Adiposity distribution and risks of twelve obesity-related cancers: a Mendelian randomization analysis

Emma Hazelwood, Lucy J. Goudswaard, Matthew A. Lee, Marina Vabistsevits, Dimitri J. Pournaras, Hermann Brenner, Daniel D Buchanan, Stephen B Gruber, Andrea Gsur, Li Li, Ludmila Vodickova, Robert C. Grant, N. Jewel Samadder, Nicholas J. Timpson, Marc J. Gunter, Benjamin Schuster-Böckler, James Yarmolinsky, Tom G. Richardson, Heinz Freisling, Neil Murphy*, Emma E. Vincent*

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26/09/24

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Can BMI tell the whole story?

Yajnik CS, Yudkin JS. The Lancet, 1999

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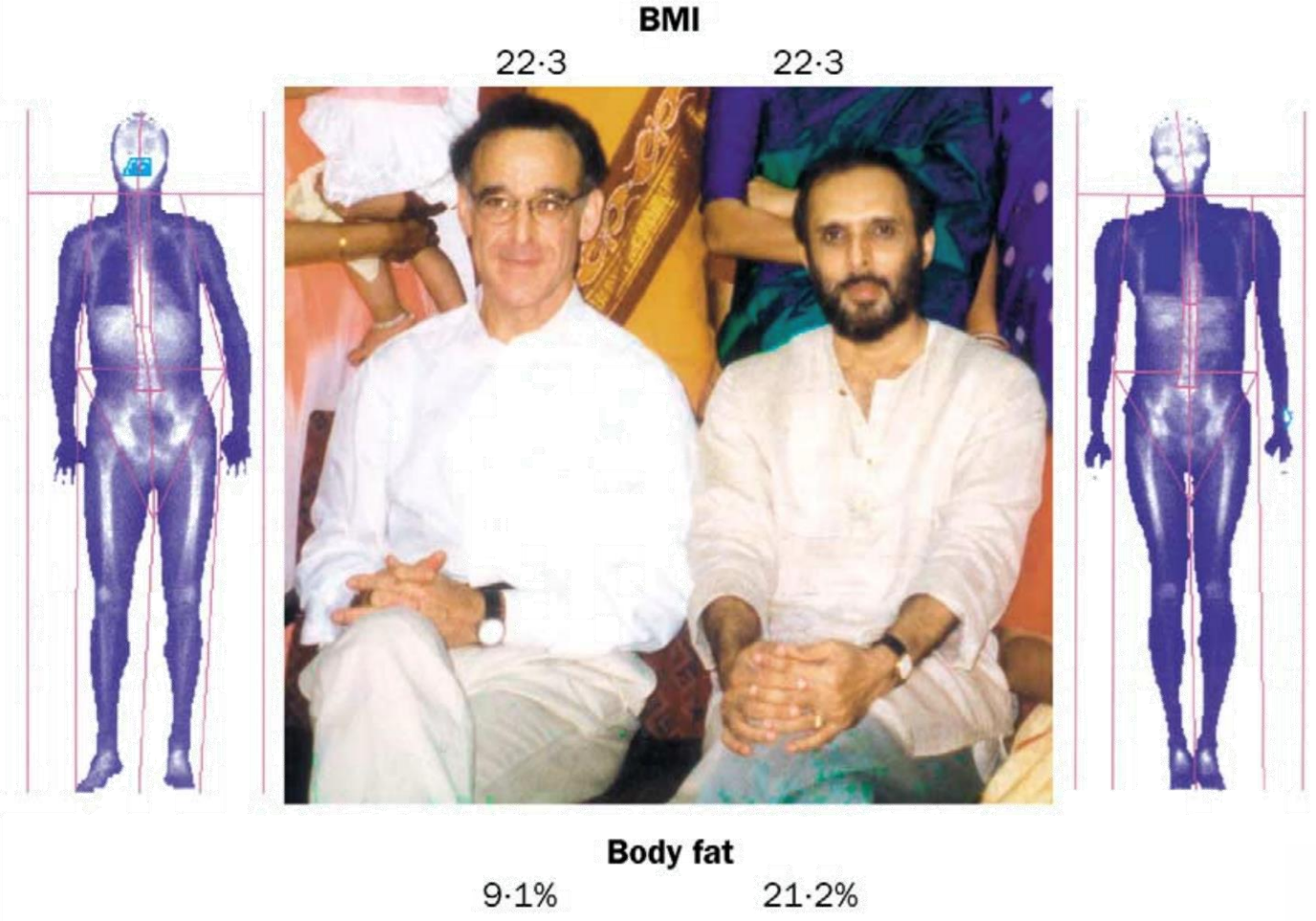
Can BMI tell the whole story?



