoid arthritis (RA).**

Methods

- The study utilized real-world data from 1,716 patients with RA receiving either of two treatments.
- Clinical Disease Activity Index (CDAI) was assessed at 0, 3, 6, 9, and 12 months in the LPC study.
- To simulate the CSC study, a single timepoint was randomly selected as the hypothetical cross-sectional time of assessment.
- Univariate and repeated measures general linear models were used to analyze the data.
  - Between-treatment differences were adjusted in both models for age, gender, duration of disease, prior treatments, and markers of inflammation.

Results

Table 1. Baseline characteristics

	Treatment					
	A		B		C	
Age: Mean (SD) years	59.62	(11.46)	60.29	(11.61)	59.94	(11.54)
Gender N(%)						
Female	6,255	73.90%	617	~74.40%	1272	83.10%
Male	231	(26.1%)	213	(25.7%)	444	(25.9%)
Disease Duration Mean (SD) years	7.18	(8.76)	8.02	(9.18)	7.59	(8.97)
CRP Mean (SD) mg/L	2.10	(3.55)	2.01	(3.05)	2.06	(3.32)
ESR Mean (SD) mm/hr	22.38	(17.13)	23.32	(16.63)	22.84	(16.89)
RF + N(%)	484	(54.6%)	494	(59.5%)	978	(57.0%)
ACCP+ N(%)	284	(32.1%)	280	(33.7%)	564	(32.9%)
Prior Treatments						
Corticosteroids N(%)	211	(23.8%)	185	(22.3%)	396	(23.1%)
NSAIDS N(%)	268	(30.2%)	230	(27.7%)	498	(29.0%)
HCQ N(%)	354	(40.0%)	336	(40.5%)	690	(40.2%)
Sulfasalazine N(%)	142	(16.0%)	140	(16.9%)	282	(16.4%)
Leflunomide N(%)	112	(12.6%)	116	(14.0%)	228	(13.3%)
Gold N(%)	7	(0.8%)	5	(0.6%)	12	(0.7%)
Biologic DMARD N(%)	359	(40.5%)	331	(39.9%)	690	(40.2%)

Abbreviations: ACCP+ = anti-cyclic citrullinated peptide-positive; CRP = C-reactive protein; DMARD = disease-modifying anti-rheumatic drug; ESR = erythrocyte sedimentation rate; HCQ = hydroxychloroquine; NSAID = nonsteroidal anti-inflammatory drug; RF + = rheumatoid factor-positive

Table 2. Estimated least squared mean CDAI

		Cross Sectional Cohort				Longitudinal Prospective Cohort			
				95% CI				95% CI	
Treatment	Month	Mean	SE	Lower Bound	Upper Bound	Mean	SE	Lower Bound	Upper Bound
A	0	29.36	0.971	27.459	31.270	27.49	1.975	23.619	31.365
	3	17.88	0.747	16.412	19.343	17.23	2.035	13.237	21.221
	6	15.55	0.729	14.125	16.983	15.86	2.118	11.704	20.012
	9	12.45	0.670	11.131	13.761	13.13	1.700	9.799	16.469
	12	10.52	1.003	8.553	12.488	12.95	1.881	9.267	16.597
B	0	31.10	0.997	29.140	33.051	27.31	1.976	23.437	31.190
	3	15.97	0.730	14.535	17.398	17.76	2.037	13.763	21.754
	6	16.17	0.732	14.735	17.606	15.24	2.120	11.086	19.401
	9	11.85	0.751	10.377	13.324	11.77	1.702	8.435	15.111
	12	12.24	1.039	10.207	14.281	12.15	1.863	8.494	15.800
Total	0	30.23	0.696	28.865	31.595	29.79	0.245	29.309	30.270
	3	16.92	0.522	15.898	17.947	16.20	0.253	15.702	16.695
	6	15.86	0.517	14.848	16.876	15.04	0.263	14.520	15.550
	9	12.15	0.503	11.161	13.135	12.09	0.211	11.679	12.505
	12	11.38	0.722	9.966	12.799	12.06	0.230	11.605	12.509

Figure 1. Estimated least squared mean CDAI

Table 3. Covariates

	P-value	
Variable	Cross-sectional Cohort	Longitudinal Prospective Cohort
Treatment	0.559	0.806
Month	0.001	0.001
Treatment * Month	0.136	0.655
Age	0.356	0.501
Gender	0.006	0.025
Disease Duration	0.051	0.025
Baseline CRP	0.061	0.003
Baseline ESR	0.764	0.734
RF	0.000	0.000
ACCP	0.055	0.001
Prior Treatments		
MTX	0.000	0.000
Corticosteroids	0.591	0.477
NSAIDS	0.001	0.000
HCQ	0.008	0.079
Sulfasalazine	0.451	0.040
Leflunomide	0.935	0.161
Gold	0.281	0.957
Biologic	0.000	0.000

Abbreviations: ACCP+ = anti-cyclic citrullinated peptide; CRP = C-reactive protein; ESR = erythrocyte sedimentation rate; HCQ = hydroxychloroquine; MTX = methotrexate; NSAID = nonsteroidal anti-inflammatory drug; RF = rheumatoid factor

Figure 3. Between-group differences

Discussion

- The results of this study showed that the CSC analysis (using general linear models) emulated the results of an LPC analysis (using a repeated measures mixed effects model).
  - Between-group differences with the two analyses were similar.
  - The two methods showed comparable statistical significance for most covariates included in the models.

Limitations

- CSC was simulated from a longitudinal study by selecting random visit numbers at different disease intervals.
- Because timing of assessment in real-world studies may be due to multiple known and unknown factors (i.e., may not be random), assessments of differential attrition and visit patterns would be required to ensure that the CSC model can be used. Adjustments for informed censoring may be necessary.
- This study was based on RA, a progressive chronic condition, where disease severity increases with time.
  - Thus, the results may not apply to diseases where severity does not follow a linear trend.
- While the example was derived from RA, it is possible that the results could be generalized to other paradigms where longitudinal assessments of disease are needed.

Conclusions

- **Cross-sectional analyses could be a valid replacement for longitudinal prospective analyses in some instances.**
- **A CSC approach offer advantages over the longitudinal studies with respect to duration and costs.**
- **Careful considerations must be given to potential issues of bias and suitability of the therapeutic area for utilization of the CSC approach.**

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Disclosures

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Poster Title

Data Reliability in Retrospective Chart Review Studies: Results and Considerations from a Novel Data Review Methodology

Objective

- The objective was to describe an alternative method for data quality review and highlight key considerations.

AUTHORS
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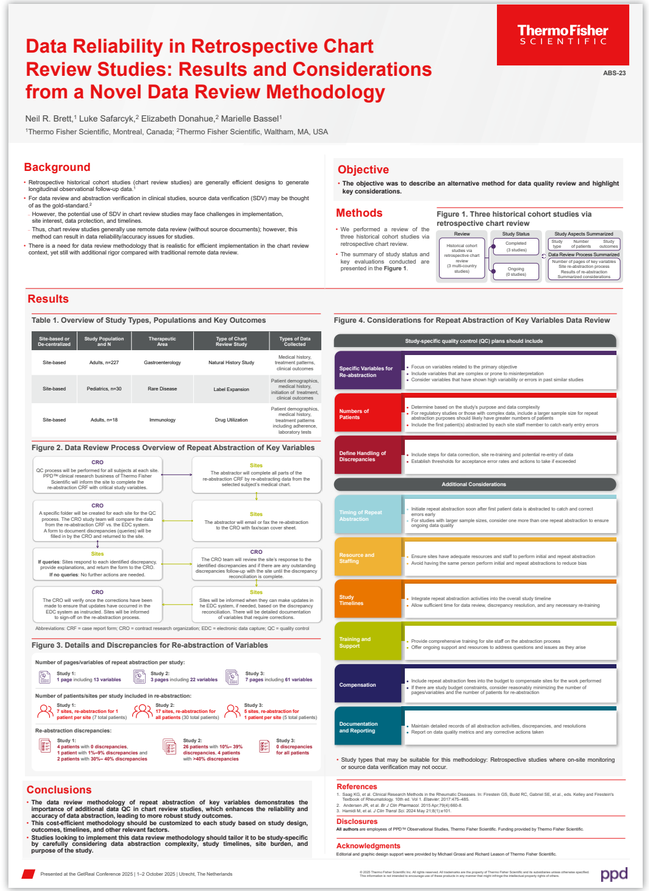

Data Reliability in Retrospective Chart Review Studies: Results and Considerations from a Novel Data Review Methodology

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ABS-23

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Background

- Retrospective historical cohort studies (chart review studies) are generally efficient designs to generate longitudinal observational follow-up data.
- For data review and abstraction verification in clinical studies, source data verification (SDV) may be thought of as the gold-standard.[2]
  - However, the potential use of SDV in chart review studies may face challenges in implementation, site interest, data protection, and timelines.
  - Thus, chart review studies generally use remote data review (without source documents); however, this method can result in data reliability/accuracy issues for studies.
- There is a need for data review methodology that is realistic for efficient implementation in the chart review context, yet still with additional rigor compared with traditional remote data review.

Objective

- The objective was to describe an alternative method for data quality review and highlight key considerations.

Methods

- We performed a review of the three historical cohort studies via retrospective chart review.
- The summary of study status and key evaluations conducted are presented in the Figure 1.

Figure 1. Three historical cohort studies via retrospective chart review

Results

Table 1. Overview of Study Types, Populations and Key Outcomes

Site-based or De-centralized	Study Population and N	Therapeutic Area	Type of Chart Review Study	Types of Data Collected
Site-based	Adults, n=227	Gastroenterology	Natural History Study	Medical history, treatment patterns, clinical outcomes
Site-based	Pediatrics, n=30	Rare Disease	Label Expansion	Patient demographics, medical history, initiation of treatment, clinical outcomes
Site-based	Adults, n=18	Immunology	Drug Utilization	Patient demographics, medical history, treatment patterns including adherence, laboratory tests

Figure 2. Data Review Process Overview of Repeat Abstraction of Key Variables

Abbreviations: CRF = case report form; CRO = contract research organization; EDC = electronic data capture; QC = quality control

Figure 3. Details and Discrepancies for Re-abstraction of Variables

Figure 4. Considerations for Repeat Abstraction of Key Variables Data Review

- Study types that may be suitable for this methodology: Retrospective studies where on-site monitoring or source data verification may not occur.

Conclusions

- **The data review methodology of repeat abstraction of key variables demonstrates the importance of additional data QC in chart review studies, which enhances the reliability and accuracy of data abstraction, leading to more robust study outcomes.**
- **This cost-efficient methodology should be customized to each study based on study design, outcomes, timelines, and other relevant factors.**
- **Studies looking to implement this data review methodology should tailor it to be study-specific by carefully considering data abstraction complexity, study timelines, site burden, and purpose of the study.**

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Poster Title

Cost-effectiveness of Radiotherapy in Uterine Serous Carcinoma (USC): A Real-world Study

Objective

- To describe the cost-effectiveness of adjuvant radiotherapy in USC patients treated in the real-world setting.

AUTHORS

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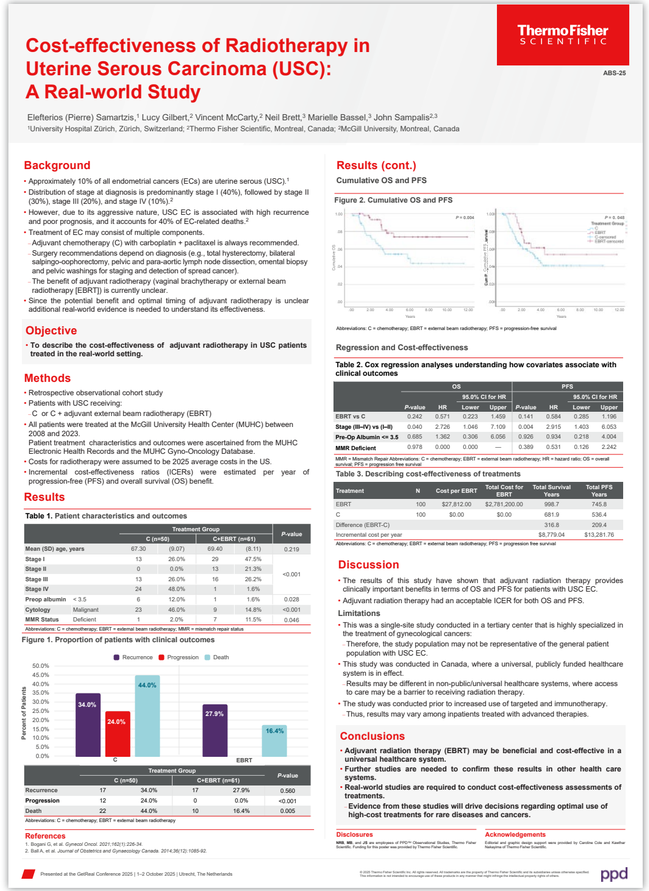

Cost-effectiveness of Radiotherapy in Uterine Serous Carcinoma (USC): A Real-world Study

ABS-25

Elefterios (Pierre) Samartzis,[1] Lucy Gilbert,[2] Vincent McCarty,[2] Neil Brett,[3] Marielle Bassel,[3] John Sampalis[2,3]
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Background

- Approximately 10% of all endometrial cancers (ECs) are uterine serous (USC).[1]
- Distribution of stage at diagnosis is predominantly stage I (40%), followed by stage II (30%), stage III (20%), and stage IV (10%).[2]
- However, due to its aggressive nature, USC EC is associated with high recurrence and poor prognosis, and it accounts for 40% of EC-related deaths.[2]
- Treatment of EC may consist of multiple components.
  - Adjuvant chemotherapy (C) with carboplatin + paclitaxel is always recommended.
  - Surgery recommendations depend on diagnosis (e.g., total hysterectomy, bilateral salpingo-oophorectomy, pelvic and para-aortic lymph node dissection, omental biopsy and pelvic washings for staging and detection of spread cancer).
  - The benefit of adjuvant radiotherapy (vaginal brachytherapy or external beam radiotherapy [EBRT]) is currently unclear.
- Since the potential benefit and optimal timing of adjuvant radiotherapy is unclear additional real-world evidence is needed to understand its effectiveness.

Objective

- **To describe the cost-effectiveness of adjuvant radiotherapy in USC patients treated in the real-world setting.**

Methods

- Retrospective observational cohort study
- Patients with USC receiving:
  - C or C + adjuvant external beam radiotherapy (EBRT)
- All patients were treated at the McGill University Health Center (MUHC) between 2008 and 2023.
  - Patient treatment characteristics and outcomes were ascertained from the MUHC Electronic Health Records and the MUHC Gyno-Oncology Database.
- Costs for radiotherapy were assumed to be 2025 average costs in the US.
- Incremental cost-effectiveness ratios (ICERs) were estimated per year of progression-free (PFS) and overall survival (OS) benefit.

Results

Table 1. Patient characteristics and outcomes

		Treatment Group				*P*-value
		C (n=50)		C+EBRT (n=61)		
Mean (SD) age, years		67.30	(9.07)	69.40	(8.11)	0.219
Stage I		13	26.0%	29	47.5%	<0.001
Stage II		0	0.0%	13	21.3%	
Stage III		13	26.0%	16	26.2%	
Stage IV		24	48.0%	1	1.6%	
Preop albumin	< 3.5	6	12.0%	1	1.6%	0.028
Cytology	Malignant	23	46.0%	9	14.8%	<0.001
MMR Status	Deficient	1	2.0%	7	11.5%	0.046

Abbreviations: C = chemotherapy; EBRT = external beam radiotherapy; MMR = mismatch repair status

Figure 1. Proportion of patients with clinical outcomes

	Treatment Group				*P*-value
	C (n=50)		C+EBRT (n=61)		
Recurrence	17	34.0%	17	27.9%	0.560
Progression	12	24.0%	0	0.0%	<0.001
Death	22	44.0%	10	16.4%	0.005

Abbreviations: C = chemotherapy; EBRT = external beam radiotherapy

References

1. Bogani G, et al. *Gynecol Oncol.* 2021;162(1):226-34.
2. Ball A, et al. *Journal of Obstetrics and Gynaecology Canada.* 2014;36(12):1085-92.

Results (cont.)

Cumulative OS and PFS

Figure 2. Cumulative OS and PFS

Abbreviations: C = chemotherapy; EBRT = external beam radiotherapy; PFS = progression-free survival

Regression and Cost-effectiveness

Table 2. Cox regression analyses understanding how covariates associate with clinical outcomes

	OS				PFS			
			95.0% CI for HR				95.0% CI for HR	
	P-value	HR	Lower	Upper	*P*-value	HR	Lower	Upper
EBRT vs C	0.242	0.571	0.223	1.459	0.141	0.584	0.285	1.196
Stage (III+IV) vs (I–II)	0.040	2.726	1.046	7.109	0.004	2.915	1.403	6.053
Pre-Op Albumin <= 3.5	0.685	1.362	0.306	6.056	0.926	0.934	0.218	4.004
MMR Deficient	0.978	0.000	0.000	—	0.389	0.531	0.126	2.242

MMR = Mismatch Repair Abbreviations: C = chemotherapy; EBRT = external beam radiotherapy; HR = hazard ratio, OS = overall survival; PFS = progression-free survival

Table 3. Describing cost-effectiveness of treatments

Treatment	N	Cost per EBRT	Total Cost for EBRT	Total Survival Years	Total PFS Years
EBRT	100	$27,812.00	$2,781,200.00	998.7	745.8
C	100	$0.00	$0.00	681.9	536.4
Difference (EBRT-C)				316.8	209.4
Incremental cost per year				$8,779.04	$13,281.76

Abbreviations: C = chemotherapy; EBRT = external beam radiotherapy; PFS = progression free survival

Discussion

- The results of this study have shown that adjuvant radiation therapy provides clinically important benefits in terms of OS and PFS for patients with USC EC.
- Adjuvant radiation therapy had an acceptable ICER for both OS and PFS.

Limitations

- This was a single-site study conducted in a tertiary center that is highly specialized in the treatment of gynecological cancers.
  - Therefore, the study population may not be representative of the general patient population with USC EC.
- This study was conducted in Canada, where a universal, publicly funded healthcare system is in effect.
  - Results may be different in non-public/universal healthcare systems, where access to care may be a barrier to receiving radiation therapy.
- The study was conducted prior to increased use of targeted and immunotherapy.
  - Thus, results may vary among inpatients treated with advanced therapies.

Conclusions

- **Adjuvant radiation therapy (EBRT) may be beneficial and cost-effective in a universal healthcare system.**
- **Further studies are needed to confirm these results in other health care systems.**
- **Real-world studies are required to conduct cost-effectiveness assessments of treatments.**
  - **Evidence from these studies will drive decisions regarding optimal use of high-cost treatments for rare diseases and cancers.**

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GetReal 2025

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Poster Title

A Real-world-derived Algorithm to Improve the Cost-effectiveness of External Beam Radiotherapy in Uterine Serous Carcinoma

Objective

- The objective was to develop and evaluate an empirical algorithm aimed at identifying patients with USC EC who would benefit from adjuvant radiotherapy.

