

Stephen Lam<sup>1,2</sup>, Bhaskar Kumar<sup>1,2</sup>, Yoon Loke<sup>2</sup>, Sophie Orme<sup>2</sup>, Ketan Dhatariya<sup>2,3</sup>

1. Department of Surgery, Norfolk and Norwich University Hospital NHS Trust, Norwich, UK.
2. Norwich Medical School, University of East Anglia, Norwich, UK.
3. Elsie Bertram Diabetes Centre, Norfolk and Norwich University Hospital NHS Trust, Norwich, United Kingdom.

## Introduction

- The relationship between elevated preoperative glycated haemoglobin (HbA<sub>1c</sub>) and adverse postoperative outcomes remains contentious.
- Previous observational work has suggested that people without diabetes but with elevated preoperative HbA<sub>1c</sub> have at least double the risk of postoperative morbidity and mortality compared to people without diabetes.<sup>1,2</sup>
- However, existing work is limited by insufficient sample sizes and potential confounding due to chronic hyperglycaemia related co-morbidity (see Figure 1)<sup>3-4</sup>
- The aim of this work was to clarify the association between preoperative HbA<sub>1c</sub> and postoperative outcomes in people without diabetes undergoing surgery using a large population-based prospective cohort design.

## Methods

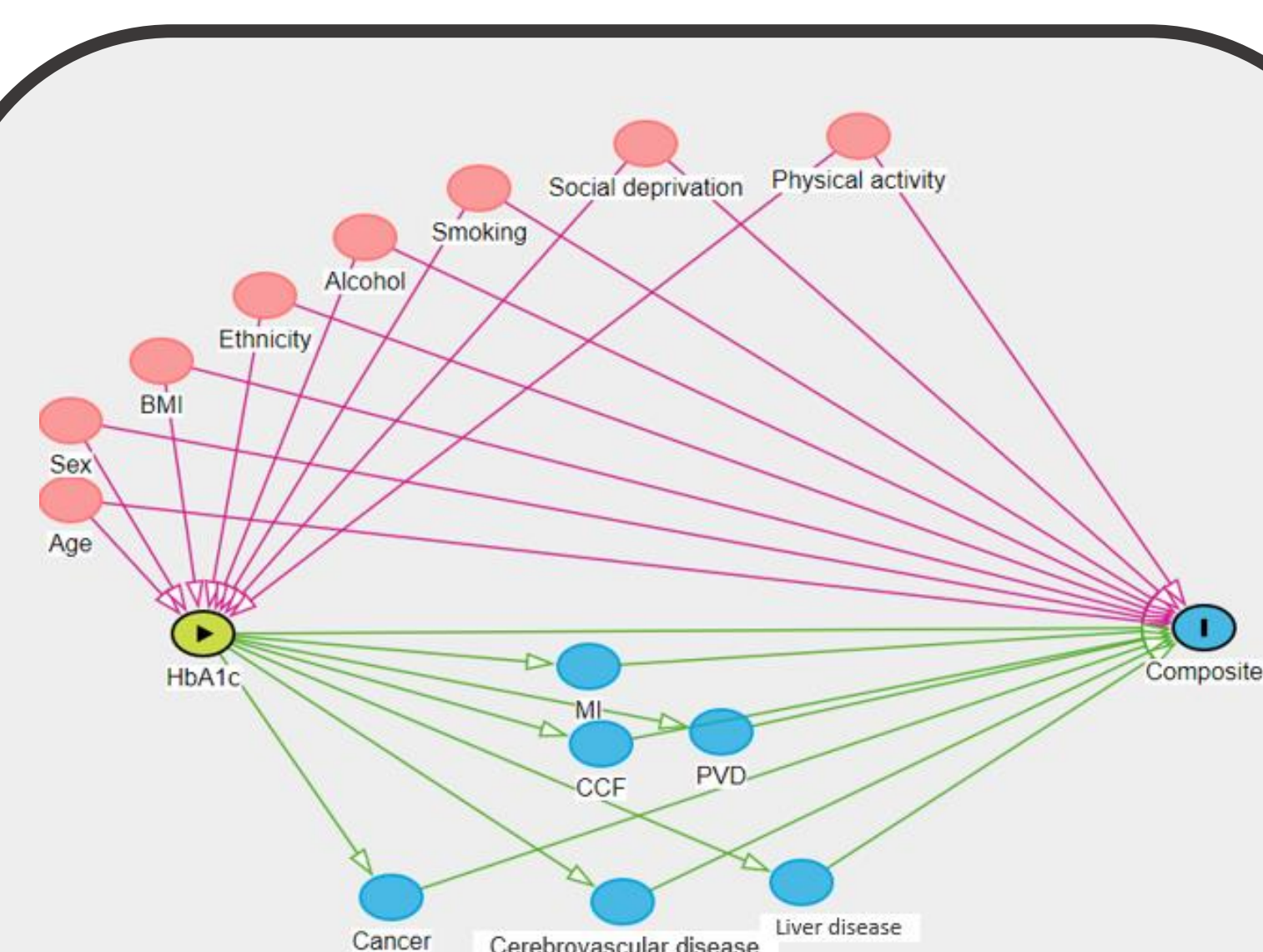
- We identified 26,653 participants in the UK Biobank who had undergone surgery within one year of recruitment.
- We stratified participants into 3 groups based on both diabetes status and baseline HbA<sub>1c</sub> (see Figure 2).
- A composite primary outcome of 30-day major post-operative complications and 90-day all cause mortality was analysed using adjusted logistic regression to estimate odds ratios per group.

