IMMUNISATION COALITION

Influenza and COVID-19 effects of and on chronic diseases

7:30 pm

A/Prof Kirsty Short

The University of Queensland

Diabetes increases the severity of influenza

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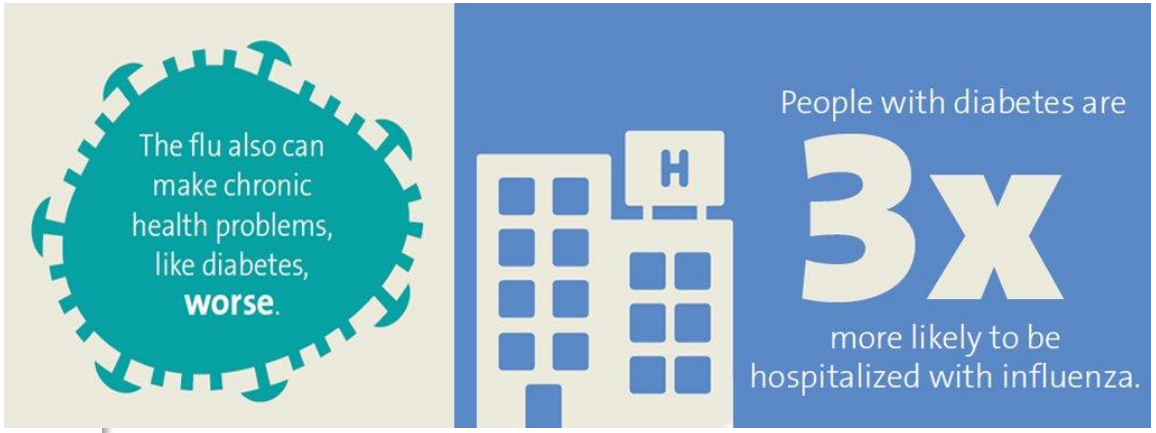
High glucose levels increase influenza-associated damage to the pulmonary epithelial-endothelial barrier

Katina D Hulme[1], Limin Yan[1], Rebecca J Marshall[1], Conor J Bloxham[2], Kyle R Upton[1], Sumaira Z Hasnain[3], Helle Bielefeldt-Ohmann[1,4], Zhixuan Loh[5], Katharina Ronacher[3,4], Keng Yih Chew[1], Linda A Gallo[2,3], Kirsty R Short[1,4]*



Rates of Severe Influenza-Associated Outcomes Among Older Adults Living With Diabetes—Influenza Hospitalization Surveillance Network (FluSurv-NET), 2012–2017

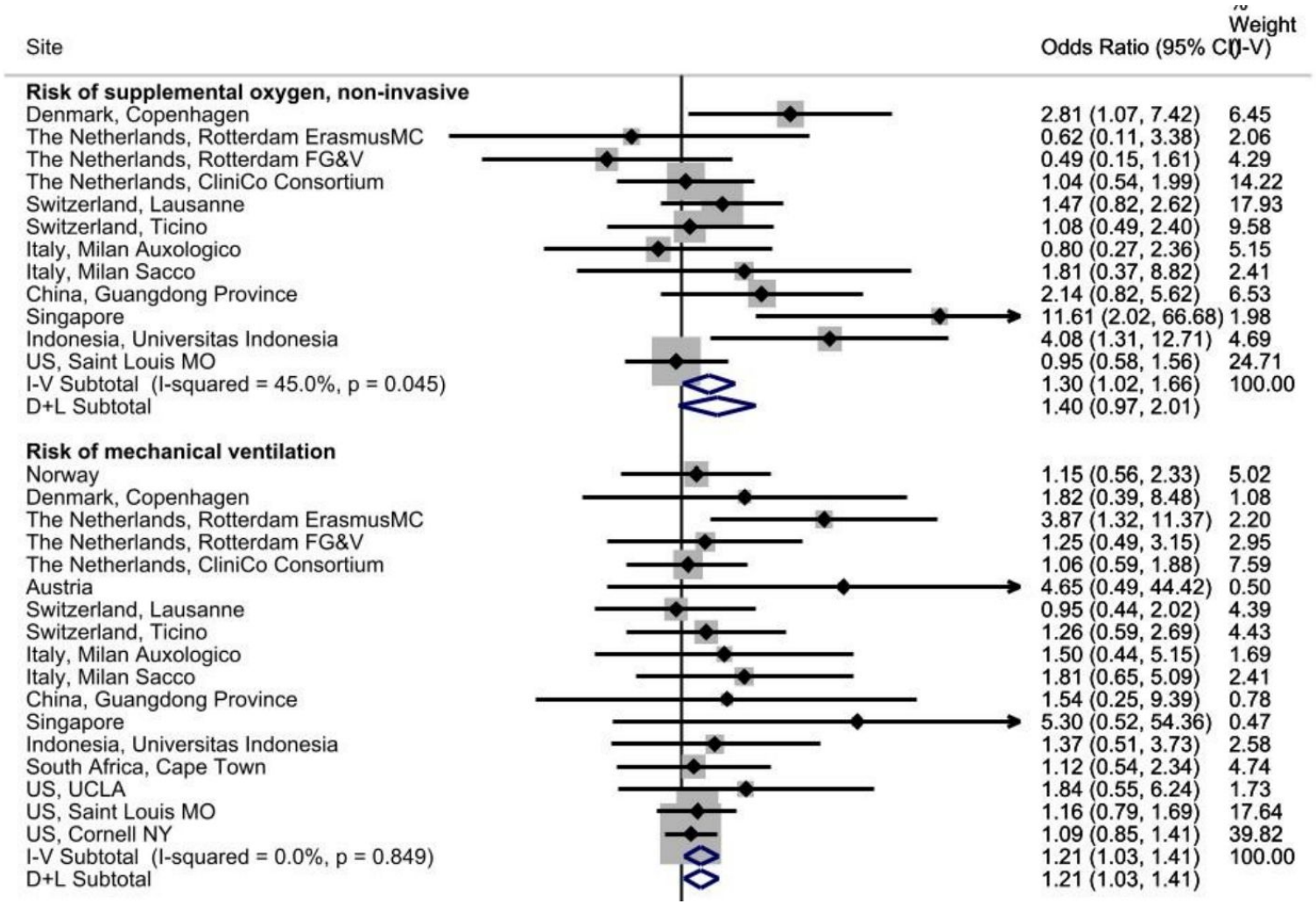
Daniel Owusu,[1,2] Melissa A. Rolfes,[2] Carmen S. Arriola,[2] Pam Daily Kirley,[3] Nisha B. Alden,[4] James Meek,[5] Evan J. Anderson,[6,7,8] Maya L. Monroe,[9] Sue Kim,[10] Ruth Lynfield,[11] Kathy Angeles,[12] Nancy Spina,[13] Christina B. Felsen,[14] Laurie Billing,[15] Ann Thomas,[16] H. Keipp Talbot,[17] William Schaffner,[17] Ryan Chatelain,[18] Carrie Reed,[2] and Shikha Garg[2]