Yajnik CS, Yudkin JS. The Lancet, 1999

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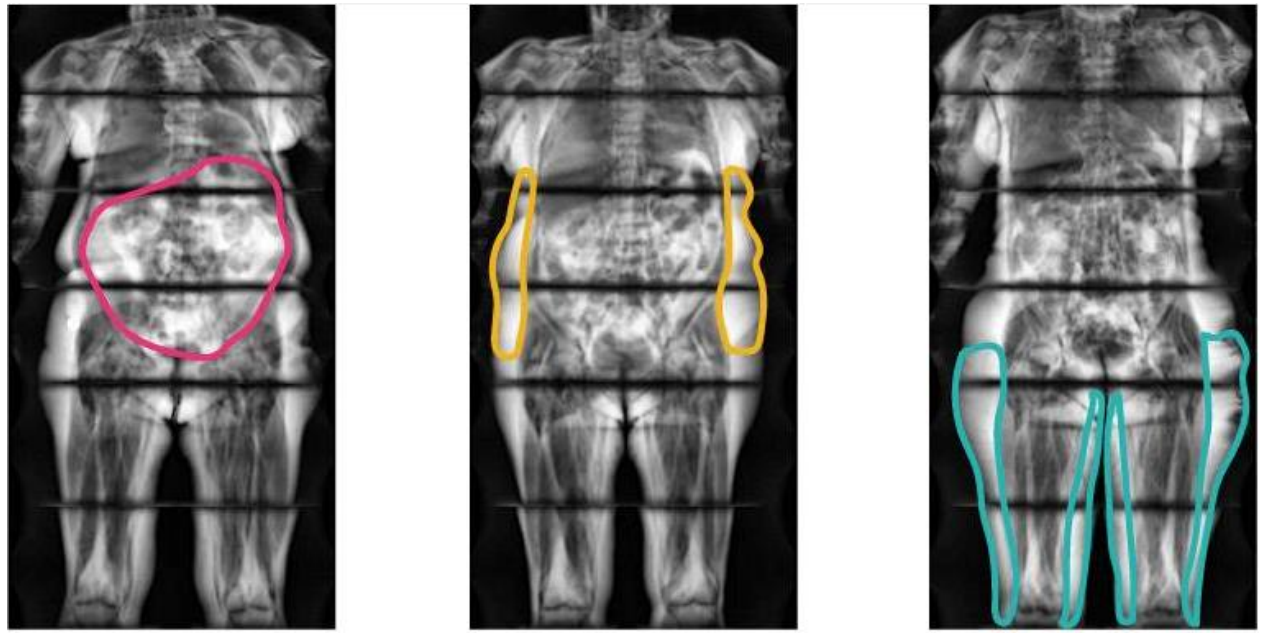
The distribution of adipose tissue throughout the body is important for cardiovascular outcomes



