

# Addressing **Instrument-Outcome Confounding** in **Mendelian Randomization** through **Representation Learning**

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**Shimeng Huang**

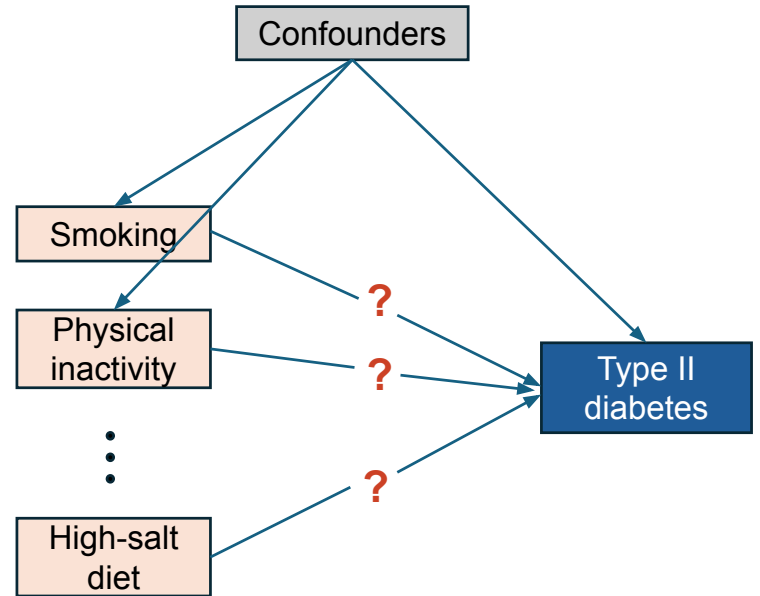
in collaboration with Matthew Robinson and Francesco Locatello