Diabetes and the Severity of Pandemic Influenza A (H1N1) Infection

Robert Allard, MD[1,2,3]
Pascale Leclerc, MSC[1,3]
Claude Tremblay, MSC[1]
Terry-Nan Tannenbaum, MD[1,2]

subjects, and those hospitalized without ICU admission, i.e., the control subjects. The associations between patient char-

Diabetes increases the severity of COVID-19



Models adjusted for: BMI categories; Age; Sex; Pre-existing cardiovascular disease; Hypertension and Pre-existing respiratory disease. Reference is patients without diabetes

American Diabetes Association. | Publications

Diabetes Care

EPIDEMIOLOGY / HEALTH SERVICES RESEARCH | APRIL 15 2021

Diabetes and Overweight/Obesity Are Independent, Nonadditive Risk Factors for In-Hospital Severity of COVID

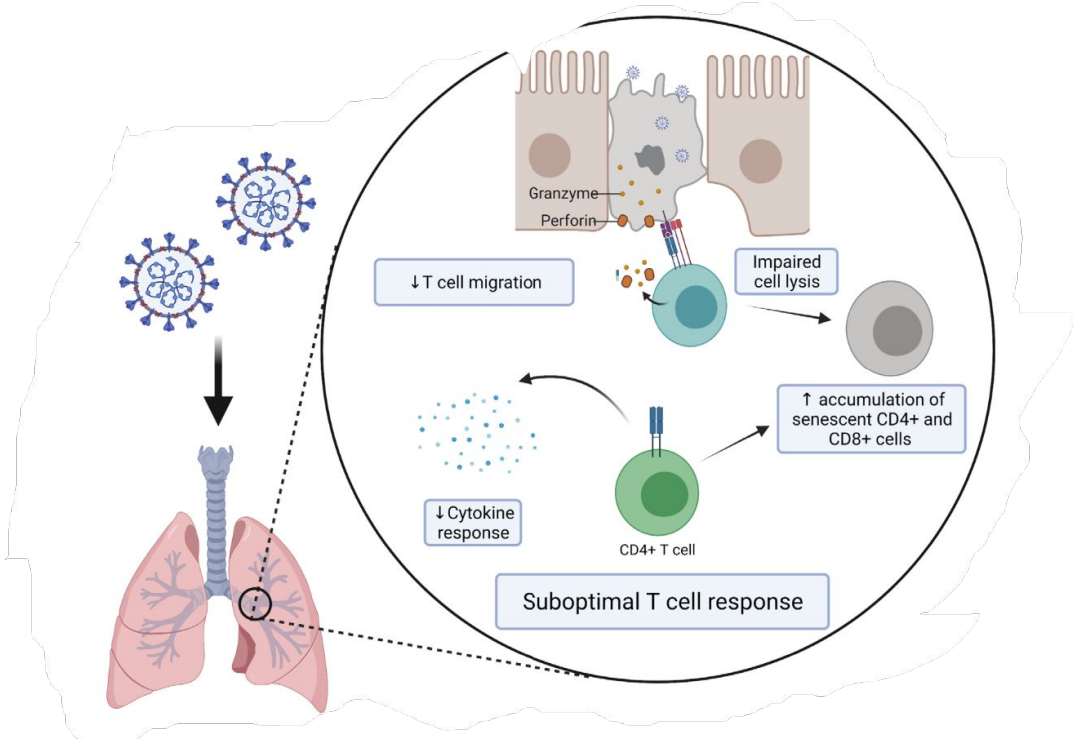
Hypothesised mechanisms

- Chronic inflammation
- Metabolic disorders impairs T cell immunity

  Decreased T cell migration

  Reduced cytokine expression after stimulation

  Accumulation of higher senescent T-cell numbers

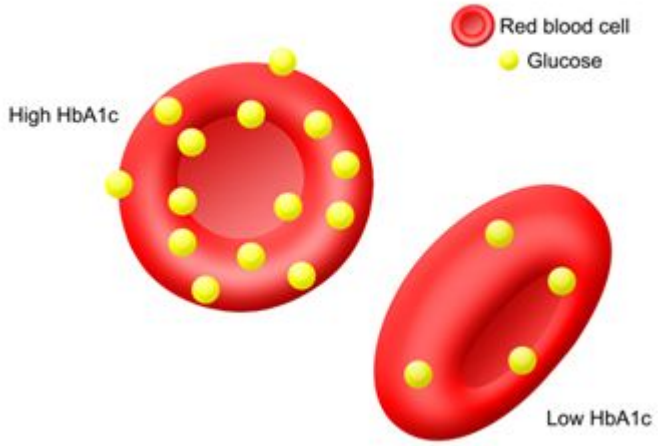


The FEBS Journal
FEBS PRESS science publishing by scientists
STATE-OF-THE-ART REVIEW

The role of T-cell immunity in COVID-19 severity amongst people living with type II diabetes

Zhen Wei Marcus Tong[1], Emma Grant[2,3], Stephanie Gras[2,3], Melanie Wu[1], Corey Smith[4], Helen L. Barrett[5,6], Linda A. Gallo[7] and Kirsty R. Short[1]

A causative role for hyperglycaemia?

