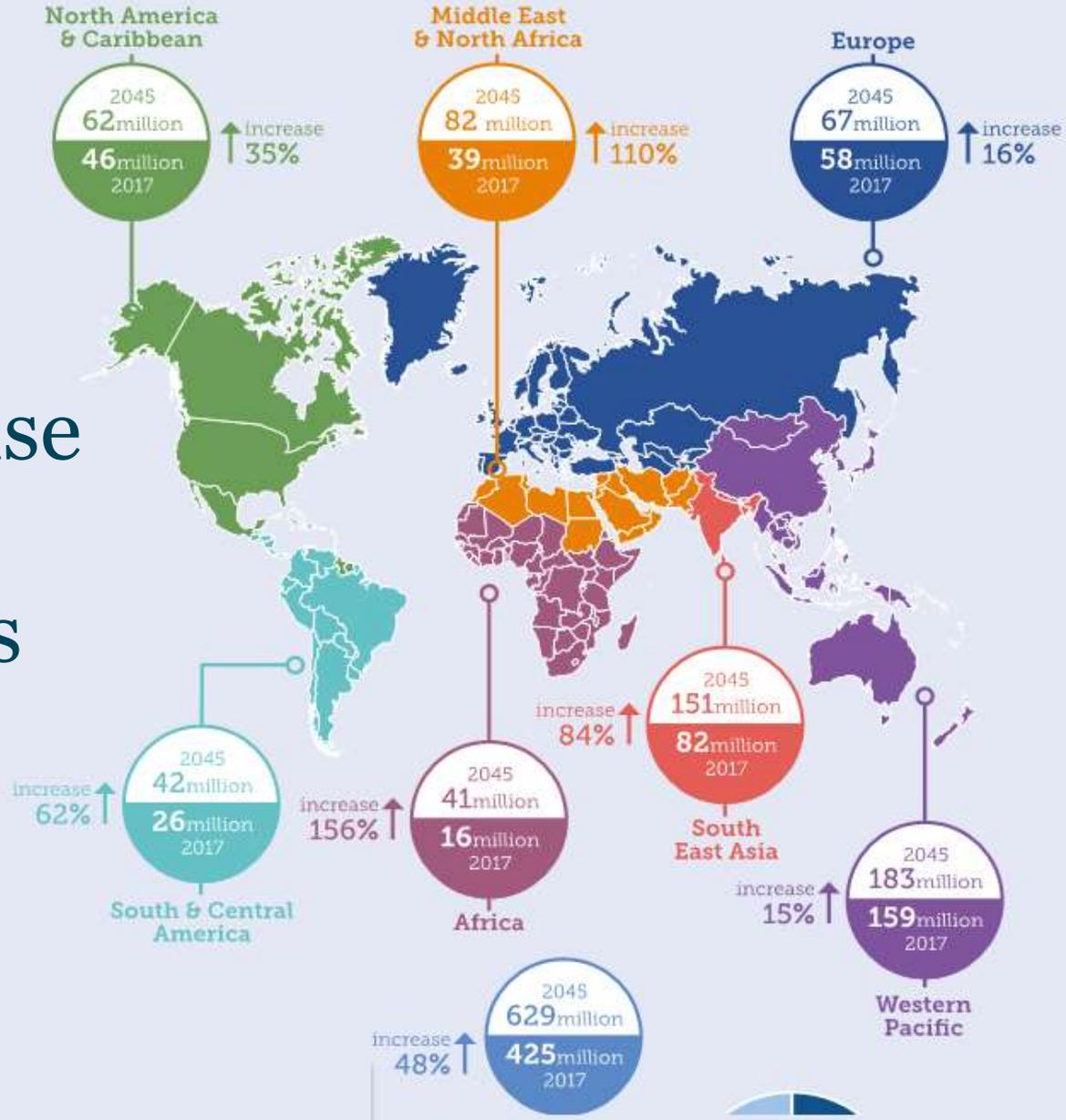# Plan

- Background

- Clinical trial in Mali (Africa)

- Umbrella review of effectiveness of herbal medicines for glycaemic control

- Systematic review of qualitative studies – how do patients and doctors feel about use of herbal medicines for diabetes?