@ICSCS 2025 in Seville, Spain



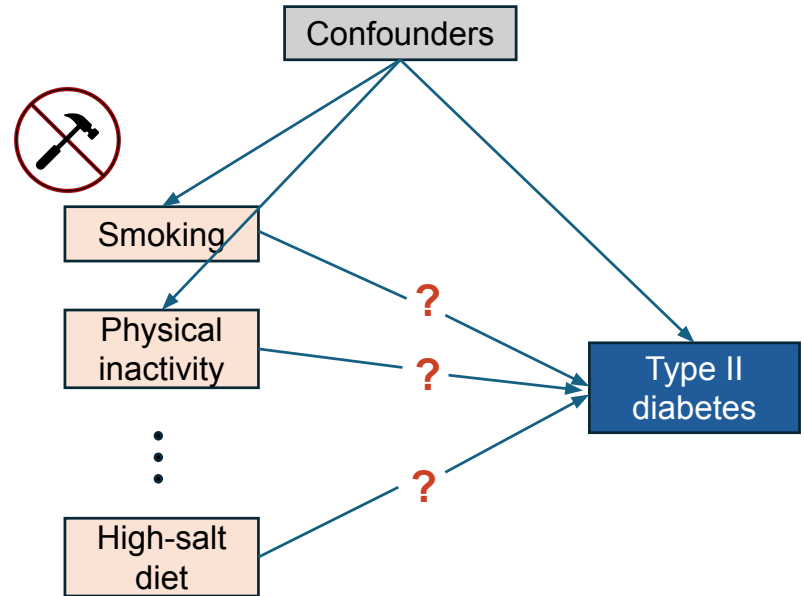
# Background: Causality in Epidemiology

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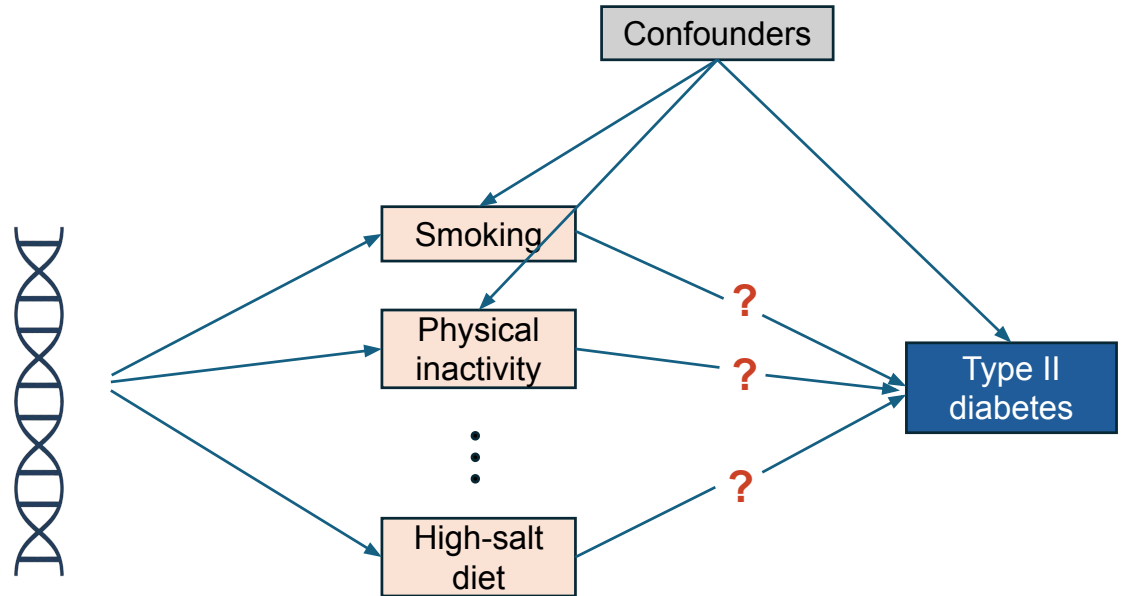
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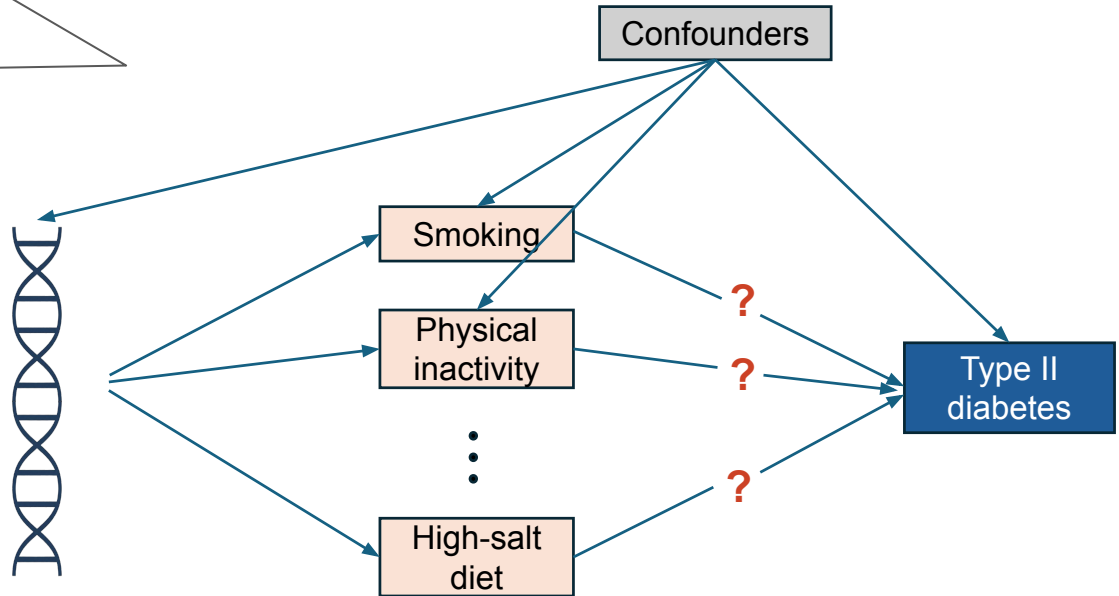