AUTHORS

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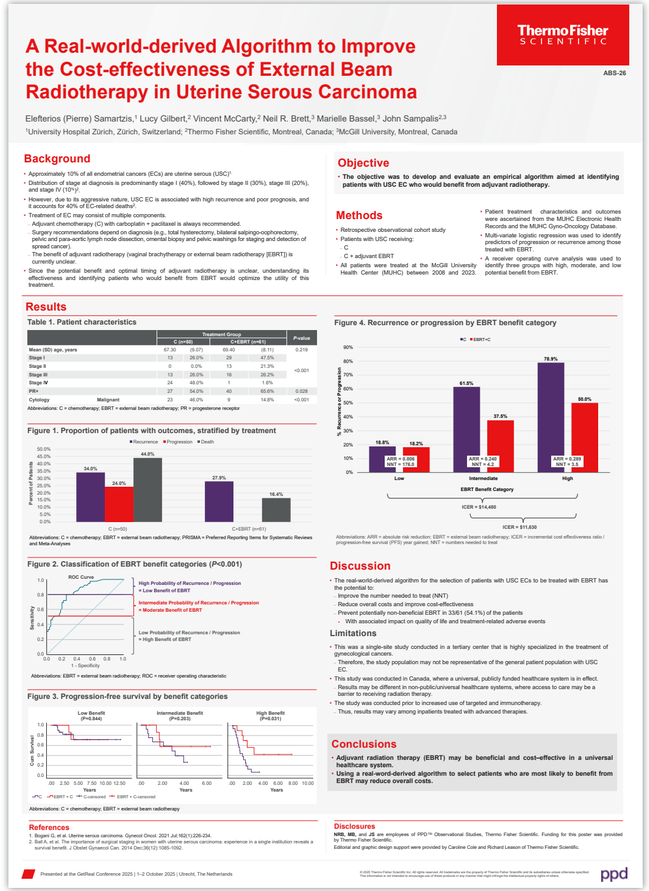

A Real-world-derived Algorithm to Improve the Cost-effectiveness of External Beam Radiotherapy in Uterine Serous Carcinoma

ThermoFisher SCIENTIFIC

ABS-26

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Background

- Approximately 10% of all endometrial cancers (ECs) are uterine serous (USC)[1]
- Distribution of stage at diagnosis is predominantly stage I (40%), followed by stage II (30%), stage III (20%), and stage IV (10%)[2]
- However, due to its aggressive nature, USC EC is associated with high recurrence and poor prognosis, and it accounts for 40% of EC-related deaths[2].
- Treatment of EC may consist of multiple components.
  - Adjuvant chemotherapy (C) with carboplatin + paclitaxel is always recommended.
  - Surgery recommendations depend on diagnosis (e.g., total hysterectomy, bilateral salpingo-oophorectomy, pelvic and para-aortic lymph node dissection, omental biopsy and pelvic washings for staging and detection of spread cancer).
  - The benefit of adjuvant radiotherapy (vaginal brachytherapy or external beam radiotherapy [EBRT]) is currently unclear.
- Since the potential benefit and optimal timing of adjuvant radiotherapy is unclear, understanding its effectiveness and identifying patients who would benefit from EBRT would optimize the utility of this treatment.

Objective

- **The objective was to develop and evaluate an empirical algorithm aimed at identifying patients with USC EC who would benefit from adjuvant radiotherapy.**

Methods

- Retrospective observational cohort study
- Patients with USC receiving:
  - C
  - C + adjuvant EBRT
- All patients were treated at the McGill University Health Center (MUHC) between 2008 and 2023.
- Patient treatment characteristics and outcomes were ascertained from the MUHC Electronic Health Records and the MUHC Gyno-Oncology Database.
- Multi-variate logistic regression was used to identify predictors of progression or recurrence among those treated with EBRT.
- A receiver operating curve analysis was used to identify three groups with high, moderate, and low potential benefit from EBRT.

Results

Table 1. Patient characteristics

	Treatment Group				*P*-value
	C (n=50)		C+EBRT (n=61)		
Mean (SD) age, years	67.30	(9.07)	69.40	(8.11)	0.219
Stage I	13	26.0%	29	47.5%	
Stage II	0	0.0%	13	21.3%	<0.001
Stage III	13	26.0%	16	26.2%	
Stage IV	24	48.0%	1	1.6%	
PR+	27	54.0%	40	65.6%	0.028
Cytology Malignant	23	46.0%	9	14.8%	<0.001

Abbreviations: C = chemotherapy; EBRT = external beam radiotherapy; PR = progesterone receptor

Figure 1. Proportion of patients with outcomes, stratified by treatment

Abbreviations: C = chemotherapy; EBRT = external beam radiotherapy; PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses

Figure 2. Classification of EBRT benefit categories (*P*<0.001)

Abbreviations: EBRT = external beam radiotherapy; ROC = receiver operating characteristic

Figure 3. Progression-free survival by benefit categories

Abbreviations: C = chemotherapy; EBRT = external beam radiotherapy

Figure 4. Recurrence or progression by EBRT benefit category

Abbreviations: ARR = absolute risk reduction; EBRT = external beam radiotherapy; ICER = incremental cost-effectiveness ratio / progression-free survival (PFS) year gained; NNT = numbers needed to treat

Discussion

- The real-world-derived algorithm for the selection of patients with USC ECs to be treated with EBRT has the potential to:
  - Improve the number needed to treat (NNT)
  - Reduce overall costs and improve cost-effectiveness
  - Prevent potentially non-beneficial EBRT in 33/61 (54.1%) of the patients
  - With associated impact on quality of life and treatment-related adverse events

Limitations

- This was a single-site study conducted in a tertiary center that is highly specialized in the treatment of gynecological cancers.
  - Therefore, the study population may not be representative of the general patient population with USC EC.
- This study was conducted in Canada, where a universal, publicly funded healthcare system is in effect.
  - Results may be different in non-public/universal healthcare systems, where access to care may be a barrier to receiving radiation therapy.
- The study was conducted prior to increased use of targeted and immunotherapy.
  - Thus, results may vary among inpatients treated with advanced therapies.

Conclusions

- **Adjuvant radiation therapy (EBRT) may be beneficial and cost-effective in a universal healthcare system.**
- **Using a real-world-derived algorithm to select patients who are most likely to benefit from EBRT may reduce overall costs.**

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Disclosures

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GetReal 2025

1–2 October 2025 | Utrecht, The Netherlands

Poster Title

Comparing Randomized Clinical Trials to Real-world Studies Evaluating the Effectiveness of a bDMARD in the Management of Crohn's Disease

Objective

- To compare patient profiles and outcomes between RCTs and RWS in the evaluation of a bDMARD treatment for CD.

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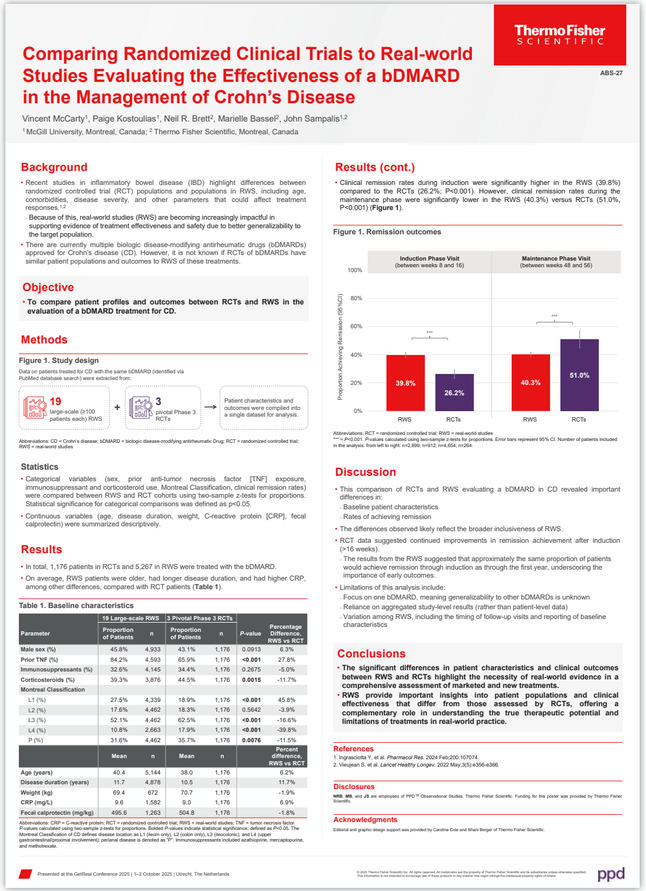

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ABS-27

Comparing Randomized Clinical Trials to Real-world Studies Evaluating the Effectiveness of a bDMARD in the Management of Crohn's Disease

Vincent McCarty[1], Paige Kostoulias[1], Neil R. Brett[2], Marielle Bassel[2], John Sampalis[1,2]

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Background

- Recent studies in inflammatory bowel disease (IBD) highlight differences between randomized controlled trial (RCT) populations and populations in RWS, including age, comorbidities, disease severity, and other parameters that could affect treatment responses.[1,2]
  - Because of this, real-world studies (RWS) are becoming increasingly impactful in supporting evidence of treatment effectiveness and safety due to better generalizability to the target population.
- There are currently multiple biologic disease-modifying antirheumatic drugs (bDMARDs) approved for Crohn's disease (CD). However, it is not known if RCTs of bDMARDs have similar patient populations and outcomes to RWS of these treatments.

Objective

- **To compare patient profiles and outcomes between RCTs and RWS in the evaluation of a bDMARD treatment for CD.**

Methods

Figure 1. Study design

Data on patients treated for CD with the same bDMARD (identified via PubMed database search) were extracted from:

Abbreviations: CD = Crohn's disease; bDMARD = biologic disease-modifying antirheumatic Drug; RCT = randomized controlled trial; RWS = real-world studies

Statistics

- Categorical variables (sex, prior anti-tumor necrosis factor [TNF] exposure, immunosuppressant and corticosteroid use, Montreal Classification, clinical remission rates) were compared between RWS and RCT cohorts using two-sample *z*-tests for proportions. Statistical significance for categorical comparisons was defined as p<0.05.
- Continuous variables (age, disease duration, weight, C-reactive protein [CRP], fecal calprotectin) were summarized descriptively.

Results

- In total, 1,176 patients in RCTs and 5,267 in RWS were treated with the bDMARD.
- On average, RWS patients were older, had longer disease duration, and had higher CRP, among other differences, compared with RCT patients **(Table 1)**.

Table 1. Baseline characteristics

	19 Large-scale RWS		3 Pivotal Phase 3 RCTs			
Parameter	**Proportion of Patients**	**n**	**Proportion of Patients**	**n**	***P*-value**	**Percentage Difference, RWS vs RCT**
Male sex (%)	45.8%	4,933	43.1%	1,176	0.0913	6.3%
Prior TNF (%)	84.2%	4,593	65.9%	1,176	**<0.001**	27.8%
Immunosuppressants (%)	32.6%	4,145	34.4%	1,176	0.2675	-5.0%
Corticosteroids (%)	39.3%	3,876	44.5%	1,176	**0.0015**	-11.7%
Montreal Classification						
L1 (%)	27.5%	4,339	18.9%	1,176	**<0.001**	45.8%
L2 (%)	17.6%	4,462	18.3%	1,176	0.5642	-3.9%
L3 (%)	52.1%	4,462	62.5%	1,176	**<0.001**	-16.6%
L4 (%)	10.8%	2,663	17.9%	1,176	**<0.001**	-39.8%
P (%)	31.6%	4,462	35.7%	1,176	**0.0076**	-11.5%
	Mean	**n**	**Mean**	**n**		**Percent difference, RWS vs RCT**
Age (years)	40.4	5,144	38.0	1,176		6.2%
Disease duration (years)	11.7	4,878	10.5	1,176		11.7%
Weight (kg)	69.4	672	70.7	1,176		-1.9%
CRP (mg/L)	9.6	1,582	9.0	1,176		6.9%
Fecal calprotectin (mg/kg)	495.6	1,263	504.8	1,176		-1.8%

Abbreviations: CRP = C-reactive protein; RCT = randomized controlled trial; RWS = real-world studies; TNF = tumor necrosis factor. *P*-values calculated using two-sample *z*-tests for proportions. Bolded *P*-values indicate statistical significance, defined as *P*<0.05. The Montreal Classification of CD defines disease location as L1 (ileum only), L2 (colon only), L3 (ileocolonic), and L4 (upper gastrointestinal/proximal involvement); perianal disease is denoted as 'P'. Immunosuppressants included azathioprine, mercaptopurine, and methotrexate.

Results (cont.)

- Clinical remission rates during induction were significantly higher in the RWS (39.8%) compared to the RCTs (26.2%; P<0.001). However, clinical remission rates during the maintenance phase were significantly lower in the RWS (40.3%) versus RCTs (51.0%, P<0.001) **(Figure 1)**.

Figure 1. Remission outcomes

Abbreviations: RCT = randomized controlled trial; RWS = real-world studies
*** = *P*<0.001. *P*-values calculated using two-sample *z*-tests for proportions. Error bars represent 95% CI. Number of patients included in the analysis: from left to right: n=2,899; n=912; n=4,834; n=264.

Discussion

- This comparison of RCTs and RWS evaluating a bDMARD in CD revealed important differences in:
  - Baseline patient characteristics
  - Rates of achieving remission
- The differences observed likely reflect the broader inclusiveness of RWS.
- RCT data suggested continued improvements in remission achievement after induction (>16 weeks).
  - The results from the RWS suggested that approximately the same proportion of patients would achieve remission through induction as through the first year, underscoring the importance of early outcomes.
- Limitations of this analysis include:
  - Focus on one bDMARD, meaning generalizability to other bDMARDs is unknown
  - Reliance on aggregated study-level results (rather than patient-level data)
  - Variation among RWS, including the timing of follow-up visits and reporting of baseline characteristics

Conclusions

- **The significant differences in patient characteristics and clinical outcomes between RWS and RCTs highlight the necessity of real-world evidence in a comprehensive assessment of marketed and new treatments.**
- **RWS provide important insights into patient populations and clinical effectiveness that differ from those assessed by RCTs, offering a complementary role in understanding the true therapeutic potential and limitations of treatments in real-world practice.**

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Disclosures

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GetReal 2025

1–2 October 2025 | Utrecht, The Netherlands

Poster Title

Comparison of Randomized Controlled Trials (RCT) with Open-label, Single-cohort, Real-world Studies (RWS) in the evaluation of pharmacologic treatment of Non-small Cell Lung Cancer (NSCLC)

Objective

- The aim of this study was to assess the validity of using ECAs derived from real-world studies in the assessment of efficacy of treatments for non-small cell lung cancer (NSCLC).
  - Efficacy outcomes assessed were objective response rate (ORR) and progression-free survival (PFS)

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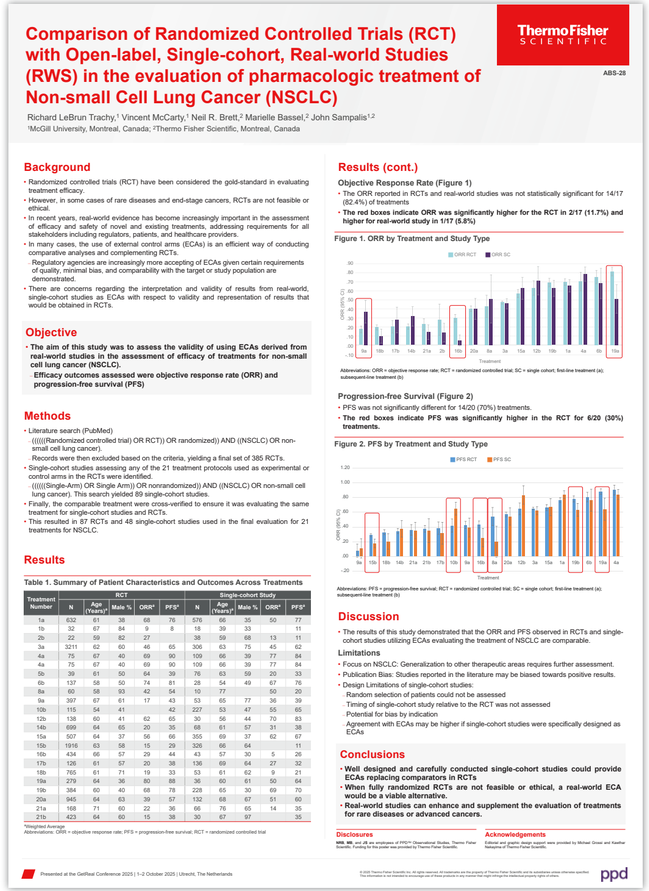

Comparison of Randomized Controlled Trials (RCT) with Open-label, Single-cohort, Real-world Studies (RWS) in the evaluation of pharmacologic treatment of Non-small Cell Lung Cancer (NSCLC)

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ABS-28

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Background

- Randomized controlled trials (RCT) have been considered the gold-standard in evaluating treatment efficacy.
- However, in some cases of rare diseases and end-stage cancers, RCTs are not feasible or ethical.
- In recent years, real-world evidence has become increasingly important in the assessment of efficacy and safety of novel and existing treatments, addressing requirements for all stakeholders including regulators, patients, and healthcare providers.
- In many cases, the use of external control arms (ECAs) is an efficient way of conducting comparative analyses and complementing RCTs.
  - Regulatory agencies are increasingly more accepting of ECAs given certain requirements of quality, minimal bias, and comparability with the target or study population are demonstrated.
- There are concerns regarding the interpretation and validity of results from real-world, single-cohort studies as ECAs with respect to validity and representation of results that would be obtained in RCTs.

Objective

- **The aim of this study was to assess the validity of using ECAs derived from real-world studies in the assessment of efficacy of treatments for non-small cell lung cancer (NSCLC).**
  - **Efficacy outcomes assessed were objective response rate (ORR) and progression-free survival (PFS)**

Methods

- Literature search (PubMed)
  - ((((((Randomized controlled trial) OR RCT)) OR randomized)) AND ((NSCLC) OR non-small cell lung cancer).
  - Records were then excluded based on the criteria, yielding a final set of 385 RCTs.
- Single-cohort studies assessing any of the 21 treatment protocols used as experimental or control arms in the RCTs were identified.
  - ((((((Single-Arm) OR Single Arm)) OR nonrandomized)) AND ((NSCLC) OR non-small cell lung cancer). This search yielded 89 single-cohort studies.
- Finally, the comparable treatment were cross-verified to ensure it was evaluating the same treatment for single-cohort studies and RCTs.
- This resulted in 87 RCTs and 48 single-cohort studies used in the final evaluation for 21 treatments for NSCLC.

Results

Table 1. Summary of Patient Characteristics and Outcomes Across Treatments

Treatment Number	RCT					Single-cohort Study				
	N	Age (Years)*	Male %	ORR*	PFS*	N	Age (Years)*	Male %	ORR*	PFS*
1a	632	61	38	68	76	576	65	35	50	77
1b	32	67	84	9	8	18	39	33		11
2b	22	59	82	27		38	59	68	13	11
3a	3211	62	60	46	65	306	63	75	45	62
4a	75	67	40	69	90	109	66	39	77	84
4a	75	67	40	69	90	109	66	39	77	84
5b	39	61	50	64	39	76	63	59	20	33
6b	137	58	50	74	81	28	54	49	67	76
8a	60	58	93	42	54	10	77		50	20
9a	397	67	61	17	43	53	65	77	36	39
10b	115	54	41		42	227	53	47	55	65
12b	138	60	41	62	65	30	56	44	70	83
14b	699	64	65	20	35	68	61	57	31	38
15a	507	64	37	56	66	355	69	37	62	67
15b	1916	63	58	15	29	326	66	64		11
16b	434	66	57	29	44	43	57	30	5	26
17b	126	61	57	20	38	136	69	64	27	32
18b	765	61	71	19	33	53	61	62	9	21
19a	279	64	36	80	88	36	60	61	50	64
19b	384	60	40	68	78	228	65	30	69	70
20a	945	64	63	39	57	132	68	67	51	60
21a	168	71	60	22	36	66	76	65	14	35
21b	423	64	60	15	38	30	67	97		35

*Weighted Average
Abbreviations: ORR = objective response rate; PFS = progression-free survival; RCT = randomized controlled trial

Results (cont.)

Objective Response Rate (Figure 1)

- The ORR reported in RCTs and real-world studies was not statistically significant for 14/17 (82.4%) of treatments
- **The red boxes indicate ORR was significantly higher for the RCT in 2/17 (11.7%) and higher for real-world study in 1/17 (5.8%)**

Figure 1. ORR by Treatment and Study Type

Abbreviations: ORR = objective response rate; RCT = randomized controlled trial; SC = single cohort; first-line treatment (a); subsequent-line treatment (b)

Progression-free Survival (Figure 2)

- PFS was not significantly different for 14/20 (70%) treatments.
- **The red boxes indicate PFS was significantly higher in the RCT for 6/20 (30%) treatments.**

Figure 2. PFS by Treatment and Study Type

Abbreviations: PFS = progression-free survival; RCT = randomized controlled trial; SC = single cohort; first-line treatment (a); subsequent-line treatment (b)

Discussion

- The results of this study demonstrated that the ORR and PFS observed in RCTs and single-cohort studies utilizing ECAs evaluating the treatment of NSCLC are comparable.

Limitations

- Focus on NSCLC: Generalization to other therapeutic areas requires further assessment.
- Publication Bias: Studies reported in the literature may be biased towards positive results.
- Design Limitations of single-cohort studies:
  - Random selection of patients could not be assessed
  - Timing of single-cohort study relative to the RCT was not assessed
  - Potential for bias by indication
  - Agreement with ECAs may be higher if single-cohort studies were specifically designed as ECAs

Conclusions

- **Well designed and carefully conducted single-cohort studies could provide ECAs replacing comparators in RCTs**
- **When fully randomized RCTs are not feasible or ethical, a real-world ECA would be a viable alternative.**
- **Real-world studies can enhance and supplement the evaluation of treatments for rare diseases or advanced cancers.**

Disclosures
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GetReal 2025

1–2 October 2025 | Utrecht, The Netherlands

Poster Title

Utility of Real-world External Control Arm (ECA) in the Evaluation of Pharmacologic Treatment of Non-small Cell Lung Cancer (NSCLC)

Objective

- The objective of this study was to compare the results observed in RCTs and real-world studies (RWS) assessing the efficacy of treatments for non-small cell lung cancer (NSCLC).
- The efficacy outcomes assessed were objective response rate (ORR), progression-free survival (PFS) and overall survival (OS).