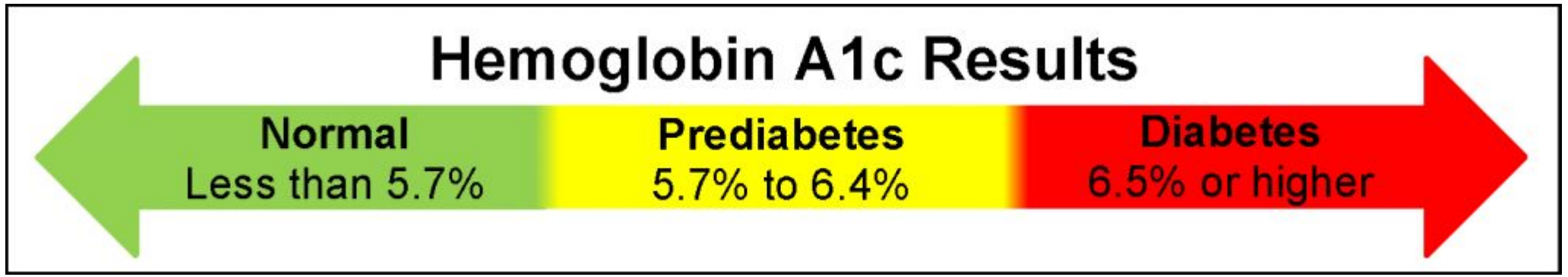


Diabetologia (2007) 50:549–554
DOI 10.1007/s00125-006-0570-3

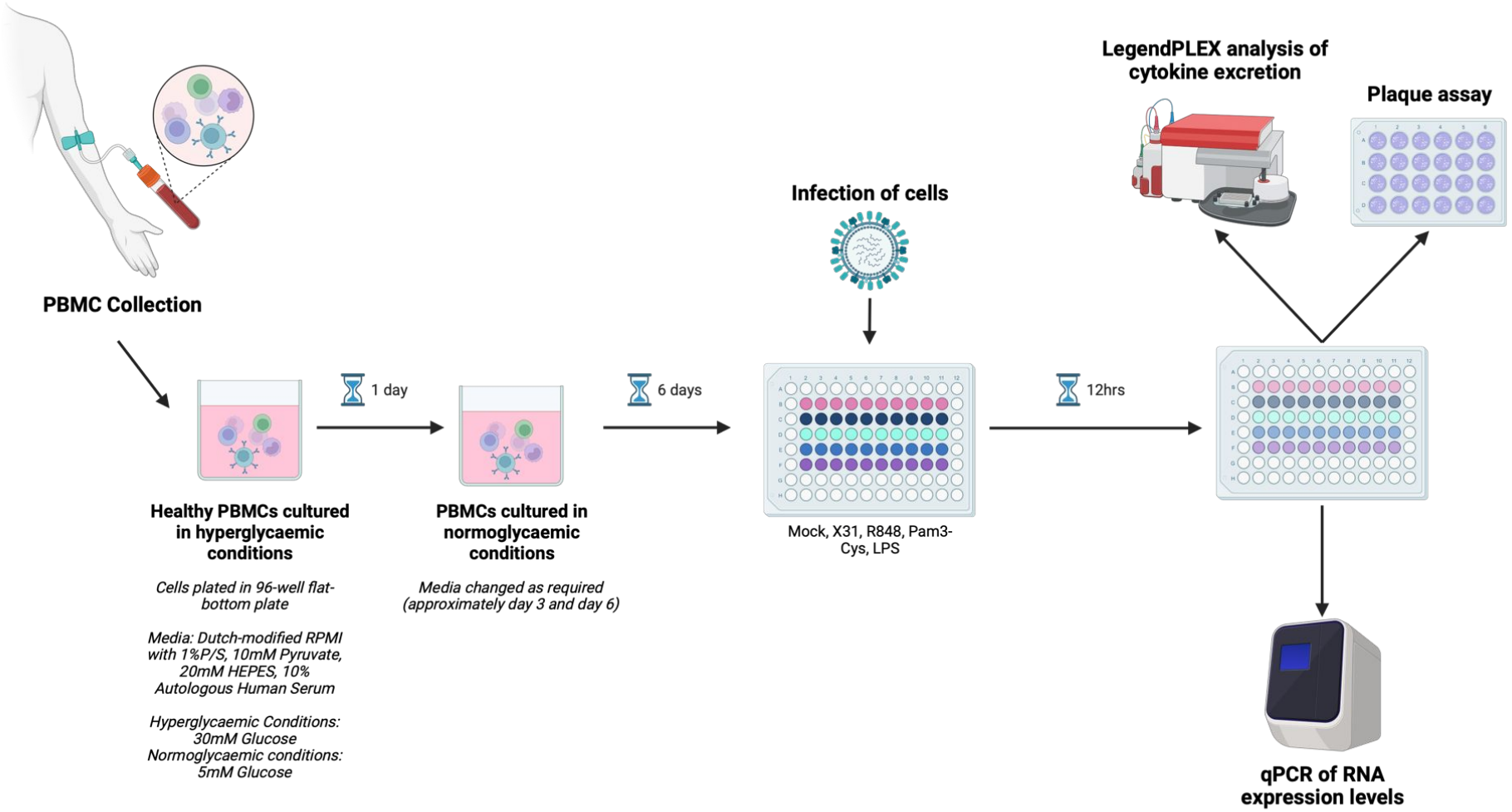
ARTICLE

Influence of diabetes and hyperglycaemia on infectious disease hospitalisation and outcome