- Priorities for future research

The global rise of Diabetes mellitus (DM)

Number of people with diabetes worldwide and per region in 2017 and 2045 (20-79 years)

North America & Caribbean
2045 62 million
46 million 2017
increase 35%

Middle East & North Africa
2045 82 million
39 million 2017
increase 110%

Europe
2045 67 million
58 million 2017
increase 16%

South & Central America
2045 42 million
26 million 2017
increase 62%

Africa
2045 41 million
16 million 2017
increase 156%

South East Asia
2045 151 million
82 million 2017
increase 84%

Western Pacific
2045 183 million
159 million 2017
increase 15%

2045 629 million
425 million 2017
increase 48%

27.06.2023
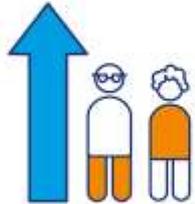
Source: IDF- 8th edition 2017

Diabetes mellitus (DM) in the UK

Almost 3.7 million
people have been diagnosed
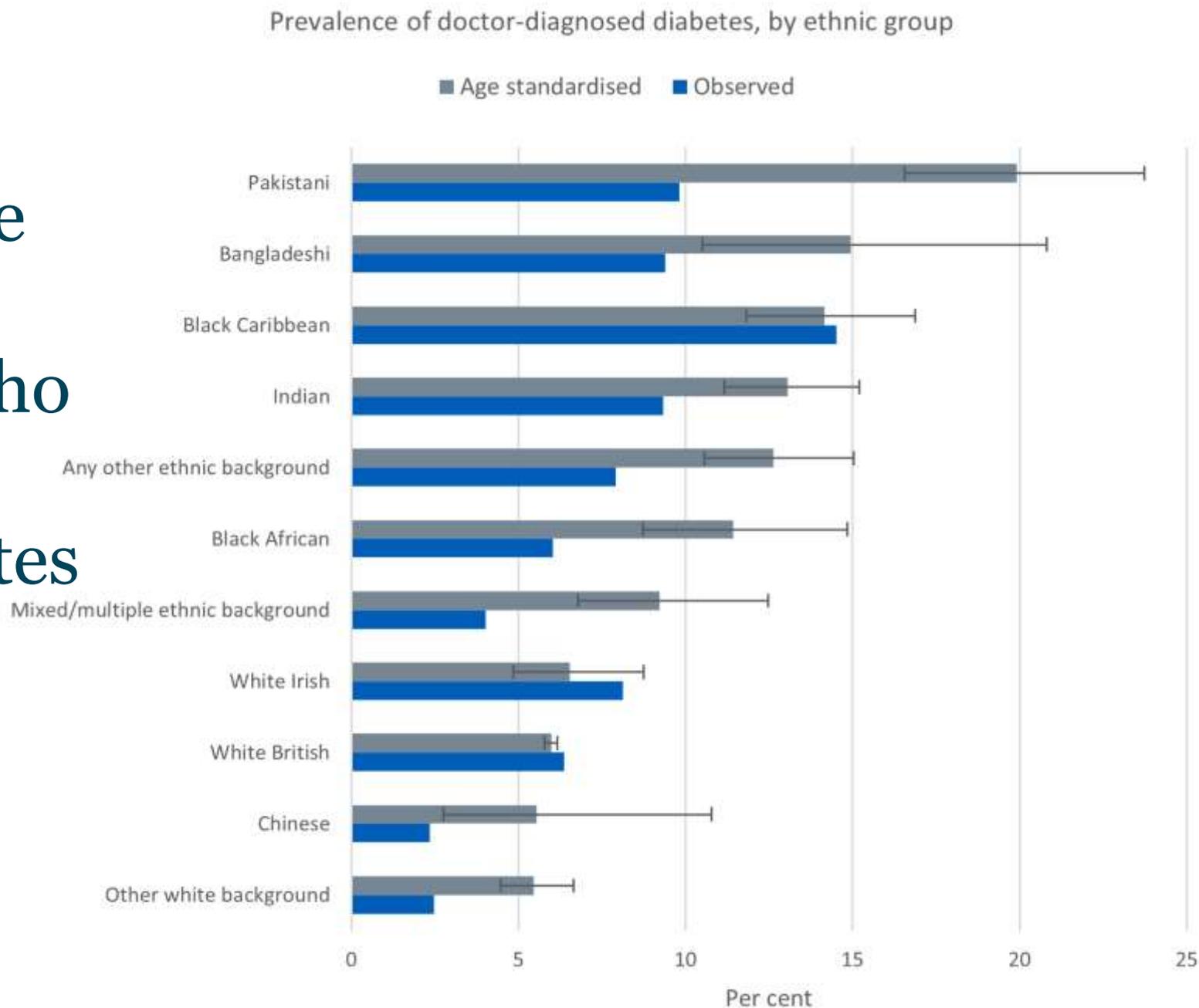with diabetes in the UK