# Background: Causality in Epidemiology

Instrument-outcome confounding  
is common in Mendelian  
Randomization studies

→ Violates IV assumptions

→ Biased causal effect



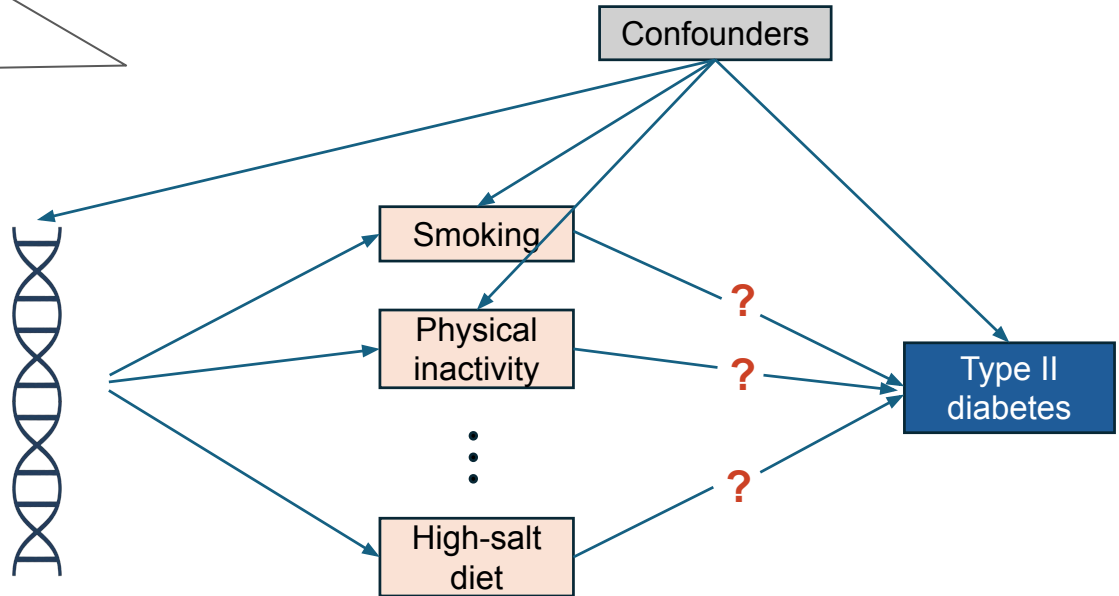
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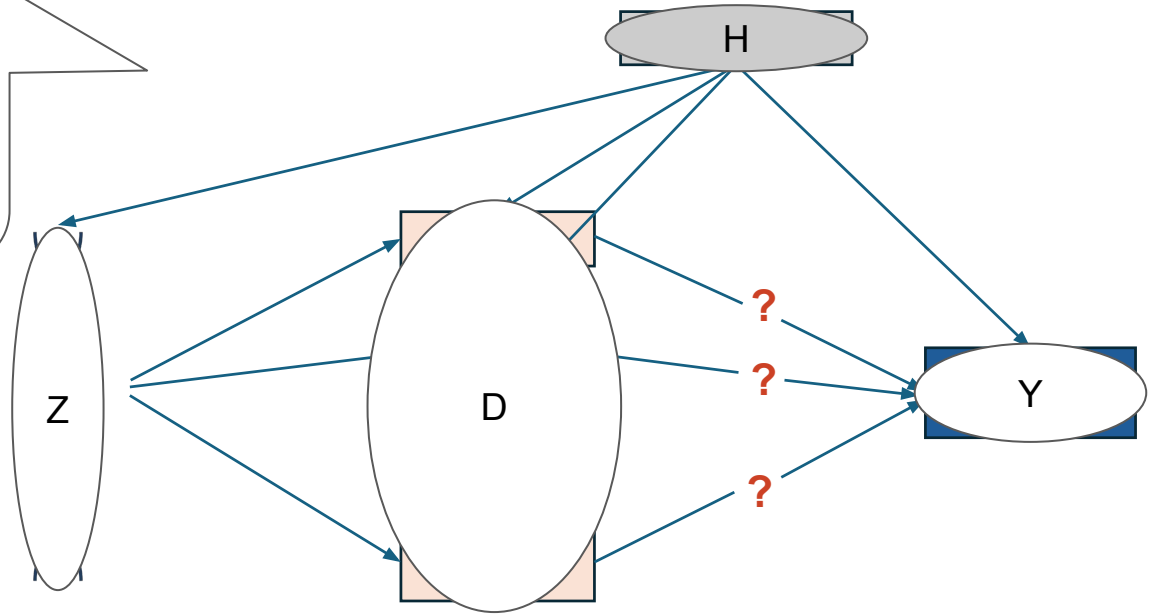
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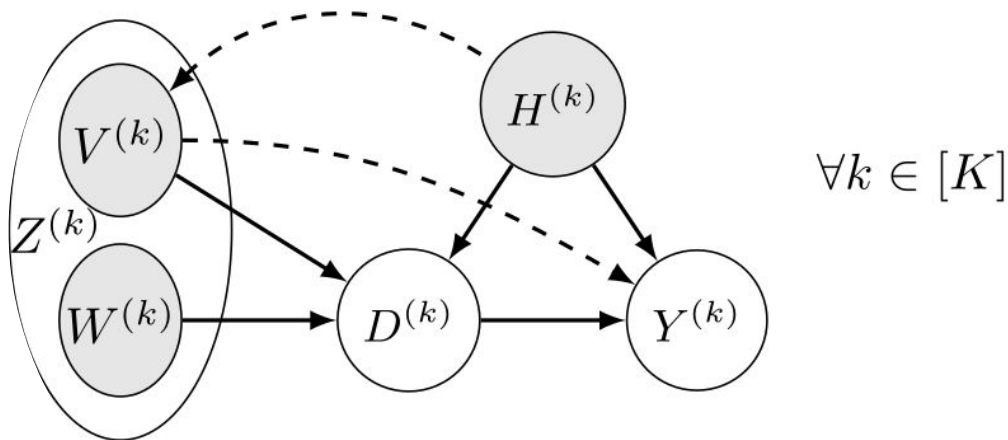
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# Method: Contrastive Learning using Multi-Population Data

