CAUSAL MEDIATION ANALYSIS

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DISCLOSURE

- No conflict of interest to declare
- Sharon Tan is funded by the National Medical Research Council Research Training Fellowship, Singapore

CASE STUDY - BACKGROUND

- Oral disease burden among persons from different income groups influenced by
  - Diet
  - Dental care utilisation
  - Oral hygiene practices

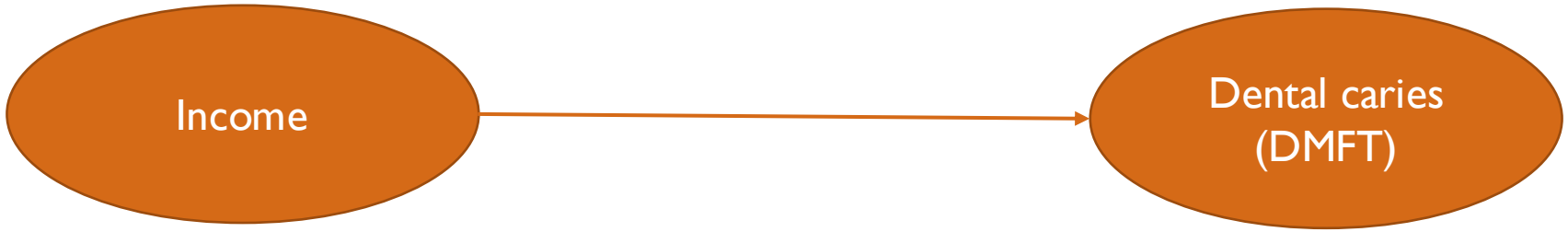
  etc.
- Studies suggest sugar consumption is associated with higher risk of dental caries (as measured by DMFT) (Moores et al, 2022)

Moores, C. J., Kelly, S. A. M., & Moynihan, P. J. (2022). Systematic Review of the Effect on Caries of Sugars Intake: Ten-Year Update. *Journal of dental research*, *101*(9), 1034–1045. https://doi.org/10.1177/00220345221082918

CASE STUDY - AIM

- To assess the influence of socioeconomic status (income) and sugar consumption on dental caries

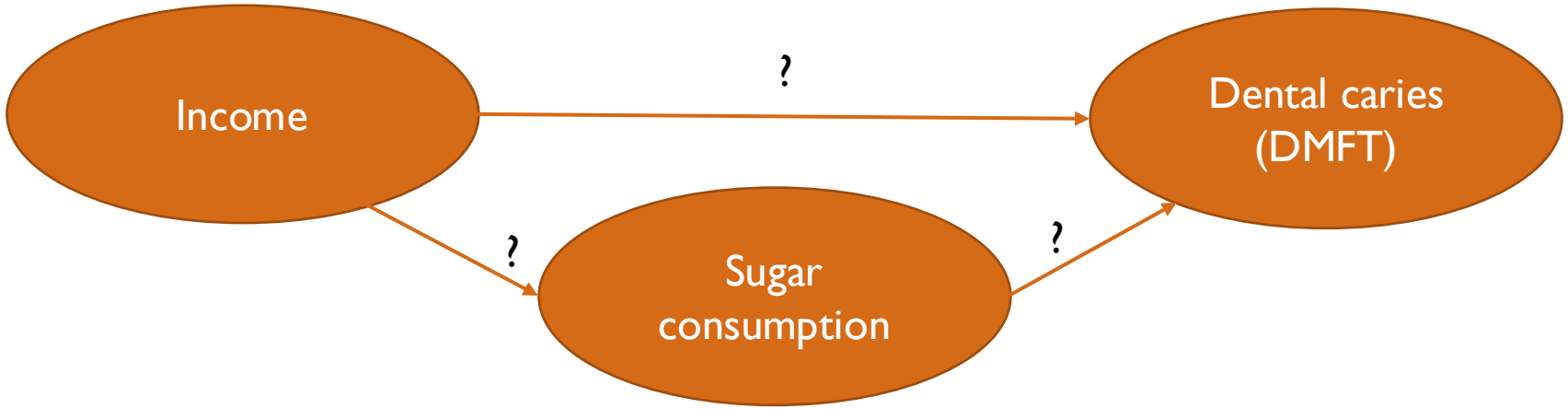
CASE STUDY - AIM



- DMFT is higher in those with lower income (Schwendicke et al 2015)