3.7m

12.3 million
people are at **increased risk**
of Type 2 diabetes

4.6 million
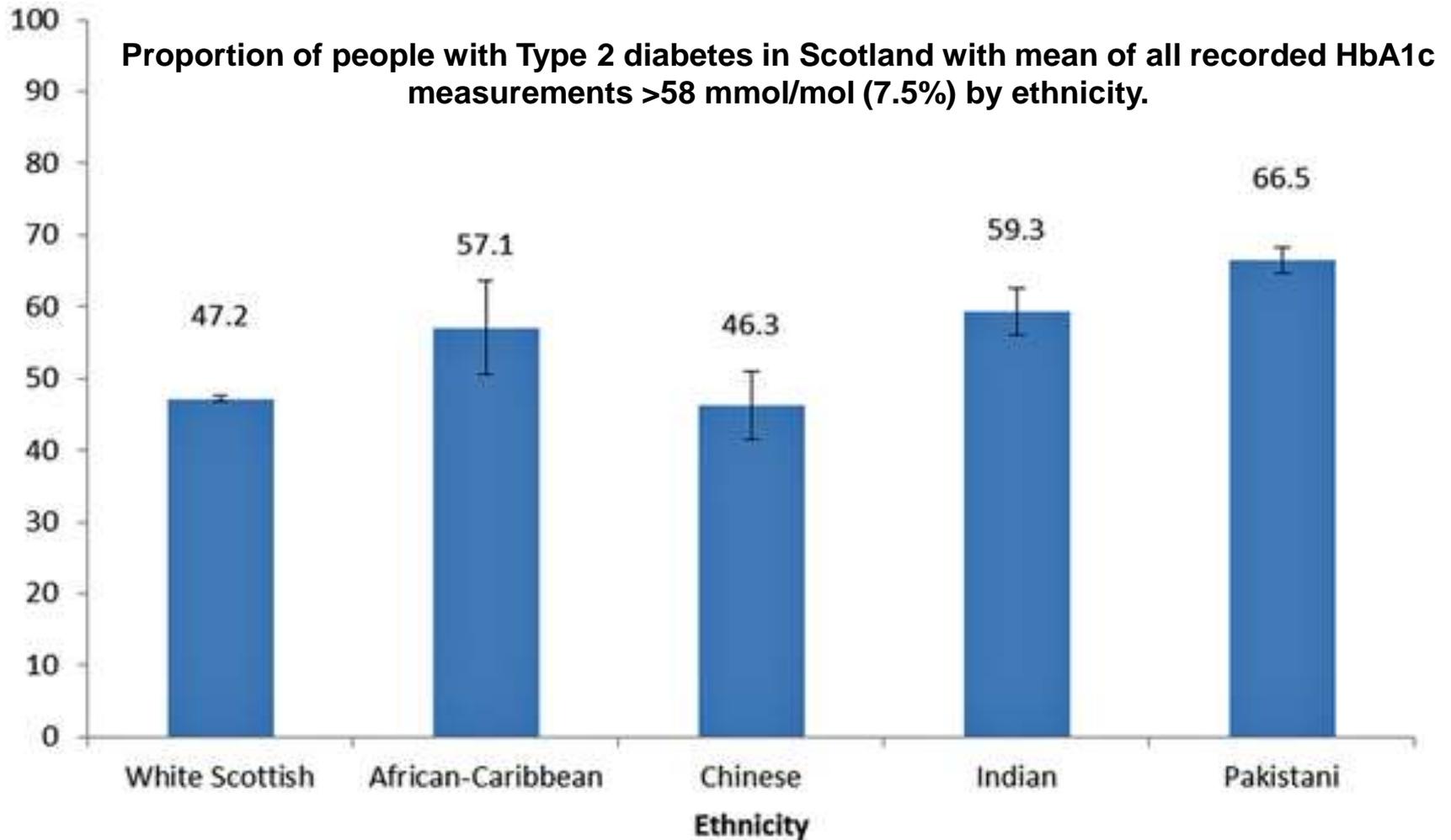people are living with
diabetes in the UK

- By 2030, 5.5 million people in the UK will have DM

- 90% are type 2 diabetes (T2DM)

- The NHS spends **£10 billion** each year on diabetes which is expected to rise to **£16.9 billion** by 2035

% of people in the UK who have diabetes

Prevalence of doctor-diagnosed diabetes, by ethnic group

■ Age standardised ■ Observed

Per cent

% of patients with poorly-controlled diabetes

Proportion of people with Type 2 diabetes in Scotland with mean of all recorded HbA1c measurements >58 mmol/mol (7.5%) by ethnicity.

