
# UKDCTN Journal Club April 2026

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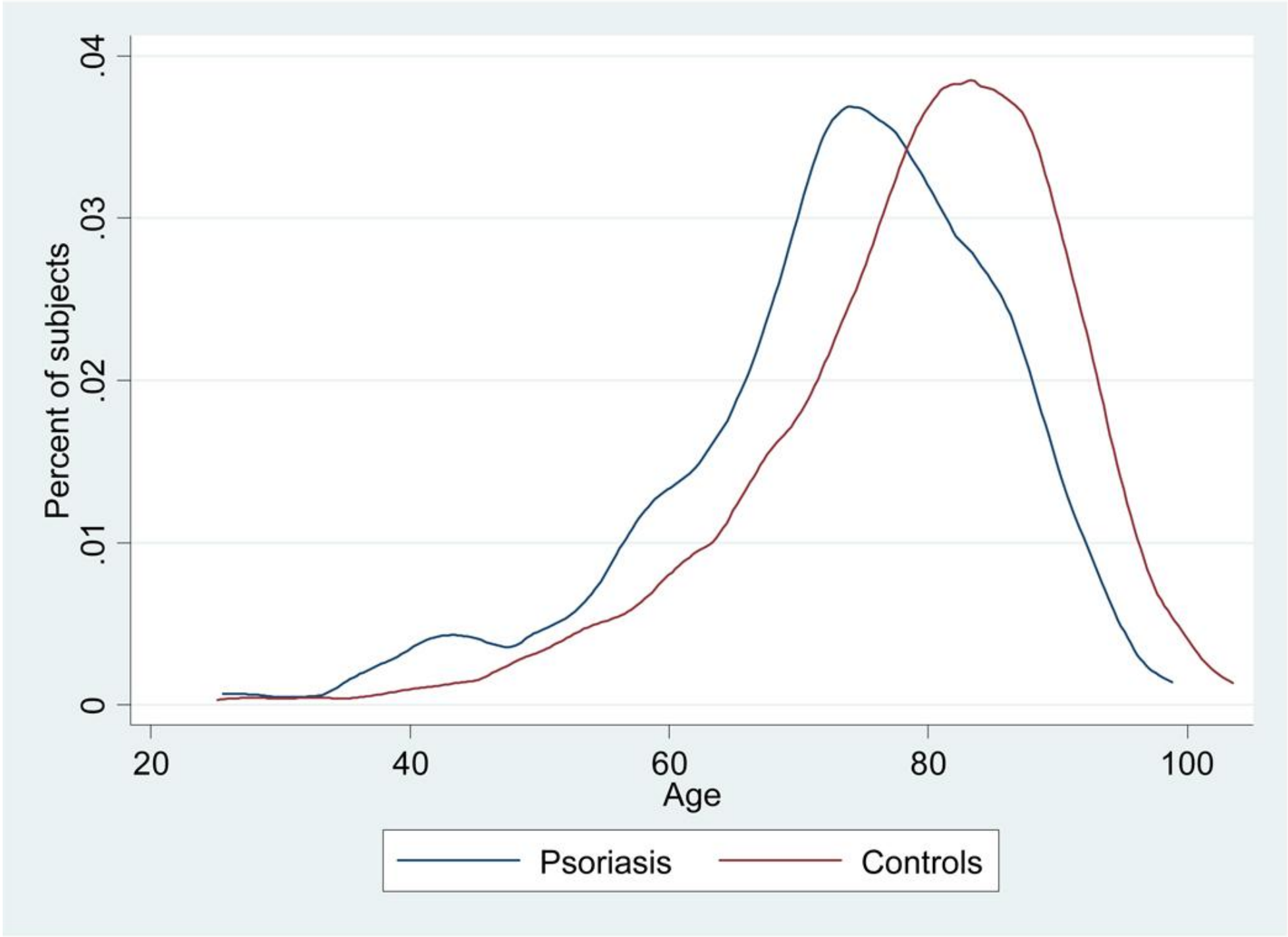
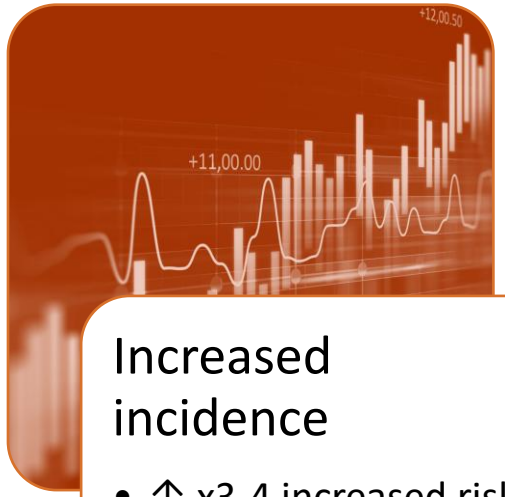



