

HIGH-VALUE
NUTRITION

Ko Ngā Kai
Whai Painga

Science Symposium_25th September 2017

Insights into diabetes susceptibility and resilience: outcomes of the TOFI_Asia Study

Dr Ivana Sequeira on behalf of the PANaMAH program

Host Institution



TOFI_Asia study: Conducted in Auckland



Multi-ethnic city hosting a wider Asian population

Cross sectional phenotyping to determine markers of diabetes risk

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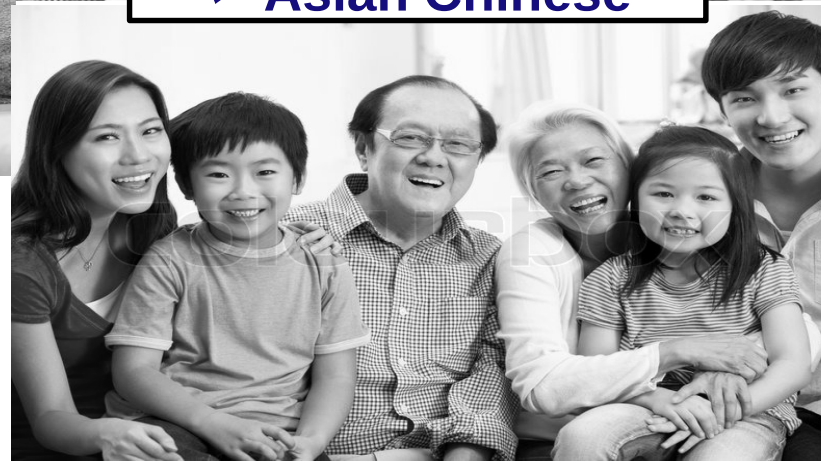
TOFI_Asia study: Conducted in Auckland



✓ European Caucasian



✓ Asian Chinese



Pre-screened: N = 383 individuals



Eligible: N = 365

And enrolled into the study

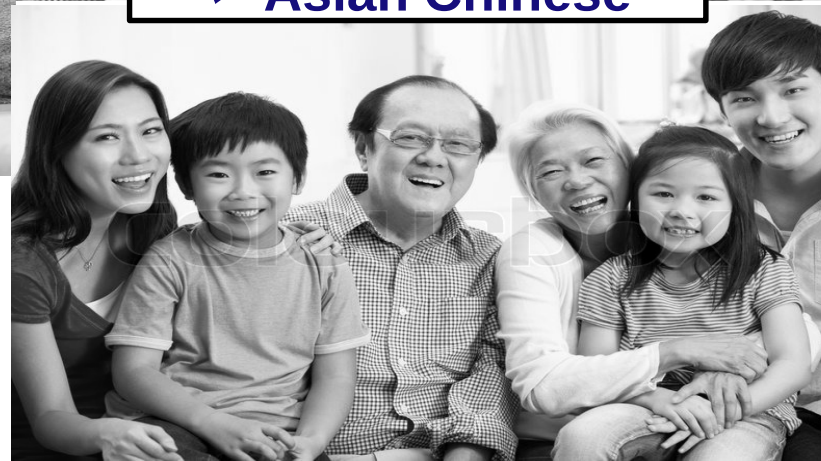
TOFI_Asia cohort: Eligibility criteria



✓ European Caucasian



✓ Asian Chinese



Both parents



18 – 70 yrs

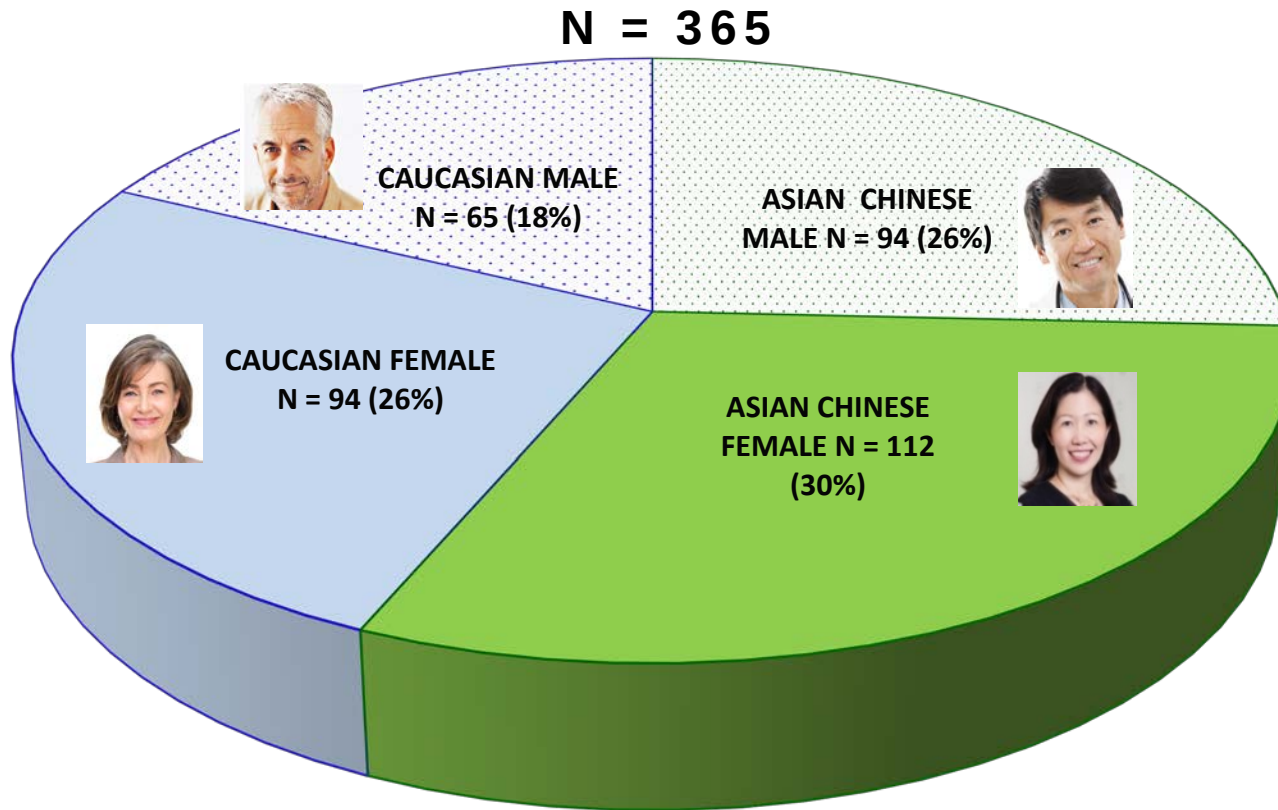


20 – 40 kg/m²

healthy

Pre-Diabetic

TOFI_Asia cohort: Successful recruitment!



159 Caucasian, 206 Asian Chinese



Dr Louise Lu

Mandarin speaking



Wilson Yip (PhD)

Cantonese speaking

TOFI_Asia study protocol: Phenotyping the cohort



N = 365 ♀♂
206 Asian Chinese
159 Caucasian

Anthropometry



Height



Weight



Waist



Hip

Study timeline: June 2016 – April 2017

National
SCIENCE
Challenges

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TOFI_Asia study protocol: Phenotyping the cohort



N = 365 ♀♂
206 Asian Chinese
159 Caucasian

Fasting blood
samples

- *Established markers*
- Fasting plasma glucose
 - Hb_{A1c}
 - Insulin
 - GI Peptides
 - Amylin, Adiponectin
 - Full lipid profile
 - Liver function tests
 - Cytokines

Study timeline: June 2016 – April 2017

TOFI_Asia study protocol: Phenotyping the cohort



N = 365 ♀♂
206 Asian Chinese
159 Caucasian

Fasting blood
samples

➤ *Novel (metabolomic) markers*
Untargeted LC-MS

agresearch

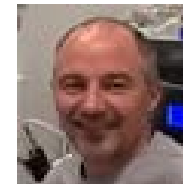


Dr Karl Fraser



Emily Wu (PhD)

International collaborators



Dr John-Charles Martin



Prof Garth Cooper

Study timeline: June 2016 – April 2017

National
SCIENCE
Challenges

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TOFI_Asia study protocol: Phenotyping the cohort

N = 365 ♀♂
206 Asian Chinese
159 Caucasian

DeXA Scan

➤ *Total body fat and abdominal fat*



Auckland City Hospital



A/Prof Lindsay Plank

Study timeline: June 2016 – April 2017

TOFI_Asia study protocol: Phenotyping the cohort

N = 365 ♀♂
206 Asian Chinese
159 Caucasian

N = 70 ♀
36 Asian Chinese
34 Caucasian



- *Lipid 'Overspill' into the organs*
Pancreas fat, Liver fat



Magnetic Resonance Imaging and Spectroscopy (MRI/S)

Study timeline: June 2016 – April 2017

TOFI_Asia study protocol: Phenotyping the cohort

AUT

Auckland City Hospital

N = 365 ♀♂
206 Asian Chinese
159 Caucasian

N = 70 ♀
36 Asian Chinese
34 Caucasian

MRI / S

➤ *Lipid 'Overspill' into the organs*
Pancreas fat, Liver fat



A/Prof Jun Lu



Dr Rinki Murphy

Study timeline: June 2016 – April 2017

National
SCIENCE
Challenges

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TOFI_Asia study protocol: Phenotyping the cohort

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159 Caucasian

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MRI / S

➤ *Lipid 'Overspill' into the organs*

Pancreas fat, Liver fat



International collaborators
renowned for MR imaging



Dr. Keiren Hollingsworth

Study timeline: June 2016 – April 2017

TOFI_Asia study protocol: Phenotyping the cohort

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206 Asian Chinese
159 Caucasian

N = 70 ♀
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➤ *Cardiorespiratory fitness*
YMCA submaximal bike test