Schwendicke, F., Dörfer, C. E., Schlattmann, P., Foster Page, L., Thomson, W. M., & Paris, S. (2015). Socioeconomic inequality and caries: a systematic review and meta-analysis. *Journal of dental research*, *94*(1), 10–18. https://doi.org/10.1177/0022034514557546

CASE STUDY - AIM



- Potential outcomes framework (Holland 1986, Rubin 2005)
- $Y_i(1) - Y_i(0)$, but one outcome will not be observed
- Causal treatment effect estimated at average level

Holland, P. W. (1986). Statistics and causal inference. *Journal of the American statistical Association*, *81*(396), 945-960.
Rubin, D. B. (2005). Causal inference using potential outcomes: Design, modeling, decisions. *Journal of the American statistical Association*

WHY CAUSAL MEDIATION?

- Goes beyond "does X $(income)$ affect Y $(DMFT)$?" to "**how** does X affect Y?"
  - via mediator M $(sugar\ consumption)$
- **Decomposes total effect** into:
  - **Indirect effect** representing the effect of income on change in dental caries that acts through sugar consumption levels
  - **Direct effect** of income (changing from low to high income) on dental caries through other pathways

WHY CAUSAL MEDIATION?

- Helps **identify mechanisms** and **improve intervention design,** by targeting the pathway that drives impact
- Supports **policy/resource decisions**
  - Act on X $(e.g. increase\ wages)$ vs act on M (e.g. educational efforts to reduce sugar consumption)
- Separate causation from mere causation by requiring clear causal assumptions

STATISTICAL ANALYSIS

- Linear regression
- Estimations of average causal mediation effects and average direct effects carried out in R
  - mediation
    - 1000 simulations, yreg – loglinear, nreg - logistic