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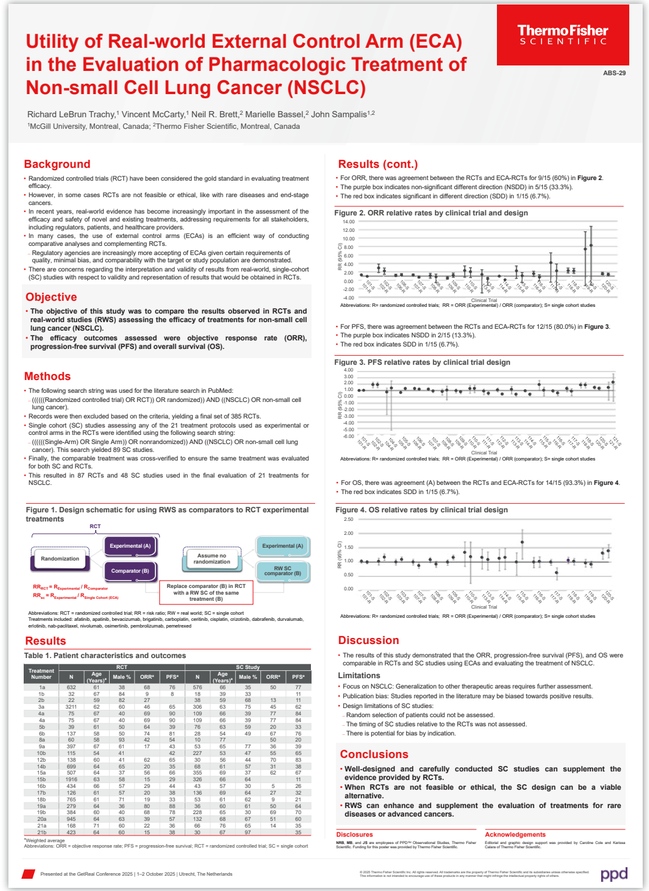

Utility of Real-world External Control Arm (ECA) in the Evaluation of Pharmacologic Treatment of Non-small Cell Lung Cancer (NSCLC)

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ABS-29

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[1]McGill University, Montreal, Canada; [2]Thermo Fisher Scientific, Montreal, Canada

Background

- Randomized controlled trials (RCT) have been considered the gold standard in evaluating treatment efficacy.
- However, in some cases RCTs are not feasible or ethical, like with rare diseases and end-stage cancers.
- In recent years, real-world evidence has become increasingly important in the assessment of the efficacy and safety of novel and existing treatments, addressing requirements for all stakeholders, including regulators, patients, and healthcare providers.
- In many cases, the use of external control arms (ECAs) is an efficient way of conducting comparative analyses and complementing RCTs.
  Regulatory agencies are increasingly more accepting of ECAs given certain requirements of quality, minimal bias, and comparability with the target or study population are demonstrated.
- There are concerns regarding the interpretation and validity of results from real-world, single-cohort (SC) studies with respect to validity and representation of results that would be obtained in RCTs.

Objective

- **The objective of this study was to compare the results observed in RCTs and real-world studies (RWS) assessing the efficacy of treatments for non-small cell lung cancer (NSCLC).**
- **The efficacy outcomes assessed were objective response rate (ORR), progression-free survival (PFS) and overall survival (OS).**

Methods

- The following search string was used for the literature search in PubMed:
  ((((Randomized controlled trial) OR RCT)) OR randomized)) AND ((NSCLC) OR non-small cell lung cancer).
- Records were then excluded based on the criteria, yielding a final set of 385 RCTs.
- Single cohort (SC) studies assessing any of the 21 treatment protocols used as experimental or control arms in the RCTs were identified using the following search string:
  ((((((Single-Arm) OR Single Arm)) OR nonrandomized)) AND ((NSCLC) OR non-small cell lung cancer). This search yielded 89 SC studies.
- Finally, the comparable treatment was cross-verified to ensure the same treatment was evaluated for both SC and RCTs.
- This resulted in 87 RCTs and 48 SC studies used in the final evaluation of 21 treatments for NSCLC.

Figure 1. Design schematic for using RWS as comparators to RCT experimental treatments

Abbreviations: RCT = randomized controlled trial; RR = risk ratio; RW = real world; SC = single cohort
Treatments included: afatinib, apatinib, bevacizumab, brigatinib, carboplatin, ceritinib, cisplatin, crizotinib, dabrafenib, durvalumab, erlotinib, nab-paclitaxel, nivolumab, osimertinib, pembrolizumab, pemetrexed

Results

Table 1. Patient characteristics and outcomes

Treatment Number	RCT					SC Study				
	N	Age, (Years)*	Male %	ORR*	PFS*	N	Age, (Years)*	Male %	ORR*	PFS*
1a	632	61	38	68	76	576	66	36	50	77
1b	32	67	84	9	8	18	39	33		11
2b	22	59	82	27		38	59	68	13	11
3a	3211	62	60	46	65	306	63	75	45	62
4a	75	67	40	69	90	109	66	39	77	84
4a	75	67	40	69	90	109	66	39	77	84
5b	39	61	50	64	39	76	63	59	20	33
6b	137	58	50	74	61	28	54	49	67	76
8a	397	67	61	57	44	53	65		36	39
9a	397	67	61	57	44	53	65	77	36	39
10b	115	54	41		42	227	53	47	55	65
12b	138	60	41	62	65	30	56	44	70	63
14b	699	64	65	20	35	68	61	57	31	38
15a	507	64	57	56	66	355	69	57	62	67
15b	1916	63	58	15	29	326	66	64		11
16b	434	66	57	29	44	43	57	30	5	26
17b	126	61	57	20	38	136	69	64	27	32
18b	765	61	71	19	33	53	61	62	9	21
19a	279	64	36	80	88	36	60	61	50	64
19b	384	60	40	68	79	228	65	30	69	70
20a	945	64	63	39	57	132	68	67	51	60
21a	168	71	60	22	36	66	76	65	14	35
21b	423	64	60	15	38	30	67	97		35

*Weighted average
Abbreviations: ORR = objective response rate; PFS = progression-free survival; RCT = randomized controlled trial; SC = single cohort

Results (cont.)

- For ORR, there was agreement between the RCTs and ECA-RCTs for 9/15 (60%) in **Figure 2**.
- The purple box indicates non-significant different direction (NSDD) in 5/15 (33.3%).
- The red box indicates significant in different direction (SDD) in 1/15 (6.7%).

Figure 2. ORR relative rates by clinical trial and design

Abbreviations: R+ randomized controlled trials; RR = ORR (Experimental) / ORR (comparator); S+ single cohort studies

- For PFS, there was agreement between the RCTs and ECA-RCTs for 12/15 (80.0%) in **Figure 3**.
- The purple box indicates NSDD in 2/15 (13.3%).
- The red box indicates SDD in 1/15 (6.7%).

Figure 3. PFS relative rates by clinical trial design

Abbreviations: R+ randomized controlled trials; RR = ORR (Experimental) / ORR (comparator); S+ single cohort studies

- For OS, there was agreement (A) between the RCTs and ECA-RCTs for 14/15 (93.3%) in **Figure 4**.
- The red box indicates SDD in 1/15 (6.7%).

Figure 4. OS relative rates by clinical trial design

Abbreviations: R+ randomized controlled trials; RR = ORR (Experimental) / ORR (comparator); S+ single cohort studies

Discussion

- The results of this study demonstrated that the ORR, progression-free survival (PFS), and OS were comparable in RCTs and SC studies using ECAs and evaluating the treatment of NSCLC.

Limitations

- Focus on NSCLC: Generalization to other therapeutic areas requires further assessment.
- Publication bias: Studies reported in the literature may be biased towards positive results.
- Design limitations of SC studies:
  Random selection of patients could not be assessed.
  The timing of SC studies relative to the RCTs was not assessed.
  There is potential for bias by indication.

Conclusions

- **Well-designed and carefully conducted SC studies can supplement the evidence provided by RCTs.**
- **When RCTs are not feasible or ethical, the SC design can be a viable alternative.**
- **RWS can enhance and supplement the evaluation of treatments for rare diseases or advanced cancers.**

Disclosures
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ObesityWeek

4–7 November 2025 | Atlanta, GA, USA

Posters

Guidance for Obesity Management: What About the Patient's Experience?

ObesityWeek 2025

4–7 November 2025 | Atlanta, GA, USA

Poster Title

Guidance for Obesity Management: What About the Patient's Experience?

Objective

- To examine the inclusion of qualitative evidence in approval packages and product labels for obesity management medications (OMMs).

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Guidance for Obesity Management: What About the Patient's Experience?

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Background

- The emergence of novel pharmacotherapies has revolutionized the treatment of obesity.
- The 2025 US FDA draft guidance for industry, titled *"Obesity and Overweight: Developing Drugs and Biological Products for Weight Reduction"*,[1] focuses on the design of trials to demonstrate the effectiveness of drugs on sustained weight reduction. However, this lacks consideration of the physical, emotional, and lifestyle impacts experienced by patients with obesity.
- The FDA recognizes the value of qualitative interviews in establishing what is important to patients during drug development.[2]
- Qualitative in-trial interviews with clinical trial participants have emerged as a leading evidence-generation tool to support the approval of innovative therapies. These interviews offer a unique opportunity to elevate the patient voice by capturing in-depth patient experience data on meaningful treatment experiences and can support the interpretation of clinical outcomes assessment (COA) and other clinical trial efficacy endpoints.

Objective

- **To examine the inclusion of qualitative evidence in approval packages and product labels for obesity management medications (OMMs)**

Methods

- To assess the inclusion of qualitative data in regulatory submissions we:
  - Identified FDA-approved OMMs for obesity using the Center for Drug Evaluation and Research (CDER) database[3]
  - Reviewed the corresponding drug approval packages and product labels

Results

- Six OMMs have been FDA approved for obesity and/or overweight between 1999 and 2025 (*see* **Table 1** for approval and last label review dates): orlistat, phentermine and topiramate, bupropion and naltrexone, liraglutide, semaglutide, and tirzepatide.
- Three OMMs included in-trial and/or other qualitative data as part of the FDA clinical/medical or other review documents.
- No OMM applications included in-trial interview data in the product label.
- Feedback from the FDA on these OMM submissions included recommendations to sponsors for submitting qualitative evidence as part of drug approval packages and the importance of well-designed in-trial research:
  - **Engage FDA early on plans for qualitative research**
  - **Provide comprehensive documentation for early and effective review of qualitative evidence**
  - **Specify and define patient-relevant functional impacts**
  - **Use patient interviews to support anchor-based analyses, content validity, and meaningful change**
  - **Use exit interviews to ask patients about satisfaction and drug effectiveness**
  - **Involve patients in qualitative research that are representative of the clinical trial population**

Results (cont.)

Table 1. FDA Review of OMM Submissions Containing In-Trial and/ or Qualitative Interview Data (N=6)

Active Ingredient/ Generic Drug Name (Brand Name), *Company*	Drug Class	FDA Approval Date and Latest Label Review Date	Qualitative Data Included	Type of FDA Review Document	Type of Qualitative Research and Objective	FDA Comments Regarding Qualitative Research
Orlistat (Xenical/Alli) *Cheplapharm/GSK plc*	Gastric and pancreatic lipase inhibitor	FDA approval: 23 Apr 1999 Latest label review: 17 Nov 2022	• Xenical: No • Alli: Yes	Medical review	**Type**: In-trial longitudinal interviews **Objective**: Assess subject-perceived study treatment effectiveness and satisfaction	• Satisfaction and drug effectiveness questions should have been reserved for the final interview.
Phentermine and topiramate (Qsymia) *Vivus*	Norepinephrine agonist/GABA agonist, glutamate antagonist	FDA approval: 7 Jul 2012 Latest label review: 19 Nov 2024	No	-	-	-
Bupropion hydrochloride and naltrexone hydrochloride (Contrave) Orexigen *Therapeutics, Inc.*	Naltrexone/bupropion: Opioid receptor antagonist/ dopamine and norepinephrine reuptake inhibitor	FDA approval: 10 Sep 2014 Latest label review: 1 Apr 2022	Yes	Medical review	**Type**: CE **Objective**: Evaluate content validity of the IWQOL-Lite	• Qualitative evidence failed to demonstrate the IWQOL-Lite was fit-for-purpose. • Interviewed patients may not be representative of clinical trial population. • Inadequate documentation of content validity. • No submission of qualitative protocols, interview guides, transcripts or publications.
Liraglutide (Saxenda) *Novo Nordisk*	GLP-1 receptor agonist	FDA approval: 23 Dec 2014 Latest label review: 1 Nov 2024	No	-	-	-
Semaglutide (Wegovy) *Novo Nordisk*	GLP-1 receptor agonist	FDA approval: 4 Jun 2021 Latest label review: 27 Nov 2024	No	-	-	-
Tirzepatide (Zepbound) *Eli Lilly*	Dual GLP-1 receptor and GIP receptor agonist	FDA approval: 8 Nov 2023 Latest label review: 2 Jul 2025	Yes	Other reviews and clinical review	**Type:** CE and CI **Objective**: 1. Explore impacts of obesity on PF 2. Evaluate content validity of the SF-36v2 3. Determine MIC on SF-36v2 PF	• Interview results did not inform meaningful change for the SF-36v2 PF domain score. • Importance of Agency review and comment on qualitative research plans early in the development program • Recommended interviews to support anchor-based analyses, content validity and MIC. • Specify and define functional impacts relevant and important to patients.

Abbreviations: CE= concept elicitation; CI= cognitive interviews; GABA = gamma-aminobutyric acid; GIP = glucose-dependent insulinotropic polypeptide; GLP-1 = glucagon-like peptide-1; IWQOL-Lite = Impact of Weight on Quality of Life-Lite; MIC= minimally importance change; PF = physical functioning; SF-36v2 = Short Form Health Survey version-2.0

Disclosures
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Editorial and graphic design support were provided by Caroline Cole and Kawthar Nakayima of Thermo Fisher Scientific.

Strengths

- To our knowledge, this is the first review of qualitative evidence in OMM regulatory submissions.
- This review has identified a gap in the FDA drug evaluation and approval process for OMMs; the focus for approvals remains on quantitative data, i.e. weight loss percentages, as evidenced in the recent FDA draft guidance for industry, with less focus on the patient voice.

Limitations

- The review was limited to approved OMMs only.
- The review focused only on the US regulatory landscape (FDA); future research should also evaluate the European landscape (EMA submissions).

Conclusions

- **The FDA recognizes the value of qualitative data to:**
  - **Capture patients' experiences with OMMs.**
  - **Support the content validity and interpretability of COA endpoints.**
- **Whilst the 2022 Patient-Focused Drug Development (PFDD) guidance encourages the inclusion of qualitative evidence:[3]**
  - **The FDA does not formally require it in submission packages.**
  - **There appears to have been a lack of opportunity to date for sponsors to collect rich qualitative data to complement COA-based endpoints.**
- **There is a need for sponsors to design more patient-centered clinical trials integrating the patient voice.**
- **The FDA recommends for sponsors of OMMs to:**
  - **Engage the FDA early**
  - **Provide comprehensive qualitative evidence**
  - **Specify and define functional impacts**
  - **Use patient interviews to support anchor-based analyses, content validity and meaningful change**
  - **Use exit interviews to ask patients about satisfaction and drug effectiveness**
  - **Ensure qualitative samples represent the clinical trial population**
- **Well-designed in-trial qualitative studies can help address FDA concerns regarding the interpretation of COA endpoints.**
- **Collecting rich qualitative data may also reduce the need for sponsors to collect additional real-world evidence research often required to supplement clinical trial data.**

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The Professional Society for Health Economics and Outcomes Research (ISPOR EU)

9–12 November 2025 | Glasgow, Scotland, UK

Posters

Exploring the Promise of Generative Artificial Intelligence (AI) for Coding and Analysing Qualitative Patient Data: Results from a Pilot Study in Non-Hodgkin's Lymphoma

Evidence of Mapping Malpractice? A Review of Mapping Algorithm Usage in NICE HealthTechnology Appraisals

From Theory to Practice: Guidance for Identifying and Selecting Mapping Algorithms for Health Economic Models

Anchors Away: Navigating Unanchored Indirect Comparisons with Multilevel Unanchored Meta-regression

An Exploration of Implementing Herd Immunity Into Static Models for Economic Evaluation of Vaccines

Using a Large Language Model (LLM) for Data Extraction of Studies: Learnings from a Targeted Literature Review (TLR) in Non-small Cell Lung Cancer (NSCLC)

Real-world Evidence on the Broader Benefits of GLP-1 RA-based Therapies: A Global Targeted Literature Review

Millennial Medical Record Data Profile: A Japanese Electronic Medical Records Database Utilising Unstructured Data for Lung Cancer Research

AI-Assisted Time-to-Event Projection: A Case Study and Broader Potential

Have Delays in Vaccine Market Access Improved in Europe and the US Over the Last Decade?

NICE Has Embraced Single-arm Trials in Technology Appraisals, but Where is the Guidance?

Comparing Alternative Extrapolation Methods Using Standard Partitioned Survival Model Functionality in the Presence of Converging Survival Data: A Case Study in Renal Cell Carcinoma

Are Clinicians Ready For A More Environmental-friendly Health Care? A Clinician Survey

Navigating Health Technology Assessment Requirements: The Current Landscape of Alzheimer's Disease Modifying Treatments

A Layered Approach to Reducing Hallucinations in LLMs for Clinical Data

Identifying Risk Profiles for Early Treatment Discontinuation in Geographic Atrophy Using Machine Learning and SHAP Clustering

Uncovering Patient Narratives of Opioid Use and Recovery Using Large Language Models for Topic and Emotion Analysis of Social Media

Enhancing Migraine Preference Research: Recommendations from a Systematic Review of Preference Studies

Integrating Real-World Evidence into Oncology Health Technology Assessment Submissions: Recent EU Examples

Evaluating High-cost Gene Therapies for Non-cancer Conditions: Insights From NICE's Standard Appraisal Process

Enhancing Targeted Literature Reviews (TLRs) with Artificial Intelligence (AI): A Methodological Approach for Conducting Efficient Targeted Searches

Navigating Evidence Requirements for Joint Clinical Assessment (JCA): Practical Considerations for Systematic Literature Reviews (SLRs) and Indirect Treatment Comparisons (ITCs)

Cost Implications of Declining MMR Coverage in England: Modelling NHS Burden and the Value of Catch-Up Vaccination

ISPOR EU 2025

9–12 November 2025 | Glasgow, Scotland, UK

Poster Title

Exploring the Promise of Generative Artificial Intelligence (AI) for Coding and Analysing Qualitative Patient Data: Results from a Pilot Study in Non-Hodgkin's Lymphoma

Objective

- Evaluate how AI performs compared with human tasks and processes.
- Provide recommendations for AI use-cases that can meet regulatory standards, using both primary and secondary analysis of qualitative data.