**Abuabara *et al.*** *Cause-specific mortality in patients with severe psoriasis: a population-based cohort study in the U.K.* ***Br J Dermatol*****.**

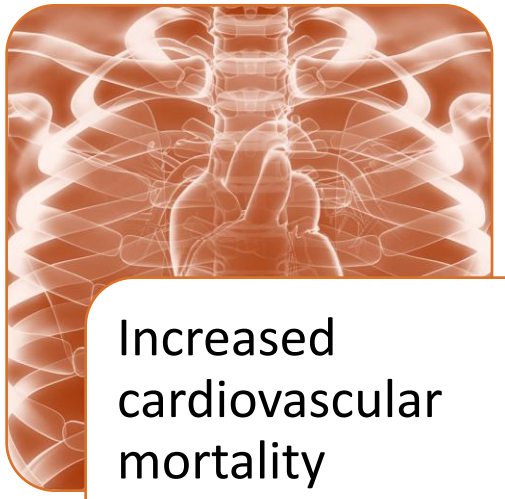
# Cardiovascular comorbidity in psoriasis




## Increased incidence

- ↑ x3-4 increased risk of stroke
- ↑ x4-5 increased risk of myocardial infarction

Gelfand *et al* 2006
Gelfand *et al* 2009



## Increased cardiovascular mortality

- 3.5 excess deaths from cardiovascular disease in psoriasis per 1000 patient-years

Abuabara *et al* 2010

# UKDCTN Journal Club April 2026

BJD Improving patient outcomes in skin disease worldwide

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Volume 194, Issue 1
January 2026

## Article Contents



JOURNAL ARTICLE EDITOR'S CHOICE

# Glucagon-like peptide-1 receptor agonists and reduced mortality, cardiovascular and psychiatric risks in patients with psoriasis: a large-scale cohort study

Henning Olbrich, Khalaf Kridin, Henner Zirpel, Gema Hernandez, Christian D Sadik, Evelyn Gaffal, Diamant Thaçi, Ralf J Ludwig

*British Journal of Dermatology*, Volume 194, Issue 1, January 2026, Pages 59–66,
https://doi.org/10.1093/bjd/ljaf346
**Published:** 03 September 2025 **Article history**

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## Abstract

### Background

# Hypothesis and research questions

**Background:**

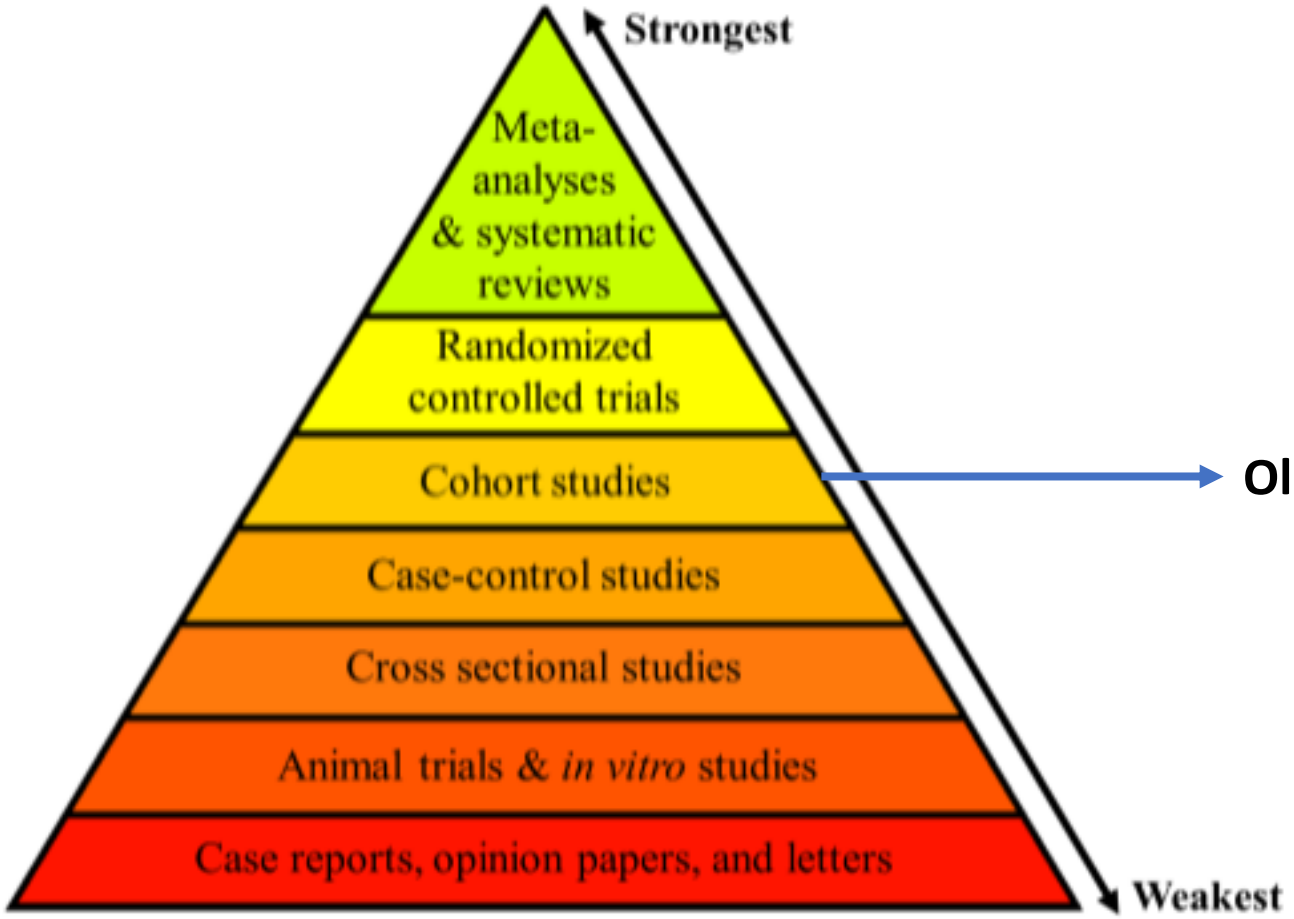
“GLP-1RAs could potentially reduce comorbidities in patients with psoriasis”