T. Benfield · J. S. Jensen · B. G. Nordestgaard

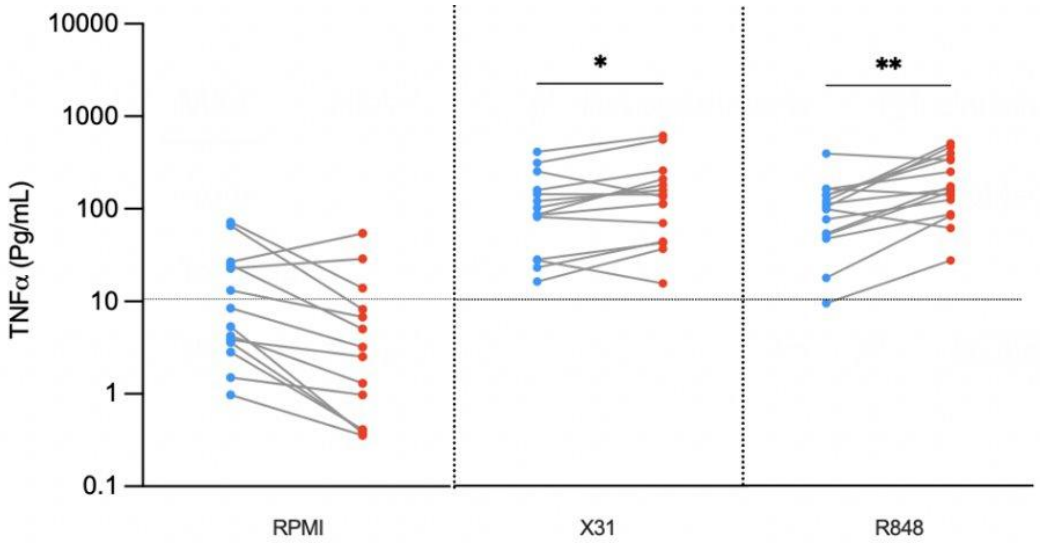


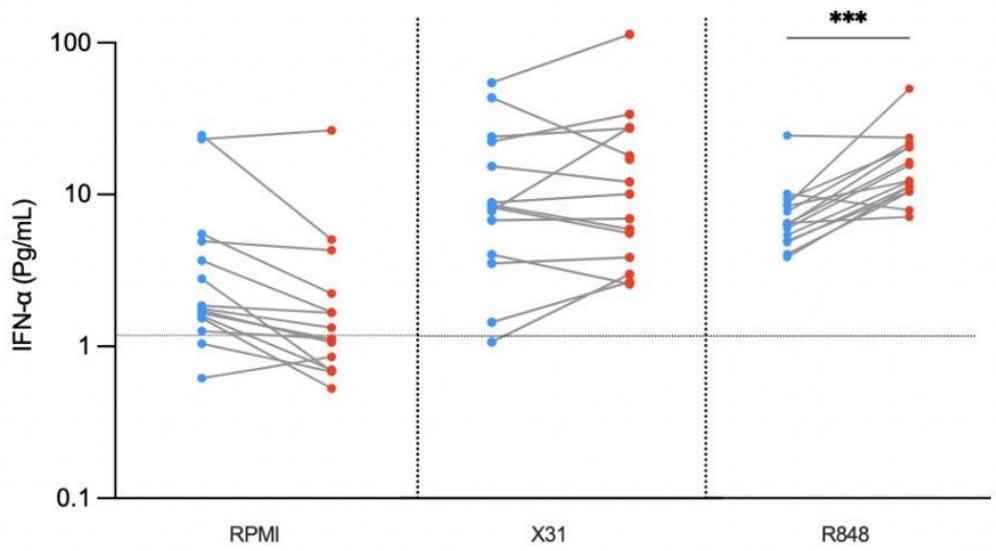
Hyperglycaemia increases the innate inflammatory response to influenza