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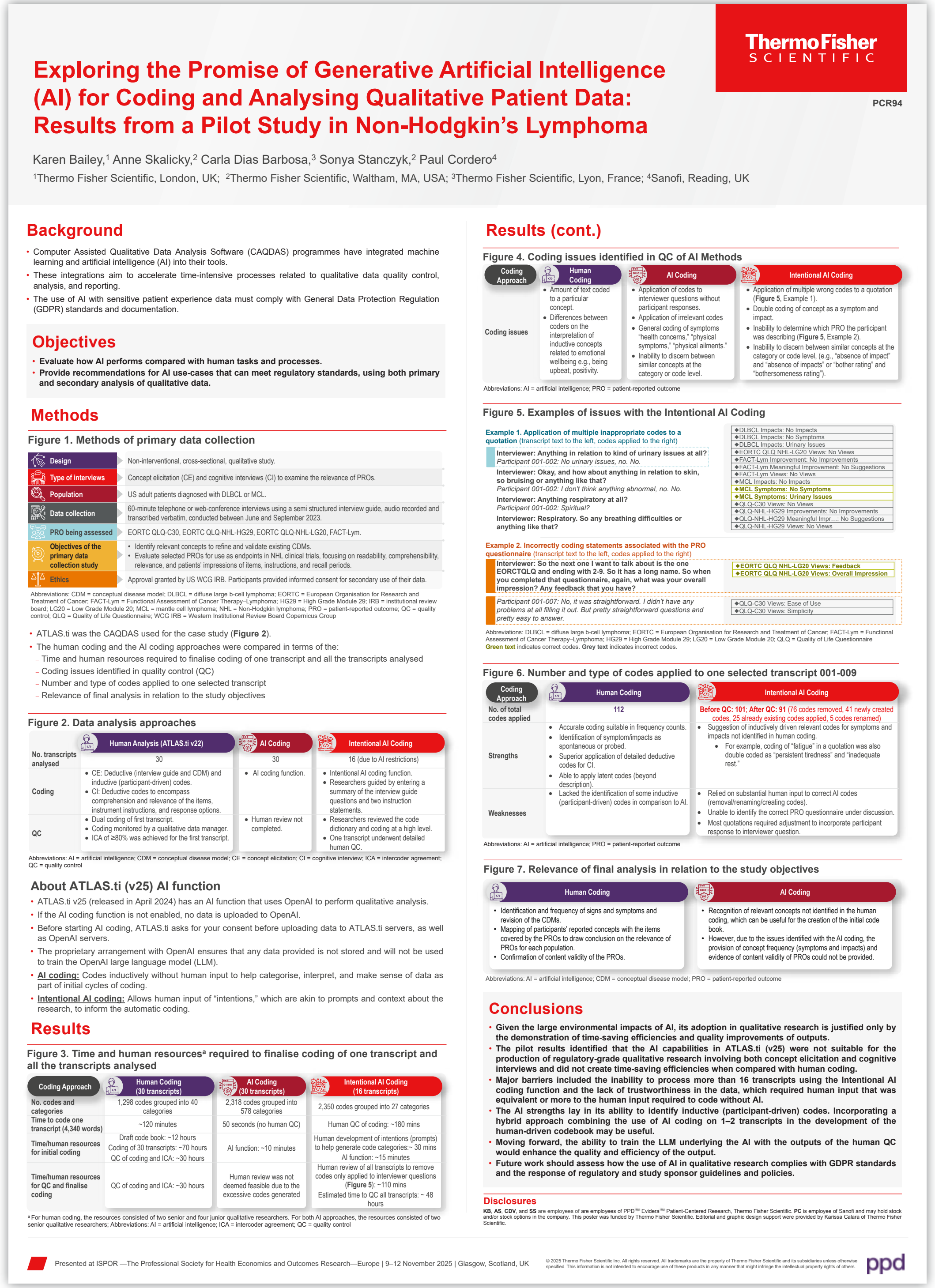

ISPOR EU 2025

9–12 November 2025 | Glasgow, Scotland, UK

Poster Title

Evidence of Mapping Malpractice? A Review of Mapping Algorithm Usage in NICE HealthTechnology Appraisals

Objective

- To review NICE appraisals published or updated over the past 5 years to:
  - Quantify the general frequency of mapping algorithm usage
  - Highlight any trends in mapping algorithm usage across appraisals over time
  - Determine which HRQoL instruments were most frequently mapped from
  - Summarise how submitting companies identified and selected candidate algorithms for use in cost-effectiveness analyses, and highlight any relevant critiques from Evidence Assessment Groups (EAGs)

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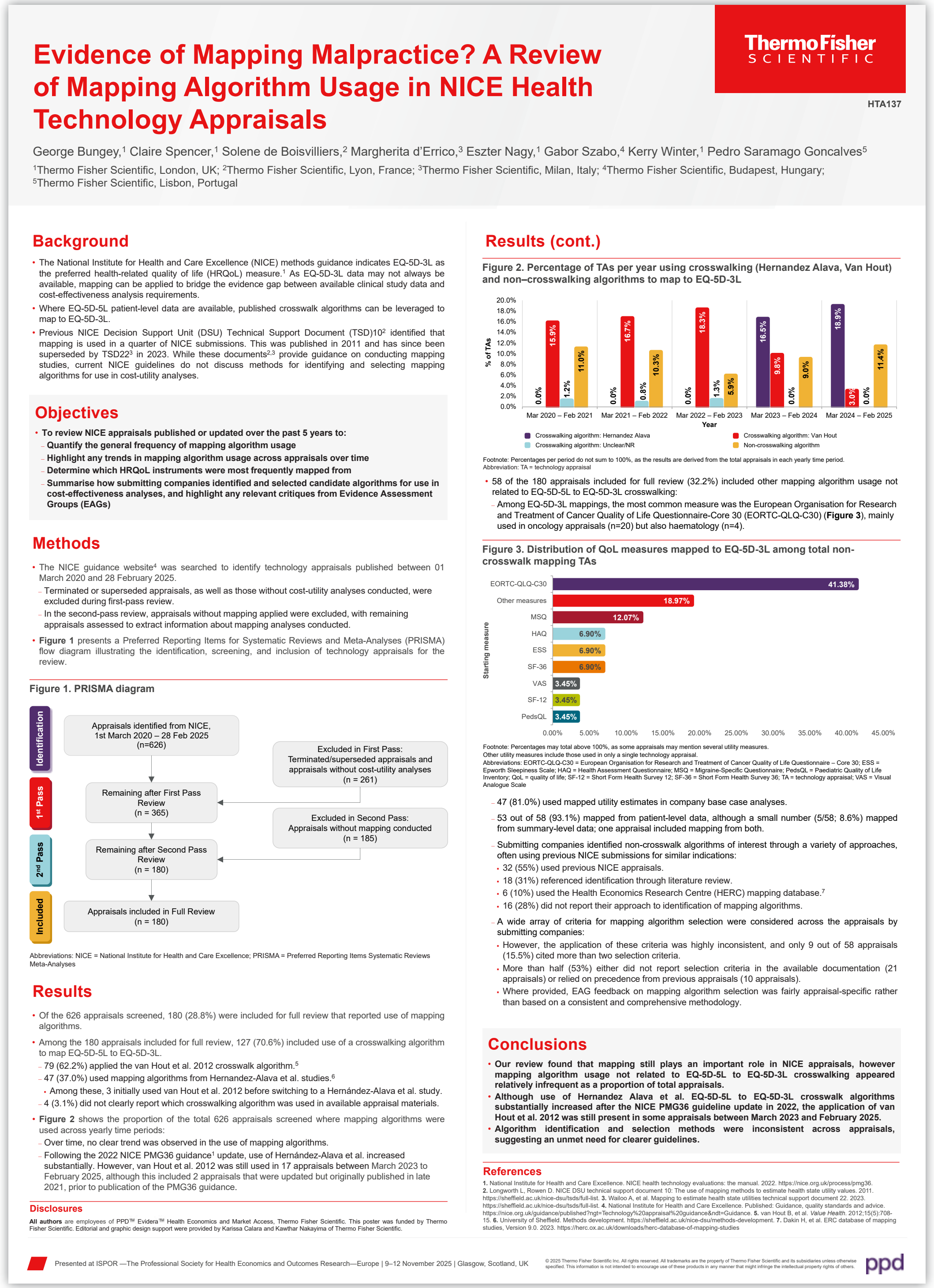

ISPOR EU 2025

9–12 November 2025 | Glasgow, Scotland, UK

Poster Title

From Theory to Practice: Guidance for Identifying and Selecting Mapping Algorithms for Health Economic Models

Objective

- Conduct a targeted search to confirm the most relevant sources available for mapping algorithms and the suitability of the HERC search strategy.
- Review pertinent discussion in existing guidance on mapping algorithms to inform selection criteria as well as identification and selection approaches adopted in recent NICE appraisals.
- Leverage findings to propose guidance for identifying and selecting mapping algorithms.

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ISPOR EU 2025

9–12 November 2025 | Glasgow, Scotland, UK

Poster Title

Anchors Away: Navigating Unanchored Indirect Comparisons with Multilevel Unanchored Meta-regression

Objective

- To address this gap, we introduce multilevel unanchored meta-regression (ML-UMR)—a novel extension of ML-NMR for unanchored comparisons—and assess its performance via simulation.

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ISPOR EU 2025

9–12 November 2025 | Glasgow, Scotland, UK

Poster Title

An Exploration of Implementing Herd Immunity Into Static Models for Economic Evaluation of Vaccines

Objective

- Aim: Compare vaccination effects on infection rate in both DTMs and Markov models.
- Develop and compare two models for the same hypothetical disease:
  - DTM: Captures person-to-person transmission and indirect (herd) effects through changing prevalence and contacts
  - Markov model: Models infection using a simpler time-step (discrete time), with transition probability from susceptible to infected informed by the DTMcritiques from Evidence Assessment Groups (EAGs)
- Evaluate impact of herd immunity on infection rate
- Analyze how different functional forms of herd effect in the Markov model influence results

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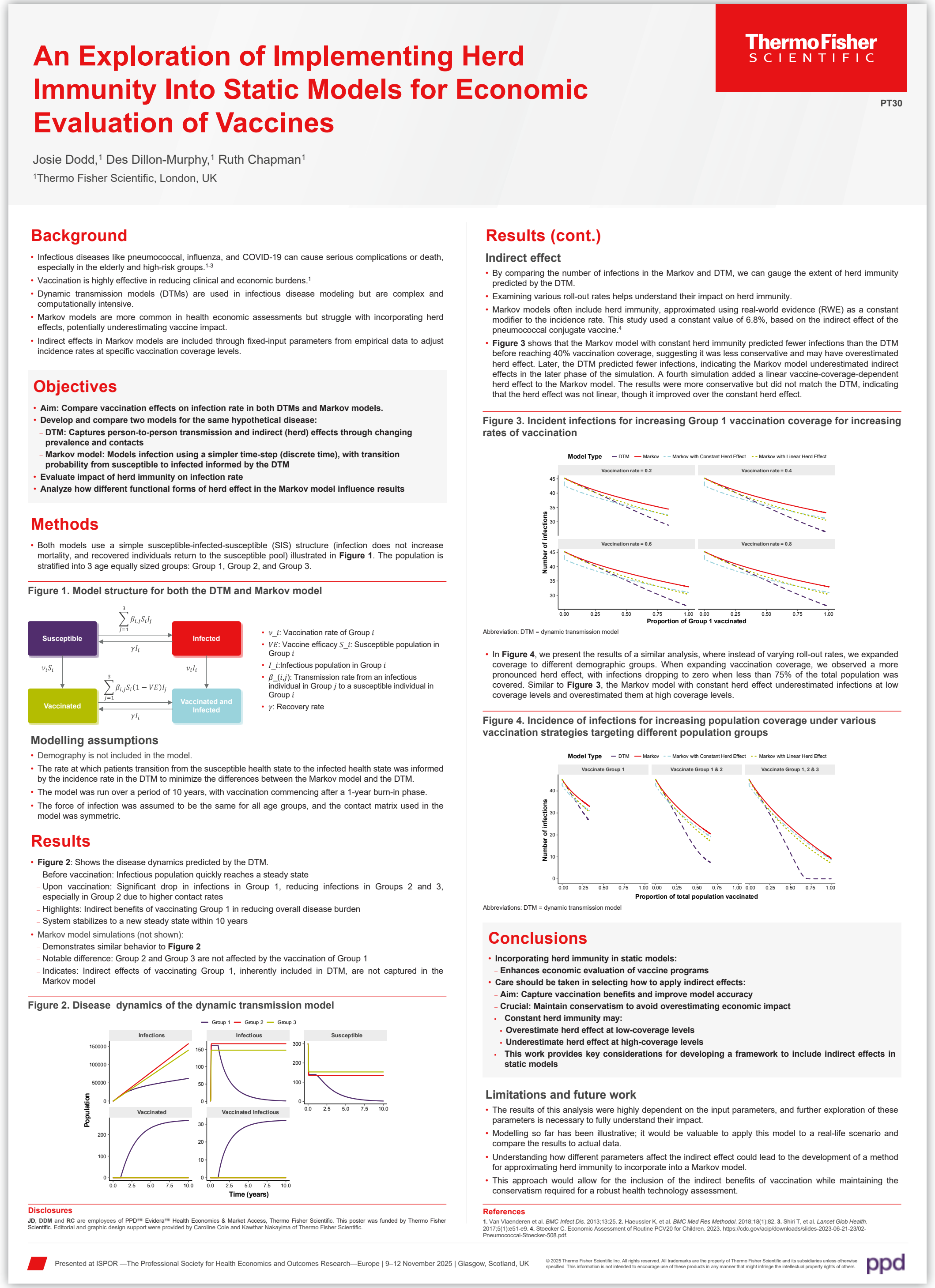

ISPOR EU 2025

9–12 November 2025 | Glasgow, Scotland, UK

Poster Title

Using a Large Language Model (LLM) for Data Extraction of Studies: Learnings from a Targeted Literature Review (TLR) in Non-small Cell Lung Cancer (NSCLC)

Objective

- This study aimed to evaluate a zero-shot GPT-4-assisted extraction approach for clinical outcomes from RWE studies in a specific cancer subpopulation to address the following objectives:
  - Identify and document challenges during data extraction, especially in RWE designs and studies with mixed populations, focusing on subsets of interest.
  - Provide recommendations for using LLMs in these instances.

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Using a Large Language Model (LLM) for Data Extraction of Studies: Learnings from a Targeted Literature Review (TLR) in Non-small Cell Lung Cancer (NSCLC)

ThermoFisher SCIENTIFIC

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Background

- Large Language Models (LLMs) streamline literature reviews by reliably extracting relevant information, thus reducing manual effort.
- We previously reported:
  - High accuracy (84%, range: 66%–96%) using zero-shot prompts for extraction of disease-specific clinical outcomes from a systematic literature review (SLR) of randomized controlled trials (RCTs) in atopic dermatitis.[1]
  - High reproducibility rates (80.6%–100%) under the same human operator and conditions, but lower reliability (65.7%–95.5%) between different operators using identical prompts.[2]
- While extraction has been tested on a broad range of therapeutic areas using RCT data,[3,4] real-world evidence (RWE) studies and complex research questions, such as those involving specific subpopulations, are not fully understood.

Objectives

- **This study aimed to evaluate a zero-shot GPT-4-assisted extraction approach for clinical outcomes from RWE studies in a specific cancer subpopulation to address the following objectives:**
  - **Identify and document challenges during data extraction, especially in RWE designs and studies with mixed populations, focusing on subsets of interest.**
  - **Provide recommendations for using LLMs in these instances.**

Methods

- A targeted literature review (TLR) assessed the comparative effectiveness and safety of immunotherapy treatments for non-small cell lung cancer (NSCLC) patients with programmed death-ligand 1 (PD-L1) expression ≥50% in RWE studies. Sixteen publications covering ten observational primary studies were included.
- Zero-shot prompts were developed, tested, and optimized for a proprietary GPT-4-based LLM using one included publication. Once satisfactory output was achieved (i.e., all predefined fields extracted with correct formatting and no critical omissions or errors after human validation), data were then extracted by the LLM for each remaining publication individually.
  - Zero-shot prompt: input given to a LLM to perform a task without any prior specific training or examples for that task; the model relies solely on the prompt and the provided documents
- Data extracted by the LLM were validated by a human investigator, with the main challenges noted during the process.
- Related publications were identified and categorized manually by a human reviewer.

Results

- The main challenges identified during the extraction and validation process were:
  1. Difficulties in isolating data for the target population (PD-L1 ≥50%) when reported as a subset of a broader NSCLC population with diverse PD-L1 expression statuses.
  2. Incorrect or missing data extracted by the LLM for subgroups (e.g., sex, age, smoking status) and fields related to study characteristics (e.g., follow-up duration, data source).
  3. Multiple files for a single study caused discrepancies from data presentation (tables, text, figures), multiple data types and timepoints, variations between main text and supplemental materials, and related publications.
- As a result of these challenges, additional extraction and re-validation of subgroup data, along with correction of formatting issues, resulted in time expenditure equal to or greater than validating manual extractions.

Limitations and recommendations

- For each identified challenge, the limitations with the extraction approach are presented in **Table 1**, along with a suggested workflow and considerations for future projects using LLMs for data extraction (**Figure 1**).

Table 1. Challenges and corresponding recommendations for future use

Data extraction challenge	Limitations	Recommendations
Mixed population studies: difficulties identifying data from the target population (PD-L1 ≥50%) within a broader population (NSCLC)	• LLM often extracts data for the overall population instead of the subpopulation of interest.	• Develop specific prompts for studies with subpopulations of interest: - Include detailed context and clearly indicate that only data for the target subpopulation are of interest.
Incorrect or missing data for subgroups	• LLM may extract incorrect/incomplete subgroup data. • The LLM used for this study did not recognize data in figures.	• Enhance prompt specificity for subgroup data. • Include detailed instructions and examples in the prompt.

Lack of recognition of related publications	• The prompt was not designed to enable the LLM to identify related publications, resulting in some redundant extractions.	• Consider two approaches:
		  1. Identify related publications manually and design specific prompts to extract only new data.
		  2. Identify related publications, compare data manually, and use LLM for extraction only if new data points are present, refining the prompt as needed.

Supplementary materials	• Multiple documents (such as the main publication and its supplement) complicate LLM processing, especially in mixed population studies with extensive subgroup data.	• Enhance prompt instructions for handling multiple documents. • Specify prioritized information for extraction. • Note relevant subpopulation data may be in supplementary material.
Formatting issues	• Inconsistent formatting in extracted data requires additional processing and standardization.	• Standardize format requirements in prompts. • Provide clear examples.
Generic platform vs platform integrated within literature review software	• Using a generic LLM interface may increase time requirements due to manual steps needed to use it for literature reviews (e.g., identifying related publications, providing examples in prompts).	• LLMs integrated into a literature-review platform are trained on structured research data extraction variables and outcomes with higher fidelity for TLRs. • Built-in linkage across related publications reduces redundant data extraction from overlapping or duplicate studies.

Note: Limitations may not be generalizable across various LLM architectures, implementations, or platform integrations.
Abbreviations: LLM = large language model; NSCLC = non-small cell lung cancer; PD-L1 = programmed death-ligand 1

Figure 1. Suggested workflow diagram and considerations for future projects using LLM for data extraction

Some LLMs now support reading Excel™ files. If available, uploading the Excel extraction table for direct population may streamline the workflow. At the time of this work, this functionality was not available
Abbreviations: LLM = large language model

Conclusions

- **LLMs can extract data from RWE studies but face significant challenges with clinical outcomes, especially for subgroups and mixed populations. Heterogeneity and limited standardization in reporting of observational studies likely contributed to errors in LLM-assisted extraction with zero-shot prompts.**
- **Further research into prompt engineering (i.e., design and execution) is needed to improve efficiency and accuracy in LLM-assisted data extraction for RWE study designs and complex research questions, particularly across multiple files per study and various types of data. Additional considerations are needed for generic LLMs versus. SLR-specific tools.**
- **Future projects should consider and evaluate the time required for human re-extraction, re-validation, and prompt development/optimization to accurately assess potential time savings.**

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Disclosures

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ISPOR EU 2025

9–12 November 2025 | Glasgow, Scotland, UK

Poster Title

Real-world Evidence on the Broader Benefits of GLP-1 RA-based Therapies: A Global Targeted Literature Review

Objective

- The goal of the study was to review published real-world benefits of GLP-1 RA-based therapies beyond their established effects on weight loss and glycaemic control.

