**The association between types of meat consumption and the risk of type 2 diabetes: a federated meta-analysis in the InterConnect project**

## The scientific rationale for the research question

Several meta-analyses of prospective cohort studies have shown that red and processed meat consumption is associated with increased risk of type 2 diabetes (T2D) [1-8]. However, these meta-analyses showed a high degree of heterogeneity, the reasons for which remain unclear[2,4,8]. Several factors may contribute, including differences in serving size, definition of meat consumption, extent of adjustment for potential confounders, or a general lack of standardisation or harmonisation for methods and variables.

In contrast to the extensive information base for red and processed meat, there is only sparse knowledge on the association of poultry consumption with T2D[3,9-12] and the association was not significant in a recent meta-analysis[13]. This evidence needs to be updated with a greater number of studies and a standardised assessment method because poultry consumption is crucial as one of the alternatives for red and processed meat consumption as a source of protein.

The available evidence from the literature-based meta-analyses was predominantly from North America and Europe, with only a few from Asia and Australia, and almost none from other areas[2,4,5,7,8]. Not currently available, but individual-participant data analysis of populations around the world would be ideal, given the rapid increase in meat consumption in non-Western populations[14,15].

Therefore, we aim to explore the association between consumption of different types of meat and T2D risk using individual-level data with the InterConnect project. InterConnect[I] is an EU funded project (FP7 grant 602068) led by the MRC Epidemiology Unit. This project seeks to optimise the use of existing data to enable new research into the causes of diabetes and obesity. A federated meta-analytical approach is used in InterConnect to 'take the analysis to the data' so that we can enable efficient analyses of individual-level data, without the need for data to leave the local data system.

In this study, we will explore the association between consumption of different types of meat and T2D incidence globally by considering geographical variation in meat consumption and T2D incidence. In addition, we will standardise the definitions for different types of meat consumption, harmonise exposure and

[I] InterConnect website: www.interconnect-diabetes.eu.

outcome variables for analysis, and adjust for consistent confounders by using the same statistical models across cohorts.

**Objectives**

1) Examine the association between consumption of different types of meat (red meat, poultry, and processed meat including processed red meat, processed poultry, and other processed meat) and the incidence of T2D across populations in different countries;

2) Investigate the dose-response relationship of meat consumption with T2D risk;

3) Explore effect modification of the association between meat consumption and T2D by age, sex, geographical area, ethnicity, and BMI.

**Data required**

**Inclusion**

- Adults aged over 18 years at baseline

**Exclusion**

- T2DM cases at baseline
- T1DM cases (prevalent and incident)
- Those with implausible energy intakes [defined by energy intake < 500 or >3500 kcal/d for women and <800 or >4200 kcal/d for men]

**Main exposures –all that are available from the list below**

- Total red meat (e.g. beef, pork, lamb, others)
- Total poultry (e.g. chicken, turkey, others)
- Total processed meat (e.g. bacon, ham, sausages, others)
- Processed red meat
- Processed white meat
- Other processed meat

Unit: at least one measure of frequency (servings/day or servings/week) and/or quantity (grams/day or grams per serving). Specify what constituted a serving in each cohort.

**Outcome** (this part has been conducted in InterConnect previously and we will follow the definition in prior InterConnect projects)

- Incident T2D event (yes or no)
- Follow-up information (date of baseline, date of diagnosis, censored date, or end date of follow-up)

- Diagnosis information: registry or medical record, medication usage, biochemical measurement, self-reported

**Main potential confounders – to include as many as possible from below list**

- Socio-demographic factors: age, sex, geographical area, ethnicity, religion, socio-economic status (education and/or occupation, income if available)
- Health variables: previous history of stroke, myocardial infarction, cancer, hypertension at baseline; also family history of diabetes
- Health-related behaviours: smoking, physical activity, alcohol (g/d if available), special diet (e.g. vegetarian, vegan)
- Adiposity: BMI, waist circumference and/or waist-hip ratio
- Dietary variables: total energy intake (kcal), fish, fruits, vegetables, sources of carbohydrates (e.g. breads, pasta, and rice separated by wholegrain status if available), legumes, dairy products, sugary beverages (or soft drinks), tea, coffee, fibre, cooking method, cooking oil or fat (g/d if available), poultry (when analysing red or processed meat); red and processed meat (when analysing poultry); being vegetarian or vegan (yes or no)

**Analysis plan**

- Perform descriptive analysis to examine the distribution of consumption of different types of meat and other covariates across baseline characteristics
- Investigate the associations between consumption of different types of meat and T2D incidence by survival analysis models (piecewise Poisson regression in DataSHIELD)
- Test for linear or non-linear trend for rate ratios (RRs) and 95% confidence intervals (CIs) for T2D according to meat intake
- Explore effect modification using multiplicative interaction test and stratified analysis by pre-defined characteristics (age, sex, ethnicity, geographical area, and BMI).
- Perform relevant sensitivity analyses, meta-regression analyses, and exploratory analyses indicated by the results.

**Specific issues about federated meta-analysis**

InterConnect will use a federated process of analysis in which individual-participant data from contributing studies are held securely at their own sites. Analytical commands will be sent as blocks of code from a computer within the network which requests each computer to undertake an analysis and return non-identifiable summary statistics (i.e. results, not data). Analyses will be performed locally so all data will stay at source.

## References


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