Negandhi PH, Ghouri N, Colhoun HM, Fischbacher CM, Lindsay RS, et al. (2013) Ethnic Differences in Glycaemic Control in People with Type 2 Diabetes Mellitus Living in Scotland. PLOS ONE 8(12): e83292. https://doi.org/10.1371/journal.pone.0083292
https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0083292

Inequalities in diabetes

Diabetes control and outcomes are worse in patients from ethnic minorities

Racial differences in all-cause mortality and future complications among **people with diabetes**

23 prospective cohort studies

2,416,516 individuals diagnosed with type 1 and/or type 2 diabetes

2-20 years follow-up duration

- Māori
- Black
- Hispanic-American
- East Asian
- South Asian
- Native-American
- Pacific Islander
- White

ALL-CAUSE MORTALITY
Māori patients show ↑88% mortality risk compared with White people

END-STAGE RENAL DISEASE
Black patients present ↑54% risk than White people

MACROVASCULAR COMPLICATIONS
Hispanic-American patients have ↓34% risk than White people

AMPUTATION
No significant differences between racial groups

# Adherence to conventional treatment

- Conventional lifestyle advice focusses on diet and exercise but many patients do not engage with these

    - EG: Survey in Glasgow - only 1/3 of had changed their diet at home

- <50% of patients take their medicines as prescribed

- Side-effects of conventional medicines are a major reason for this

- This leads to worse control of diabetes, more complications and suffering for patients, and more costs for the NHS

# Use of herbal medicines for diabetes

- The NHS provides no information to patients about natural remedies and which could be effective

- Most patients don't tell their GP about herbal medicines they are taking

- Globally, 50-60% of people living with diabetes use some form of CAM / natural remedies along with conventional medicines

  - India - 67% of patients choose naturopathy or Ayurveda

  - UK: 2/3 of Pakistani community prefer to use natural remedies

  - Africa: a wide range of plants are used

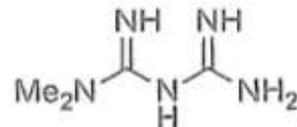# Plants as a source of antidiabetic medicines

- Ebers Papyrus of 1550 BC suggested a high-fibre diet of wheat grains and ochre

- Chinese herbal medicine has been used to treat diabetes for >1500 years

- *Galega officinalis* ("Goat's rue")

  - contains guanidine and galegine – inhibit hepatic glucose production

  - modified to create metformin
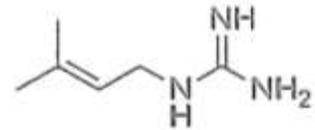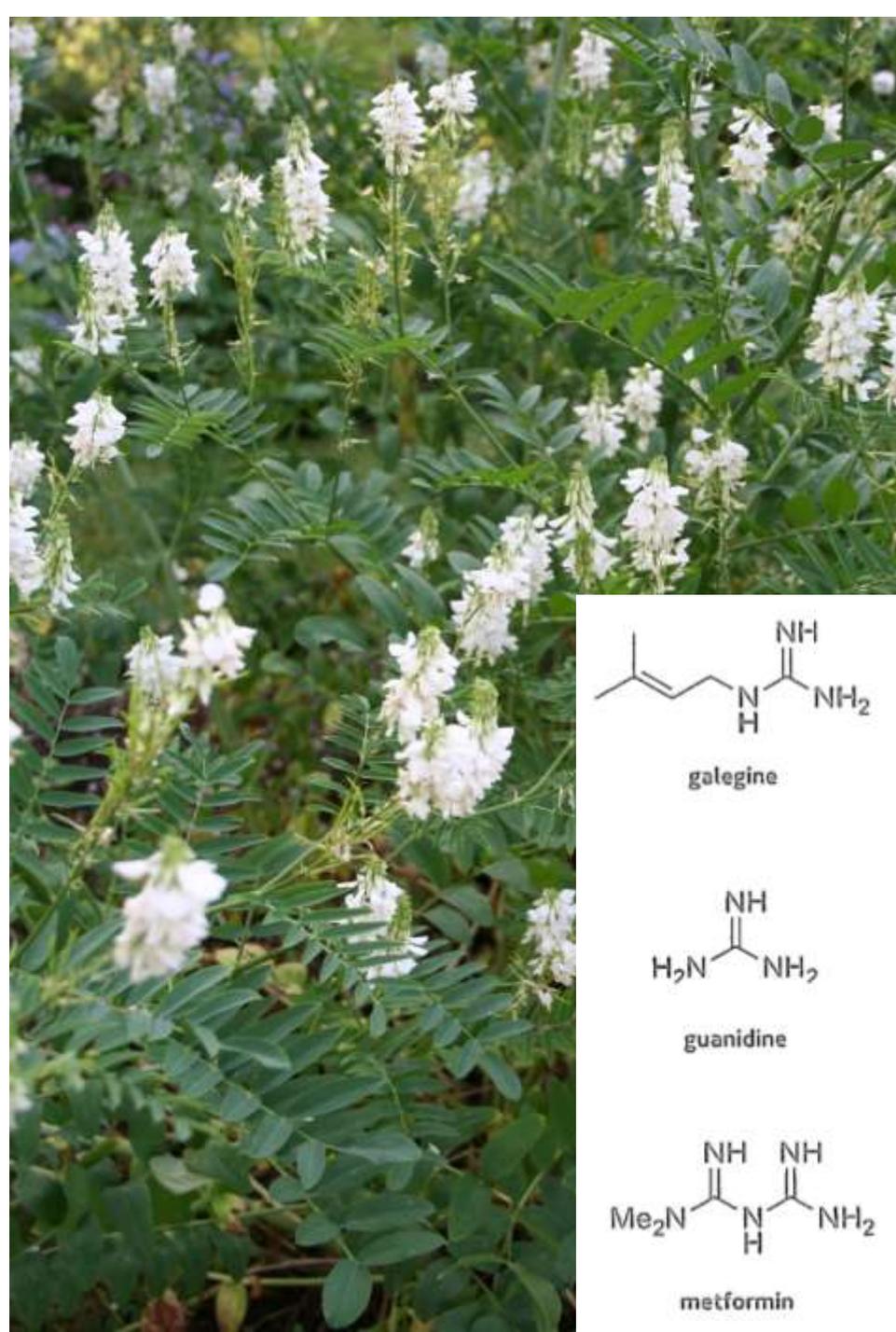
galegine
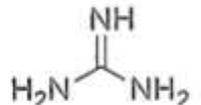
guanidine

