# 4. Results

# Contents

# Results

## Simulation Study

### Data Simulation

Data were successfully simulated as intended. A selection of representative visualisations are presented in Figure 1.

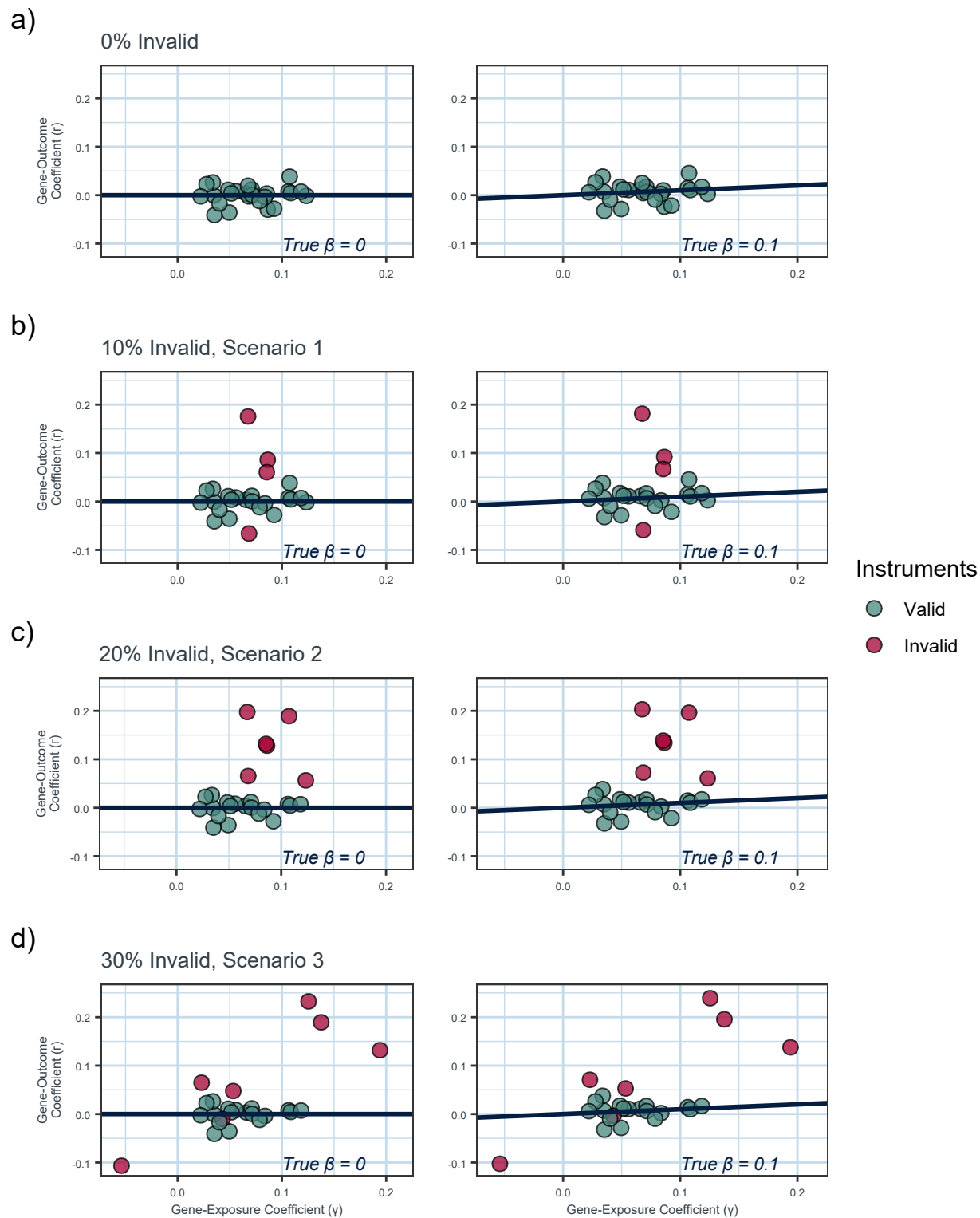**Analysis of Simulated Data**

A summary is shown in Table 1 and 2

Figure 1: Plots of a representative simulated dataset; all plots shown simulate genetic instruments from the same index from the same random seed. Left and right columns demonstrate null and positive true causal effects ( = 0 and  = 0.1), respectively. The proportion of invalid genetic instruments, i.e. those with pleiotropic effects, increases 10% each row. Plots a) and b) ….

