Objective:
Glucose-insulin pharmacokinetic-pharmacodynamic (PK-PD) models can be used for improved glycemic control of critically ill patients. A key component of glucose-insulin PK-PD models is pancreatic insulin secretion. There is limited data in the literature quantifying insulin secretion in critically ill patients at physiologic levels. This study creates a model pancreatic insulin secretion in critically ill patients to improve glucose-insulin system modeling.

Method:
19 patients from the Christchurch Hospital ICU enrolled in a prospective clinical trial studying sepsis each had arterial blood samples assayed for insulin and C-peptide. Two sets of four samples were taken from each patient, with each set collected over 60mins. Blood glucose (BG) data was collected with a bedside glucometer. C-peptide data was deconvolved using the model of van Cauter et al. to determine pre-hepatic insulin secretion rates (Uen). Data from literature suggested a maximum secretion rate of 16U/hr. A minimum rate of 1U/hr was also adopted. There were no diagnosed type 1 diabetics.

Result:
Regression analysis indicated endogenous secretion could be modeled as a function of BG only. There was clear separation of secretion levels between normal glucose tolerant (NGT) and impaired glucose tolerant (IGT) patients. Hence, Uen was modeled as a constrained linear function of BG (in mmol/L) for NGT and IGT patients separately with $R^2=0.55$ and 0.58 respectively.

NGT: $\text{Uen} = 16.5 \times \text{BG} - 62.4$, constrained to $[16.7 \text{ to } 266.7]$ (mU/min)
IGT: $\text{Uen} = 6.2 \times \text{BG} - 40.2$, constrained to $[16.7 \text{ to } 266.7]$ (mU/min)

Conclusion:
This work presents a simple model of pancreatic insulin secretion in critically ill patients based on clinical data. The model is a function of blood glucose level and glucose tolerance status and can be easily incorporated into glucose-insulin PK-PD models.