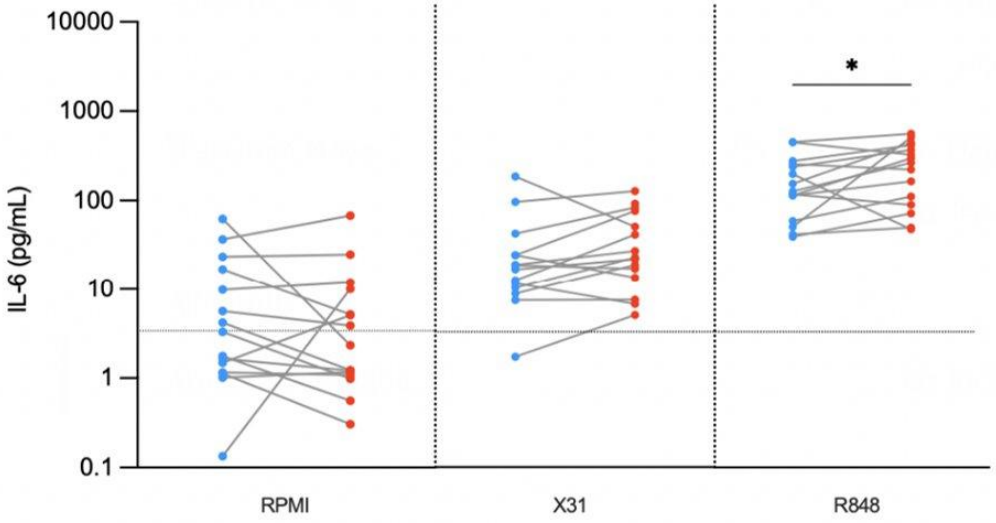


Hocking et al., unpublished

Hyperglycaemia increases the innate inflammatory response to influenza







Normoglycemic

Hyperglycemic

Belle Hocking

Elle Noye

Hocking et al., unpublished

T cell responses and hyperglycaemia

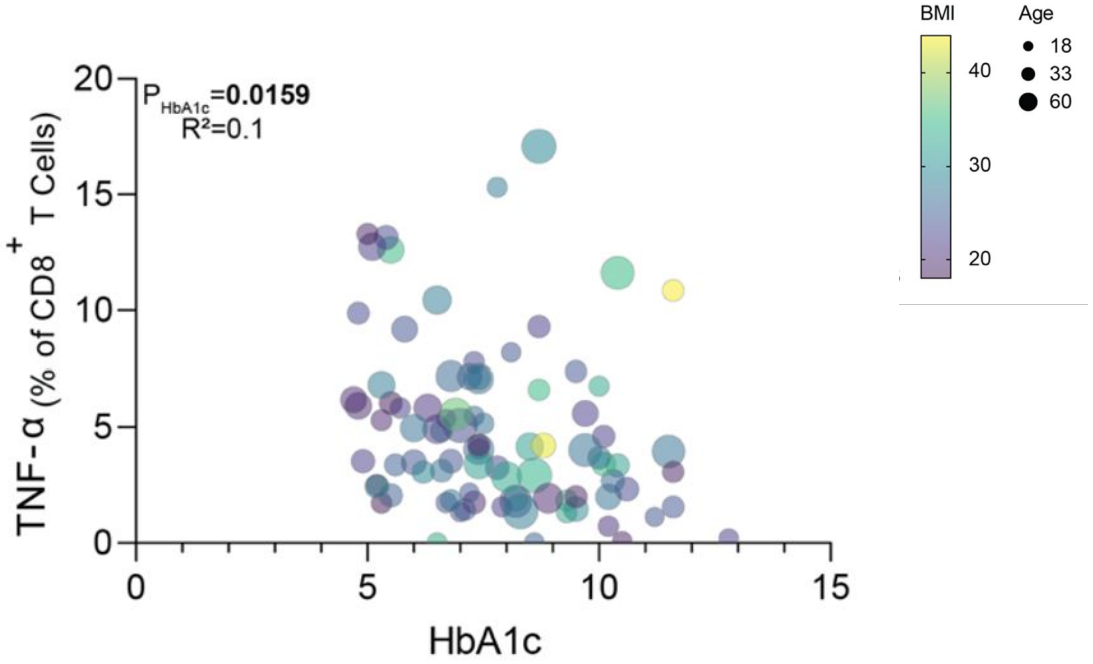
IMMUNISATION COALITION

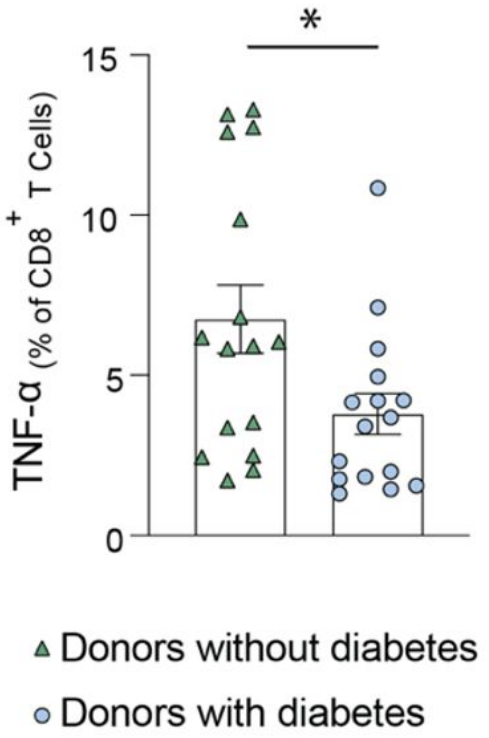
	Donors without diabetes (n=16)	Donors with diabetes (n=72)	*P*-value
Age, years	28.1 ± 5.4	30.6 ± 11.6	0.874
Female/Male (% Female)	11/5 (68.8%)	44/28 (60.3%)	0.776
BMI (kg/m^2)	23 ± 4.6	27 ± 5.4	**0.006 (*)**
Ethnicity, % Caucasian	68.8%	83.6%	0.157
HbA1c (%)	5.2 ± 0.3	8.4 ± 1.7	**<0.0001 (*)**
T1DM/T2DM (% T1DM)	N/A	66/6 (90.4%)	N/A
Insulin treatment	N/A	66/6 (90.4%)	NA
Duration of Diabetes (years)	N/A	14.8 ± 7.2	N/A
Non-steroidal anti-inflammatory drug (NSAID) use (% use)	0/16 (0%)	4/68 (5.5%)	>0.999