Table 1: Summary of 1000 Simulated Mendelian Randomisation Studies With Null Causal Effect

| N | Proportion of Invalid IVs | F | $R^2$ | Weighted Median | | MR Hevo | |
|---|---|---|---|---|---|---|---|
| | | | | Mean Estimate (Mean SE) | Positive Rate | Mean Estimate (Mean SE) | Positive Rate |
| Scenario 1: Balanced pleiotropy, InSIDE assumption satisfied | | | | | | | |
| 10,000 | 0.0 | 11.7 | 2.8% | 0.001 (0.078) | 0.2 | 0.000 (0.001) | 0.0 |
| 10,000 | 0.1 | 11.7 | 2.8% | 0.026 (0.086) | 1.5 | 0.032 (0.001) | 0.0 |
| 10,000 | 0.2 | 11.7 | 2.8% | 0.022 (0.092) | 2.0 | 0.037 (0.002) | 0.0 |
| 10,000 | 0.3 | 11.7 | 2.8% | 0.014 (0.093) | 1.6 | 0.022 (0.002) | 0.0 |
| Scenario 2: Directional pleiotropy, InSIDE assumption satisfied | | | | | | | |
| 10,000 | 0.0 | 11.7 | 2.8% | 0.001 (0.078) | 0.3 | 0.000 (0.001) | 0.0 |
| 10,000 | 0.1 | 11.7 | 2.8% | 0.020 (0.087) | 0.8 | 0.039 (0.001) | 0.0 |
| 10,000 | 0.2 | 11.7 | 2.8% | 0.050 (0.093) | 4.1 | 0.098 (0.002) | 1.5 |
| 10,000 | 0.3 | 11.7 | 2.8% | 0.066 (0.094) | 5.8 | 0.126 (0.002) | 3.6 |

IV: Instumental Variable, SE: Standard Error
Data from 1000 Simulated Mendelian Randomisation Studies
Null Causal Effect (β = 0)

Table 2: Summary of 1000 Simulated Mendelian Randomisation Studies With Positive Causal Effect

| N | Proportion of Invalid IVs | F | $R^2$ | Weighted Median | | MR Hevo | |
|---|---|---|---|---|---|---|---|
| | | | | Mean Estimate (Mean SE) | Positive Rate | Mean Estimate (Mean SE) | Positive Rate |
| Scenario 1: Balanced pleiotropy, InSIDE assumption satisfied | | | | | | | |
| 10,000 | 0.0 | 11.7 | 2.8% | 0.070 (0.079) | 4.9 | 0.085 (0.001) | 6.2 |
| 10,000 | 0.1 | 11.7 | 2.8% | 0.094 (0.087) | 11.0 | 0.118 (0.001) | 12.6 |
| 10,000 | 0.2 | 11.7 | 2.8% | 0.089 (0.093) | 10.3 | 0.124 (0.002) | 5.6 |
| 10,000 | 0.3 | 11.7 | 2.8% | 0.081 (0.094) | 8.7 | 0.108 (0.002) | 1.6 |
| Scenario 2: Directional pleiotropy, InSIDE assumption satisfied | | | | | | | |
| 10,000 | 0.0 | 11.7 | 2.8% | 0.070 (0.079) | 5.3 | 0.085 (0.001) | 5.9 |
| 10,000 | 0.1 | 11.7 | 2.8% | 0.089 (0.088) | 9.0 | 0.124 (0.001) | 11.9 |
| 10,000 | 0.2 | 11.7 | 2.8% | 0.119 (0.094) | 17.7 | 0.187 (0.002) | 32.3 |
| 10,000 | 0.3 | 11.7 | 2.8% | 0.133 (0.095) | 23.3 | 0.216 (0.002) | 46.1 |
| Scenario 3: Directional pleiotropy, InSIDE assumption not satisfied | | | | | | | |
| 10,000 | 0.0 | 11.7 | 2.8% | 0.070 (0.079) | 5.2 | 0.085 (0.001) | 5.7 |
| 10,000 | 0.1 | 13.7 | 3.3% | 0.150 (0.089) | 35.0 | 0.137 (0.001) | 25.1 |
| 10,000 | 0.2 | 14.9 | 3.6% | 0.213 (0.1) | 55.8 | 0.202 (0.002) | 45.2 |
| 10,000 | 0.3 | 12.8 | 3.1% | 0.169 (0.099) | 37.1 | 0.191 (0.002) | 29.1 |

IV: Instumental Variable, SE: Standard Error
Data from 1000 Simulated Mendelian Randomisation Studies
Positive Causal Effect (β = 0.1)

Table reference[1]

Word count: 48

1. Bowden J, Smith GD, Haycock PC, Burgess S. Consistent Estimation in Mendelian Randomization with Some Invalid Instruments Using a Weighted Median Estimator. Genetic Epidemiology [Internet]. 2016 Apr [cited 2024 Oct 22];40(4):304. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC4849733/