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Artificial intelligence and digital transformation in research and healthcare

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Who Participates?

Quantifying the healthy-volunteer effect in a real-world RCT

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Background and aims

Background:

Understanding whether RCT participants represent the broader patient population is critical for applying trial evidence in clinical practice. Healthy volunteer bias may limit external validity and has yet to be quantified.

Aim:

To compare outcomes, demographics, comorbidities, and preventive behaviours of those who volunteer for an RCT, with those who

Methods

BedMed

Setting: Antihypertensive timing trial recruiting via PCP-mailed letter

Data Source: Linked electronic health data available on all Alberta residents

Participants: 326 PCPs → 52,891 invited patients → 1,858 (3.5%) volunteers

Measures: Baseline characteristics + adverse events (e.g. MACE, death, hip #)

Primary Comparison: PCP-invited volunteers vs PCP-invited decliners

Secondary Comparisons: Eligible PCP pts vs Eligible Albertans; Social

Results

Outcomes: **MACE 0.47** (95%CI 0.41-0.53; p < 0.0001); **Death 0.33** (95%CI 0.27-0.40; p < 0.0001); Hip fracture 0.65 (95%CI 0.45-0.93; p=0.02); New Dx Dementia 0.55 (95%CI 0.45-0.68; p < 0.0001); **Nursing home admission 0.30** (95%CI 0.20-0.46; p<0.0001)

Demographics: Female 55.0 vs 54.3% (NSS); Median age 68 vs 67 yrs (NSS); ↓**80+ yrs** (10.3% vs 19.6%); Most **affluent** quintile↑ (23.1% vs 16.5%; Material deprivation index)

Comorbidities: **Prior 6 mo in hospital 4.0 vs 10.8%** (p < 0.0001); Diabetes 26.5 vs 35.4% (p < 0.0001); Heart Failure 6.2 vs 14.0% (p < 0.0001); COPD 11.1 vs 18.9% (p < 0.0001) **Prevention:** **Shingles vaccine 17.2 vs 6.9%** (p < 0.0001); PAP smear (♀) 73.4 vs 50.2% (p < 0.0001); Mammogram (♀) 73.4 vs

Limits and conclusions

Limitations: These findings stem from a single RCT where participants received a letter of invitation from their family doctor. Higher pressure recruitment methods (e.g. approaching potential participants in person), or other approaches resulting in a higher % enrollment, likely have more representative trial populations.

Conclusions: "Healthy volunteer bias" can meaningfully reduce the risk of all adverse health outcomes – diminishing the intervention's apparent **NNT** and lessening the likelihood of detecting **adverse effects**. Wherever possible, recruitment methods that maximize the % enrolment should be