“Recent real-world data have also shown reduced risks of certain psychiatric complications, such as suicidal ideations and drug abuse”

**Hypothesis:**

“We hypothesized that patients with psoriasis could benefit from GLP-1RA treatment due to their special comorbidity risk”

# Hierarchy of evidence




**Olbrich *et al* 2026**

# RCT evidence

## 1. Does GLP-1RA treatment reduce the risk of cardiovascular events?

ORIGINAL ARTICLE

### Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes

**Authors**: A. Michael Lincoff, M.D. , Kirstine Brown-Frandsen, M.D., Helen M. Colhoun, M.D., John Deanfield, M.D., Scott S. Emerson, M.D., Ph.D., Sille Esbjerg, M.Sc., Søren Hardt-Lindberg, M.D., Ph.D., +9 , for the SELECT Trial Investigators* Author Info & Affiliations

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CURRENT ISSUE SPECIALTIES TOPICS

ORIGINAL ARTICLE

### Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes

**Authors**: Steven P. Marso, M.D., Gilbert H. Daniels, M.D., Kirstine Brown-Frandsen, M.D., Peter Kristensen, M.D., E.M.B.A., Johannes F.E. Mann, M.D., Michael A. Nauck, M.D., Steven E. Nissen, M.D., +8 , for the LEADER Steering Committee on behalf of the LEADER Trial Investigators* Author Info & Affiliations

Published July 28, 2016 | N Engl J Med 2016;375:311-322 | DOI: 10.1056/NEJMoa1603827 | VOL. 375 NO. 4
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ARTICLES · Volume 394, Issue 10193, P121-130, July 13, 2019 Download Full Issue

### Dulaglutide and cardiovascular outcomes in type 2 diabetes (REWIND): a double-blind, randomised placebo-controlled trial

Prof Hertzel C Gerstein, MD [a] · Prof Helen M Colhoun, MD [b] · Prof Gilles R Dagenais, MD [c] · Rafael Diaz, MD [d] · Mark Lakshmanan, MD [e] · Prof Prem Pais, MD [f] · et al. Show more

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## 2. Does GLP-1RA treatment reduce the risk of mental health outcomes?

JAMA Psychiatry

Home Issues Multimedia

Home | JAMA Psychiatry | Vol. 82, No. 7

Original Investigation

### Glucagon-Like Peptide 1 Receptor Agonists and Mental Health

A Systematic Review and Meta-Analysis

Aureliane C. S. Pierret, MBBChir[1,2,12]; Yuya Mizuno, PhD[2,8,9]; Pippa Saunders, BSc[4]; et al

Author Affiliations | Article Information

## 3. Does GLP-1RA treatment reduce the mortality risk?

ARTICLES · Volume 9, Issue 10, P653-662, October 2021 Download Full Issue

### Cardiovascular, mortality, and kidney outcomes with GLP-1 receptor agonists in patients with type 2 diabetes: a systematic review and meta-analysis of randomised trials

Prof Naveed Sattar, MD [a,†] · Matthew M Y Lee, MBChB [a,†] · Søren L Kristensen, MD [b,†] · Prof Kelley R H Branch, MD [c] · Prof Stefano Del Prato, MD [d] · Nardev S Khurmi, MD [e] · et al. Show more

Affiliations & Notes Article Info Linked Articles (1)

# Hypothesis and research questions

**Background:**

“GLP-1RAs could potentially reduce comorbidities in patients with psoriasis”

“Recent real-world data have also shown reduced risks of certain psychiatric complications, such as suicidal ideations and drug abuse”

**Hypothesis:**

“We hypothesized that patients with psoriasis could benefit from GLP-1RA treatment due to their special comorbidity risk”

**Research questions:**

What is the biological effect of GLP1RA treatment on major forms of comorbidity in people with psoriasis?