Agrawal et al. Nature Communications, 2023

VAT = visceral adipose tissue

ASAT = Abdominal subcutaneous adipose tissue

GFAT = gluteofemoral adipose tissue

- **Is this also important in cancer risk?**

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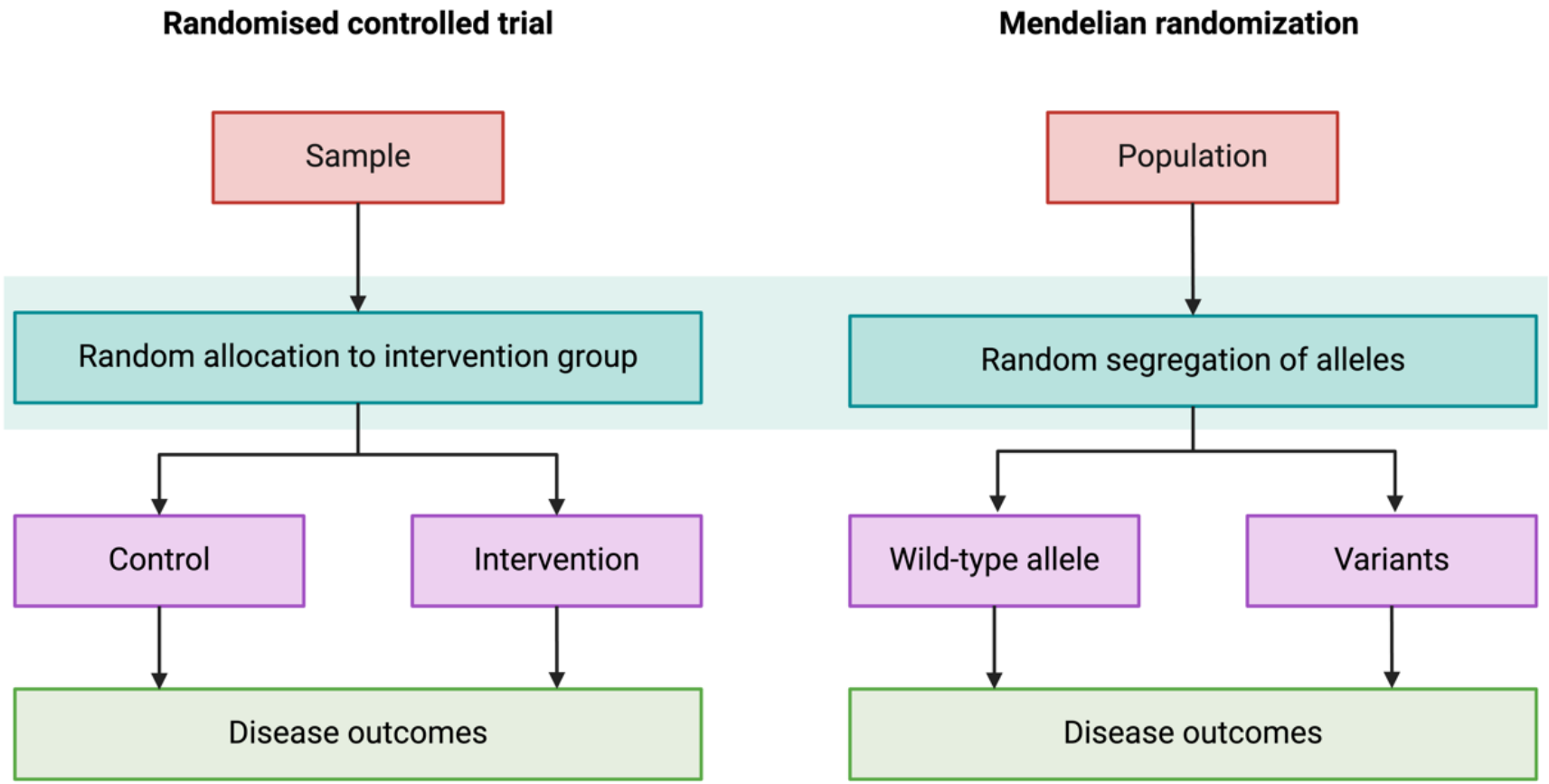
Mendelian randomization (MR)