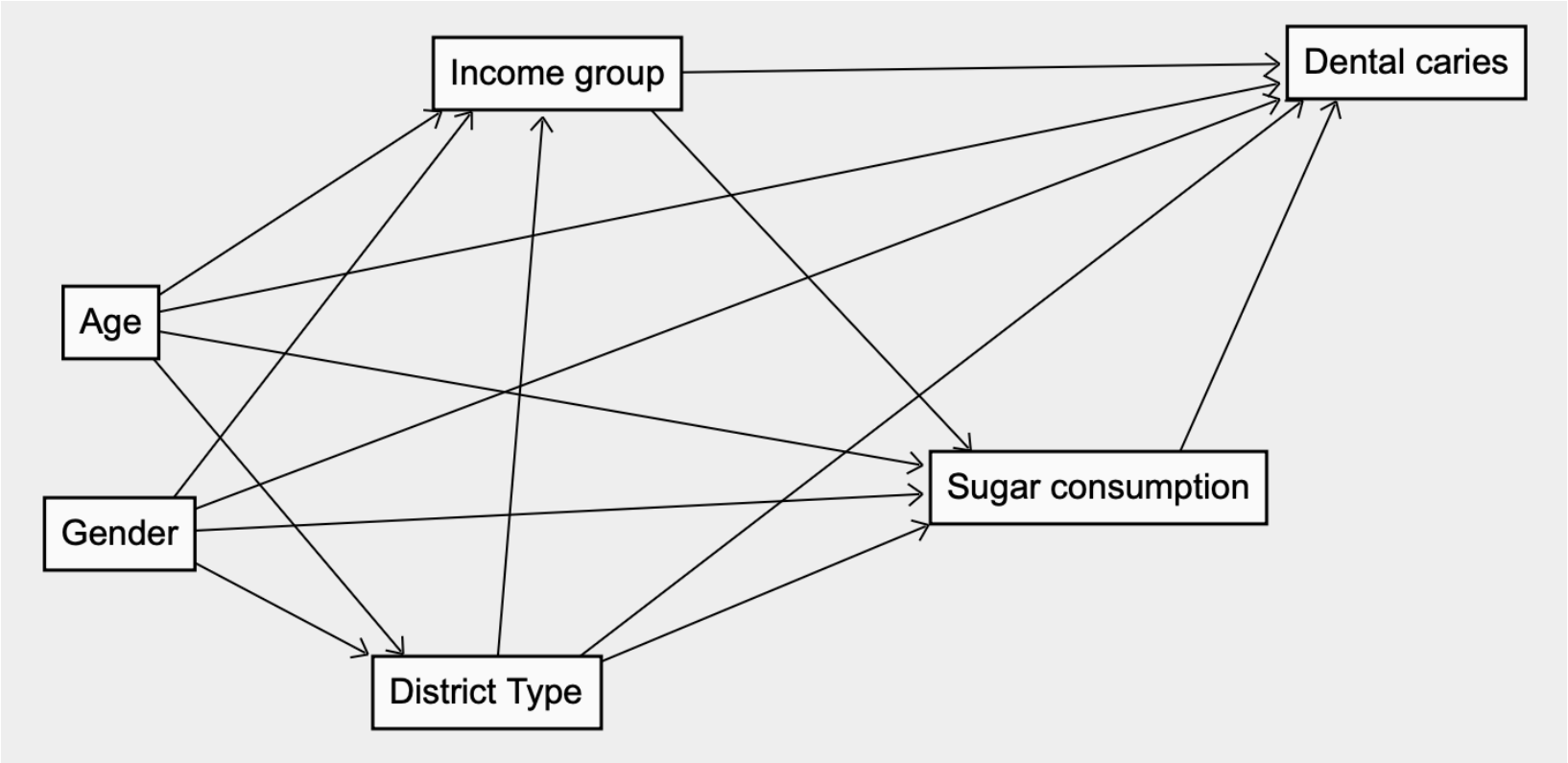
LOAD DATA AND PACKAGE

```r
setwd("~/Downloads/")
df <- readRDS("df.rds")

# Install once (only if not already installed)
if (!requireNamespace("mediation", quietly = TRUE)) {
  install.packages("mediation")
}

# Load it for use in the current R session
library("mediation")
```

DIRECTED ACYCLIC GRAPH



EXPOSURE	MEDIATOR	COVARIATES	OUTCOME
Income a=0 Low gross monthly household income a=1 High gross monthly household income	**Sugar consumption** (grams, continuous)	X -> Y/ X -> M/ M -> Y confounders - **Gender** (male/female) - **Age** (continuous) - **District Type** (public/private)	**DMFT** (continuous) **Caries** (yes/no)

MEDIATION (CONTINUOUS OUTCOME)

```
set.seed(2014)

med.fit <- lm(sugar_consumption ~ income_high + age_adult + gender + district_type, data = df)

out.fit <- lm(dmft ~ sugar_consumption + income_high + age_adult + gender + district_type, data = df)

med.out <- mediate(med.fit, out.fit, treat = "income_high", mediator = "sugar_consumption", robustSE = TRUE, sims
= 1000)
summary(med.out)
```

Linear regression

1000 simulations (quasi-Bayesian Monte Carlo method based on normal approximation)

Robust standard error: White's heteroskedasticity-consistent estimator for covariance matrix

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```

```
##
## Causal Mediation Analysis
##
## Quasi-Bayesian Confidence Intervals
##
##                Estimate 95% CI Lower 95% CI Upper   p-value
## ACME           -3.37749     -3.61150     -3.11365 < 2.2e-16 ***
## ADE            -1.84406     -2.16181     -1.55755 < 2.2e-16 ***
## Total Effect   -5.22155     -5.44421     -4.99514 < 2.2e-16 ***
## Prop. Mediated  0.64696      0.59504      0.69614 < 2.2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Sample Size Used: 5000
##
##
## Simulations: 1000
```

Moving from low to high income, direct effect was reduction in DMFT of -1.8.