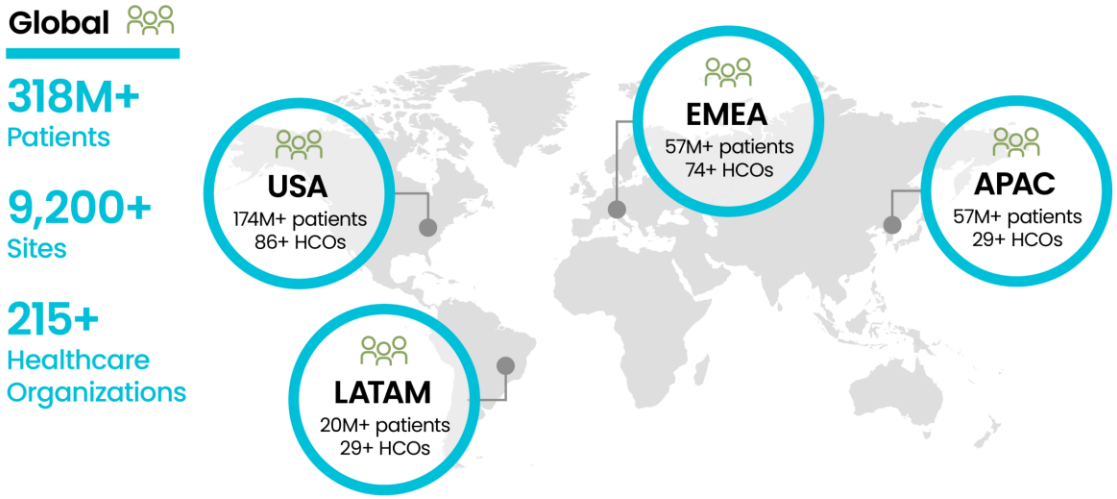
# Study breakdown (SPICO)