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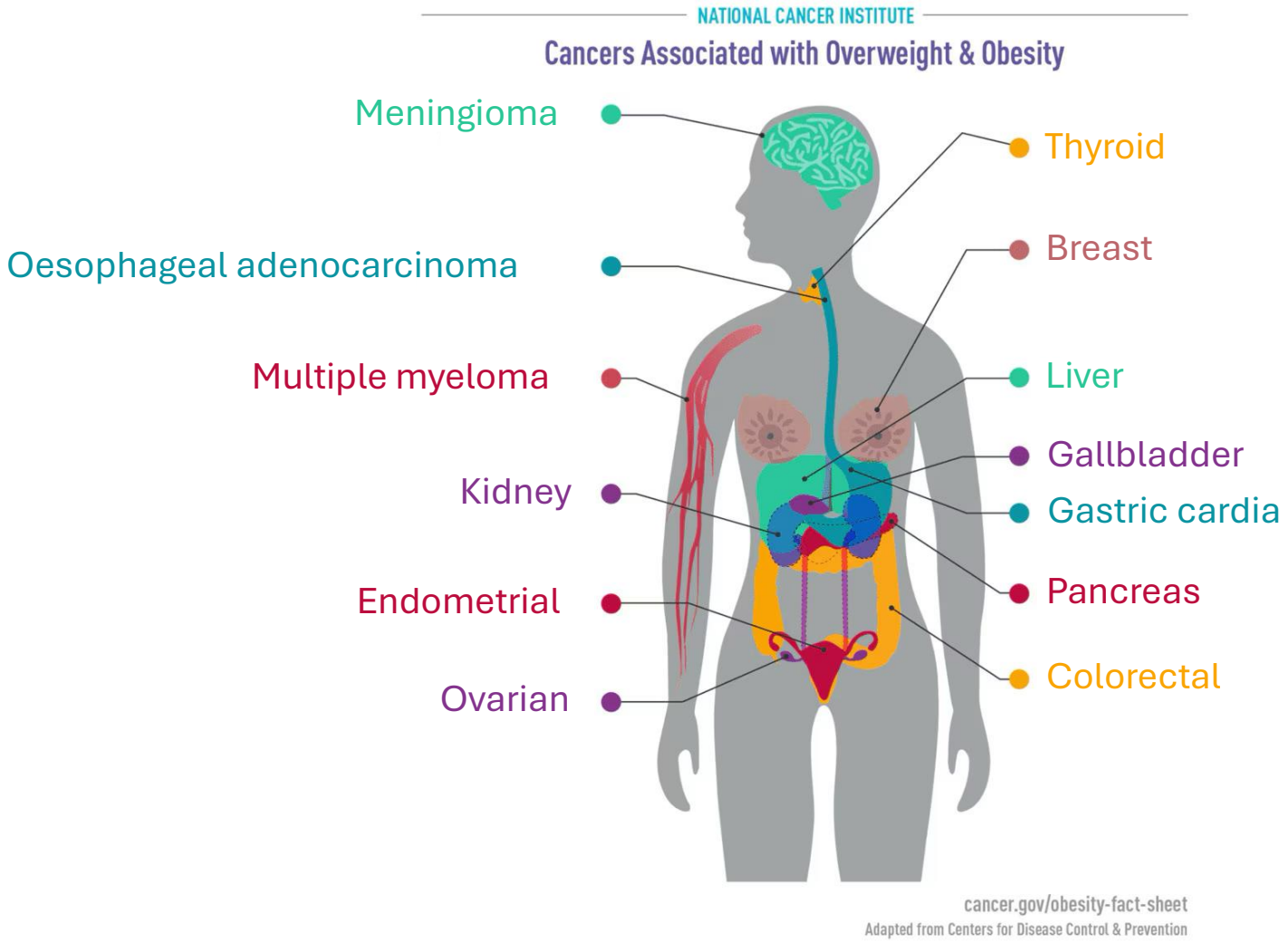
Does adiposity distribution affect obesity-related cancer risk?