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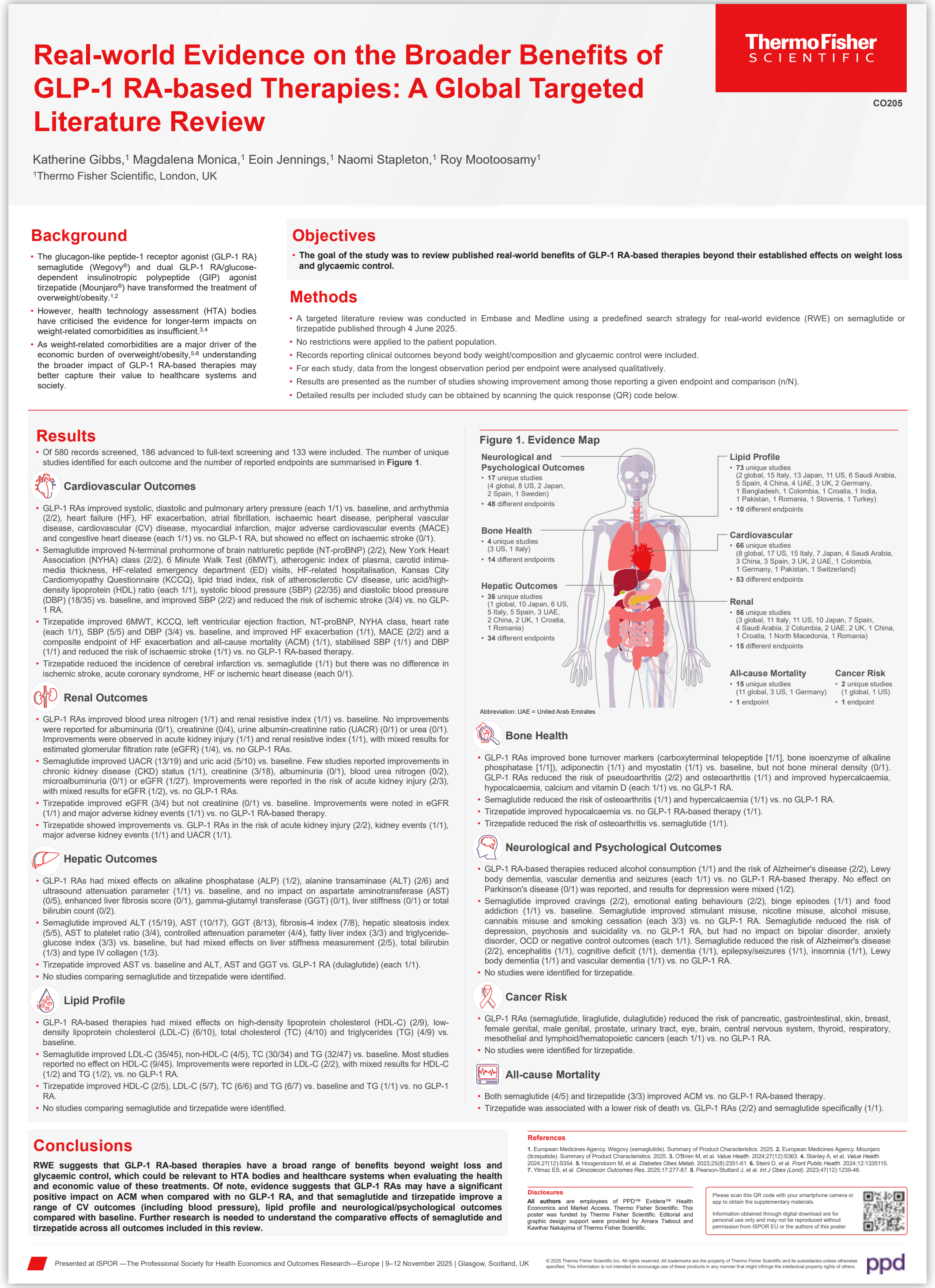

ISPOR EU 2025

9–12 November 2025 | Glasgow, Scotland, UK

Poster Title

Millennial Medical Record Data Profile: A Japanese Electronic Medical Records Database Utilising Unstructured Data for Lung Cancer Research

Objective

- The goal of this study was to describe the characteristics of MMR data, illustrating its utility for lung cancer research.

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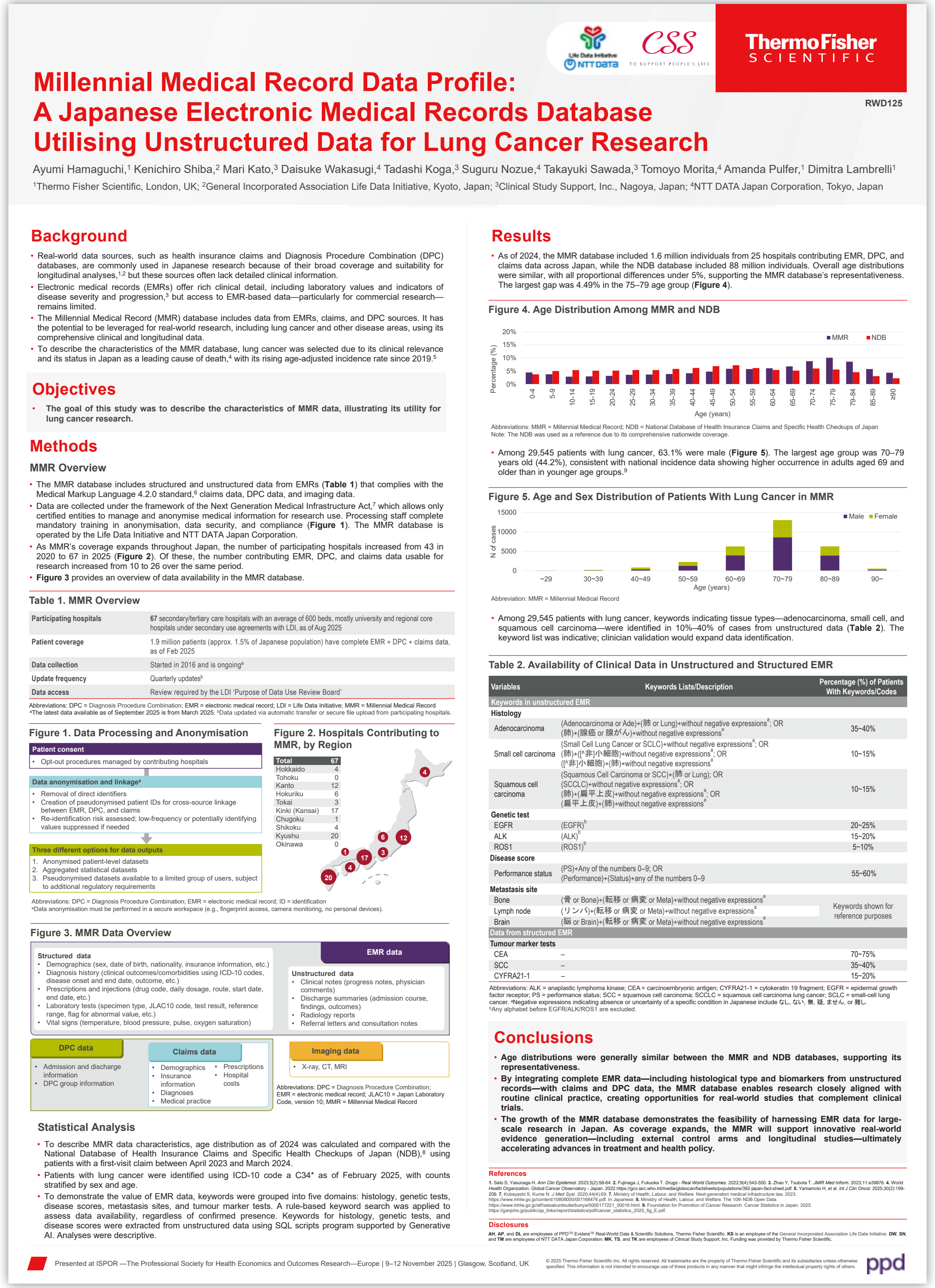

ISPOR EU 2025

9–12 November 2025 | Glasgow, Scotland, UK

Poster Title

AI-Assisted Time-to-Event Projection:
A Case Study and Broader Potential

Objective

- We explored the use of large language models (LLMs) (e.g., Chat-GPT, Gemini) to assist with understanding the prognosis of the study population to establish plausible ranges of life expectancy or median survival times.

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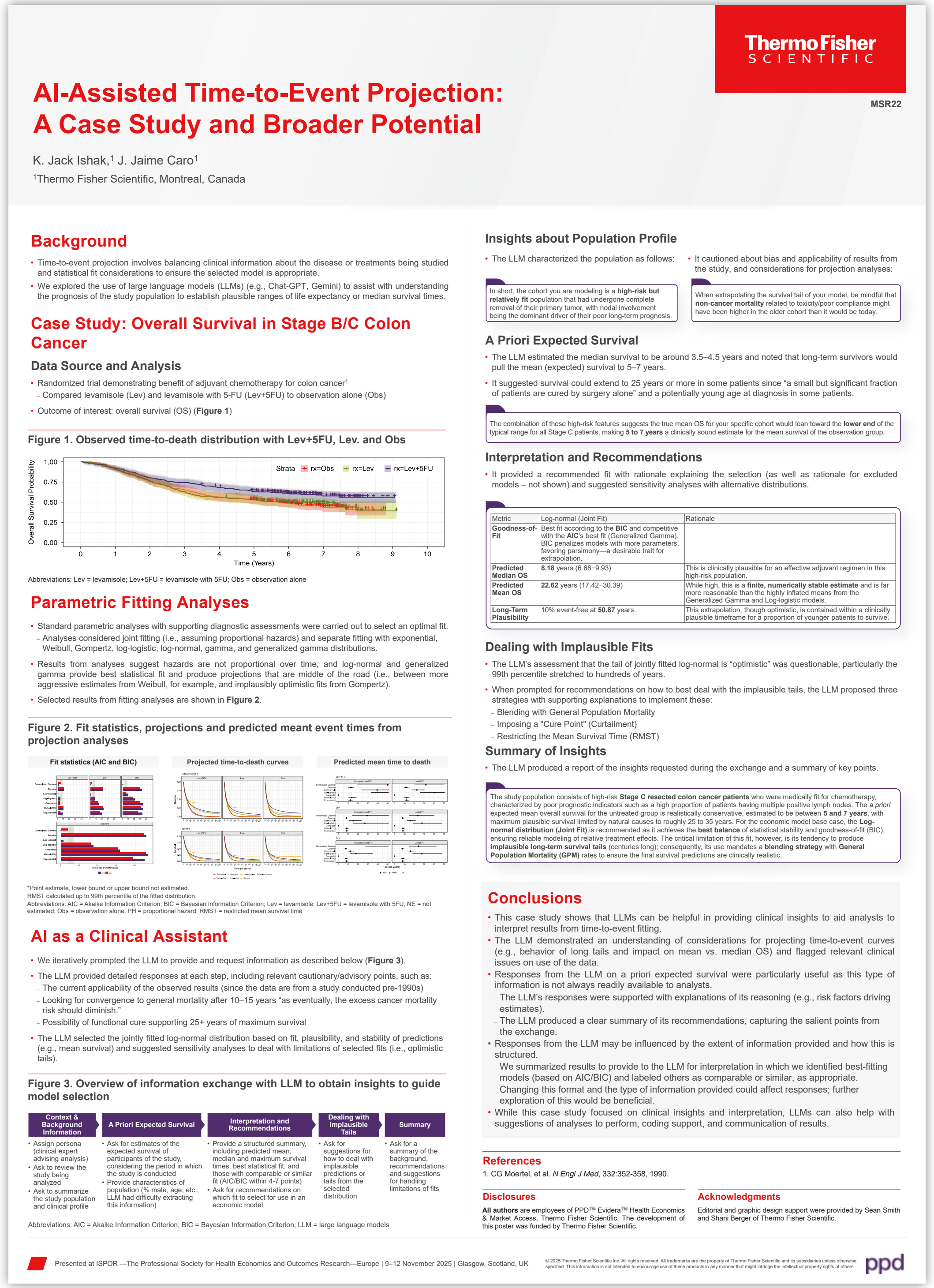

ISPOR EU 2025

9–12 November 2025 | Glasgow, Scotland, UK

Poster Title

Have Delays in Vaccine Market Access Improved in Europe and the US Over the Last Decade?

Objective

- To determine if delays between vaccine licensure and National Immunization Technical Advisory Group (NITAG) evaluation have improved over the last decade.

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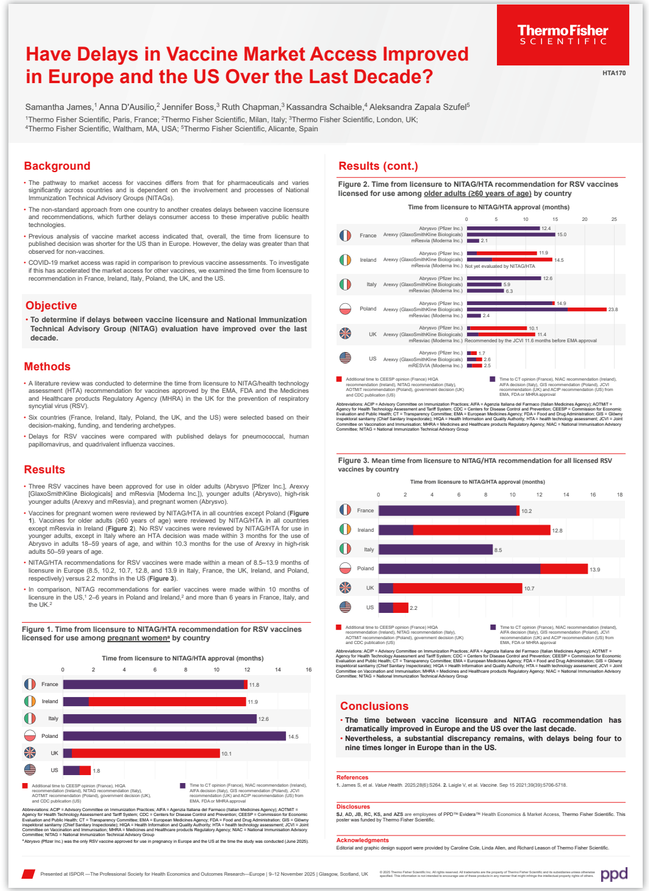

Have Delays in Vaccine Market Access Improved in Europe and the US Over the Last Decade?

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HTA170

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Background

- The pathway to market access for vaccines differs from that for pharmaceuticals and varies significantly across countries and is dependent on the involvement and processes of National Immunization Technical Advisory Groups (NITAGs).
- The non-standard approach from one country to another creates delays between vaccine licensure and recommendations, which further delays consumer access to these imperative public health technologies.
- Previous analysis of vaccine market access indicated that, overall, the time from licensure to published decision was shorter for the US than in Europe. However, the delay was greater than that observed for non-vaccines.
- COVID-19 market access was rapid in comparison to previous vaccine assessments. To investigate if this has accelerated the market access for other vaccines, we examined the time from licensure to recommendation in France, Ireland, Italy, Poland, the UK, and the US.

Objective

- **To determine if delays between vaccine licensure and National Immunization Technical Advisory Group (NITAG) evaluation have improved over the last decade.**

Methods

- A literature review was conducted to determine the time from licensure to NITAG/health technology assessment (HTA) recommendation for vaccines approved by the EMA, FDA and the Medicines and Healthcare products Regulatory Agency (MHRA) in the UK for the prevention of respiratory syncytial virus (RSV).
- Six countries (France, Ireland, Italy, Poland, the UK, and the US) were selected based on their decision-making, funding, and tendering archetypes.
- Delays for RSV vaccines were compared with published delays for pneumococcal, human papillomavirus, and quadrivalent influenza vaccines.

Results

- Three RSV vaccines have been approved for use in older adults (Abrysvo [Pfizer Inc.], Arexvy [GlaxoSmithKline Biologicals] and mRESVIA [Moderna Inc.]), younger adults (Abrysvo), high-risk younger adults (Arexvy and mResvia), and pregnant women (Abrysvo).
- Vaccines for pregnant women were reviewed by NITAG/HTA in all countries except Poland (**Figure 1**). Vaccines for older adults (≥60 years of age) were reviewed by NITAG/HTA in all countries except mResvia in Ireland (**Figure 2**). No RSV vaccines were reviewed by NITAG/HTA for use in younger adults, except in Italy where an HTA decision was made within 3 months for the use of Abrysvo in adults 18–59 years of age, and within 10.3 months for the use of Arexvy in high-risk adults 50–59 years of age.
- NITAG/HTA recommendations for RSV vaccines were made within a mean of 8.5–13.9 months of licensure in Europe (8.5, 10.2, 10.7, 12.8, and 13.9 in Italy, France, the UK, Ireland, and Poland, respectively) versus 2.2 months in the US (**Figure 3**).
- In comparison, NITAG recommendations for earlier vaccines were made within 10 months of licensure in the US,[1] 2–6 years in Poland and Ireland,[2] and more than 6 years in France, Italy, and the UK.[2]

Figure 1. Time from licensure to NITAG/HTA recommendation for RSV vaccines licensed for use among pregnant women[a] by country

Abbreviations: ACIP = Advisory Committee on Immunization Practices; AIFA = Agenzia Italiana del Farmaco (Italian Medicines Agency); AOTMiT = Agency for Health Technology Assessment and Tariff System; CDC = Centers for Disease Control and Prevention; CEESP = Commission for Economic Evaluation and Public Health; CT = Transparency Committee; EMA = European Medicines Agency; FDA = Food and Drug Administration; GIS = Gliwice Hospital Sanitary Inspectorate; HQA = Health Information and Quality Authority; HTA = health technology assessment; JCVI = Joint Committee on Vaccination and Immunisation; MHRA = Medicines and Healthcare products Regulatory Agency; NAC = National Immunization Advisory Committee; NITAG = National Immunization Technical Advisory Group

[a]*Abrysvo* (Pfizer Inc.) was the only RSV vaccine approved for use in pregnancy in Europe and the US at the time the study was conducted (June 2025).

Results (cont.)

Figure 2. Time from licensure to NITAG/HTA recommendation for RSV vaccines licensed for use among older adults (≥60 years of age) by country

Abbreviations: ACIP = Advisory Committee on Immunization Practices; AIFA = Agenzia Italiana del Farmaco (Italian Medicines Agency); AOTMiT = Agency for Health Technology Assessment and Tariff System; CDC = Centers for Disease Control and Prevention; CEESP = Commission for Economic Evaluation and Public Health; CT = Transparency Committee; EMA = European Medicines Agency; FDA = Food and Drug Administration; GIS = Gliwice Hospital Sanitary Inspectorate; HQA = Health Information and Quality Authority; HTA = health technology assessment; JCVI = Joint Committee on Vaccination and Immunisation; MHRA = Medicines and Healthcare products Regulatory Agency; NAC = National Immunization Advisory Committee; NITAG = National Immunization Technical Advisory Group

Figure 3. Mean time from licensure to NITAG/HTA recommendation for all licensed RSV vaccines by country

Abbreviations: ACIP = Advisory Committee on Immunization Practices; AIFA = Agenzia Italiana del Farmaco (Italian Medicines Agency); AOTMiT = Agency for Health Technology Assessment and Tariff System; CDC = Centers for Disease Control and Prevention; CEESP = Commission for Economic Evaluation and Public Health; CT = Transparency Committee; EMA = European Medicines Agency; FDA = Food and Drug Administration; GIS = Gliwice Hospital Sanitary Inspectorate; HQA = Health Information and Quality Authority; HTA = health technology assessment; JCVI = Joint Committee on Vaccination and Immunisation; MHRA = Medicines and Healthcare products Regulatory Agency; NAC = National Immunization Advisory Committee; NITAG = National Immunization Technical Advisory Group

Conclusions

- **The time between vaccine licensure and NITAG recommendation has dramatically improved in Europe and the US over the last decade.**
- **Nevertheless, a substantial discrepancy remains, with delays being four to nine times longer in Europe than in the US.**

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Disclosures

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ISPOR EU 2025

9–12 November 2025 | Glasgow, Scotland, UK

Poster Title

NICE Has Embraced Single-arm Trials in Technology Appraisals, but Where is the Guidance?

Objective

- This study aimed to identify published guidance by National Institute for Health and Care Excellence (NICE) on SAT use in reimbursement submissions and to evaluate the acceptance of technology appraisals (TA) that use evidence solely from SATs across different therapeutic areas.