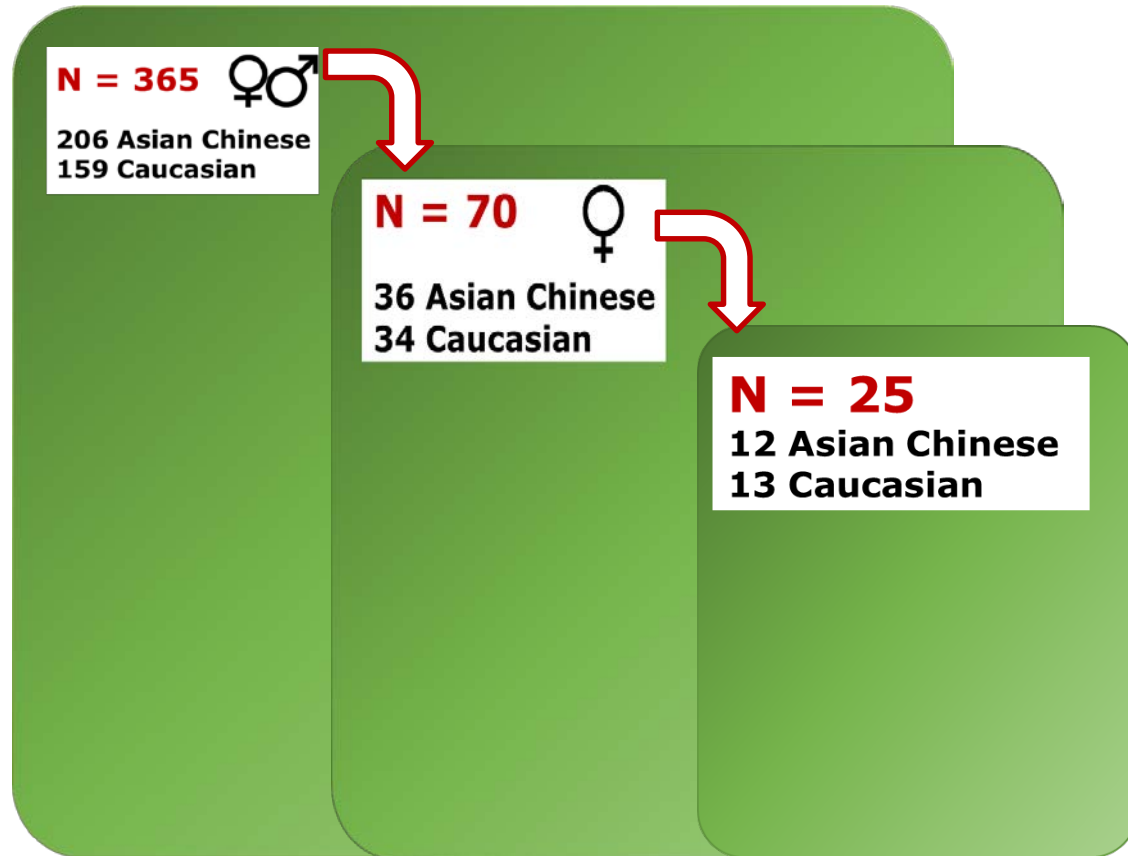


Dr. Nick Gant

HVN Poster presentation,
Wilson Yip (PhD)

Study timeline: June 2016 – April 2017

TOFI_Asia study protocol: Phenotyping the cohort



➤ *Pancreatic β -cell function
as a measurement of insulin secretion*

Intravenous glucose tolerance test
(ivGTT)

Study timeline: June 2016 – April 2017

Summarise *Early* data from the TOFI cohort

N = 365 ♀♂

206 Asian Chinese
159 Caucasian



N = 70 ♀

36 Asian Chinese
34 Caucasian



Study timeline: June 2016 – April 2017

TOFI cohort: Summary of early results

N = 365 ♀♂
206 Asian Chinese
159 Caucasian



	CAUCASIAN	CHINESE ASIAN	p value
Height (m)	1.72 ± 0.1	1.66 ± 0.1	<0.001
Weight (kg)	80.0 ± 15.7	75.9 ± 14.4	0.009
BMI (kg/m ²)	26.8 ± 4.6	27.4 ± 3.9	ns
Age (yrs)	42.4 ± 16.	41.2 ± 13.3	ns
Total body fat (%)	33.8 ± 10.2	35.0 ± 7.2	ns
Abdominal fat (%)	36.9 ± 14.1	41.0 ± 9.0	<0.001

NOT AS TALL

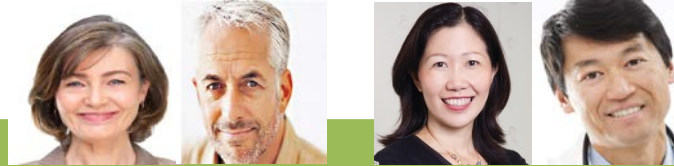
Mean ± SD

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TOFI cohort: Summary of early results

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WEIGHED LESS

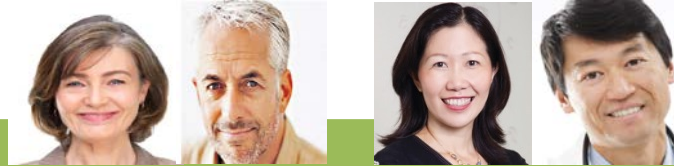
Mean ± SD

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TOFI cohort: Summary of early results

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but SIMILAR BMI

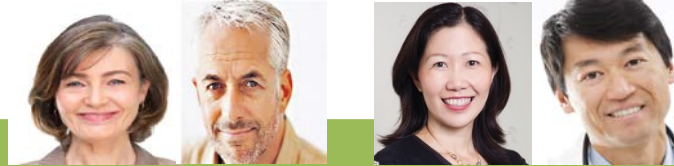
Mean ± SD

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TOFI cohort: Summary of early results

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SIMILAR AGE

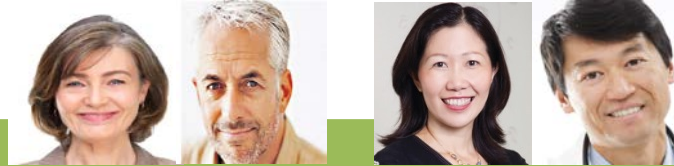
Mean ± SD

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TOFI cohort: Summary of early results

N = 365 ♀♂
206 Asian Chinese
159 Caucasian



DEXA

	CAUCASIAN	CHINESE ASIAN	p value
Height (m)	1.72 ± 0.1	1.66 ± 0.1	<0.001
Weight (kg)	80.0 ± 15.7	75.9 ± 14.4	0.009
BMI (kg/m ²)	26.8 ± 4.6	27.4 ± 3.9	ns
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Total body fat (%)	33.8 ± 10.2	35.0 ± 7.2	ns
Abdominal fat (%)	36.9 ± 14.1	41.0 ± 9.0	<0.001

**GREATER
ABDOMINAL FAT**

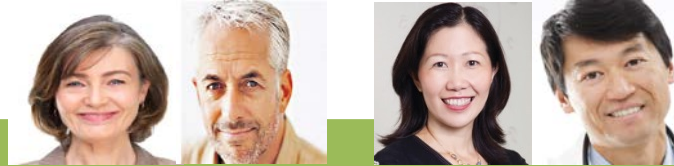
Mean ± SD

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TOFI cohort: Summary of early results

N = 365 ♀♂
206 Asian Chinese
159 Caucasian



Established
BLOOD
markers
for
diabetes risk

	CAUCASIAN	CHINESE ASIAN	<i>p</i> value
Fasting plasma glucose (mmol/L)	5.1 ± 0.6	5.4 ± 0.7	<0.001
Hb_{A1c} (mmol/mol)	33.3 ± 3.6	35.9 ± 4.1	<0.001

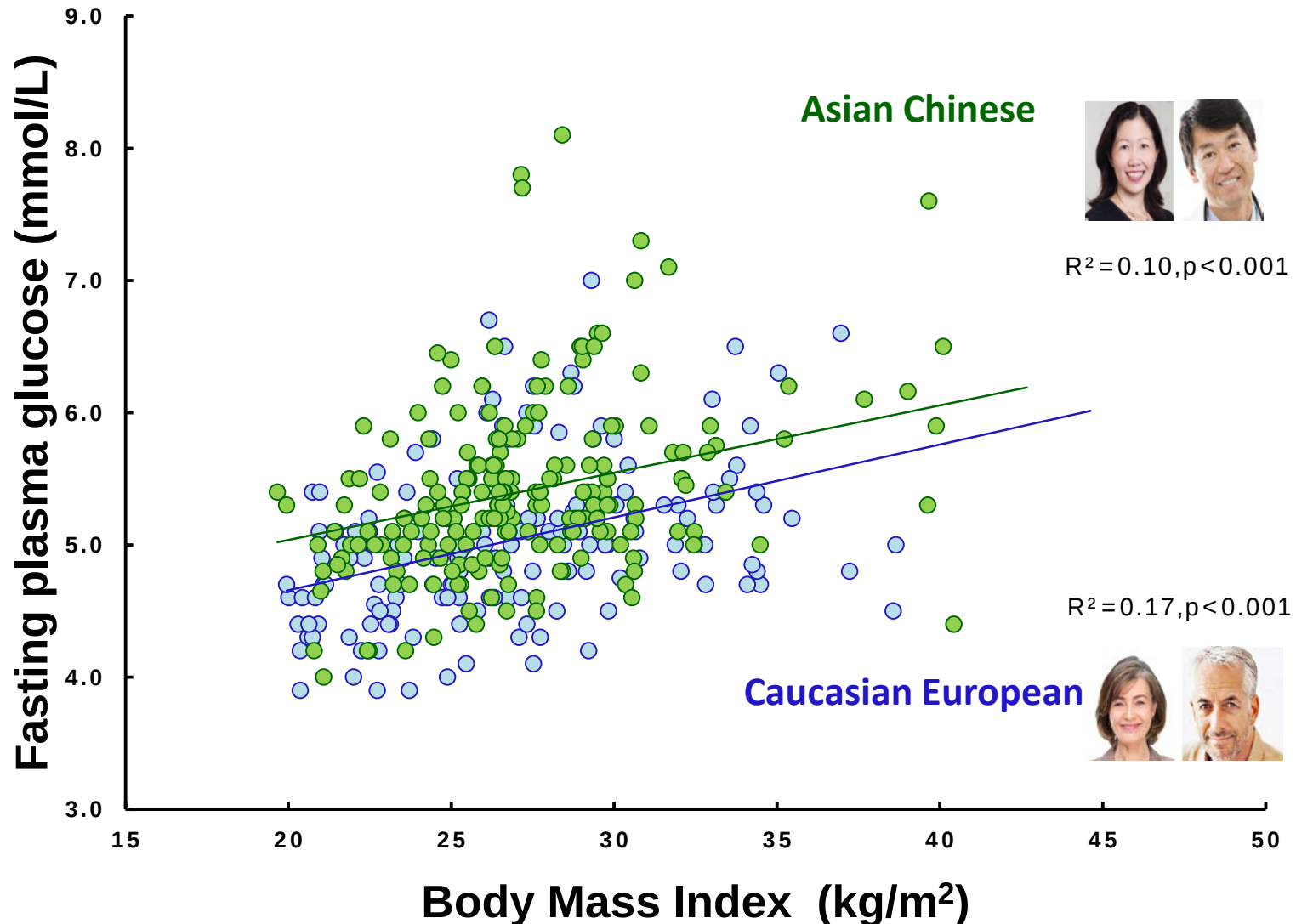
**BOTH HIGHER in
Asian Chinese**

Mean ± SD

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Established risk markers in the TOFI cohort