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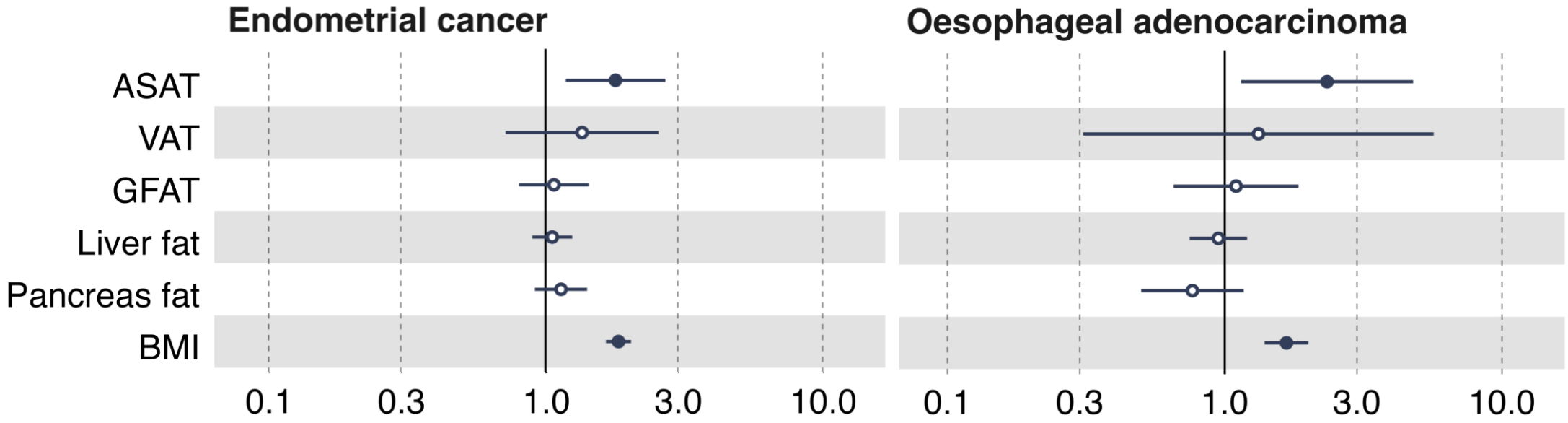
Of the cancers we looked at, we see the strongest evidence for an effect of subcutaneous fat on risk



ASAT = Abdominal subcutaneous adipose tissue; VAT = visceral adipose tissue; GFAT = gluteofemoral adipose tissue

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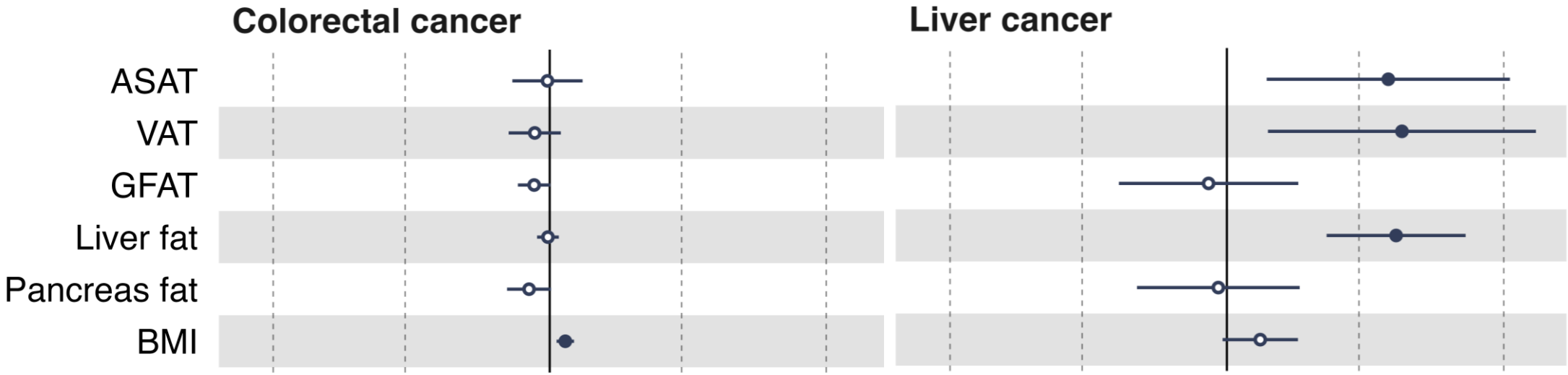
Adiposity distribution seems to be important for some cancer types, but not others