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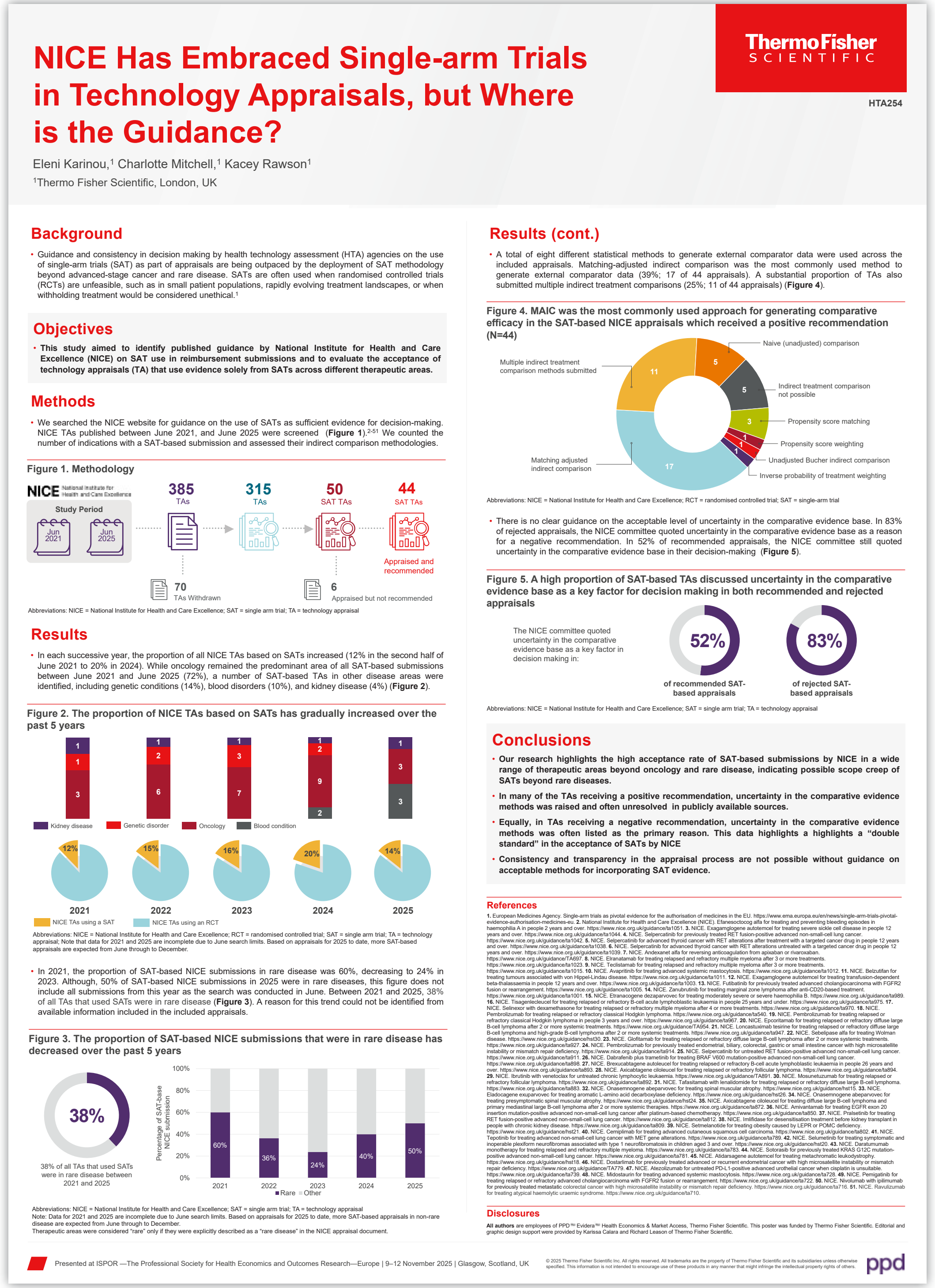

ISPOR EU 2025

9–12 November 2025 | Glasgow, Scotland, UK

Poster Title

Comparing Alternative Extrapolation Methods Using Standard Partitioned Survival Model Functionality in the Presence of Converging Survival Data: A Case Study in Renal Cell Carcinoma

Objective

- The objective of this case study was to explore the impact of combining typical functionalities (treatment effect waning, KM+parametric fit) included in partitioned survival models (PSMs) with standard parametric models as alternative extrapolation approaches, compared to conservatively assuming equivalence at the crossing point or unadjusted extrapolation, considering multiple OS data cuts from the CLEAR trial.

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Comparing Alternative Extrapolation Methods Using Standard Partitioned Survival Model Functionality in the Presence of Converging Survival Data: A Case Study in Renal Cell Carcinoma

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EE141

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Background

- In specific circumstances, combinations of parametric survival extrapolations may produce implausible crossings between two comparators due to the characteristics of the underlying Kaplan-Meier (KM) data.
- This was observed with the CLEAR trial[1] data in NICE TA858[2] when comparing lenalidomide in combination with pembrolizumab (LEN+PEM) versus sunitinib (SUN) in patients with renal cell carcinoma (RCC).
- In the August 2020 cut of CLEAR trial data, while LEN+PEM showed improved overall survival (OS) in the short term, crossing occurred between the KM curves at approximately 33 months.

Objectives

- **The objective of this case study was to explore the impact of combining typical functionalities (treatment effect waning, KM+parametric fit) included in partitioned survival models (PSMs) with standard parametric models as alternative extrapolation approaches, compared to conservatively assuming equivalence at the crossing point or unadjusted extrapolation, considering multiple OS data cuts from the CLEAR trial.**

Methods

- Published OS data from the CLEAR trial were digitized using WebPlotDigitizer software[3] and pseudo-individual patient data generated by Guyot Algorithm.[4] A series of standard parametric distributions was then fitted in the R flexsurv package to the August 2020 data cut.
- Six standard parametric functions were then fitted (exponential, Weibull, lognormal, loglogistic, Gompertz, generalized gamma). Models were selected based on statistical, visual fit, comparisons of hazard profiles for the parametric models against smoothed hazard plots for the KM data, and on the basis of plausibility of long-term predictions according to UK clinical expert expectations for SUN from technology appraisal (TA) 858 by the National Institute for Health and Care Excellence (NICE; <20% at 10 years).[4] In line with NICE decision support unit (DSU) technical support document (TSD) 14 guidance,[5] the same type of parametric model was selected for both comparators in the absence of a strong rationale to support different types.
- Given the crossing of OS KM curves observed in the CLEAR trial and potential uncertainty around long-term extrapolations for OS, the following approaches were also explored: (1) assuming equivalence at the crossing point; (2) assuming equivalent efficacy to SUN for LEN+PEM at the start of convergence between the two treatments, after which LEN+PEM OS hazards are set equal to SUN; (3) exploring a combined KM+parametric extrapolation approach using a truncated KM curve.
- Long-term extrapolations were then visually compared with the final data cut KM curve (July 2022).[6]

Results

Unadjusted Extrapolations

- Joint parametric distributions were not suitable due to curve crossings on the log-cumulative hazard plot with clearly non-parallel hazard plots, as well as the result of the formal assessment of the proportional hazards (PH) assumption via the Schoenfeld residuals test (P<0.0001)
- Among individual fits, the Gompertz and log-normal distributions produced the best statistical fit according to both Akaike information criterion (AIC) and Bayesian information criterion (BIC) for LEN+PEM and SUN, respectively. Most SUN fits showed relatively poor visual fit to the observed data, and almost all produced aggressive curve crossing.(**Figure 1** and **Figure 2**). The exponential models, while producing poor visual fits, were considered the most plausible set of single-fit distributions given clinical expert expectations for long-term OS discussed in NICE TA858[2] (<20% for patients starting treatment with SUN) without curve crossing and were selected for both comparators in line with NICE DSU TSD14 guidance[5].
- Among the remaining individual fits, the Weibull model produced the least sharp curve crossing and met clinical expert expectations from NICE TA858[2] for long-term OS in the SUN arm. This model was explored for both comparators in the equivalence assumption approach.

Figure 1. Long-term Single Parametric OS Predictions for LEN+PEM Using August 2020 Data Cut

Abbreviations: KM = Kaplan-Meier; LEN+PEM = lenalidomide in combination with pembrolizumab; OS = overall survival

Figure 2. Long-term Single Parametric OS Predictions for SUN Using August 2020 Data Cut

Abbreviations: KM = Kaplan-Meier; LEN+PEM = lenalidomide in combination with pembrolizumab; OS = overall survival

Results (cont.)

Method 1: Equivalence Assumption

- Single Weibull models were applied in combination with the SUN equivalency assumption mechanic to allow for a smoother convergence between LEN+PEM and SUN curves without actual crossing. This approach helped avoid overpredicting the tail of the original KM curve; however, it resulted in more conservative extrapolation for LEN+PEM compared with the unadjusted individual exponential fit and underprediction of the tail of the final KM curve.

Figure 3. Approaches for Long-term OS Predictions for LEN+PEM

Abbreviations: KM = Kaplan-Meier; LEN+PEM = lenalidomide in combination with pembrolizumab; OS = overall survival; SUN = sunitinib; Tx = treatment

In Methods 2 and 3, two switch points were explored (24 and 30 weeks) as curves are closely overlapping; only 30-week switch point data is visualized for both methods

Method 2: Treatment Effect Waning

- The treatment effect waning approach for LEN+PEM explored two switch points: (1) at 24 and (2) at 30 weeks, after which the OS hazard of LEN+PEM was set equal to that of SUN. The switch points were selected based on visual inspection of the KM curves; at these times, curves appeared to begin converging. For LEN+PEM the Gompertz model, the best statistical fit according to both AIC and BIC, was used.
- Both switch points produced nearly overlapping sets of curves. In both cases, the treatment effect waning approach helped avoid overpredicting the tail of the original KM curve, similar to Method 1, while producing a conservative extrapolation for LEN+PEM compared with the unadjusted individual exponential fit with underprediction of the tail of the final curve.

Method 3: KM+Parametric Extrapolation

- The KM+parametric extrapolation approach for LEN+PEM used an individual exponential fit and explored two switch points: (1) at 24 and (2) at 30 weeks; at these times, curves appeared to begin converging on the original KM plot. Both switch points produced nearly overlapping sets of curves. Both approaches resulted in a slightly better visual fit to the observed data to the original unadjusted exponential fit. Compared with the KM curves, the KM+parametric extrapolation approach produced an overprediction of the original 2020 data cut KM data but produced a close fit to the tail of the final 2022 data cut KM curve.
- The KM+parametric extrapolation approach for SUN used an individual exponential fit and explored three switch points: (1) at 47 months, corresponding to the maximum follow-up for the SUN arm at the August 2020 data cut off; (2) at 36 months, when the number of patients at risk dropped below 10; and (3) at 30 months, shortly before the original curves crossed. Switching at 47 months resulted in a clinically implausible estimate (>20% at 10 years), whereas the other two switch points resulted in slightly more optimistic extrapolations compared to the original unadjusted exponential fit.

Figure 4. Approaches for Long-term OS Predictions for SUN

Abbreviations: KM = Kaplan-Meier; SUN = sunitinib

Conclusions

- **The results of our case study show that relatively straightforward functionalities commonly implemented in PSMs may provide reasonable alternative extrapolations to support further scenario analyses in the presence of clinically implausible converging survival extrapolations between study arms, especially in cases where proportional hazards are clearly violated and joint parametric fits appear inappropriate, as seen for the CLEAR trial data.**
- **However, careful rationalization of appropriate switch points for treatment effect waning and KM+parametric approaches is required.**

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Disclosures

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ISPOR EU 2025

9–12 November 2025 | Glasgow, Scotland, UK

Poster Title

Are Clinicians Ready For A More Environmental-friendly Health Care?
A Clinician Survey

Objective

- To identify examples for how environmental sustainability has influenced clinical practices to date and to understand expectations for its future impact.
- To test attitudes towards considering sustainability in healthcare decisions and to measure conceptual acceptance of trading off efficacy and safety outcomes, costs, and physician time for environmental benefit.

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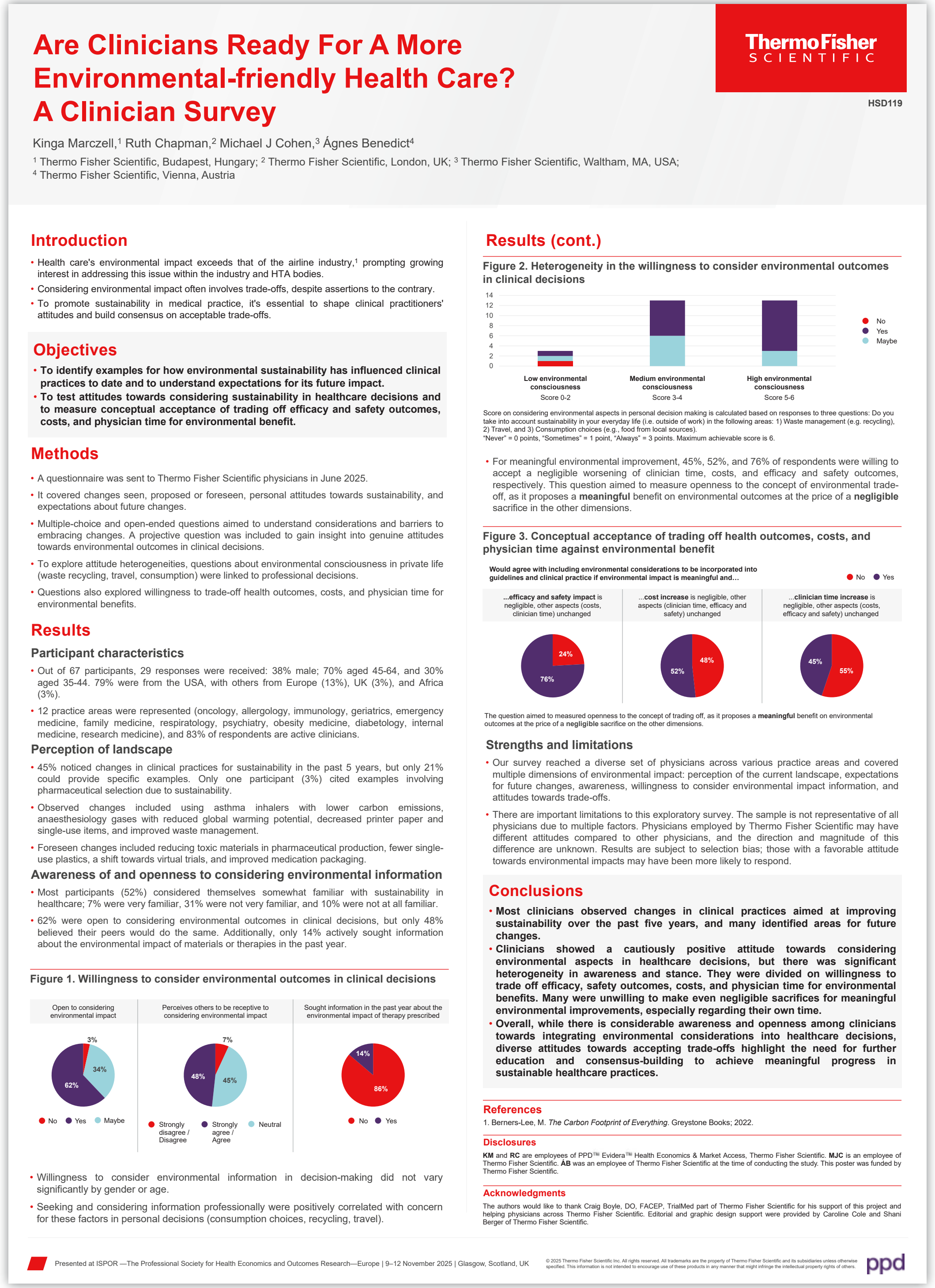

ISPOR EU 2025

9–12 November 2025 | Glasgow, Scotland, UK

Poster Title

Navigating Health Technology Assessment Requirements:
The Current Landscape of Alzheimer's Disease Modifying Treatments

Objective

- Our research aims to provide an overview of DMT health technology assessment (HTA) appraisals and highlight the challenges faced by manufacturers when the clinical value and cost-effectiveness of DMTs for AD are under evaluation.

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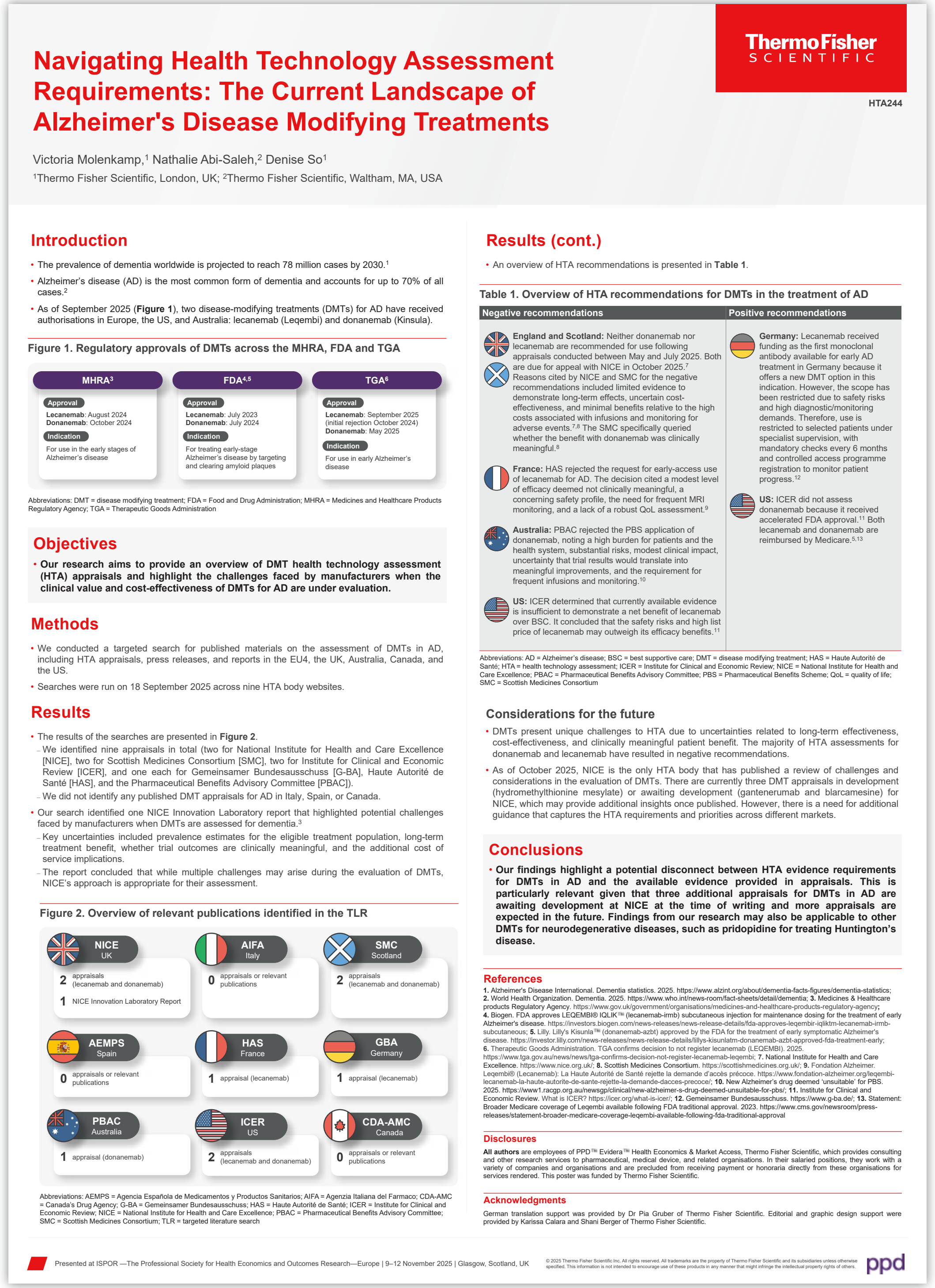

ISPOR EU 2025

9–12 November 2025 | Glasgow, Scotland, UK

Poster Title

A Layered Approach to Reducing Hallucinations in LLMs for Clinical Data

Objective

- The main objective of this study is to reduce hallucinations in LLMs when applied to structured (e.g., tabular EHR data) and unstructured (e.g., clinical text) sources.
- To design a two-layer framework where (1) refined prompts enforce factual, contextspecific outputs and (2) LangChain operationalizes RAG with agentic control.
- To demonstrate, through case examples, how prompt validation and retrieval-aware orchestration improve factual grounding and transparency in clinical and research workflows.
- To provide a scalable, interpretable, and compliant approach for deploying LLMs in healthcare analytics and decision support.