**Study design:**

Retrospective cohort study

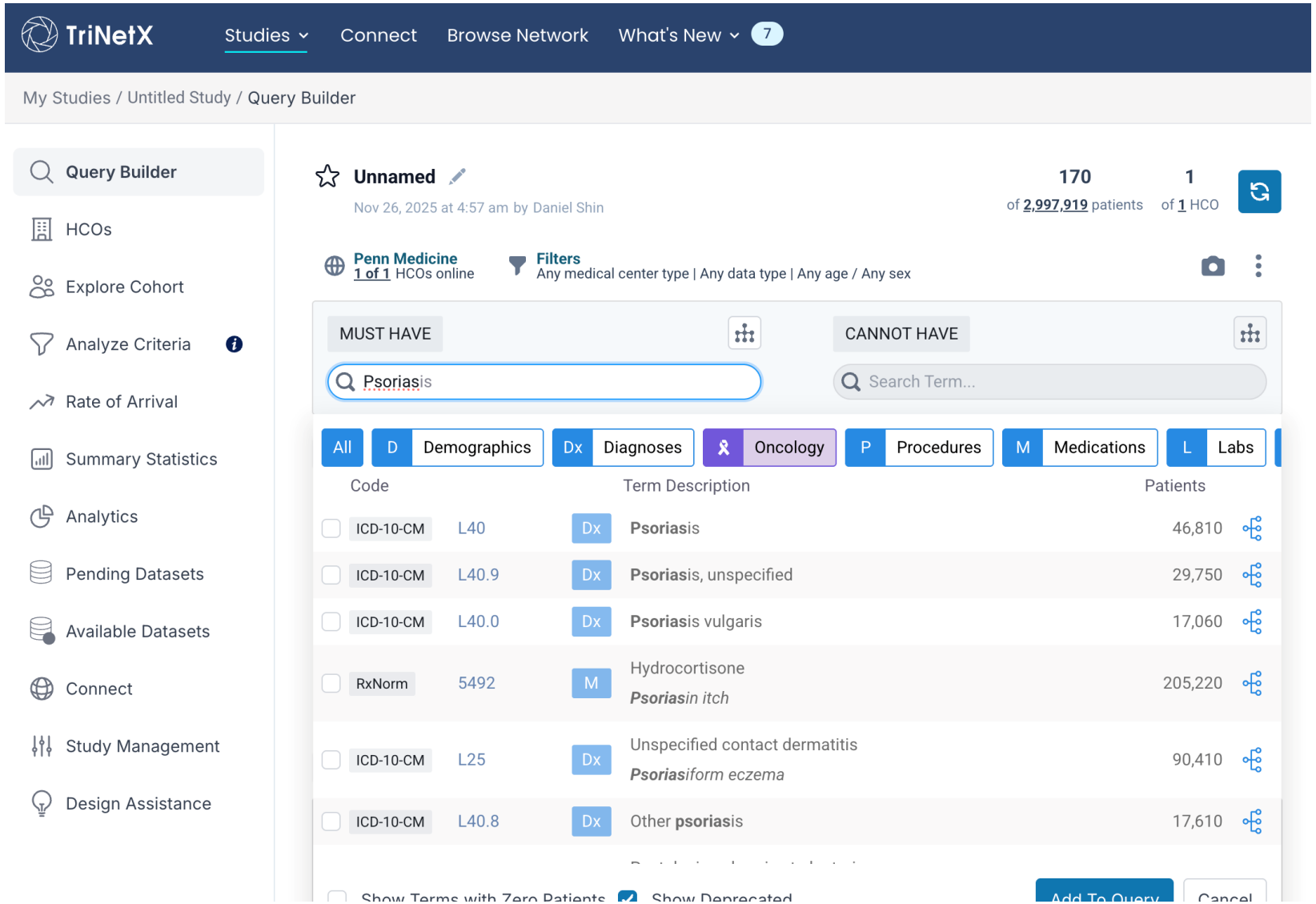
**Population/ participants:**

# TriNetX dataset




- Federated electronic health record (EHR) network providing real-time access to de-identified data from healthcare organisations worldwide.
- 150 million patient records, 128 organisations across 17 countries (as of 2024).
- **Exposures:** Medications (e.g. biologics) or disease exposures (e.g., psoriasis)
- **Outcomes:** Adverse events or diseases
- Includes an in-built propensity-score matching tool to balance measured covariates between treatment groups.
- **Strengths:** scale, speed, and accessibility.

# TriNetX dataset



# Study breakdown (SPICO)

**Study design:**

Retrospective cohort study

**Population/ participants:**

Adults (≥18 years) with psoriasis and obesity or type 2 diabetes from the US TriNetX network (>110 million EHRs), with 3048 patients per group after propensity score matching (initially 3636 vs 8410)

- *Psoriasis (L40), type 2 diabetes (E08–E13), and obesity (E65–E68) defined using ICD-10 codes from encounters*

**Exposure/ Comparator:**

GLP-1RA Tx for ≥24 months

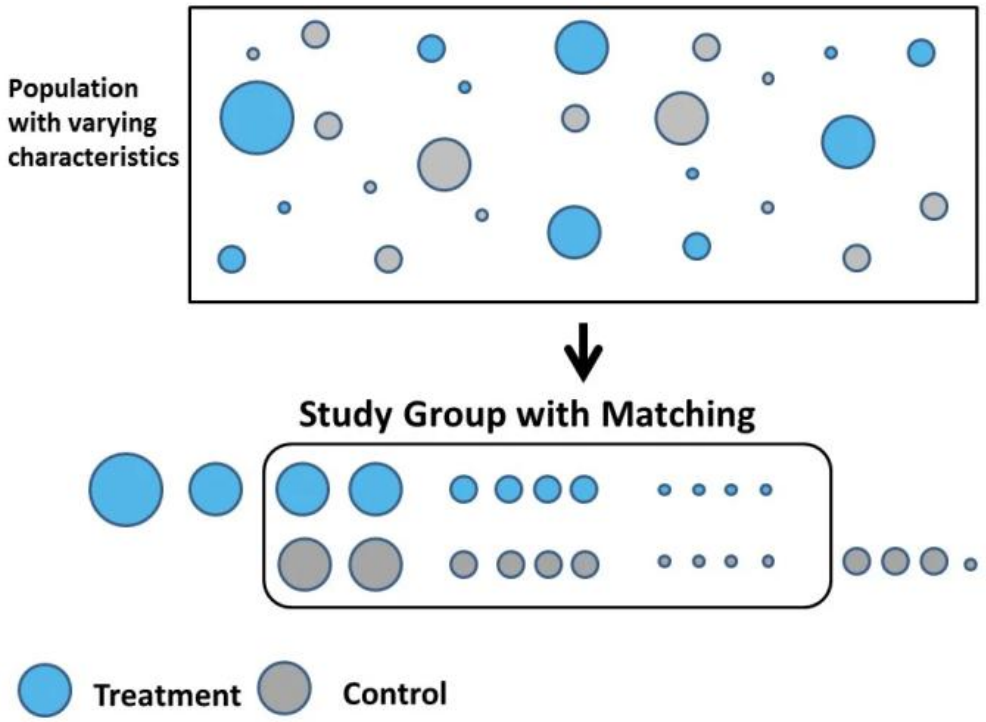
vs

Other systemic antidiabetic or anti-obesity medications

**Outcomes:**
*(Up to 2-year follow-up after treatment initiation)*

- MACE (major adverse cardiovascular events)
- Psychiatric outcomes: *alcohol abuse, substance abuse, and suicidal ideation*
- All-cause mortality
- Autoimmune outcomes: *IBD and uveitis*
- Adverse drug events