metformin

Moringa oleifera Lam.
(Moringaceae)
= drumstick tree / horseradish tree

Moringa oleifera

- Traditional food - Leaves are very rich in proteins, vitamins and minerals – eg 4x richer in Vit A than carrots
- Used as medicine for diabetes in many tropical countries
- In vitro: inhibits sucrase and α-D-glucosidase (like acarbose)
- In animals:
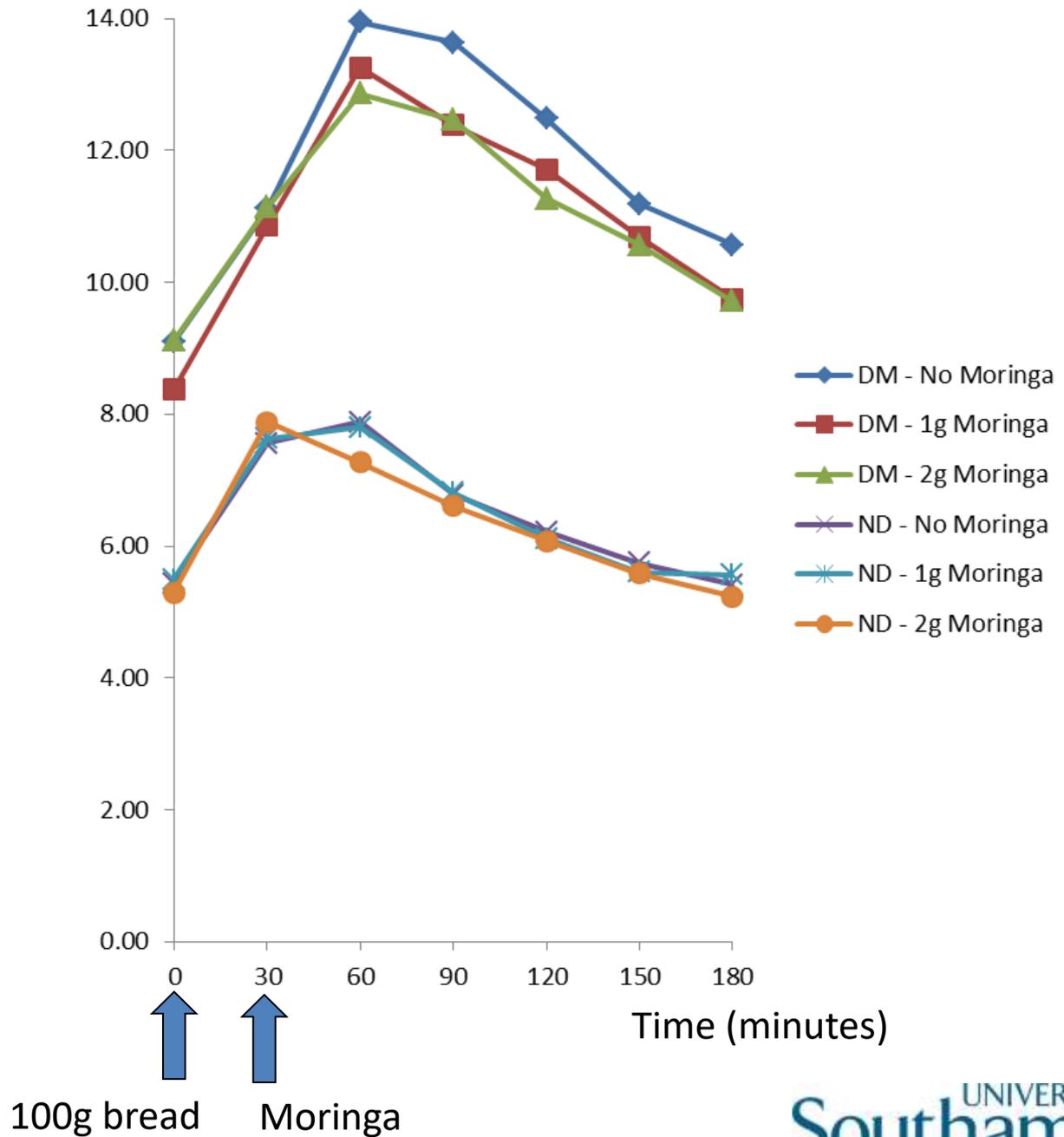 - Reduces blood glucose in diabetic animals