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Average causal mediation effect (Indirect effect) through sugar consumption was reduction in DMFT of – 3.4.

```
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##
##
## Simulations: 1000
```

Total effect =
Direct + Indirect effect

COUNTERFACTUAL THEORY

- Controlled direct effect (CDE)
  "how much the outcome would change on average if the mediator were controlled at level *m* uniformly in the population, but the treatment were changed from level *a** = 0 to level *a* =1"
- Natural direct effect (NDE)
  "how much the outcome would change if the exposure were set at level *a=1* versus level *a**=0 but for each individual the mediator were kept at the level it would have taken in the absence of the exposure"
- Natural indirect effect (NIE)
  "how much the outcome would change on average if the exposure were controlled at level *a=1*, but the mediator were changed from the level it would take if *a**=0 to the level it would take if *a=1"*
- Total effect (*TE*)
  "how much the outcome would change overall for a change in the exposure from level *a**=0 to level *a*=1"

Valeri, L., & Vanderweele, T. J. (2013). Mediation analysis allowing for exposure-mediator interactions and causal interpretation: theoretical assumptions and implementation with SAS and SPSS macros. *Psychological methods*, *18*(2), 137–150. https://doi.org/10.1037/a0031034

CASUAL INTERPRETATION ASSUMPTIONS

- Exchangeability/ Ignorability/ Conditional independence
- Identifiability of controlled direct effect
  - (1) No unmeasured confounding of treatment-outcome relationship
  - (2) No unmeasured confounding of mediator-outcome relationship
- Identifiability of natural direct & indirect effects
  - (1) + (2) +
  - (3) No unmeasured confounding of treatment-mediator relationship
  - (4) No mediator-outcome confounder that is affected by treatment

conditional on pretreatment covariates C

Nguyen, T. Q., Schmid, I., Ogburn, E. L., & Stuart, E. A. (2022). Clarifying causal mediation analysis: Effect identification via three assumptions and five potential outcomes. *Journal of causal inference*, *10*(1), 246–279. https://doi.org/10.1515/jci-2021-0049

SENSITIVITY TESTING FOR SEQUENTIAL IGNORABILITY

```
sens.out <- medsens(med.out, rho.by = 0.1, effect.type = "indirect", sims = 100)
summary(sens.out)
```

```
##
## Mediation Sensitivity Analysis for Average Causal Mediation Effect
##
## Sensitivity Region
##
##      Rho   ACME 95% CI Lower 95% CI Upper R^2_M*R^2_Y* R^2_M~R^2_Y~
## [1,] 0.4 0.0941      -0.1249       0.3132          0.16       0.0077
##
## Rho at which ACME = 0: 0.4
## R^2_M*R^2_Y* at which ACME = 0: 0.16
## R^2_M~R^2_Y~ at which ACME = 0: 0.0077
```

The higher the R^_2M*R^2_Y value, the more robust the mediation results

OTHER ASSUMPTIONS

- Time-independence
  - Fairly consistent socioeconomic position over time
  - Prospective studies
- Correct temporal order (e.g. X→ M→ Y)
- Positivity/ Overlap/ Common support
  - Non-zero probability of people belonging to high and low income groups given the covariates
  - Non-zero probability of sugar consumption taking on different values when people switch income groups
- Consistency/ SUTVA (stable unit treatment value assumption)
  - Treatment for low income group (or high income group) does not affect outcome of the other group

Nguyen, T. Q., Schmid, I., Ogburn, E. L., & Stuart, E. A. (2022). Clarifying causal mediation analysis: Effect identification via three assumptions and five potential outcomes. *Journal of causal inference*, *10*(1), 246–279. https://doi.org/10.1515/jci-2021-0049

SOME EXAMPLES

Socioeconomic Inequalities in Oral Frailty Among Older Adults: A Causal Mediation Analysis on the Role of Prevention From Tooth Loss

Mieko Fujita [1,2], Kenji Takeuchi [1,3,4,✉], Yudai Tamada [1,3], Taro Kusama [1,4], Tatsuo Yamamoto [5], Katsunori Kondo [6,7], Ken Osaka [1]

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PMCID: PMC12624153 PMID: 40873151

ABSTRACT

Background

Although social inequalities in oral health have been suggested, the link between socioeconomic status (SES) and oral frailty (OF) remains unclear. We aimed to investigate the inequalities in OF according to SES and the extent to which inequalities are mitigated by preventing tooth loss.