# Confounding




- **1:1 propensity score matching using logistic regression–derived scores**
  - Included demographics (age, sex, race, socioeconomic factors)
  - Included cardiometabolic comorbidities (e.g. hypertension, diabetes, obesity, dyslipidaemia)
  - Included psychiatric conditions (e.g. mood and anxiety disorders, substance use)
  - Included other major diseases and medication use (including insulin)
- Achieved good post-matching balance

# Results

MACE (major adverse cardiovascular events)

**Reduction in MACE:**
Composite MACE: HR **0.561** (95% CI 0.442–0.714; P<0.001)
Heart failure: HR **0.534** (95% CI 0.408–0.700; P<0.001)
Stroke: HR **0.352** (95% CI 0.228–0.542; P<0.0001)

Psychiatric outcomes: *alcohol abuse, substance abuse, and suicidal ideation*

**Reduction in Psychiatric outcomes:**
Alcohol abuse: HR **0.346** (95% CI 0.174–0.685; P=0.009)
Substance abuse: HR **0.510** (95% CI 0.350–0.743; P=0.002)
Suicidal ideation: **not statistically significant**

All-cause mortality

**Reduction in all-cause mortality:**
HR **0.219** (95% CI 0.123–0.391; P<0.001)

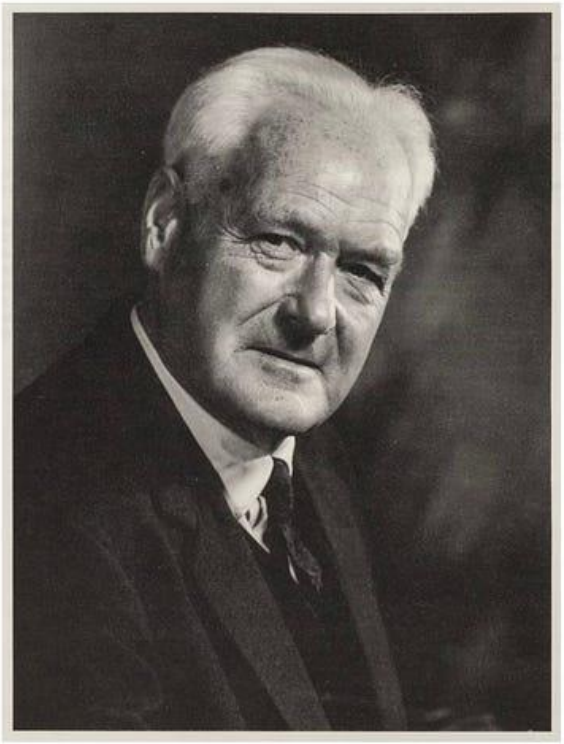
Autoimmune outcomes: *IBD and uveitis*

**Autoimmune outcomes:**
Crohn disease, ulcerative colitis, uveitis: **no significant difference**

Adverse drug events

**Adverse drug events**
Hypoglycaemia, nausea/vomiting, constipation: **no increased risk**

# Example of evidentiary criteria (from epidemiology)



**The Environment and Disease: Association or Causation?**

by Sir Austin Bradford Hill CBE DSC FRCP(hon) FRS
(*Professor Emeritus of Medical Statistics, University of London*)