Katina Hulme

Hulme et al., 2024

Hyperglycaemia is associated with reduced TNFa production by CD8+ T cells



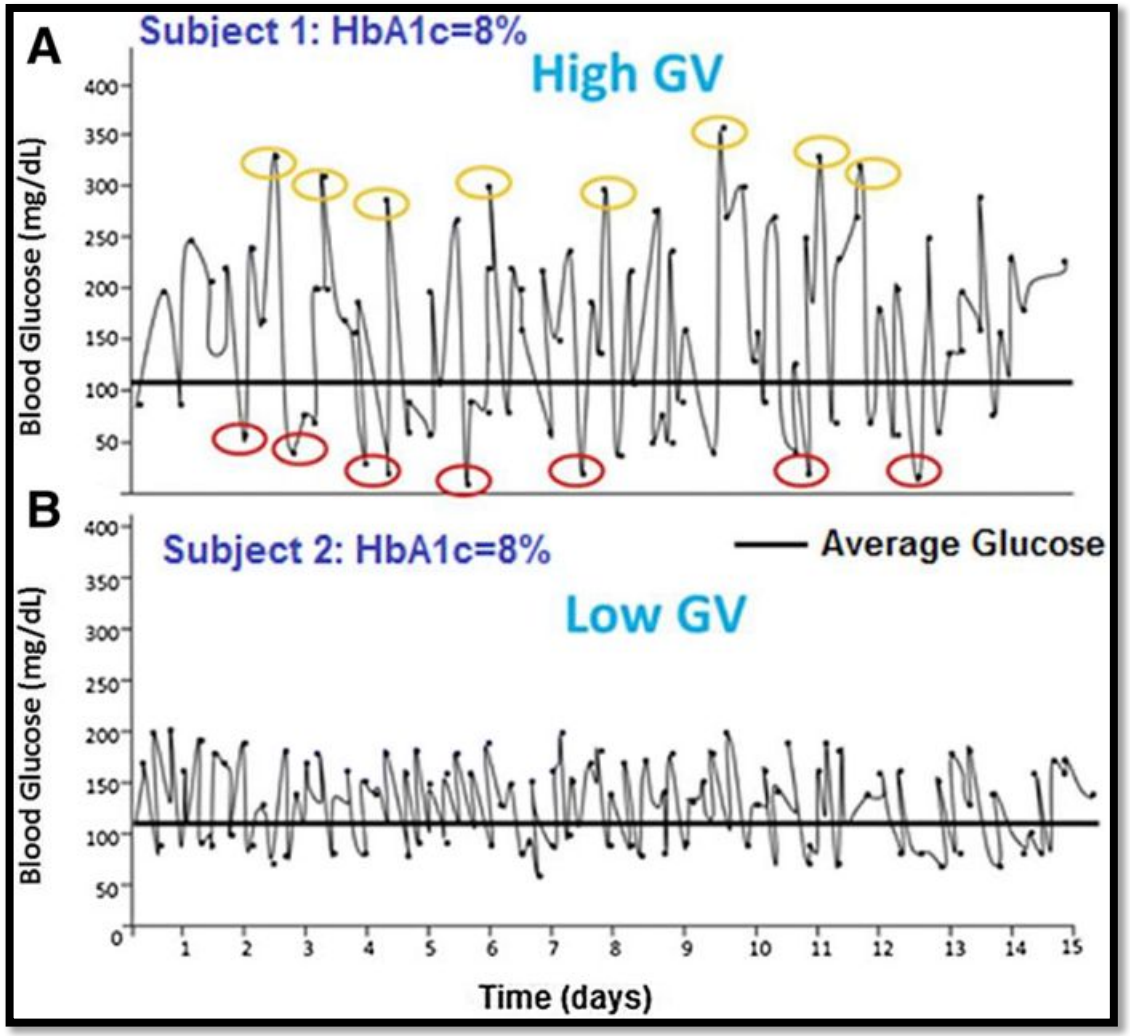


Hulme et al., 2024

Is hyperglycaemia an oversimplification?

IMMUNISATION COALITION

$$Coefficient\ of\ Variation\ (CV) = \frac{amplitude\ SD}{glucose\ mean}\ x\ 100\%$$



Acta Diabetologica (2021) 58:1701–1704
https://doi.org/10.1007/s00592-021-01779-7

SHORT COMMUNICATION

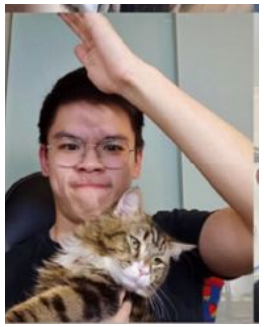
High glycaemic variability is associated with progression of COVID-19

Caroline Wei Shan Hoong[1] · Xier Emily Yeo[2] · Yi Lin[2] · Say Tat Ooi[2,3] · Ester Yeoh[4,5]

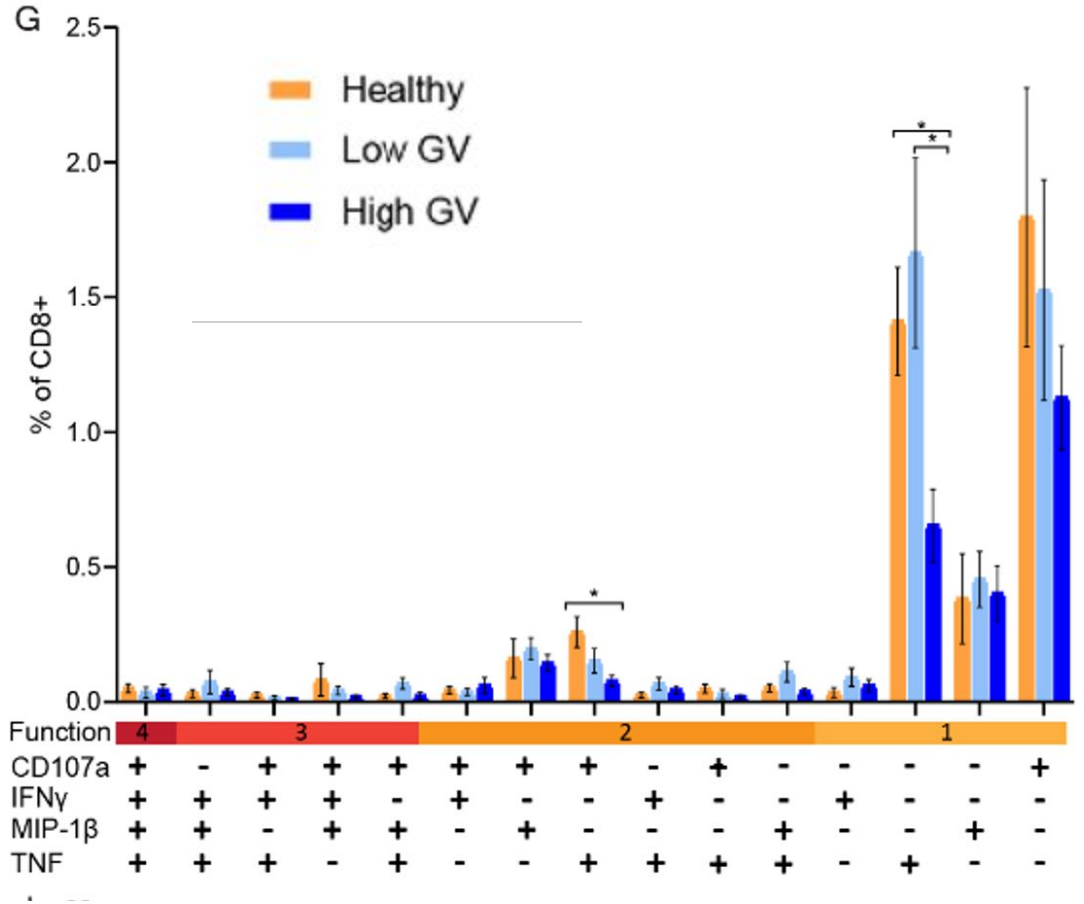
High GV associated with reduced TNFa production by CD8+ T cells