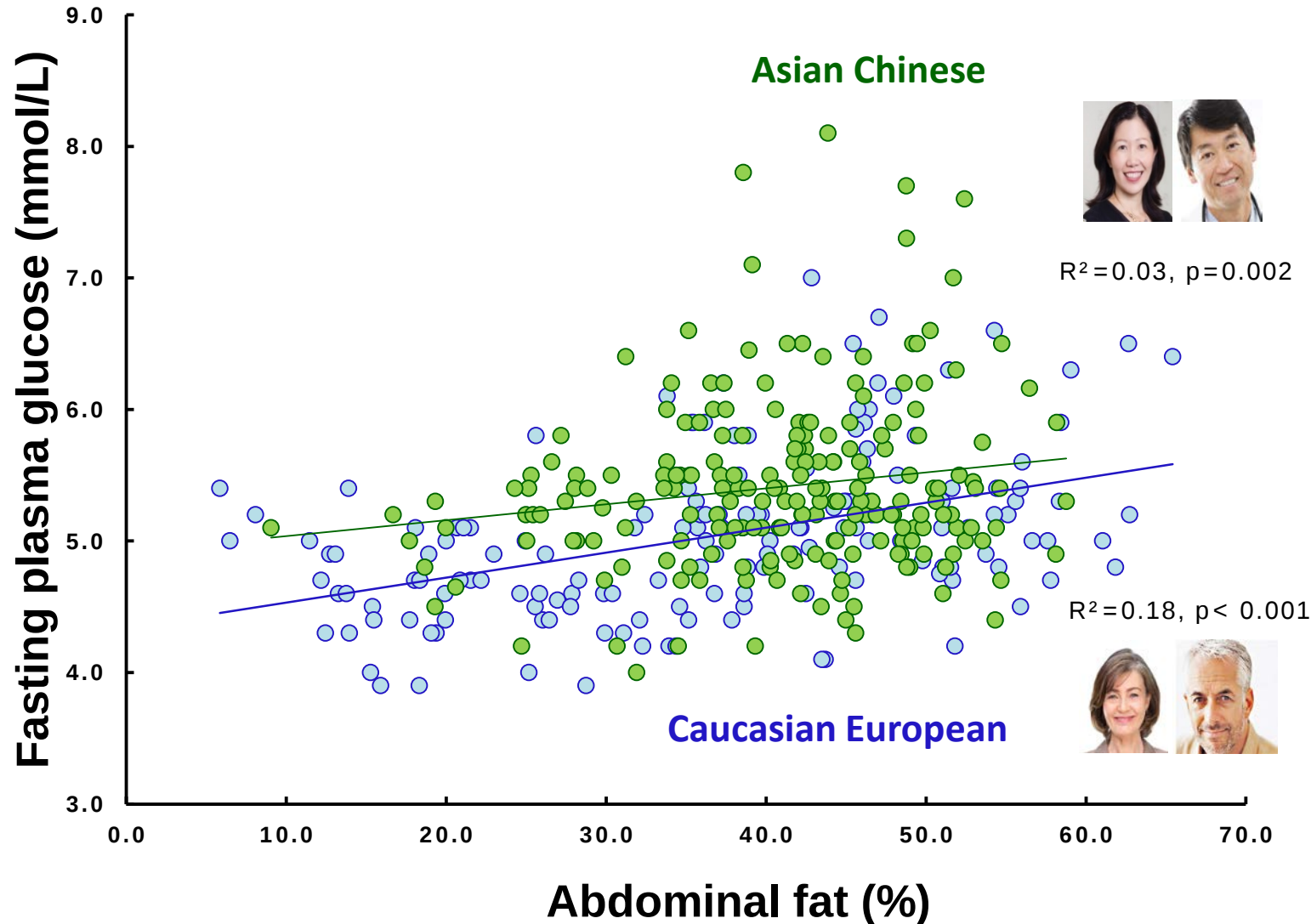
As expected, fasting glucose levels are significantly correlated with BMI in both Ethnicities

If anything Asian Chinese are slightly higher

Established risk markers in the TOFI cohort



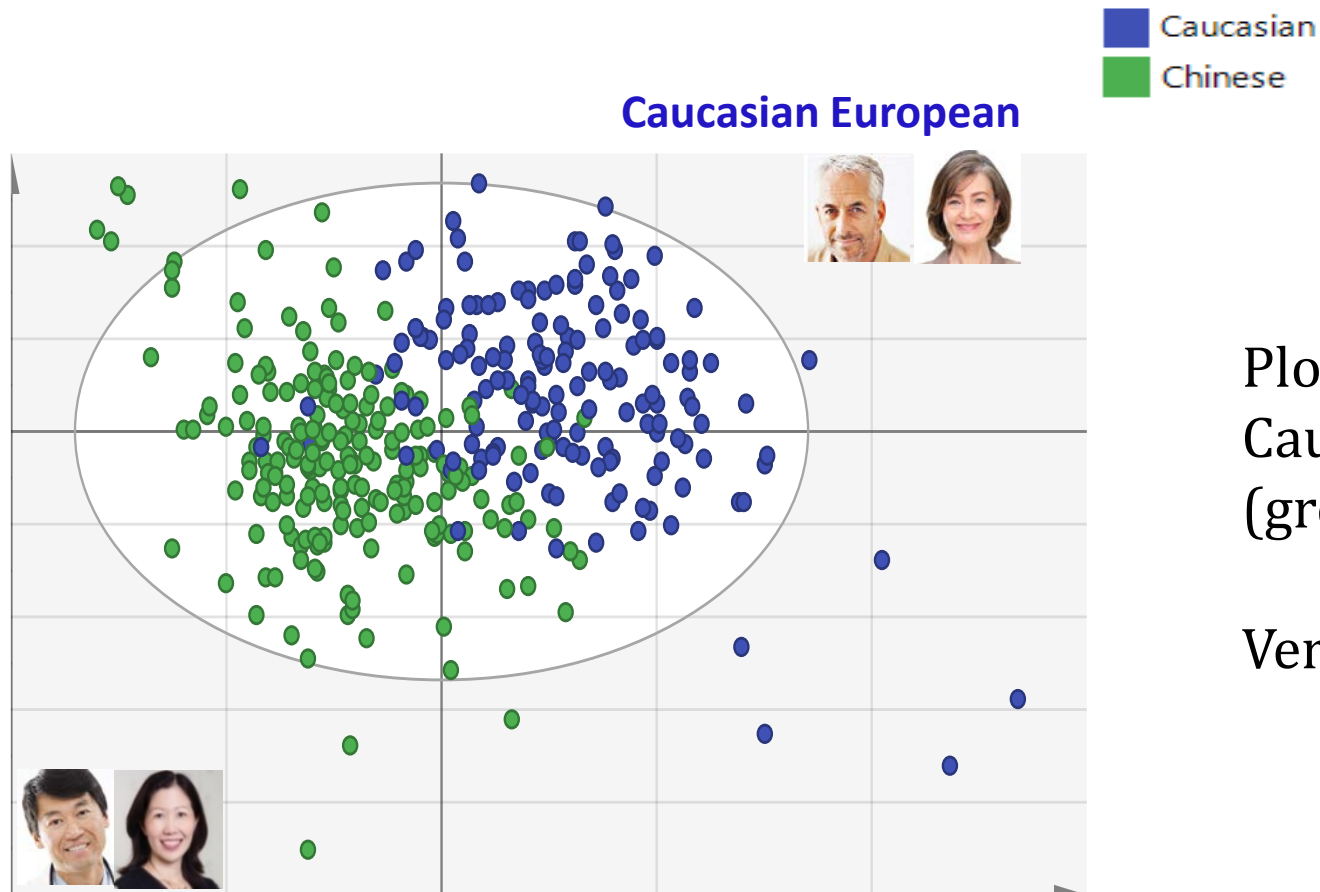
DeXA - fat around the abdomen



Not surprising, fasting glucose levels are also significantly correlated with abdominal fat in both Ethnicities

Again Asian Chinese are slightly higher

Novel (metabolomic) markers in the TOFI cohort



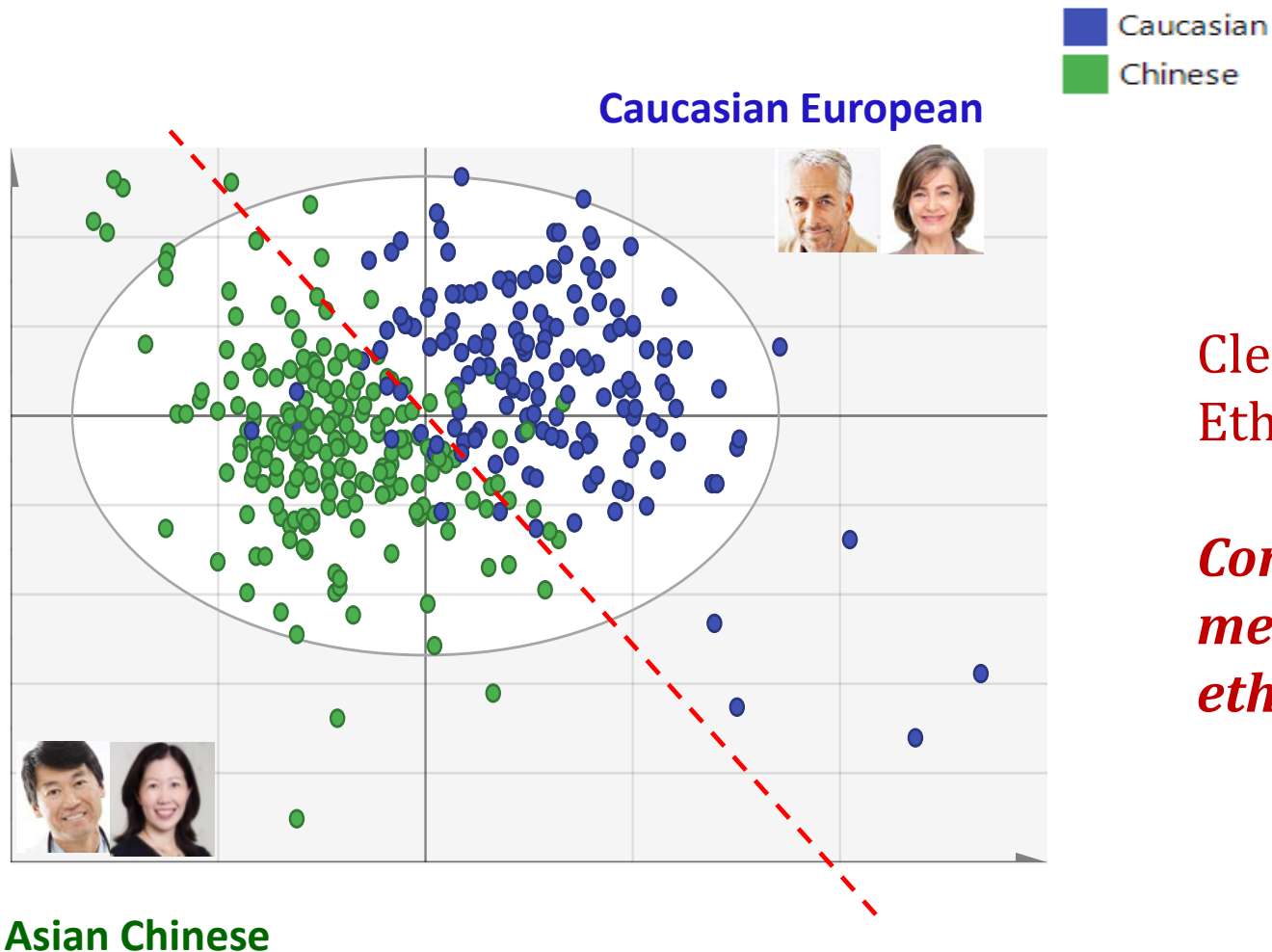
Plot shows *novel blood metabolites*
Caucasians (blue) and Asian Chinese
(green)

Very interesting findings!

