Abstract title: **Incident sepsis in people with or without type 2 diabetes: The Fremantle Diabetes Study Phase II**

**Background and aims:** Sepsis (life-threatening organ dysfunction caused by a dysregulated host response to infection) has high mortality (>10%). People with type 2 diabetes have a 2- to 6-fold increased risk of sepsis compared to people without diabetes but contemporary data are limited. This study aims to i) determine the incidence of sepsis in a community-dwelling cohort of people with type 2 diabetes compared with matched people without diabetes ii) explore associates of incident sepsis.

**Methods:** The Fremantle Diabetes Study Phase II is a longitudinal observational study conducted in an urban community of 157,000 people. We followed 1,430 participants with type 2 diabetes and 5,720 de-identified age-, sex- and postcode-matched people without diabetes from entry to first record of incident sepsis in the Western Australian Hospital Morbidity Data Collection or Death Register, onset of diabetes (for the matched cohort, defined as first hospitalisation for/with diabetes) or death or end-2021, whichever came first.

**Results:** The combined cohorts had mean age 66 years and 52% were male. At entry, 2.0% of those with type 2 diabetes had a prior hospitalisation for/with sepsis vs 0.8% of matched counterparts (*P*<0.001). During 73,139 person-years of follow-up, 169 (11.8%) participants with type 2 diabetes and 288 (5.0%) people without diabetes had incident sepsis (*P*<0.001). The overall IRR was 2.38 (95% CI: 1.96, 2.89). After adjustment, type 2 diabetes remained significantly associated with double the risk of incident sepsis (HR (95% CI: 2.16 (1.78, 2.62)). For the type 2 diabetes cohort, age, male sex, Aboriginal ancestry, current smoking, insulin use, fasting serum glucose, heart rate, distal symmetrical polyneuropathy, cerebrovascular disease, and logNT-proBNP were significantly associated with incident sepsis.

**Conclusions:** People living with type 2 diabetes experience double the risk of incident sepsis. Modifiable risk factors include smoking and hyperglycaemia, but prevention of chronic complications is also imperative.