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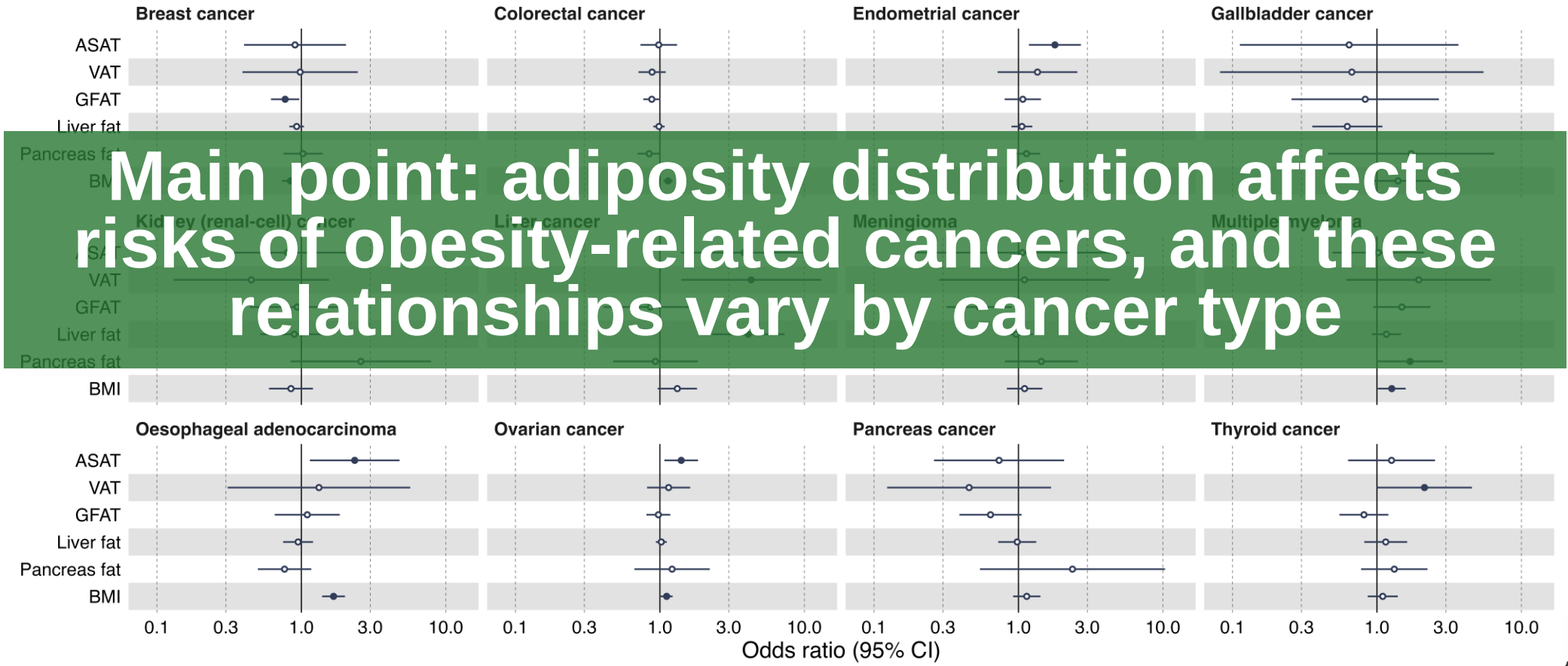
Does adiposity distribution affect obesity-related cancer risk? Yes



Main point: adiposity distribution affects risks of obesity-related cancers, and these relationships vary by cancer type

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Can we identify molecular traits that can explain these effects?

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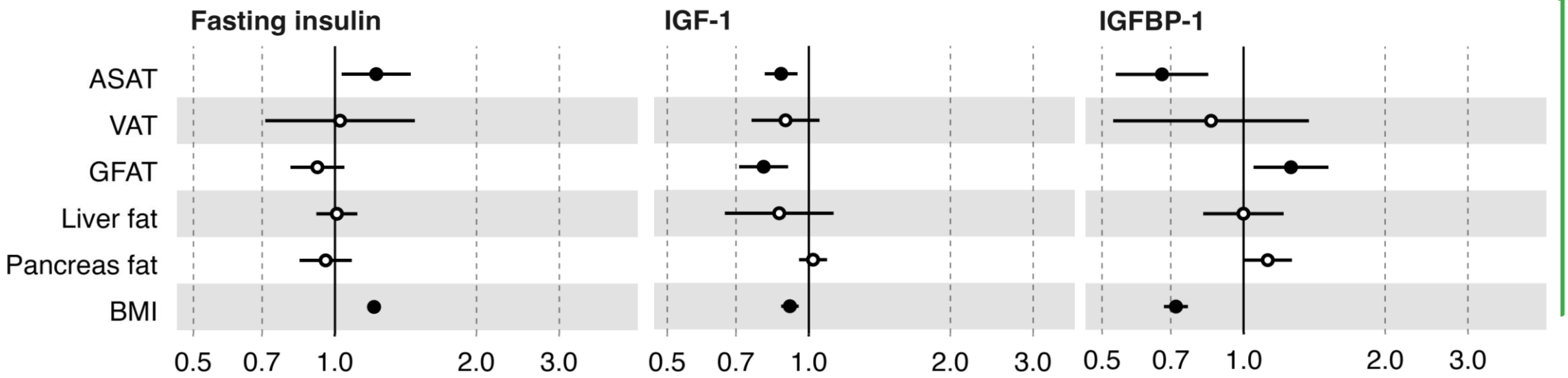