Asian Chinese

Partial least squares discriminatory analyses

Novel (metabolomic) markers in the TOFI cohort



Clear and robust separation between Ethnicities

Considerably different blood metabolite profiles between the two ethnic groups

Partial least squares discriminatory analyses

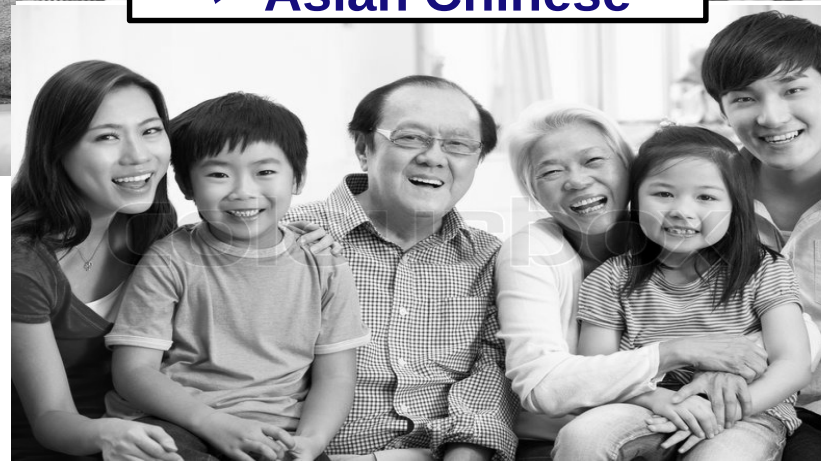
Early findings from Established & Novel markers suggest...



✓ **European Caucasian**



✓ **Asian Chinese**



Very important that these studies are focused on Asian Chinese consumers

In line with Chinese regulatory requirements for validating health claims

TOFI-MRI cohort: Summary of early results

N = 365 ♀♂
206 Asian Chinese
159 Caucasian



N = 70 ♀
36 Asian Chinese
34 Caucasian



Study timeline: June 2016 – April 2017

TOFI-MRI cohort: Summary of early results



Only scanned **women** so far

- Due to gender differences in body composition

N = 70 ♀
36 Asian Chinese
34 Caucasian



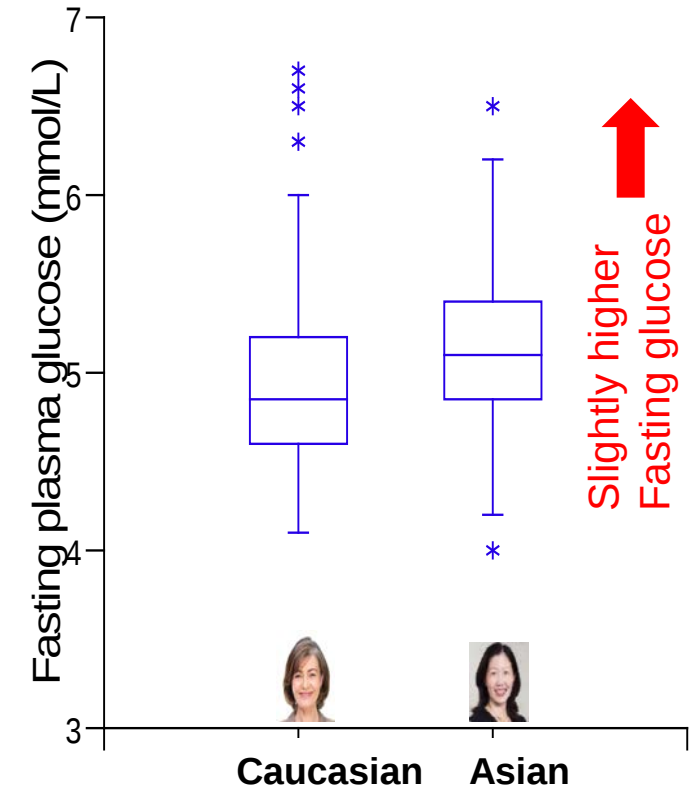
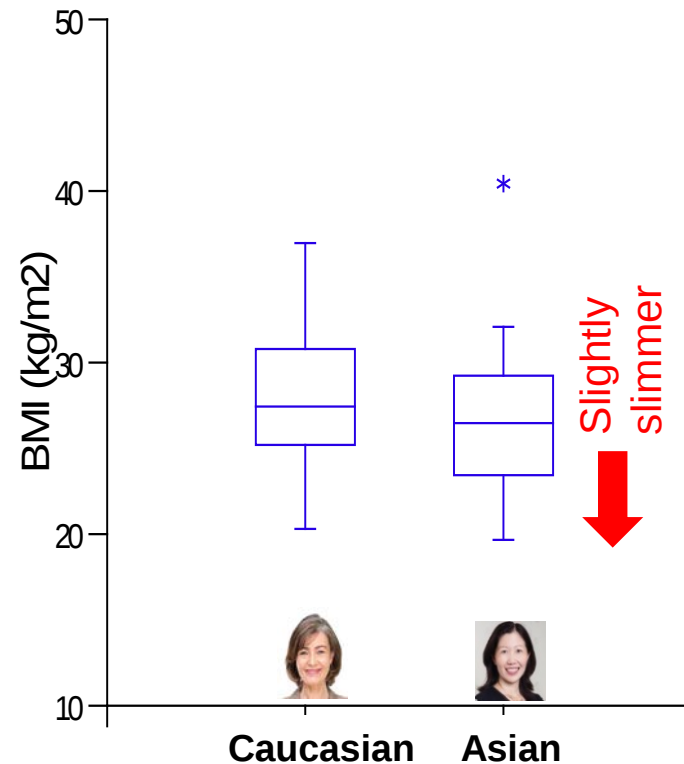
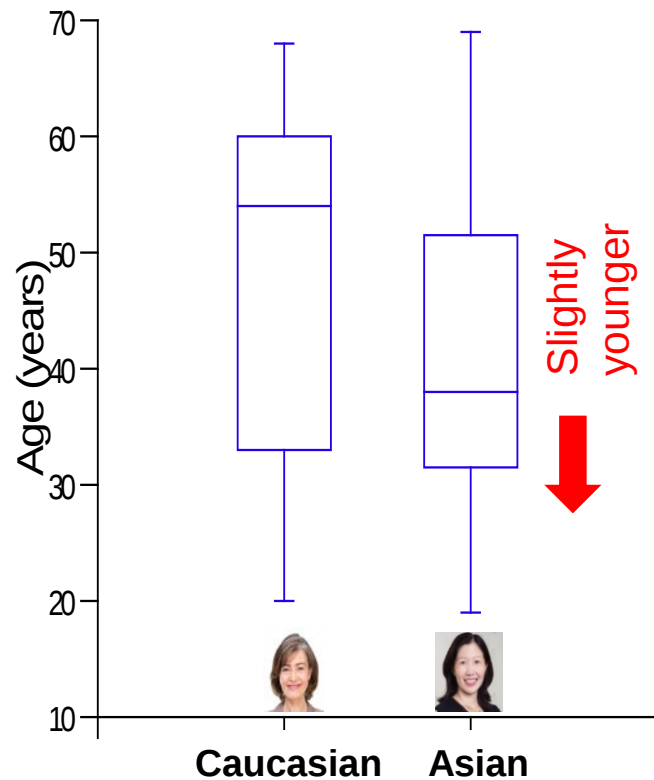
First analysis of MRI scans

- Undergoing review with **UK collaborators** – globally-leading research group for pancreatic fat MRI imaging & analyses

Study timeline: June 2016 – April 2017

TOFI-MRI cohort: Summary of early results

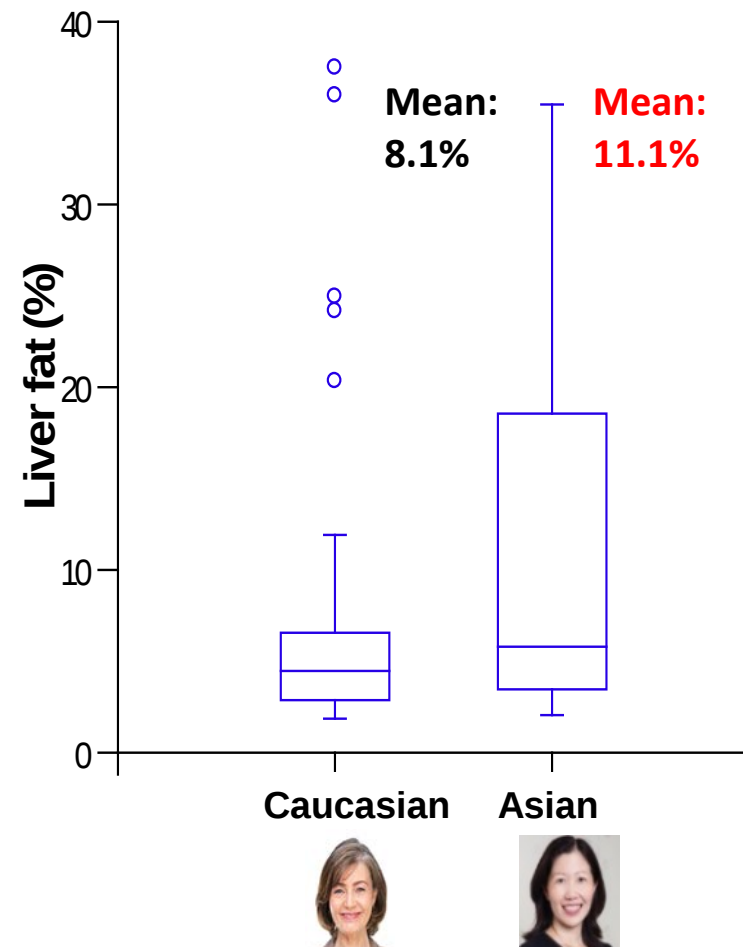
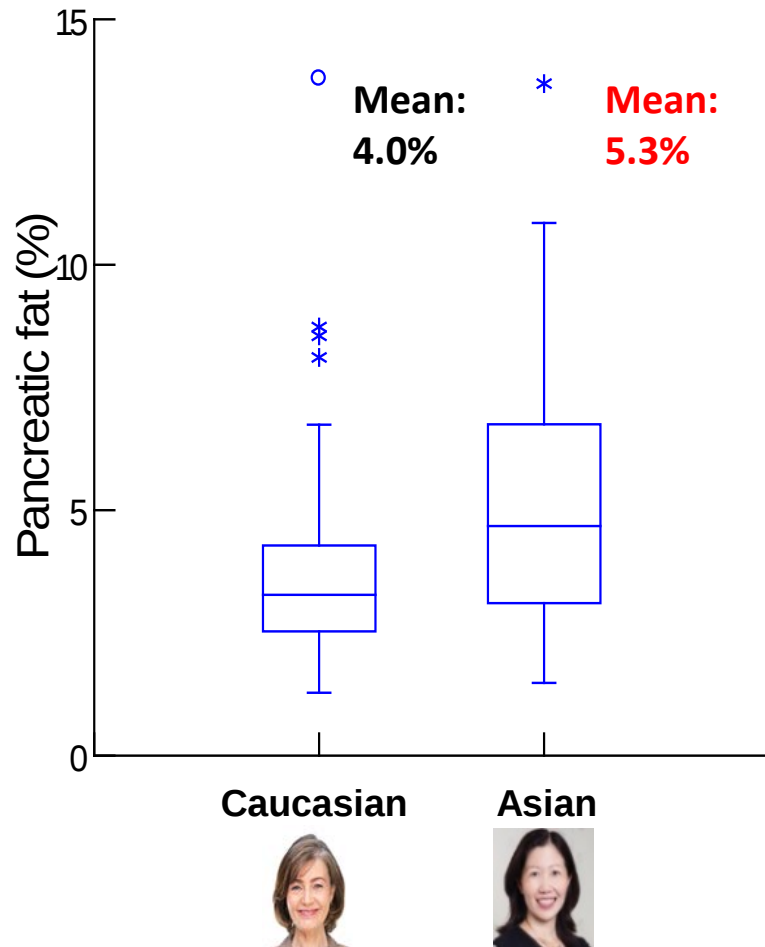
N = 70 ♀
36 Asian Chinese
34 Caucasian