IMMUNISATION COALITION

	Low glycaemic variability group (n=13)		High glycaemic variability group (n=19)		P value[2]
	Mean (SD)	%	Mean (SD)	%	
Age (years)	29.88 (±11.69)	-	26.49 (±6.67)	-	0.6172
Sex (male/female)	4/13	30.8%	6/19	31.6%	0.5993
BMI (kg/m^2)	26.33 (±4.79)		26.45 (±4.94)		>0.9999
HbA1c (%)	7.92 (±1.75)	-	7.75 (±1.42)	-	0.5505
Diabetes duration (years)	14.54 (±9.12)	-	15.15 (±5.24)	-	0.6151
Average blood glucose (mmol/L)[3]	11.83 (±3.54)	-	9.83 (±2.65)	-	0.0823
CV (%)	27.01 (±4.32)	-	39.15 (±3.25)	-	<0.0001 (****)
Type of insulin treatment (injection/pump)[4]	4/9	30.8%	9/10	47.4%	0.3477



Marcus Tong



Tong et al., under review

Vaccination in people living with diabetes

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- General consensus is that people living with diabetes have equivalent humoral immunity and cellular immunity to mRNA SARS-CoV-2 vaccines and vaccination is highly effective in preventing disease severity

- However, this varies across diabetes subtype, time post-vaccination, type of vaccine, number of vaccine ities (e.g. renal function)

DIABETES AND COVID19 ARTICLES | AUGUST 21 2022

Immunogenicity and Safety of SARS-CoV-2 mRNA Vaccines in a Cohort of Patients With Type 1 Diabetes FREE

Francesca D'Addio; Gianmarco Sabiu; Vera Usuelli; Emma Assi; Ahmed Abdelsalam; Anna Maestroni; Andy Joe Seelam; Moufida Ben Nasr; Cristian Loretelli; Davide Mileto; Giada Rossi; Ida Pastore; Laura Montefusco; Paola S. Morpurgo; Laura Plebani; Antonio Rossi; Enrica Chebat; Andrea M. Bolla; Maria Elena Lunati; Chiara Mameli ; Maddalena Macedoni; Spinello Antinori; Stefano Rusconi; Maurizio Gallieni; Cesare Berra; Franco Folli ; Massimo Galli; Maria Rita Gismondo; Gianvincenzo Zuccotti; Paolo Fiorina

The majority of patients with T1D did not show any increase in the SARS-CoV-2–specific cytotoxic response compared with the robust increase observed in all subjects without diabetes

- General consensus is that people living with diabetes have equivalent humoral immunity to influenza vaccines (cellular immunity not as relevant) and vaccination is highly effective in preventing severe disease

- The effects of vaccination appear to be more effective when using higher dose and quadrivalent vaccines

A Bidirectional Relationship

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- A US Center of Disease Control (CDC) analysis of a large electronic health-care database of 353 164 adults with COVID-19 and 1 640 776 controls with no evidence of infection, suggested that people with COVID-19 had an increased risk of new onset type 1 diabetes and type 2 diabetes (*MMWR Morb Mortal Wkly Rep.* 2022; **71**: 713-717)

- A German cohort study of 35 865 people with COVID-19 showed higher risk of newly diagnosed type 2 diabetes than an equal number of matched controls with acute upper respiratory tract infections (*Diabetologia.* 2022; **65**: 949-954)

- Data from the US Department of Veterans Affairs to characterise the risk and 12-month burden of diabetes in 181 280 people with SARS-CoV-2 infection versus two control groups: 4 118 441 contemporary controls who were enrolled during the same time but did not get infected with SARS-CoV-2 and 4 286 911 historical controls from before the pandemic (*Lancet Diabetes Endocrinology* 2022; **11:**11-13)

  - Compared with both the contemporary and historical controls, people with SARS-CoV-2 had increased risk of incident diabetes and incident use of antihyperglycemic therapy in the post-acute phase

  - Among people with COVID-19, the risk of diabetes increased in a graded fashion according to baseline risk

A Bidirectional Relationship – Why?