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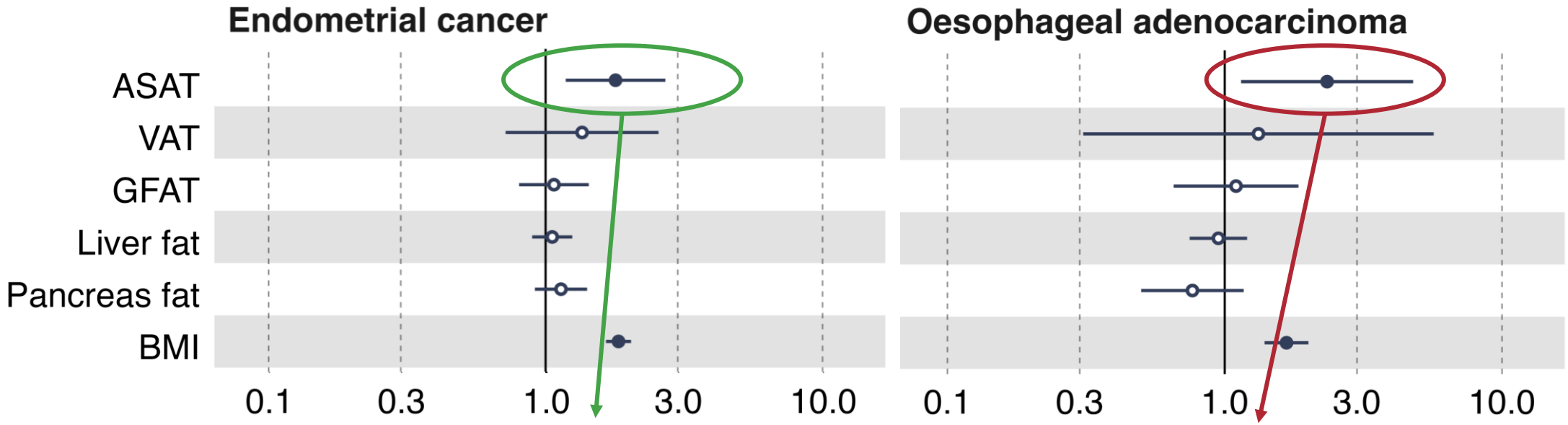
Do these molecular traits influence cancer risks? Yes – but molecular traits vary by cancer type



Sex hormones (including testosterone and SHBG)

Insulin-related traits (IGFBP-1)

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Conclusions

- Adiposity distribution does seem to be important for (some) obesity-related cancers
- But these effects are not straightforward and vary by cancer type
- The underlying molecular traits also vary by cancer type

Acknowledgements

Lucy J. Goudswaard, Matthew A. Lee, Marina Vabistsevits, Dimitri J. Pournaras, Hermann Brenner, Daniel D Buchanan, Stephen B Gruber, Andrea Gsur, Li Li, Ludmila Vodickova, Robert C. Grant, N. Jewel Samadder, Nicholas J. Timpson, Marc J. Gunter, Benjamin Schuster-Böckler, James Yarmolinsky, Tom G. Richardson, Heinz Freisling, Neil Murphy, Emma E. Vincent

GECCO, CCFR, CORECT, BCAC, ECAC, OCAC, UK Biobank, FinnGen, Twin Study, MAGIC, DECODE, BEACON

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CANCER RESEARCH UK

MRC Integrative Epidemiology Unit

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Thank you for listening!

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