Box plots showing median and interquartile range

TOFI-MRI cohort: Summary of early results

N = 70 ♀
36 Asian Chinese
34 Caucasian



**ORGAN FAT
HIGHER in Asian
Chinese women**

Despite being
slightly younger &
slightly slimmer

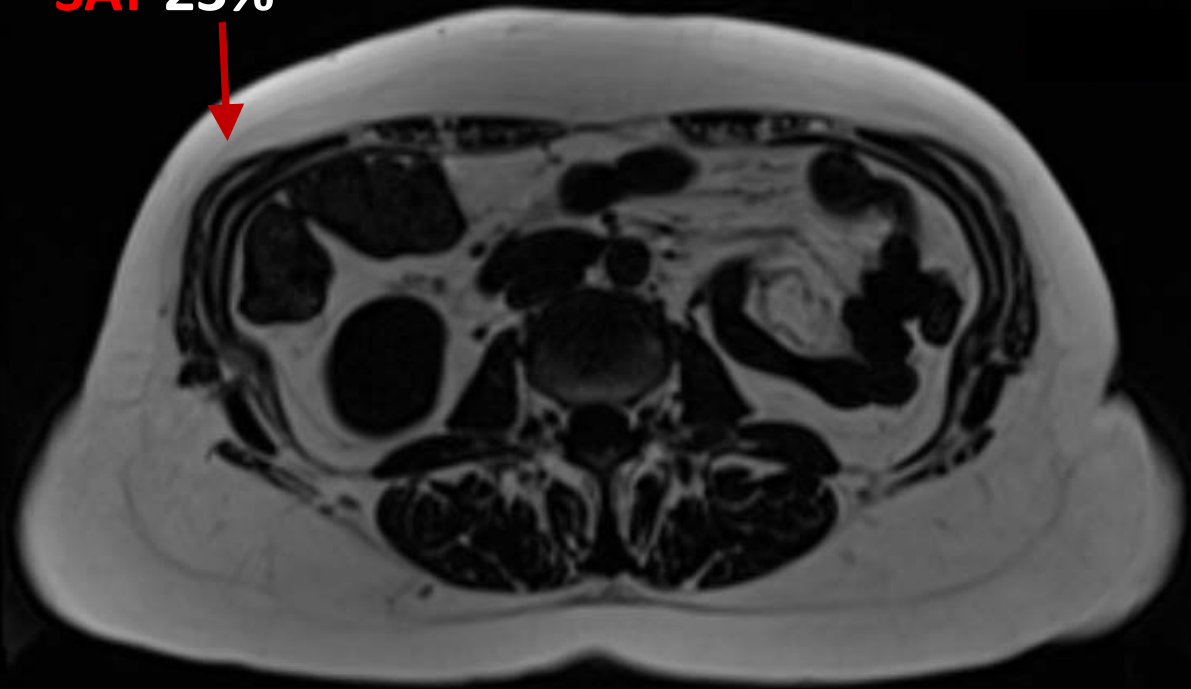
Box plots showing median and interquartile range

MRI SCAN

Caucasian female, 56 y

BMI 35 kg/m²

SAT 23%



FAT IMAGE (3 mm)