Preparation of plant

Mean blood glucose (mmol/l)

Time (minutes)

DM - No Moringa
DM - 1g Moringa
DM - 2g Moringa
ND - No Moringa
ND - 1g Moringa
ND - 2g Moringa

100g bread   Moringa

UNIVERSITY OF
Southampton

Mean paired reduction in blood glucose (mmol/l)

at different time intervals after eating 100g white bread, and Moringa 30 minutes later, compared to no Moringa (p<0.05, paired t-test)*

Group	Dose of Moringa	60 mins (95% CI)	90 mins (95% CI)	120 mins (95% CI)
Diabetic	1g	0.70 (-0.39 to 1.78)	1.26 (0.07 to 2.46)*	0.76 (-0.26 to +1.80)
	2g	1.04 (-0.21 to 2.29)	1.04 (- 0.18 to 2.27)	1.25 (0.24 to 2.26)*

- Post-prandial blood glucose was reduced by about 1 mmol/l in diabetic patients having ingested *M. oleifera* leaf powder.

- Need a larger RCT measuring impact on HbA1c over 2-3 months

Umbrella review of herbal medicines for controlling blood glucose in type 2 diabetes

- Search of 4 databases (Medline, Embase, Cochrane, CINAHL)

- Inclusion criteria:

    - Systematic reviews of randomised controlled trials

    - In patients with type 2 diabetes

    - Measuring effect on HbA1c

    - Compared to placebo or standard treatment

- 34 systematic reviews were included

https://www.frontiersin.org/articles/10.3389/fphar.2021.777561/full

Effect of medicinal plants on HbA1c (%)
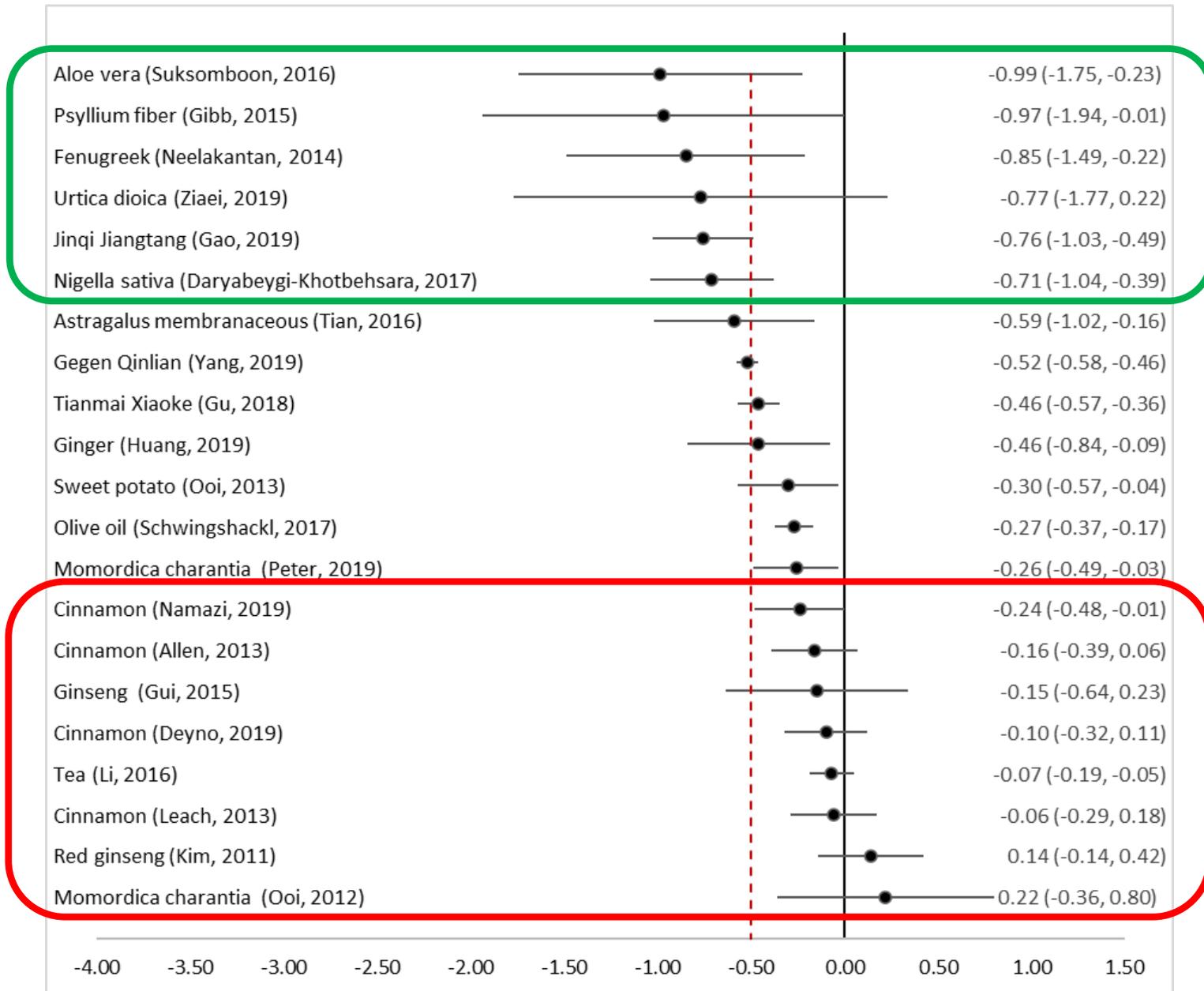
Aloe vera