*Proceedings of the Royal Society of Medicine* *Meeting January 14 1965*

**Strength:** Strong association hints at causality.

**Consistency:** Findings repeat across studies/populations.

**Specificity:** Association tied to a specific cause-effect combination.

**Temporality:** Cause comes before effect.

**Dose-response gradient:** Effect rises with greater exposure.

**Plausibility:** Reasonable mechanism established or theorised.

**Coherence:** No major conflict with existing knowledge.

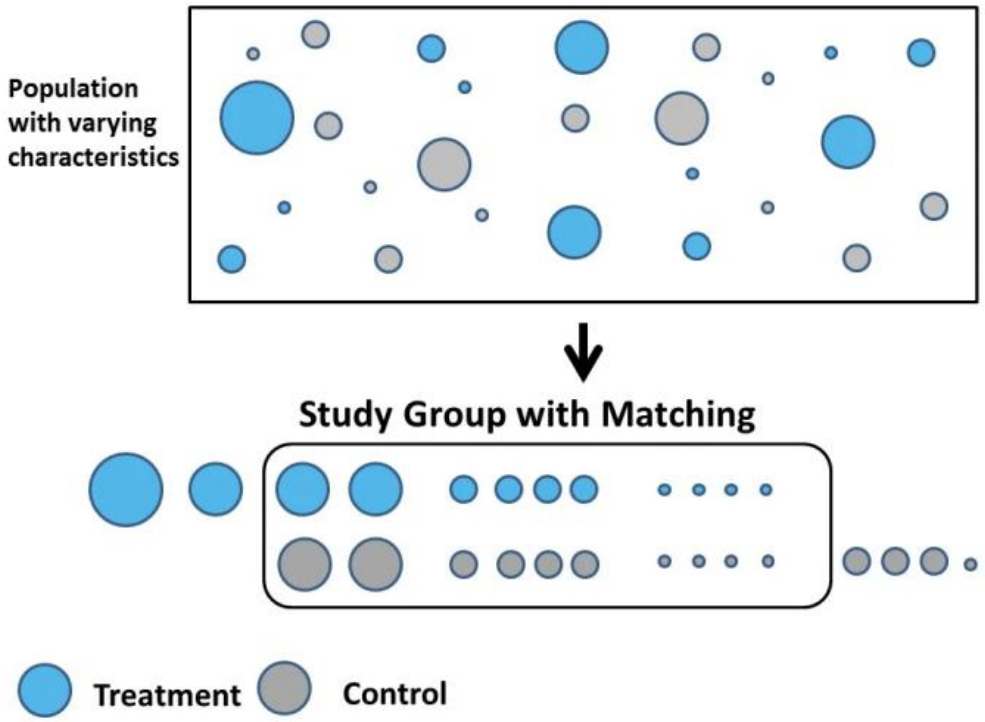
**Experiment:** Testing cause through any intervention (RCT, FAFO, etc).

**Analogy:** Causal link seen in similar situations.

**Alternative explanations:** Chance, bias, confounding considered.

# Limitations: Sources of bias

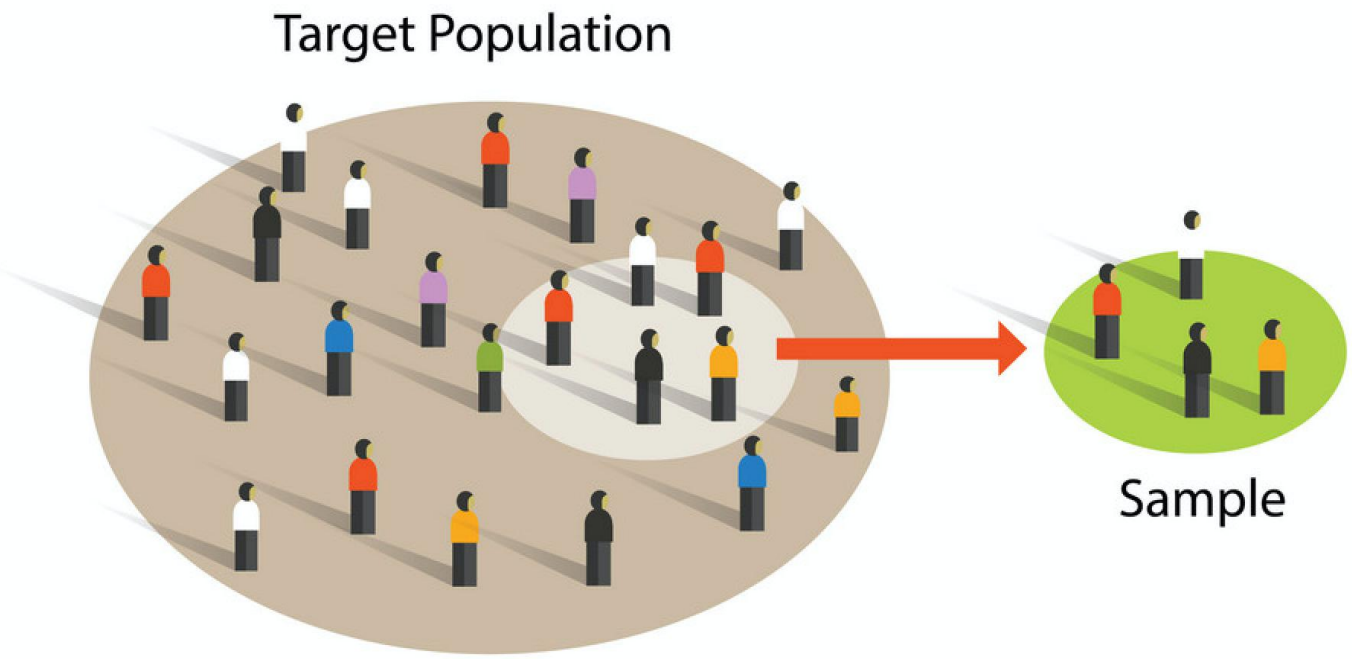
**Confounding** | **Selection bias** | **Information bias**




- **Only adjusts for measured variables** → key factors like psoriasis severity, lifestyle, adherence not captured
- **EHR data incomplete/misaligned** → important covariates may be missing or misclassified (information bias)
- No control for unmeasured socioeconomic or healthcare engagement factors