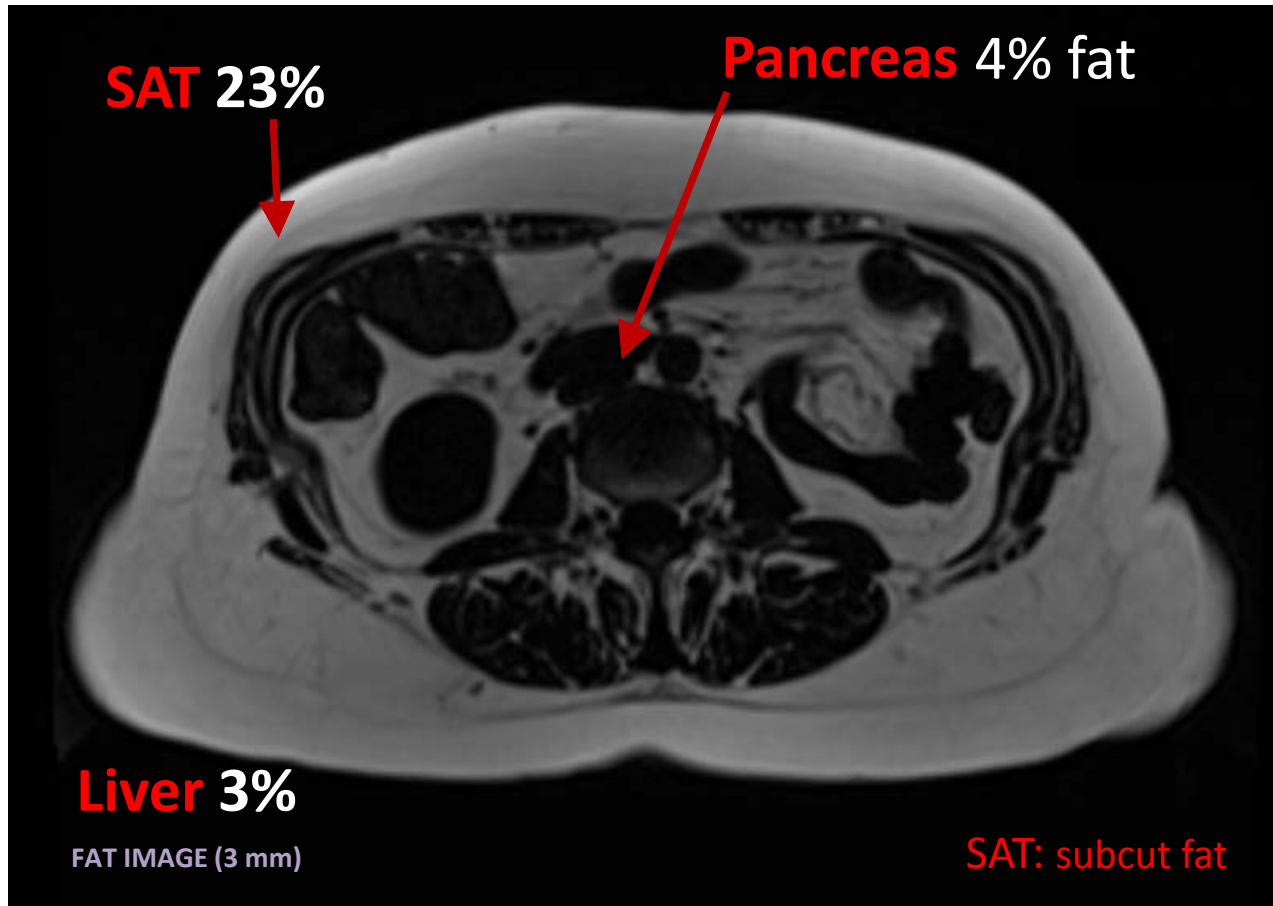
SAT: subcut fat



MRI SCAN

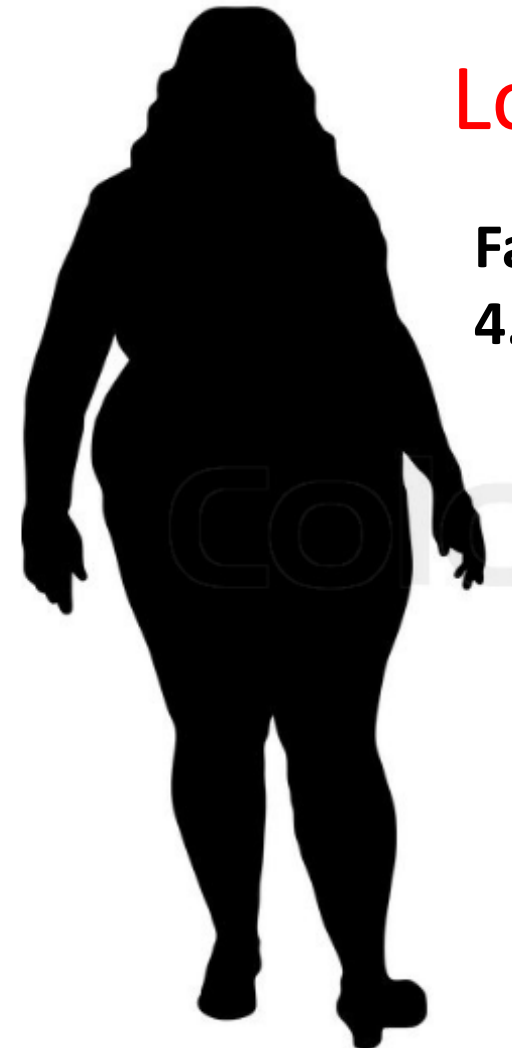
Caucasian female, 56 y

BMI 35 kg/m²



Low Risk

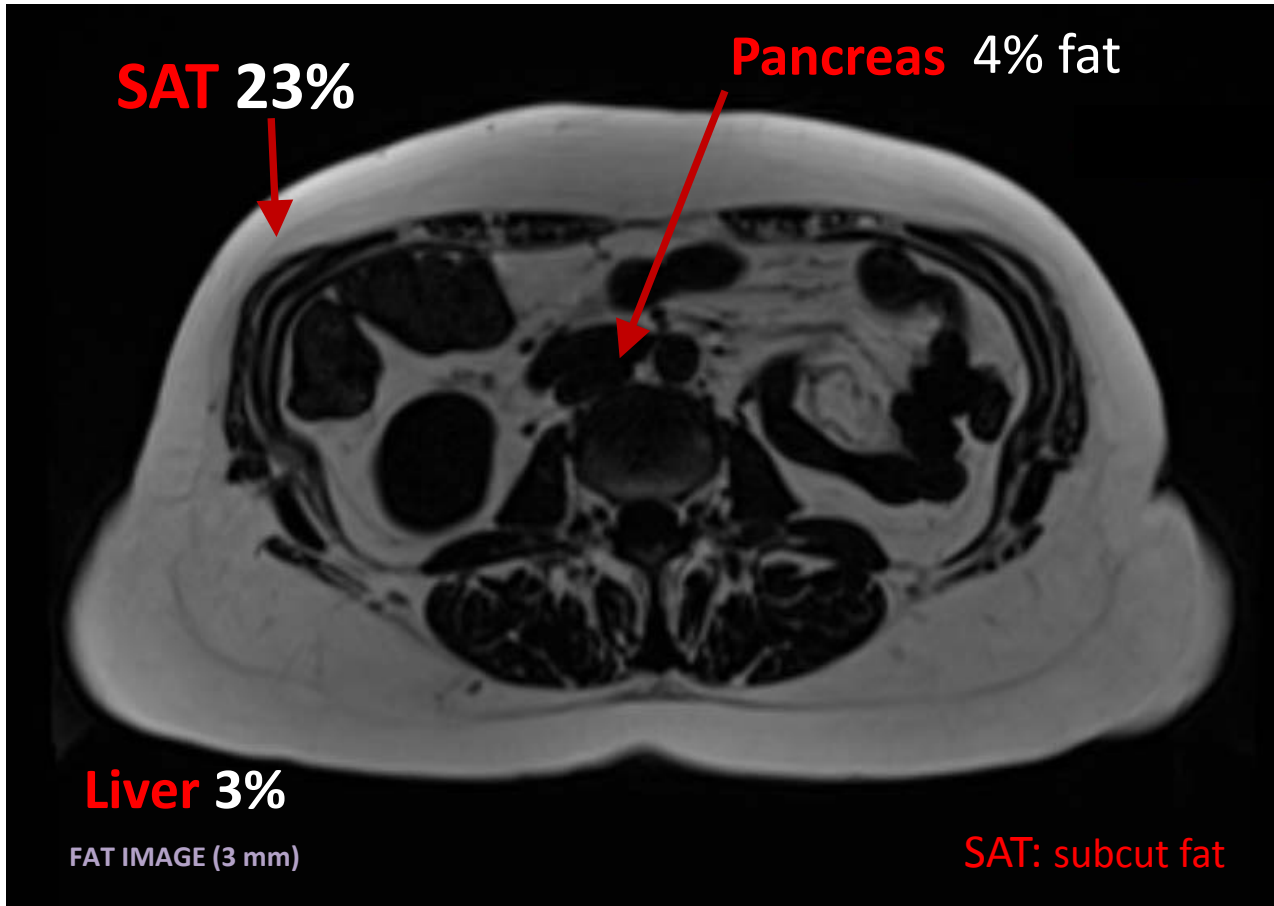
Fasting glucose
4.96 mmol/L



MRI SCAN

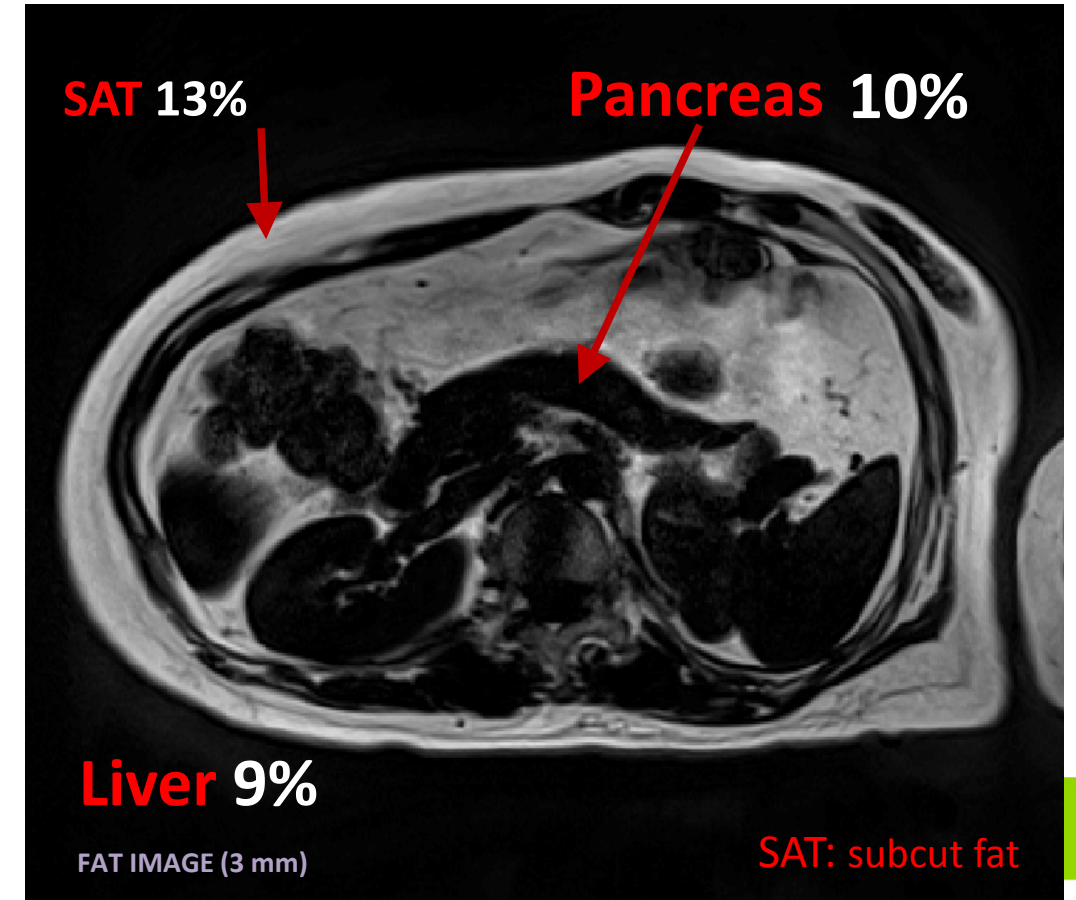
Caucasian female, 56 y

BMI 35 kg/m²



Asian Chinese female, 45 y

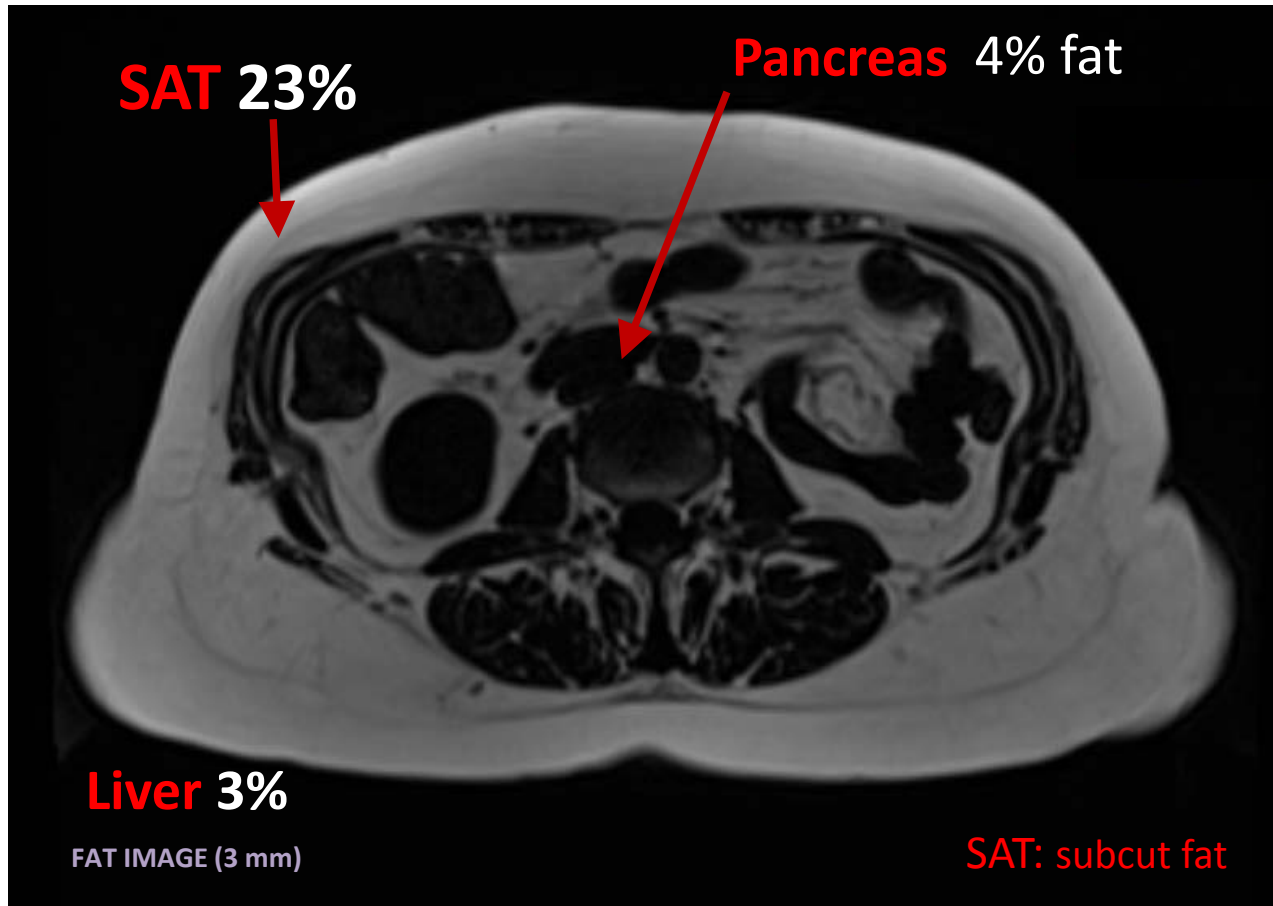
BMI 23 kg/m²