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Suppose we can decompose  $Z$  into two parts,  $V$  and  $W$ ...

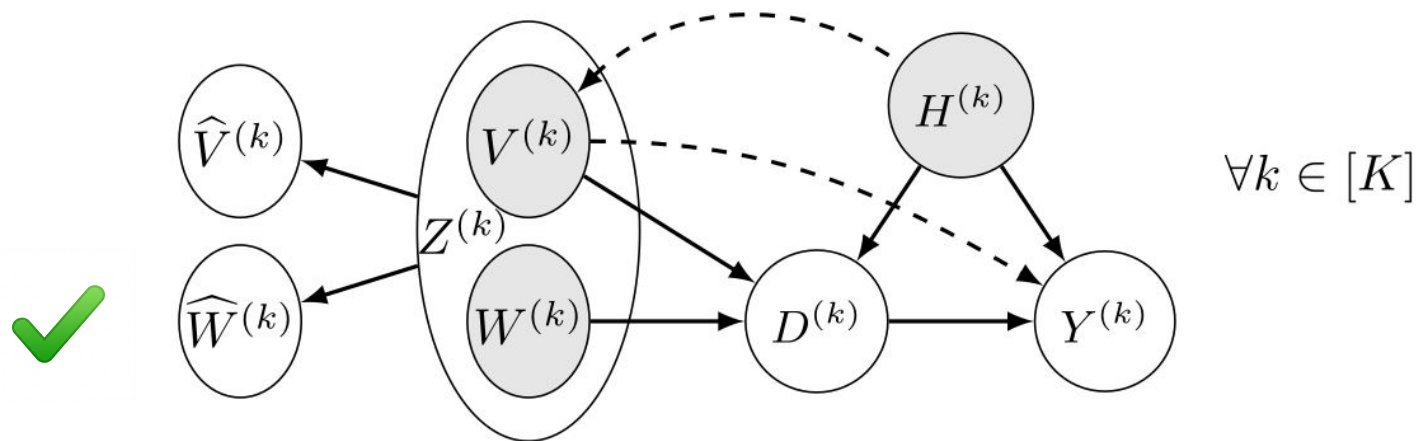


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# Key Findings

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**Identifiability of  $W$  and  $V$ :** Under certain assumptions