- Popular remedy for skin complaints

- Very easy to grow at home

- Overall, reduced HbA1c by 0.99%

- Fresh crushed leaves (15g twice daily) or fresh juice (150ml once daily) were the most effective preparations

Psyllium fibre

- Commonly prescribed as a laxative

- Reduced HbA1c by an average of 0.97%

- Optimal dose was 5g twice daily after meals

- BUT – based on 3 trials only

- Conflict of interest –funded by Proctor & Gamble

Fenugreek seeds

- Reduced HbA1c by 0.85% on average

- one of the most popular remedies used for diabetes in India, China and South Asian communities in the UK

- used as a spice in Indian food and is generally regarded as safe.

- contain gel-forming fibres which delay gastric emptying and interfere with glucose absorption from the intestines

- stimulate release of insulin.

XVII, 3.   106.Leguminosae

433.Trigonella Foenum graecum L   Griechisches Heu.

Nigella sativa seeds

- Very popular in Middle East

- Part of diet

- Reduced HbA1c by 0.71%

- Most effective preparation was powder, 2g/day

Other promising herbal remedies

- Many were not included in our umbrella review because there has not been a systematic review of Randomised controlled trials

- Several complex Chinese herbal medicines – see Cochrane review

23

Gymnema sylvestre

- Ayurvedic remedy for diabetes

- Gurmar = "sugar destroyer"

- Gymnemic acid inhibits perception of sweetness

- May inhibit glucose absorption from intestine

- Improves diabetic control (types 1 and 2)

What do patients think about using herbs for type 2 diabetes?

- Systematic review of 22 qualitative (interview) studies

  - 7 from high-income countries (1 in UK)

  - 12 from middle-income countries

  - 3 from low-income countries

Themes

Facilitators to taking herbal medicine
- Cultural beliefs
- Self-management
- Accessibility
- Influence from friends, family and healthcare professionals

Barriers to following conventional treatment
- Patients' lack of knowledge about modern medicine
- Cultural reasons
- Side effects of modern medicine
- Resistance to taking tablets or medication

Doctor-patient relationship
- Patients not informing doctors about using herbal medicines
- Doctors not recommending herbal medicines as one of the options
- Barriers to taking herbal medicines

Double-blind medicine

I'm not discussing any herbs with the doctor because when you tell him about herbs he says 'nonsense', 'foolishness' so I continue to drink the herb. I put the medication aside for a while, go on the herb, and then back to the medication.

Female patient with type 2 diabetes, Western Jamaica

If I ask the patient whether he/she has been using herbal medicine and found that he/she was using any herb, I wouldn't take any decision towards using herb because I don't have any knowledge about a specific herb and the conventional anti-diabetic drug interactions

GP, Ethiopia

The need for evidence-based advice

As a doctor, I have no idea about the real physiological effects of these products. If I do recommend them that would imply that I should be responsible to answer to any question and doubt of my patients.

Doctor, Mauritius

My doctor is a Nigerian that supports both herbs and medication. I would love my Nigerian doctor to give me the herbs because I know he has an herb book and he knows which ones are best so I can get a list.