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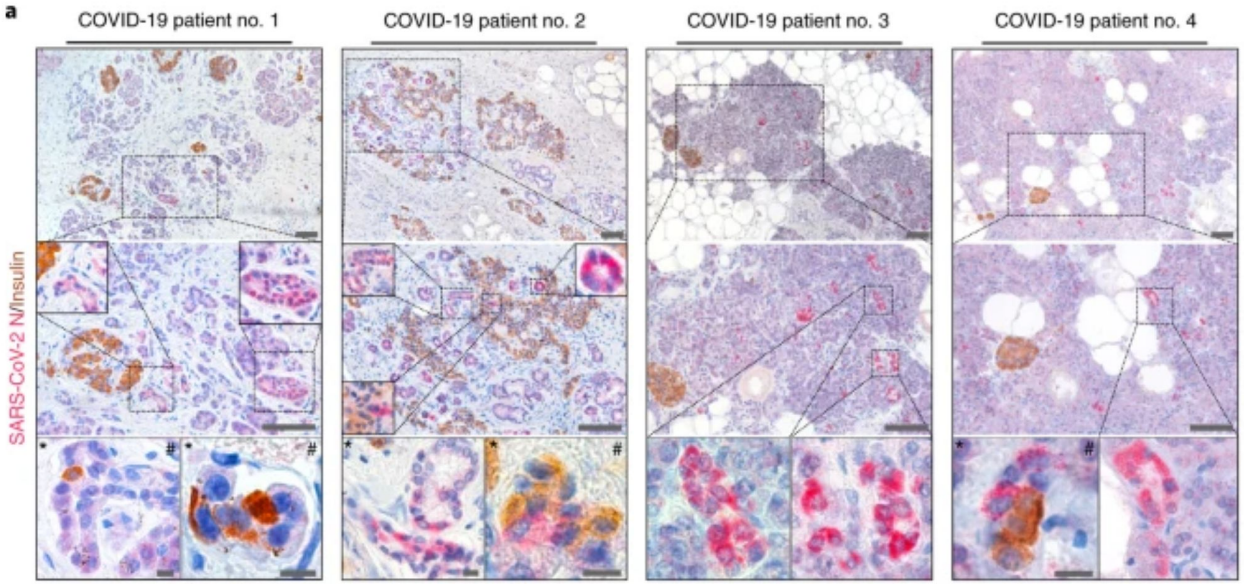
- SARS-CoV-2 infects cells of the human exocrine and endocrine pancreas ex vivo and in vivo.
- Human β-cells express viral entry proteins, and SARS-CoV-2 infects and replicates in cultured human islets.
- Infection is associated with morphological, transcriptional and functional changes, including reduced numbers of insulin-secretory granules in β-cells and impaired glucose-stimulated insulin secretion
- In COVID-19 full-body postmortem examinations, SARS-CoV-2 nucleocapsid protein was detected pancreatic



narker NKX6.1 and are in close proximity to the

nature metabolism ARTICLES
https://doi.org/10.1038/s42255-021-00347-1
Check for updates

SARS-CoV-2 infects and replicates in cells of the human endocrine and exocrine pancreas

Does a Bidirectional Relationship Exist with vaccination?

IMMUNISATION COALITION

Incidence of diabetes following COVID-19 vaccination and SARS-CoV-2 infection in Hong Kong: A population-based cohort study

Xi Xiong, David Tak Wai Lui, Matthew Shing Hin Chung, Ivan Chi Ho Au, Francisco Tsz Tsun Lai, Eric Yuk Fai Wan, Celine Sze Ling Chui, Xue Li, Franco Wing Tak Cheng, Ching-Lung Cheung, Esther Wai Yin Chan, Chi Ho Lee, Yu Cho Woo, [...], Ian Chi Kei Wong [view all]

- There was no evidence of increased risks of incident diabetes following COVID-19 vaccination.
- The risk of incident diabetes increased following SARS-CoV-2 infection, mainly type 2 diabetes.
- Subgroup analysis revealed no evidence of increased risk of incident diabetes among fully vaccinated COVID-19 survivors.

COVID-19 Vaccination Prior to SARS-CoV-2 Infection Reduced Risk of Subsequent Diabetes Mellitus: A Real-World Investigation Using U.S. Electronic Health Records

Tina Yi Jin Hsieh; Renin Chang ; Su-Boon Yong; Pei-Lun Liao ; Yao-Min Hung ; James Cheng-Chung Wei

- 65% higher risk of new-onset diabetes in SARS-CoV-2–infected individuals compared to noninfected counterparts.
- COVID-19 survivors who received COVID-19 vaccinations experienced a reduced risk of new-onset diabetes, with a dose-dependent effect

Conclusions and implications for patient care

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- Vaccination against SARS-CoV-2/influenza virus decreases the risk of severe respiratory viral infections in people living with diabetes
- Vaccination also reduces the risk of diabetes developing following SARS-CoV-2 infection
- Still numerous questions to answer about vaccine efficacy in people living with diabetes: diabetes subtype, time post-vaccination, type of vaccine, number of vaccine doses, infecting viral strain and co-morbidities (e.g. renal function)
- Severe respiratory viral disease in people living with diabetes may be driven by hyperglycaemia: importance of maintaining HbA1c targets
- Glycaemic variability may also play a role: added impetus to make CGMs available to people living with diabetes, including people with type 2 diabetes

Acknowledgements

- **University of Queensland**
  - Kirsty Short
  - Keng Yih Chew
  - Katina Hulme
  - Ellesandra Noye
  - Nathalie Verzele
  - Melanie Wu
- **Mater Research**
  - Helen Barett
  - Emily Dorey
  - Soi Law
- **University of Sunshine coast**
  - Linda Gallo
- **University of Melbourne**
  - Katherine Kedzierska
  - Louise C. Rowntree
  - Carolien E. van de Sandt
- **La Trobe University**
  - Stephanie Gras
  - Emma Grant
- **Sorbonne Université**
  - Fawaz Alzaid
  - Jean-Pierre Riveline
  - Jean-Baptiste Julla
  - Charline Potier