MRI SCAN

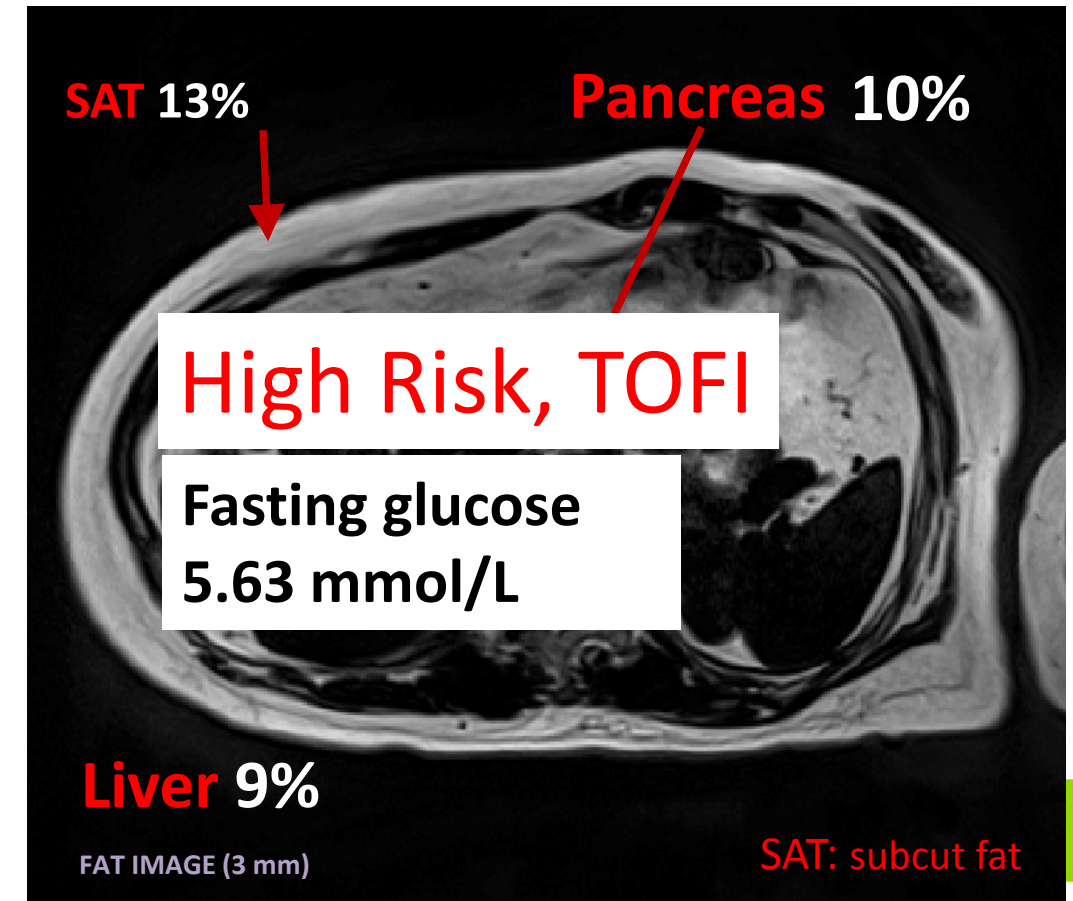
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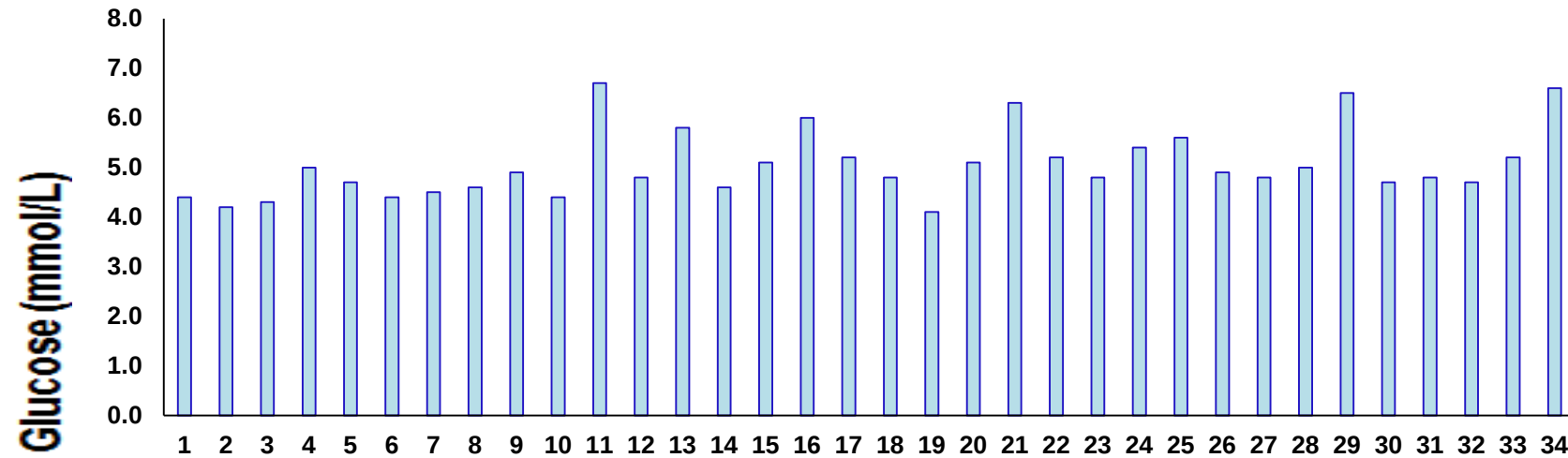


Asian Chinese female, 45 y

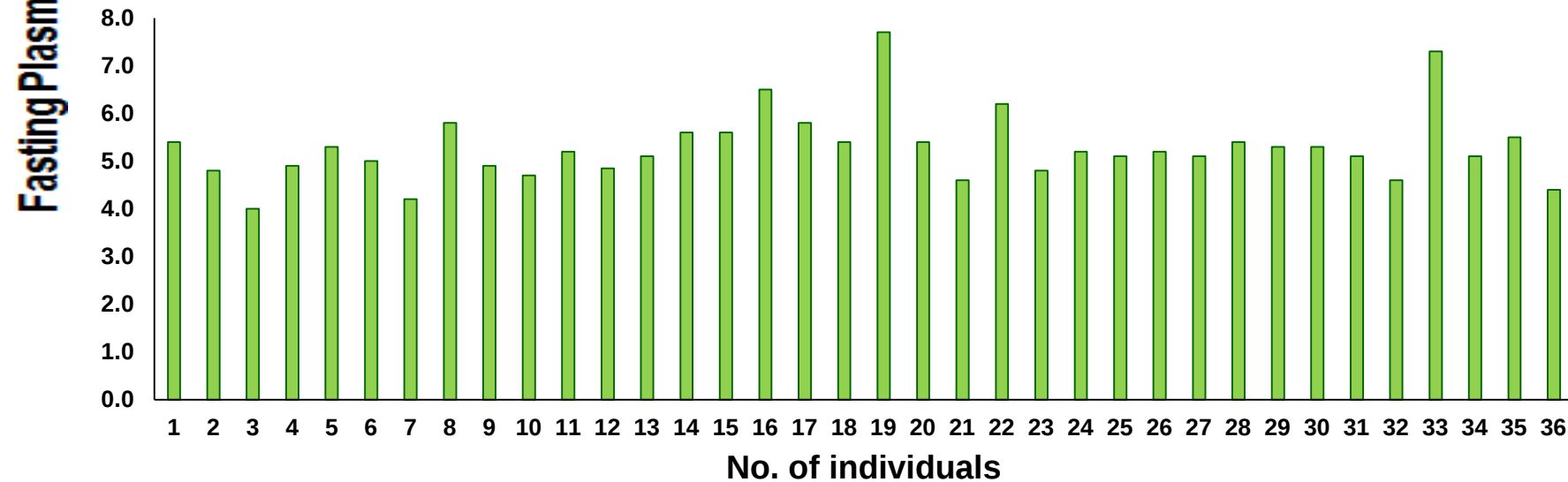
BMI 23 kg/m²



Individual women in the MRI cohort....

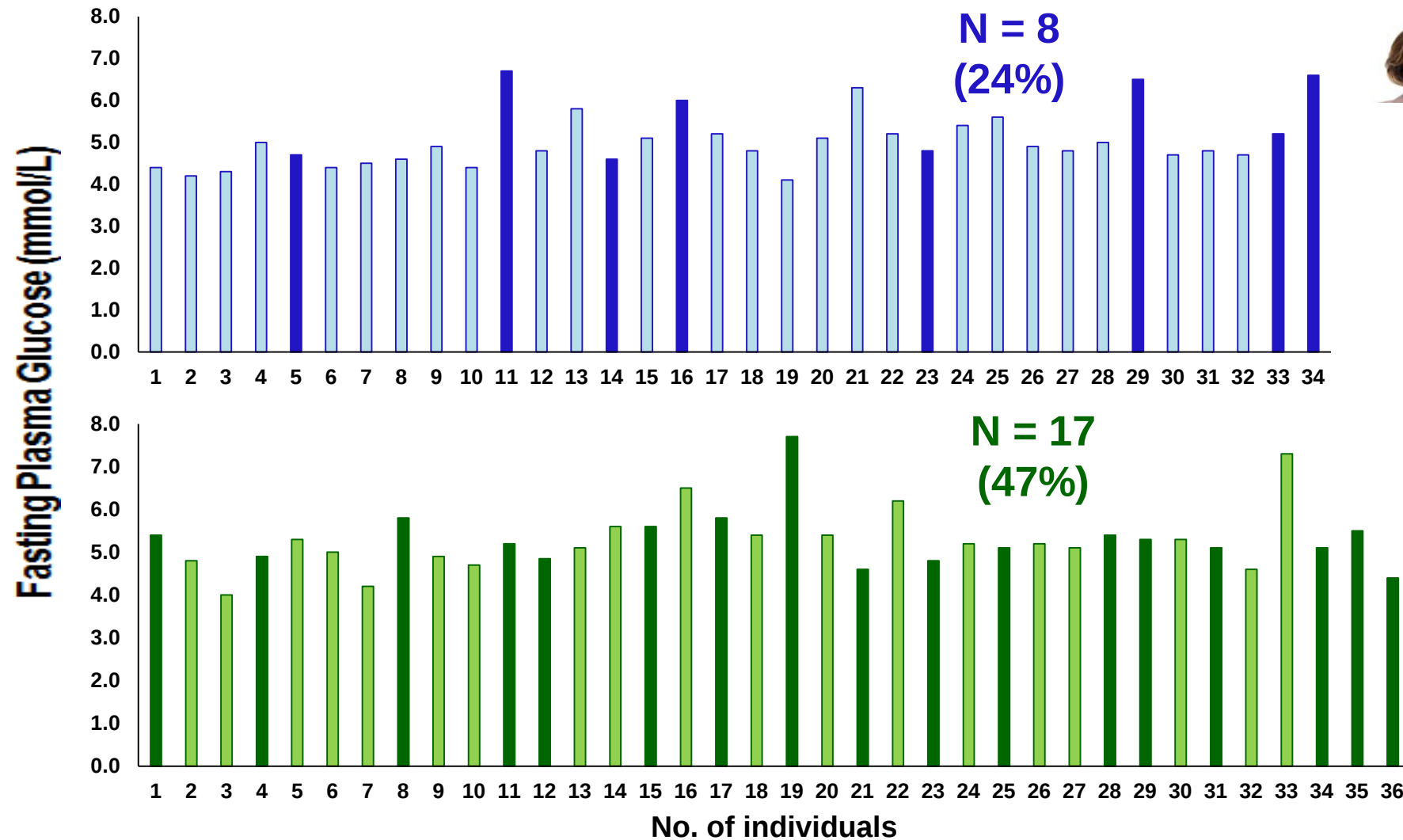


Caucasian European
N = 34



Asian Chinese
N = 36

(i) Women with high pancreatic fat (early data)