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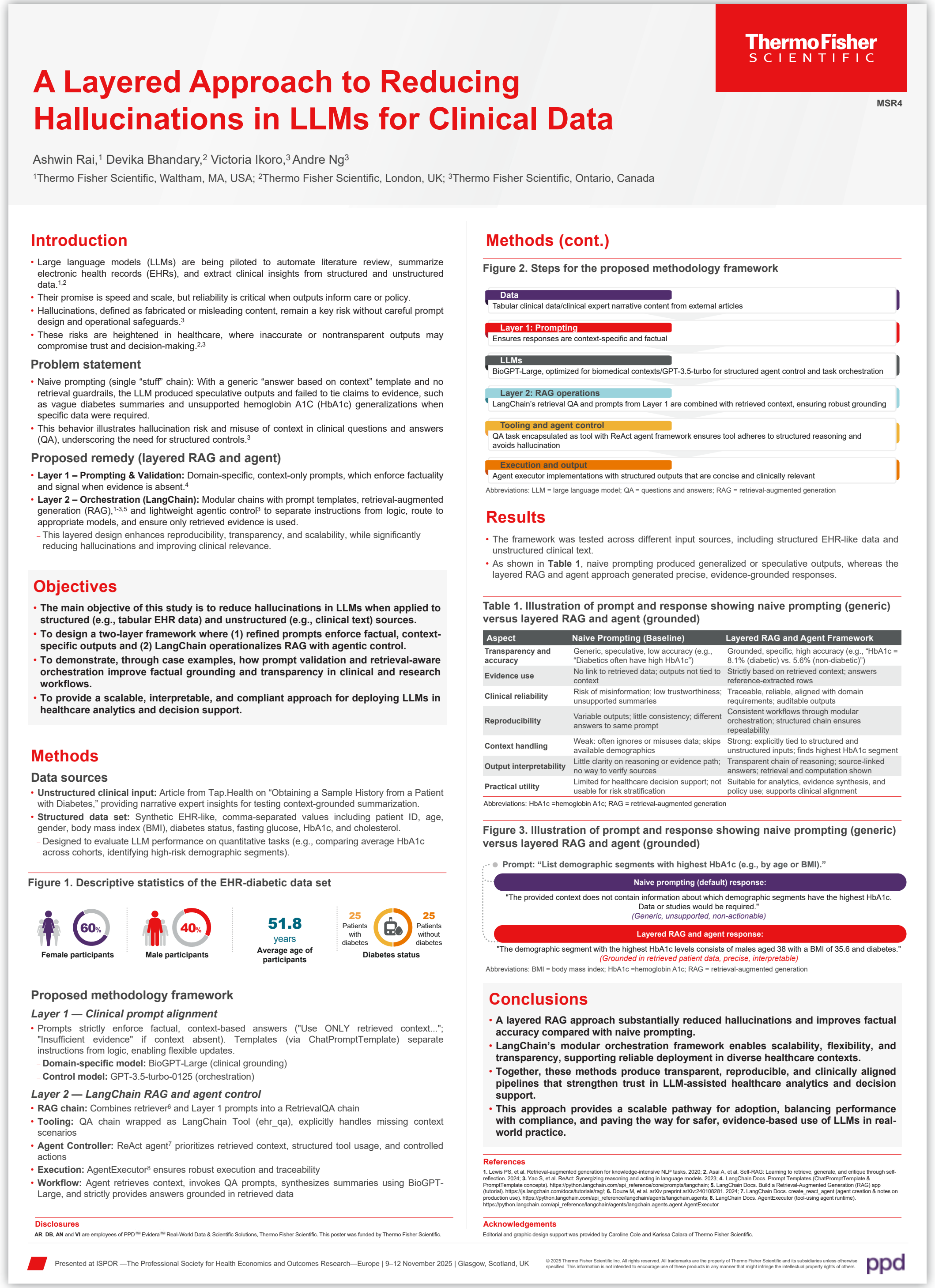

ISPOR EU 2025

9–12 November 2025 | Glasgow, Scotland, UK

Poster Title

Identifying Risk Profiles for Early Treatment Discontinuation in Geographic Atrophy Using Machine Learning and SHAP Clustering

Objective

- The main objective of this study was to develop a machine learning algorithm to identify patients at risk of dropout.
- For each patient, the algorithm would produce a risk score for adherence based on their individual patient journey.
- By utilizing a data-driven approach, we sought to explore the clinical, behavioral, and psychosocial factors behind patients' decisions to be non-adherent.
- The ultimate goal was to subsequently create a toolkit for healthcare professionals to implement a tailored retention strategy.

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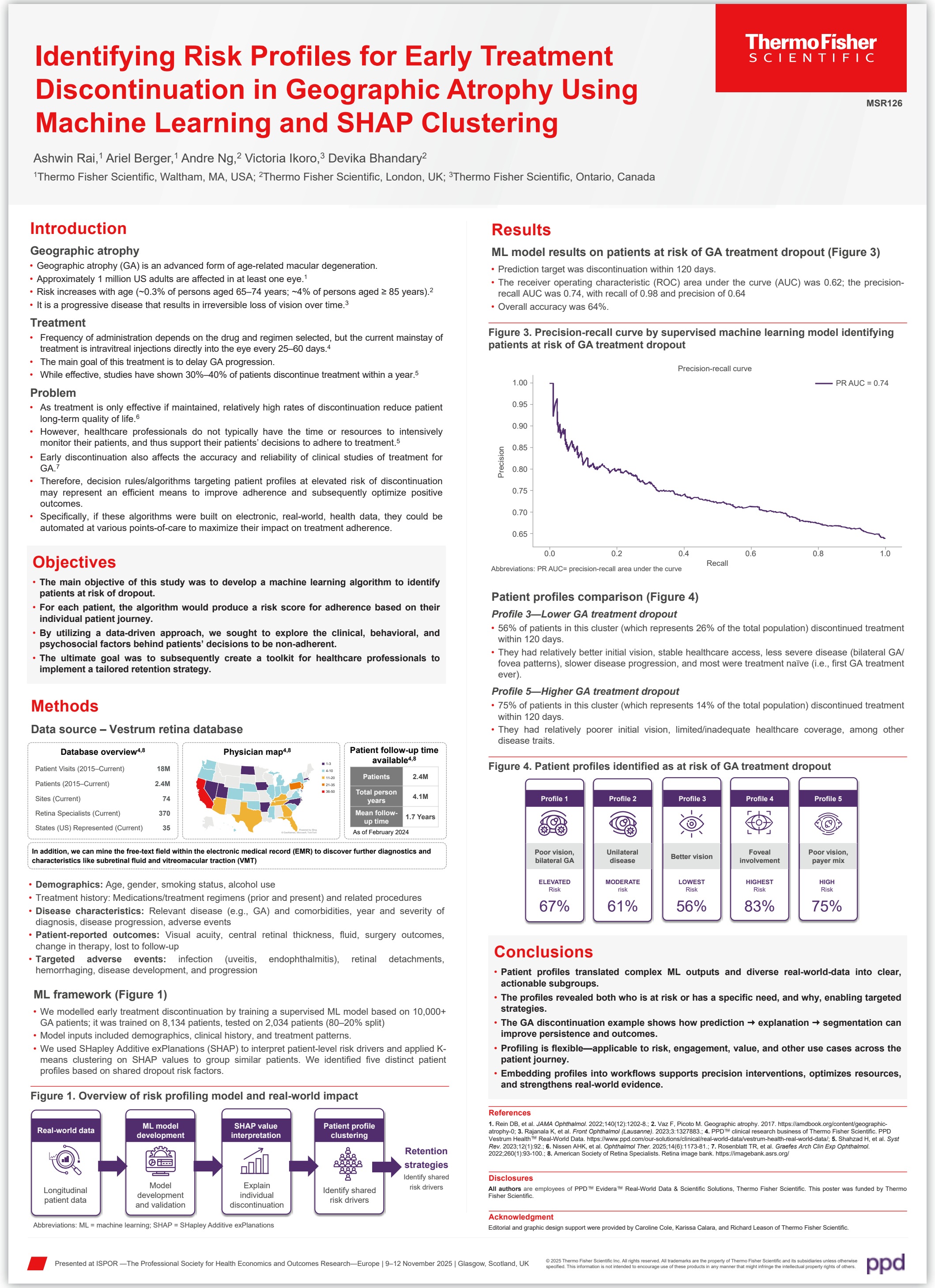

ISPOR EU 2025

9–12 November 2025 | Glasgow, Scotland, UK

Poster Title

Uncovering Patient Narratives of Opioid Use and Recovery Using Large Language Models for Topic and Emotion Analysis of Social Media

Objective

- To apply LLM–based topic modeling to patient-authored opioid-related discussions from online forums, identifying major themes in lived experience.
- To perform LLM-based emotion analysis across narratives, characterizing emotional burdens such as fear, sadness, hope, and relief.
- To generate scalable, interpretable insights from unstructured patient narratives that can inform tailored interventions, patient support resources, and health policy.

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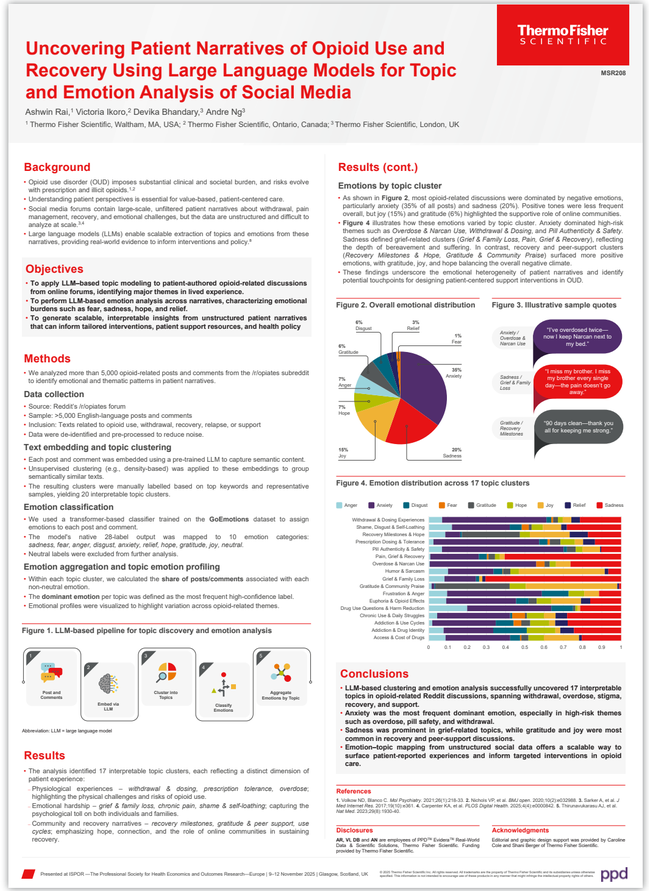

Uncovering Patient Narratives of Opioid Use and Recovery Using Large Language Models for Topic and Emotion Analysis of Social Media

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MSR208

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Background

- Opioid use disorder (OUD) imposes substantial clinical and societal burden, and risks evolve with prescription and illicit opioids.[1,2]
- Understanding patient perspectives is essential for value-based, patient-centered care.
- Social media forums contain large-scale, unfiltered patient narratives about withdrawal, pain management, recovery, and emotional challenges, but the data are unstructured and difficult to analyze at scale.[3,4]
- Large language models (LLMs) enable scalable extraction of topics and emotions from these narratives, providing real-world evidence to inform interventions and policy.[4]

Objectives

- **To apply LLM–based topic modeling to patient-authored opioid-related discussions from online forums, identifying major themes in lived experience.**
- **To perform LLM-based emotion analysis across narratives, characterizing emotional burdens such as fear, sadness, hope, and relief.**
- **To generate scalable, interpretable insights from unstructured patient narratives that can inform tailored interventions, patient support resources, and health policy**

Methods

- We analyzed more than 5,000 opioid-related posts and comments from the /r/opiates subreddit to identify emotional and thematic patterns in patient narratives.

Data collection

- Source: Reddit's /r/opiates forum
- Sample: >5,000 English-language posts and comments
- Inclusion: Texts related to opioid use, withdrawal, recovery, relapse, or support
- Data were de-identified and pre-processed to reduce noise.

Text embedding and topic clustering

- Each post and comment was embedded using a pre-trained LLM to capture semantic content.
- Unsupervised clustering (e.g., density-based) was applied to these embeddings to group semantically similar texts.
- The resulting clusters were manually labelled based on top keywords and representative samples, yielding 20 interpretable topic clusters.

Emotion classification

- We used a transformer-based classifier trained on the **GoEmotions** dataset to assign emotions to each post and comment.
- The model's native 28-label output was mapped to 10 emotion categories: *sadness, fear, anger, disgust, anxiety, relief, hope, gratitude, joy, neutral.*
- Neutral labels were excluded from further analysis.

Emotion aggregation and topic emotion profiling

- Within each topic cluster, we calculated the **share of posts/comments** associated with each non-neutral emotion.
- The **dominant emotion** per topic was defined as the most frequent high-confidence label.
- Emotional profiles were visualized to highlight variation across opioid-related themes.

Figure 1. LLM-based pipeline for topic discovery and emotion analysis

Abbreviation: LLM = large language model

Results

- The analysis identified 17 interpretable topic clusters, each reflecting a distinct dimension of patient experience:
  - Physiological experiences – *withdrawal & dosing, prescription tolerance, overdose*; highlighting the physical challenges and risks of opioid use.
  - Emotional hardship – *grief & family loss, chronic pain, shame & self-loathing*; capturing the psychological toll on both individuals and families.
  - Community and recovery narratives – *recovery milestones, gratitude & peer support, use cycles*; emphasizing hope, connection, and the role of online communities in sustaining recovery.

Results (cont.)

Emotions by topic cluster

- As shown in **Figure 2**, most opioid-related discussions were dominated by negative emotions, particularly anxiety (35% of all posts) and sadness (20%). Positive tones were less frequent overall, but joy (15%) and gratitude (6%) highlighted the supportive role of online communities.
- **Figure 4** illustrates how these emotions varied by topic cluster. Anxiety dominated high-risk themes such as *Overdose & Narcan Use, Withdrawal & Dosing,* and *Pill Authenticity & Safety*. Sadness defined grief-related clusters (*Grief & Family Loss, Pain, Grief & Recovery*), reflecting the depth of bereavement and suffering. In contrast, recovery and peer-support clusters (*Recovery Milestones & Hope, Gratitude & Community Praise*) surfaced more positive emotions, with gratitude, joy, and hope balancing the overall negative climate.
- These findings underscore the emotional heterogeneity of patient narratives and identify potential touchpoints for designing patient-centered support interventions in OUD.

Figure 2. Overall emotional distribution

Figure 3. Illustrative sample quotes

Figure 4. Emotion distribution across 17 topic clusters

Conclusions

- **LLM-based clustering and emotion analysis successfully uncovered 17 interpretable topics in opioid-related Reddit discussions, spanning withdrawal, overdose, stigma, recovery, and support.**
- **Anxiety was the most frequent dominant emotion, especially in high-risk themes such as overdose, pill safety, and withdrawal.**
- **Sadness was prominent in grief-related topics, while gratitude and joy were most common in recovery and peer-support discussions.**
- **Emotion–topic mapping from unstructured social data offers a scalable way to surface patient-reported experiences and inform targeted interventions in opioid care.**

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9–12 November 2025 | Glasgow, Scotland, UK

Poster Title

Enhancing Migraine Preference Research: Recommendations from a Systematic Review of Preference Studies

Objective

- To examine how preference studies are designed and reported in the context of migraine treatment, with the aim of informing the design and conduct of future studies.

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ISPOR EU 2025

9–12 November 2025 | Glasgow, Scotland, UK

Poster Title

Integrating Real-World Evidence into Oncology Health Technology Assessment Submissions: Recent EU Examples

Objective

- The aim of this research was to review RWE included in oncology HTA submissions in selected European countries and to identify barriers to its successful application.

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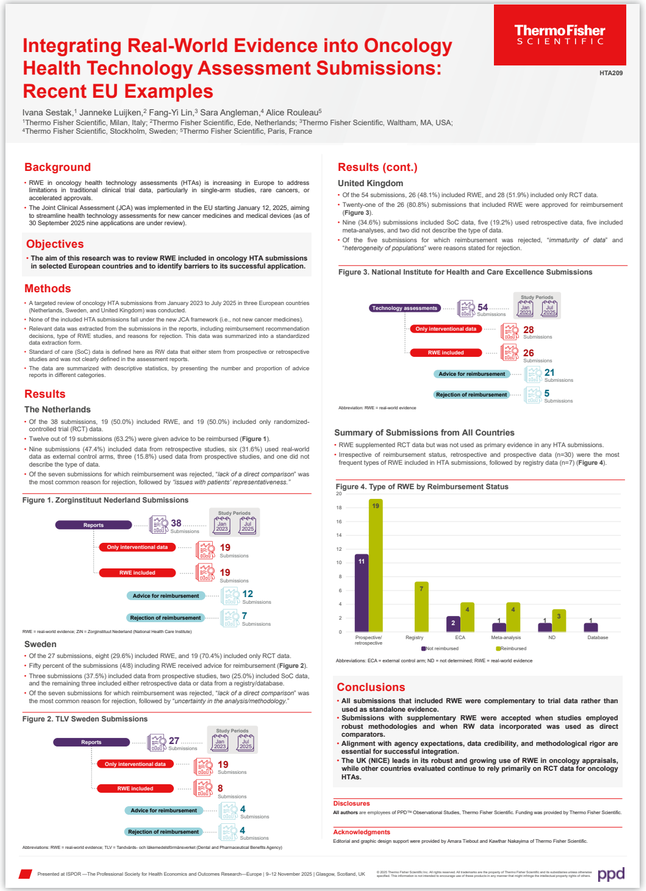

Integrating Real-World Evidence into Oncology Health Technology Assessment Submissions: Recent EU Examples

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HTA209

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Background

- RWE in oncology health technology assessments (HTAs) is increasing in Europe to address limitations in traditional clinical trial data, particularly in single-arm studies, rare cancers, or accelerated approvals.
- The Joint Clinical Assessment (JCA) was implemented in the EU starting January 12, 2025, aiming to streamline health technology assessments for new cancer medicines and medical devices (as of 30 September 2025 nine applications are under review).

Objectives

- **The aim of this research was to review RWE included in oncology HTA submissions in selected European countries and to identify barriers to its successful application.**

Methods

- A targeted review of oncology HTA submissions from January 2023 to July 2025 in three European countries (Netherlands, Sweden, and United Kingdom) was conducted.
- None of the included HTA submissions fall under the new JCA framework (i.e., not new cancer medicines).
- Relevant data was extracted from the submissions in the reports, including reimbursement recommendation decisions, type of RWE studies, and reasons for rejection. This data was summarized into a standardized data extraction form.
- Standard of care (SoC) data is defined here as RW data that either stem from prospective or retrospective studies and was not clearly defined in the assessment reports.
- The data are summarized with descriptive statistics, by presenting the number and proportion of advice reports in different categories.

Results

The Netherlands

- Of the 38 submissions, 19 (50.0%) included RWE, and 19 (50.0%) included only randomized-controlled trial (RCT) data.
- Twelve out of 19 submissions (63.2%) were given advice to be reimbursed (**Figure 1**).
- Nine submissions (47.4%) included data from retrospective studies, six (31.6%) used real-world data as external control arms, three (15.8%) used data from prospective studies, and one did not describe the type of data.
- Of the seven submissions for which reimbursement was rejected, "*lack of a direct comparison*" was the most common reason for rejection, followed by "*issues with patients' representativeness.*"

Figure 1. Zorginstituut Nederland Submissions

RWE = real-world evidence; ZIN = Zorginstituut Nederland (National Health Care Institute)

Sweden

- Of the 27 submissions, eight (29.6%) included RWE, and 19 (70.4%) included only RCT data.
- Fifty percent of the submissions (4/8) including RWE received advice for reimbursement (**Figure 2**).
- Three submissions (37.5%) included data from prospective studies, two (25.0%) included SoC data, and the remaining three included either retrospective data or data from a registry/database.
- Of the seven submissions for which reimbursement was rejected, "*lack of a direct comparison*" was the most common reason for rejection, followed by "*uncertainty in the analysis/methodology.*"

Figure 2. TLV Sweden Submissions

Abbreviations: RWE = real-world evidence; TLV = Tandvårds- och läkemedelsförmånsverket (Dental and Pharmaceutical Benefits Agency)

Results (cont.)

United Kingdom

- Of the 54 submissions, 26 (48.1%) included RWE, and 28 (51.9%) included only RCT data.
- Twenty-one of the 26 (80.8%) submissions that included RWE were approved for reimbursement (**Figure 3**).
- Nine (34.6%) submissions included SoC data, five (19.2%) used retrospective data, five included meta-analyses, and two did not describe the type of data.
- Of the five submissions for which reimbursement was rejected, "*immaturity of data*" and "*heterogeneity of populations*" were reasons stated for rejection.

Figure 3. National Institute for Health and Care Excellence Submissions

Abbreviation: RWE = real-world evidence

Summary of Submissions from All Countries

- RWE supplemented RCT data but was not used as primary evidence in any HTA submissions.
- Irrespective of reimbursement status, retrospective and prospective data (n=30) were the most frequent types of RWE included in HTA submissions, followed by registry data (n=7) (**Figure 4**).