# Limitations: Sources of bias

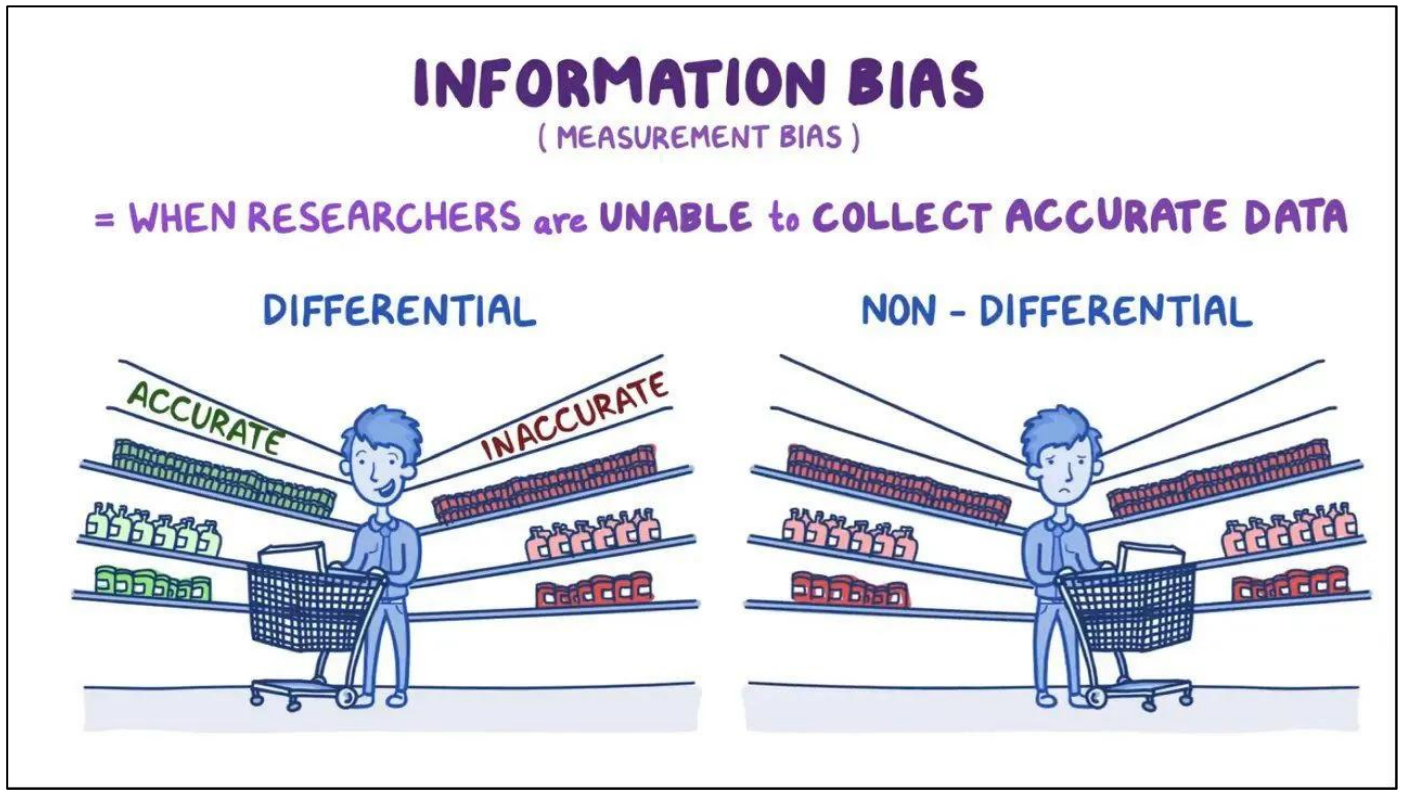
**Confounding** | **Selection bias** | **Information bias**




- **Over-representation of hospital/academic populations** → more severe disease (75% from academic centres)
- High healthcare utilisers more likely captured (Missing not at random bias)

# Limitations: Sources of bias

**Confounding** | **Selection bias** | **Information bias**




- **Misclassification from ICD coding** (diagnoses may be inaccurate/inconsistent)
- **Exposure misclassification** (prescriptions ≠ actual use/adherence)
- **Outcome misclassification** (events outside network not recorded)

# Take home points

- Start with the **research question/hypothesis**
- Break the study into key elements:
  - **Population, exposure, comparator**
  - **Outcomes**
  - **Confounding + how it was managed**
  - **Sources of selection and information bias**
- Ask: **do the results make sense?** (e.g. Bradford Hill – plausibility)
- **Do not take findings at face value** → interpret in context of bias and design
- **Build skill with practice** → aim to read one paper regularly (e.g. BJD epidemiology)