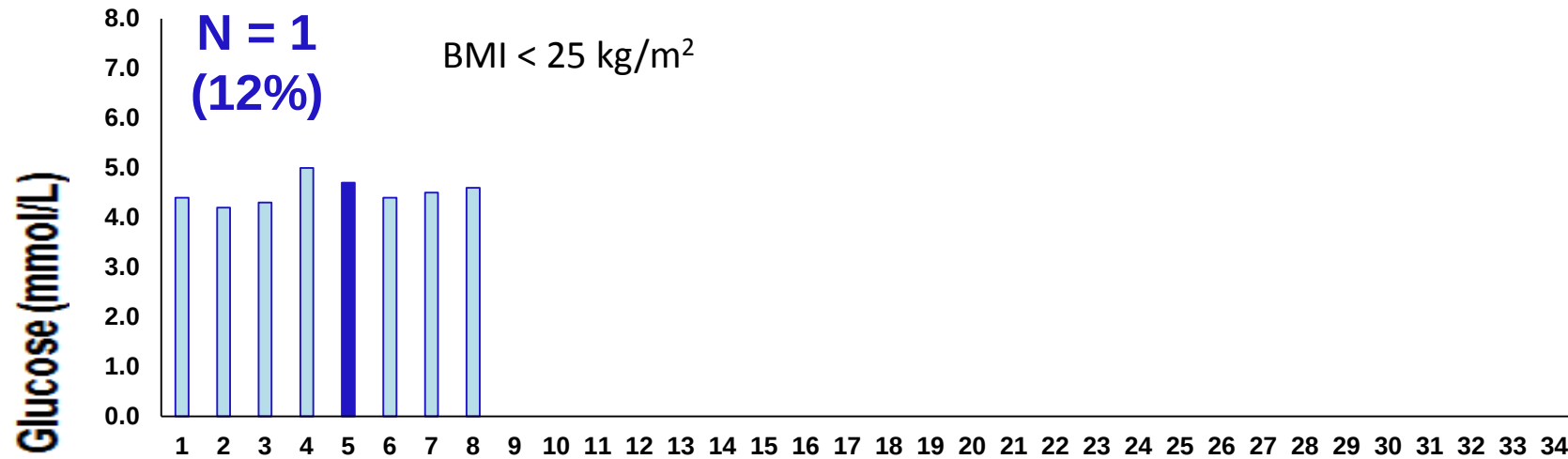


Caucasian European
N = 34



Asian Chinese
N = 36

(ii) Lean women with high pancreatic fat: who is **TOFI**?

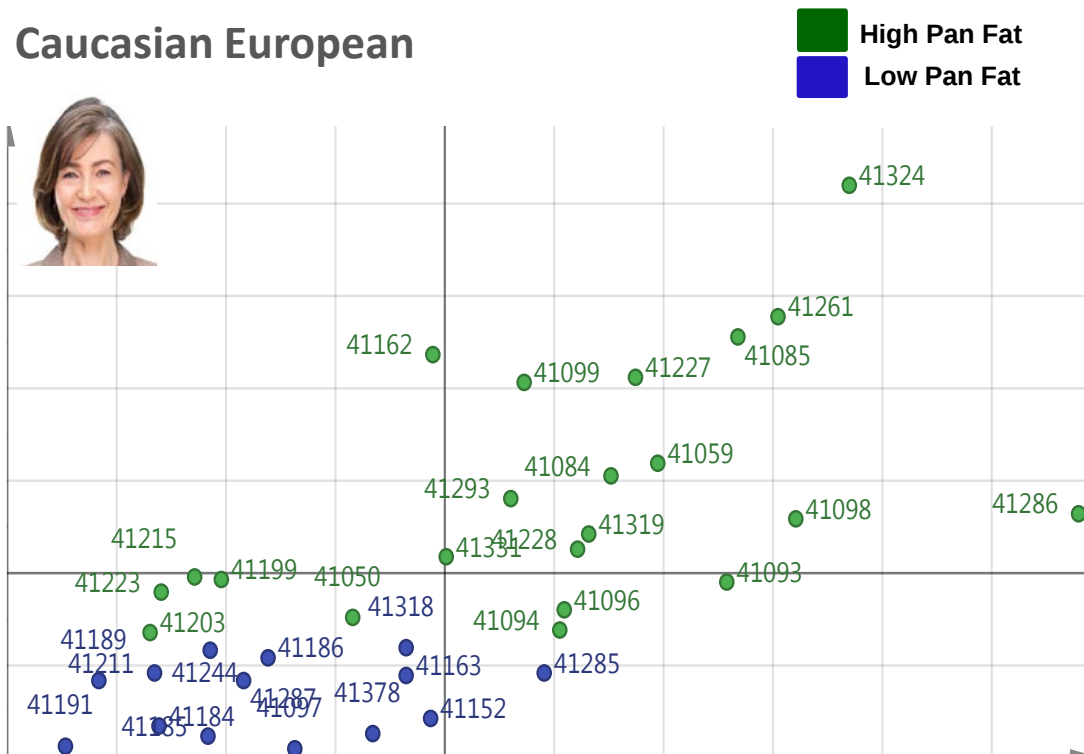


Caucasian European
N = 34



Asian Chinese
N = 36

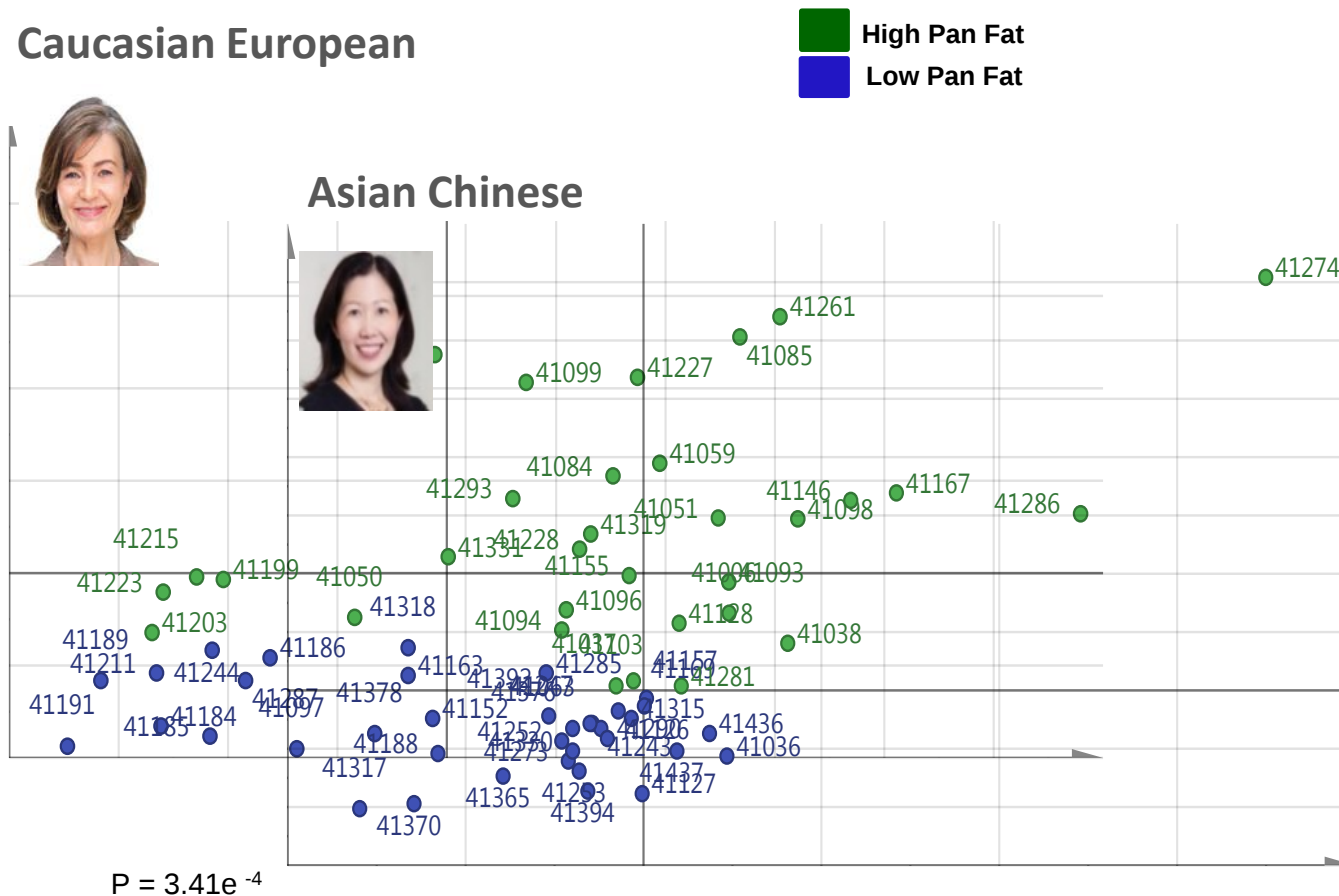
Are there *Novel (metabolomics)* risk markers for pancreatic fat?



$P = 3.41e^{-4}$

Yes, strong correlations between some blood metabolites with high (green) and low (blue) pancreatic fat

The early findings from *Novel* risk markers suggest...



There may be fundamental differences between the two ethnicities around biomarkers that represent high pancreatic fat

Orthogonal Partial least squares analyses

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Where to from here.....



✓ European Caucasian



✓ Asian Chinese



PANaMAH Phase I:
TOFI_Asia study



*Phenotyping
will continue*

PANaMAH Phase II



*Longer term F&B
interventions*

Collaboration with **Nuku** cluster