**Table 1: Logistic Regression analyses to estimate the odds of the composite primary outcome (major 30-day post-operative complications and 90-day mortality) by disease status**

Disease status	Age and sex adjusted OR (95% CI), p-value	Adjusted for total effect OR (95% CI), p-value	Adjusted for direct effect OR (95% CI), p-value
No diagnosis of diabetes HbA <sub>1c</sub> <42 mmol/mol	Ref.	Ref.	Ref.
No diagnosis of diabetes HbA <sub>1c</sub> ≥42 mmol/mol	1.49 (1.10-2.01), p=0.01	1.43 (1.02-2.02), p=0.04	1.37 (0.97-1.93), p=0.07
Prevalent diabetes	2.21 (1.80-2.72), p<0.0001	2.00 (1.53-2.54), p<0.0001	1.79 (1.37-2.31), p<0.0001

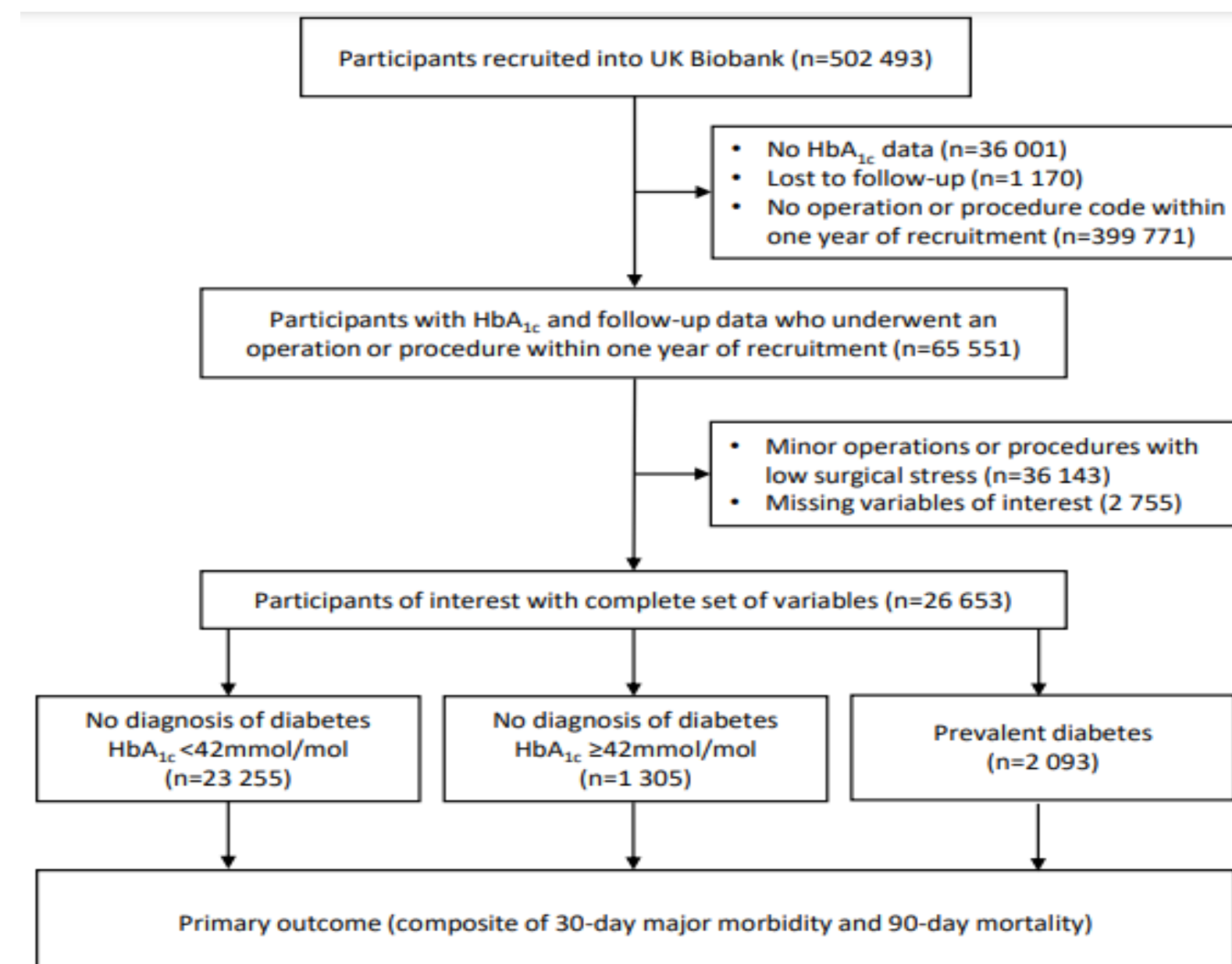
Total effect adjustment=age, sex, body mass index (continuous), ethnicity (white, mixed, Asian, Black, other), alcohol frequency (daily, 3-4 times/week, 1-2 times/week, 1-3 times/month, rarely, never), smoking status (never, former, current) Townsend deprivation index (1-5), International Physical Activity Index (low, moderate, high), and assessment centre location.