$$\hat{W} = AW + c$$

can be learned by contrasting data from multiple populations, as well as

$$\hat{V} = BV + d$$

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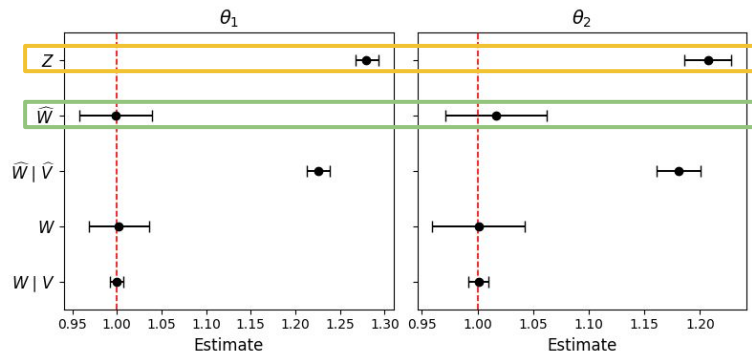
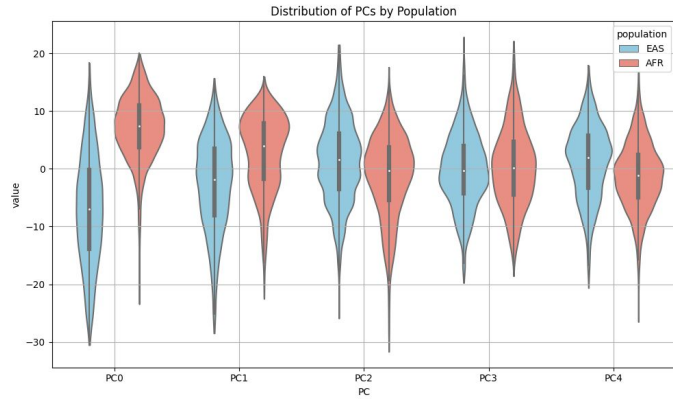
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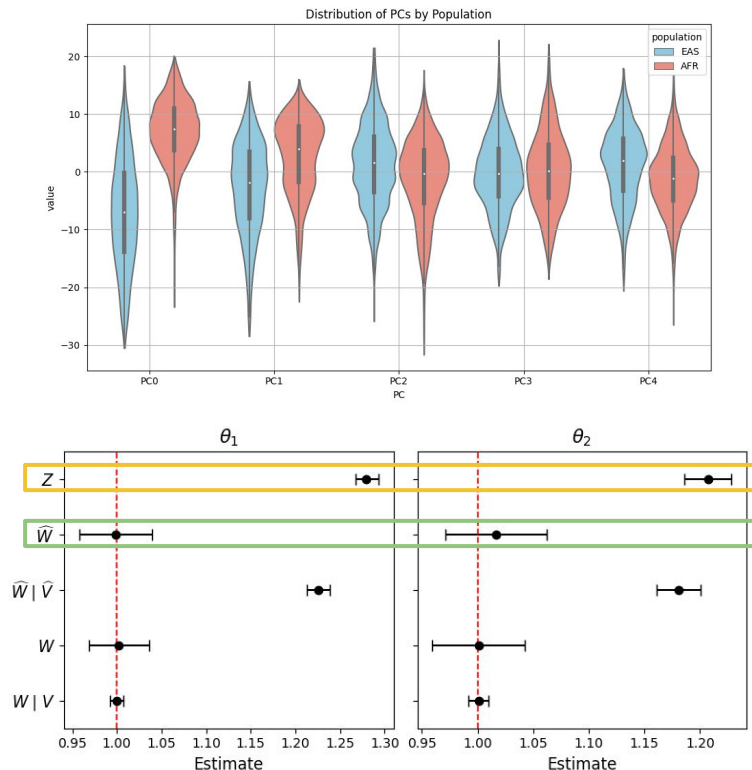
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**Average causal effect (ACE) estimation:**  $\hat{W}$  can identify the ACE as long as  $W$  can, and it *may* be helpful to control  $\hat{V}$ .

# Results and Conclusion



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We leverage representation learning in MR under violation of **instrument-outcome confounding**.

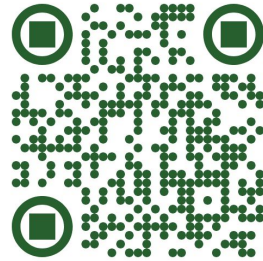
We adapt and extend the theoretical results of **contrastive learning** for identifying the invariant component of the instruments.

We show empirically that autoencoders satisfying the **invariance constraint** can identify a valid instrument for MR.

# Thank you for your attention!

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