Diabetic patient, Cameroon (38)

Priorities for future research

- Continue improving the evidence base on herbal medicines for T2DM

- Updated systematic review of clinical trials of Fenugreek

- High quality clinical trials of promising herbs eg *Moringa*

- Qualitative study with T2DM patients from ethnic minorities in the UK to better understand their support needs

- Co-design evidence-based support for patients with T2DM, using the "person-based approach"

- Trials to assess feasibility and effectiveness of this approach to improve diabetes outcomes

PROPOSAL: EAT SOMETHING YOU LIKE...CHOOSE FROM THE LIST!

-- list of hypoglycemic foods

-- choice

-- information

-- try

-- test

... can be tested in a clinical study (even RCT: usual care + choice *versus* usual care)

Providing evidence-based information

Black cumin *(Nigella sativa)*

Scientific name: *Nigella sativa* L.

Common names: Nigella, Black seed, Black cumin, Small Fennel, Black Caraway, Fennel flower, Roman coriander or Kalonji.

Part used: Seed.

Practical information:

-- **Where to buy it:** Seeds are found on the market, in speciality grocery stores and Herbal shops. You can also find black cumin oil, seed powder, and capsules.

-- **Storage:** The seeds must be stored under dry conditions to maintain their characteristic spicy flavour. Their viability is for 2 to 3 years when fully ripe. Broken seeds deteriorate rapidly; do not keep them over long periods.

Preparation and dosage:

-- **Black cumin seeds:** Consume 2 g/day (equal to 1 level teaspoon) given in two times (means ½ level teaspoon twice a day). Seeds must be crushed or well-chewed to increase their efficacy; it is also possible to consume them stir-fried, but you should avoid other modes of preparation (baked, cooked for a long time, etc.), as this may alter their hypoglycaemic properties.

-- **Black cumin oil:** Consume 1 g/day of black cumin oil (equal to ¼ teaspoon), can be found in the form of capsules or bulk.

Precautions, interactions, and adverse effects:

Black cumin can be consumed safely at the usual doses.

In functional dyspeptic patients, mild adverse effects such as nausea, bloating, and burning sensation have been reported after administration of black cumin. However, in general, black cumin improves liver and kidney functions.

Black cumin should not be taken by patients under phenobarbitone sodium.

Black cumin increases intestinal absorption of amoxicillin, thus enhancing its availability and pharmacological effect.

Pregnancy and Breastfeeding:

Despite no systematically controlled studies in pregnant women or during breastfeeding, black cumin can be consumed safely at the usual doses as a common food product.

Recipes:

Black cumin seeds are widely used in food as spices and condiments. Black cumin seeds add a nutmeg-like flavour to foods, a carrot-like smell and an aromatic, somewhat acrid oil taste.

Trial of impact of "advice"

Advantages	**Disadvantages**

- Circumvents regulatory issues with trials of a single product

- Pragmatic, "real-world" evidence

- Cannot control quality of product

- May not be accepted by official bodies (eg NICE) to make recommendations

PhD: Improving self-management of type 2 diabetes in patients of African heritage in the UK

- Co-funded by NIHR SPCR (School for Primary Care Research) and Pukka Herbs

- Systematic literature review on self-management of diabetes

- Qualitative interviews on self-management of diabetes in patients of African origin in the UK

- Designing and piloting an "advice" intervention using the patient-based approach.

What do we hope will be the impact?

- Better understanding of the support needed by T2DM patients from ethnic minorities in the UK

- Culturally appropriate, evidence-based advice on diet including natural / herbal remedies

- Patients feel more motivated to engage with self-management of diabetes

- Improved glycaemic control and improved diabetic outcomes, particularly for patients at highest risk (ethnic minorities).

Improving type 2 diabetes outcomes for people of African ethnic backgrounds.
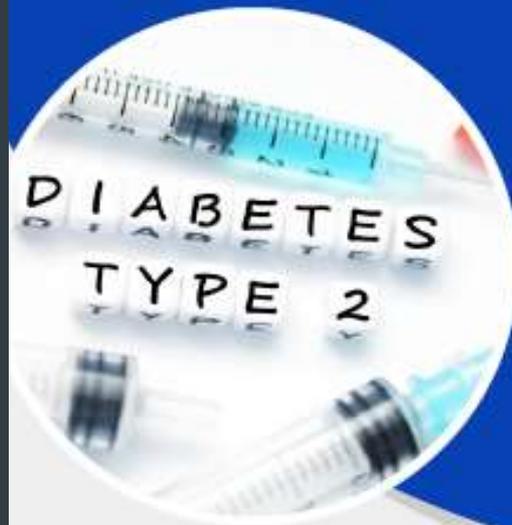
DIABETES TYPE 2

P.P.I panel
Patient Public Involvement

NEEDED

ELIGIBILITY

- Identify as being from an African ethnic background.
- Have type 2 diabetes
- Live in the U.K
- Be willing to contribute to service improvement.

University of **Southampton**

For more information, please contact:
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