Direct effects adjustment=as per total effect model + comorbidity (myocardial infarction, congestive cardiac failure, peripheral vascular disease, cancer, cerebrovascular disease, and liver disease)



HbA<sub>1c</sub>= Glycated haemoglobin, BMI=body mass index, MI=myocardial infarction, CCF=congestive cardiac disease, PVD=peripheral vascular disease, Composite=30-day major postoperative complication and 90-day all-cause mortality. The blue risk factors represent mediators through which HbA<sub>1c</sub> also acts

**Figure 1: Directed Acyclic Graph of the presumed causal pathway for HbA<sub>1c</sub> and the composite primary outcome**



**Figure 2: Study Flow Diagram**

## Results

- Elevated preoperative HbA<sub>1c</sub> in people without diabetes was associated with an increased risk of complications (OR 1.43, 95% CI 1.02-2.02), but the association was confounded by end organ comorbidity (adjusted OR 1.37, 95% CI 0.97-1.93).

## Conclusions

- HbA<sub>1c</sub> can be used as a preoperative risk marker for postoperative complications in people without diabetes.
- However, in people without diabetes but with elevated HbA<sub>1c</sub> increased postoperative risk is likely attributed to underlying comorbid disease.
- As such, our findings suggest that in order to prevent adverse postoperative outcomes, optimisation of pre-existing comorbidities should take precedence over the diabetes.

## References:

1. Kwon S, Thompson R, Dellinger P, et al. Importance of perioperative glycaemic control in general surgery: a report from the Surgical Care and Outcomes Assessment Program. *Ann Surg* 2013;257(1):8-14.
2. Gustafsson UO, Thorell A, Soop M, et al. Haemoglobin A1c as a predictor of postoperative hyperglycaemia and complications after major colorectal surgery. *Br J Surg* 2009;96(11):1358-64.
3. O'Sullivan CJ, Hynes N, Mahendran B, et al. Haemoglobin A1c (HbA1C) in non diabetic and diabetic vascular patients. Is HbA1C an independent risk factor and predictor of adverse outcome? *Eur J Vasc Endovasc Surg* 2006;32(2):188-97.
4. Kreutziger J, Schlaepfer J, Wenzel V, et al. The role of admission blood glucose in outcome prediction of surviving patients with multiple injuries. *J Trauma* 2009;67(4):704-8.