Figure 4. Type of RWE by Reimbursement Status

Abbreviations: ECA = external control arm; ND = not determined; RWE = real-world evidence

Conclusions

- **All submissions that included RWE were complementary to trial data rather than used as standalone evidence.**
- **Submissions with supplementary RWE were accepted when studies employed robust methodologies and when RW data incorporated was used as direct comparators.**
- **Alignment with agency expectations, data credibility, and methodological rigor are essential for successful integration.**
- **The UK (NICE) leads in its robust and growing use of RWE in oncology appraisals, while other countries evaluated continue to rely primarily on RCT data for oncology HTAs.**

Disclosures

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Poster Title

Evaluating High-cost Gene Therapies for Non-cancer Conditions: Insights From NICE's Standard Appraisal Process

Objective

- To assess the factors considered during NICE's appraisals of gene therapies for non-cancer conditions via standard STA and to determine whether the Innovative Medicines Fund (IMF) was employed to enable NICE's recommendations for high-cost, non-cancer therapies that do not meet the criteria for HST.

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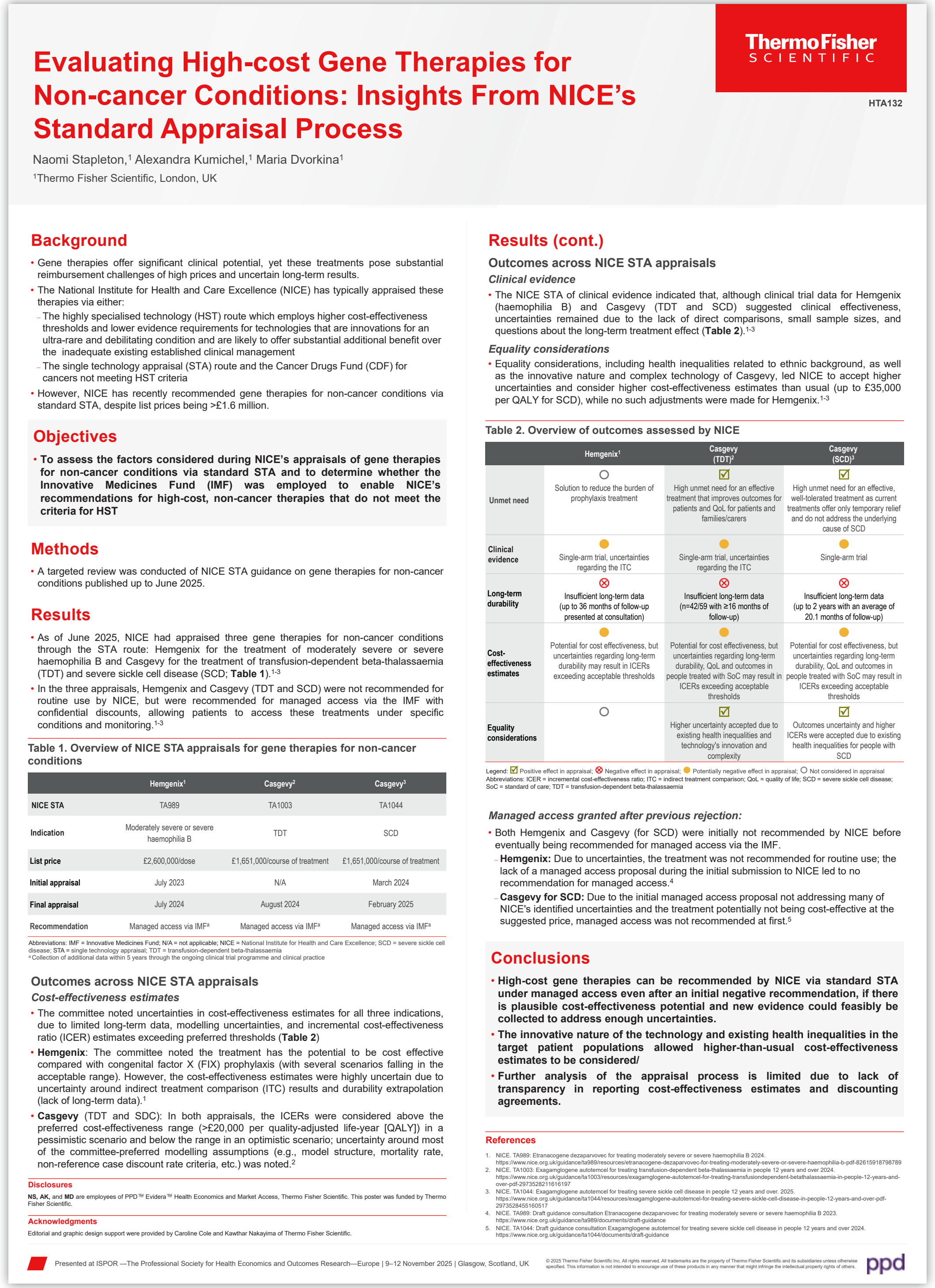

Evaluating High-cost Gene Therapies for Non-cancer Conditions: Insights From NICE's Standard Appraisal Process

HTA132

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Background

- Gene therapies offer significant clinical potential, yet these treatments pose substantial reimbursement challenges of high prices and uncertain long-term results.
- The National Institute for Health and Care Excellence (NICE) has typically appraised these therapies via either:
  - The highly specialised technology (HST) route which employs higher cost-effectiveness thresholds and lower evidence requirements for technologies that are innovations for an ultra-rare and debilitating condition and are likely to offer substantial additional benefit over the inadequate existing established clinical management
  - The single technology appraisal (STA) route and the Cancer Drugs Fund (CDF) for cancers not meeting HST criteria
- However, NICE has recently recommended gene therapies for non-cancer conditions via standard STA, despite list prices being >£1.6 million.

Objectives

- **To assess the factors considered during NICE's appraisals of gene therapies for non-cancer conditions via standard STA and to determine whether the Innovative Medicines Fund (IMF) was employed to enable NICE's recommendations for high-cost, non-cancer therapies that do not meet the criteria for HST**

Methods

- A targeted review was conducted of NICE STA guidance on gene therapies for non-cancer conditions published up to June 2025.

Results

- As of June 2025, NICE had appraised three gene therapies for non-cancer conditions through the STA route: Hemgenix for the treatment of moderately severe or severe haemophilia B and Casgevy for the treatment of transfusion-dependent beta-thalassaemia (TDT) and severe sickle cell disease (SCD; **Table 1**).[1-3]
- In the three appraisals, Hemgenix and Casgevy (TDT and SCD) were not recommended for routine use by NICE, but were recommended for managed access via the IMF with confidential discounts, allowing patients to access these treatments under specific conditions and monitoring.[1-3]

Table 1. Overview of NICE STA appraisals for gene therapies for non-cancer conditions

	Hemgenix[1]	Casgevy[2]	Casgevy[3]
NICE STA	TA989	TA1003	TA1044
Indication	Moderately severe or severe haemophilia B	TDT	SCD
List price	£2,600,000/dose	£1,651,000/course of treatment	£1,651,000/course of treatment
Initial appraisal	July 2023	N/A	March 2024
Final appraisal	July 2024	August 2024	February 2025
Recommendation	Managed access via IMF[a]	Managed access via IMF[a]	Managed access via IMF[a]

Abbreviations: IMF = Innovative Medicines Fund; N/A = not applicable; NICE = National Institute for Health and Care Excellence; SCD = severe sickle cell disease; STA = single technology appraisal; TDT = transfusion-dependent beta-thalassaemia
[a] Collection of additional data within 5 years through the ongoing clinical trial programme and clinical practice

Outcomes across NICE STA appraisals

Cost-effectiveness estimates

- The committee noted uncertainties in cost-effectiveness estimates for all three indications, due to limited long-term data, modelling uncertainties, and incremental cost-effectiveness ratio (ICER) estimates exceeding preferred thresholds (**Table 2**)
- **Hemgenix**: The committee noted the treatment has the potential to be cost effective compared with congenital factor X (FIX) prophylaxis (with several scenarios falling in the acceptable range). However, the cost-effectiveness estimates were highly uncertain due to uncertainty around indirect treatment comparison (ITC) results and durability extrapolation (lack of long-term data).[1]
- **Casgevy** (TDT and SDC): In both appraisals, the ICERs were considered above the preferred cost-effectiveness range (>£20,000 per quality-adjusted life-year [QALY]) in a pessimistic scenario and below the range in an optimistic scenario; uncertainty around most of the committee-preferred modelling assumptions (e.g., model structure, mortality rate, non-reference case discount rate criteria, etc.) was noted.[2]

Disclosures

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Results (cont.)

Outcomes across NICE STA appraisals

Clinical evidence

- The NICE STA of clinical evidence indicated that, although clinical trial data for Hemgenix (haemophilia B) and Casgevy (TDT and SCD) suggested clinical effectiveness, uncertainties remained due to the lack of direct comparisons, small sample sizes, and questions about the long-term treatment effect (**Table 2**).[1-3]

Equality considerations

- Equality considerations, including health inequalities related to ethnic background, as well as the innovative nature and complex technology of Casgevy, led NICE to accept higher uncertainties and consider higher cost-effectiveness estimates than usual (up to £35,000 per QALY for SCD), while no such adjustments were made for Hemgenix.[1-3]

Table 2. Overview of outcomes assessed by NICE

	Hemgenix[1]	Casgevy (TDT)[2]	Casgevy (SCD)[3]
Unmet need	○ Solution to reduce the burden of prophylaxis treatment	☑ High unmet need for an effective treatment that improves outcomes for patients and QoL for patients and families/carers	☑ High unmet need for an effective, well-tolerated treatment as current treatments offer only temporary relief and do not address the underlying cause of SCD
Clinical evidence	● Single-arm trial, uncertainties regarding the ITC	● Single-arm trial, uncertainties regarding the ITC	● Single-arm trial
Long-term durability	⊗ Insufficient long-term data (up to 36 months of follow-up presented at consultation)	⊗ Insufficient long-term data (n=42/59 with ≥16 months of follow-up)	⊗ Insufficient long-term data (up to 2 years with an average of 20.1 months of follow-up)
Cost-effectiveness estimates	● Potential for cost effectiveness, but uncertainties regarding long-term durability may result in ICERs exceeding acceptable thresholds	● Potential for cost effectiveness, but uncertainties regarding long-term durability, QoL and outcomes in people treated with SoC may result in ICERs exceeding acceptable thresholds	● Potential for cost effectiveness, but uncertainties regarding long-term durability, QoL and outcomes in people treated with SoC may result in ICERs exceeding acceptable thresholds
Equality considerations	○	☑ Higher uncertainty accepted due to existing health inequalities and technology's innovation and complexity	☑ Outcomes uncertainty and higher ICERs were accepted due to existing health inequalities for people with SCD

Legend: ☑ Positive effect in appraisal; ⊗ Negative effect in appraisal; ● Potentially negative effect in appraisal; ○ Not considered in appraisal
Abbreviations: ICER = incremental cost-effectiveness ratio; ITC = indirect treatment comparison; QoL = quality of life; SCD = severe sickle cell disease; SoC = standard of care; TDT = transfusion-dependent beta-thalassaemia

Managed access granted after previous rejection:

- Both Hemgenix and Casgevy (for SCD) were initially not recommended by NICE before eventually being recommended for managed access via the IMF.
  - **Hemgenix:** Due to uncertainties, the treatment was not recommended for routine use; the lack of a managed access proposal during the initial submission to NICE led to no recommendation for managed access.[4]
  - **Casgevy for SCD:** Due to the initial managed access proposal not addressing many of NICE's identified uncertainties and the treatment potentially not being cost-effective at the suggested price, managed access was not recommended at first.[5]

Conclusions

- **High-cost gene therapies can be recommended by NICE via standard STA under managed access even after an initial negative recommendation, if there is plausible cost-effectiveness potential and new evidence could feasibly be collected to address enough uncertainties.**
- **The innovative nature of the technology and existing health inequalities in the target patient populations allowed higher-than-usual cost-effectiveness estimates to be considered/**
- **Further analysis of the appraisal process is limited due to lack of transparency in reporting cost-effectiveness estimates and discounting agreements.**

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Poster Title

Enhancing Targeted Literature Reviews (TLRs) with Artificial Intelligence (AI): A Methodological Approach for Conducting Efficient Targeted Searches

Objective

- To describe the approach used for TLRs on a variety of topics using Advancement Probability and estimate time-savings.

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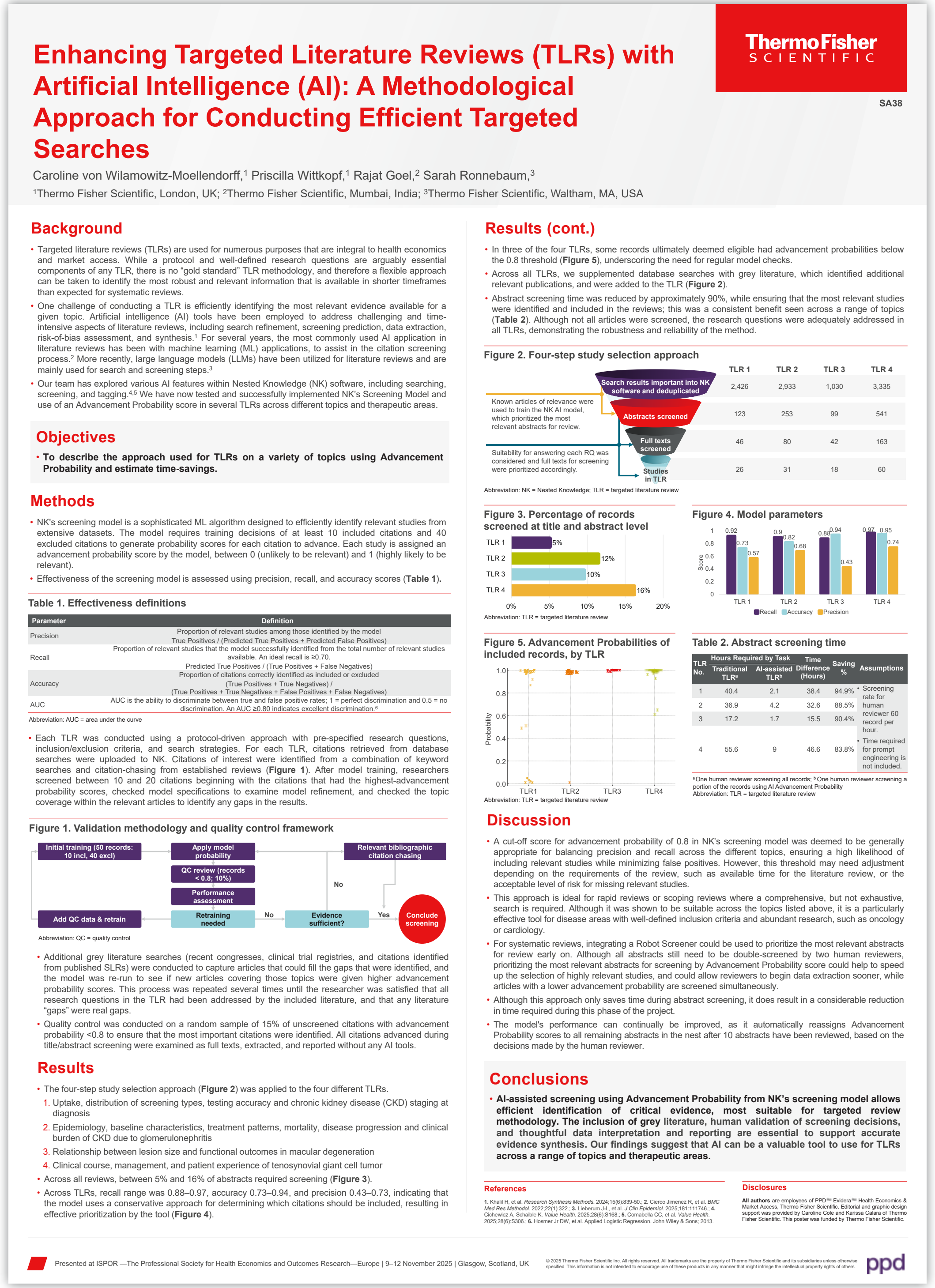

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Poster Title

Navigating Evidence Requirements for Joint Clinical Assessment (JCA): Practical Considerations for Systematic Literature Reviews (SLRs) and Indirect Treatment Comparisons (ITCs)

Objective

- Outline key methodological differences in systematic literature review (SLR) and indirect treatment comparison (ITC) requirements between the MS Coordination Group on Health Technology Assessment (HTA CG),[2] NICE,[3] and Cochrane[4].
- Discuss practical considerations for conducting JCA-compliant SLRs and ITCs.

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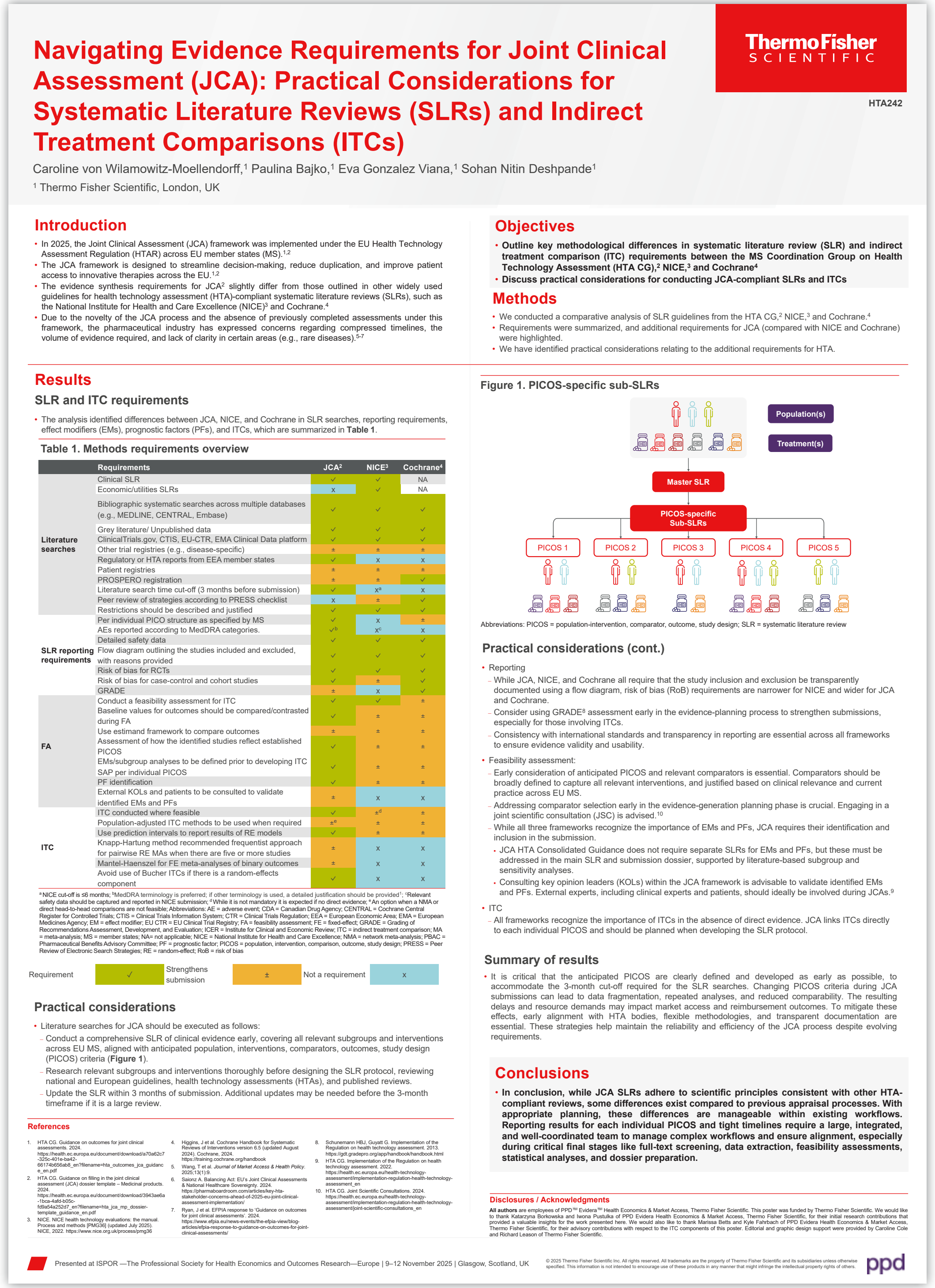

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Poster Title

Cost Implications of Declining MMR Coverage in England: Modelling NHS Burden and the Value of Catch-Up Vaccination

Objective

- The primary objectives were to estimate (1) NHS and societal costs associated with reduced MMR coverage since 2019/2020; (2) the cost of delivering catch-up vaccination to unprotected children; and (3) the future economic burden if the observed decline continues.

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