Methods

We used cross-sectional data from 21 542 functionally independent participants aged ≥ 65 (48.5% men) from the Japan Gerontological Evaluation Study. The prevalence of OF, number of teeth, and educational attainment (EA) and equivalent income (EI) were used as outcome, mediator and explanatory variables, respectively. A Poisson regression model was used to examine the association between SES and OF. Causal mediation analysis was performed to calculate the prevalence ratios (PRs) and 95% confidence intervals (CIs) of the controlled direct effects (CDEs) of the number of teeth. The proportion eliminated (PE) of the ≥ 20 remaining teeth was calculated.

Results

Overall 7984 participants had OF. The prevalence of OF was 1.45 times higher in participants with ≤ 9 years of EA and 1.38 times higher in participants with an EI of < $20.000. The estimated total effect (TE) of low EA or low EI on the prevalence of OF was mediated by the number of teeth (TE PR, 1.30 [95% CI, 1.25–1.35]; CDE PR, 1.22 [95% CI, 1.10–1.33]; PE, 28.2%) or (TE PR, 1.26 [95% CI, 1.22–1.31]; CDE PR, 1.23 [95% CI, 1.14–1.32]; PE, 12.9%).

Conclusion

OF showed a clear social gradient based on SES. However, this association could be mediated by the remaining ≥ 20 teeth.

Keywords: frailty, Japan, mediation analyses, social class, tooth loss

RESEARCH ARTICLES | MARCH 29 2025

Mediation Effect of Dental Caries in the Relationship between Parental Locus of Control and Oral Health-Related Quality of Life

Subject Area: Dental Medicine , Further Areas

Special Collection: Karger e-Journal Backfile Collection 2025

Sharon Hui Xuan Tan; Ankur Singh; Kok Hian Tan; Johan Gunnar Eriksson; Chin-ying Stephen Hsu

Caries Res (2025) 59 (6): 567–579.
https://doi.org/10.1159/000545620 Article history
PubMed:40159221

Abstract

Introduction: The study aimed to assess the direct and indirect effect of parental locus of control (LoC) on child oral health-related quality of life. ***Methods:*** As part of the Growing Up in Singapore towards Healthy Outcomes (GUSTO) multicenter longitudinal cohort study, sociodemographic characteristics of parents and their children were obtained at recruitment. Oral health status and dental caries outcomes were assessed at the 5th year post-natal visit and administered alongside the LoC questionnaire. Intraoral examinations were carried out by 3 trained calibrated dental professionals using the modified International Caries Detection and Assessment System (ICDAS-II) criteria. At the 6-year post-natal visit, the Early Childhood Oral Health Impact Scale (ECOHIS) was administered to mothers to assess the oral health-related quality of life (OHRQoL) of their child. Statistical analysis of the direct effects of parental LoC on OHRQoL and the causal mediation effects of dental caries were carried out using the potential outcomes approach with 1,000 simulations. ***Results:*** A total of 312 parent-child dyads were included in this prospective cohort study. At the 5th year post-natal visit, the median decayed, missing, and filled surfaces (dmfs) was 2 (IQR 0–5), while the median LoC was 47 (IQR 43–50). The total effect of parental LoC on ECOHIS was −2.05 (95% CI: −4.03 to −0.08), of which the direct effect through dmfs was −1.45 (95% CI: −3.41 to 0.47). The percentage of the total effect of parental LoC on ECOHIS that was mediated by the presence of dental caries was 29.5% for dmfs, including incipient caries (ICDAS 1–6). The proportion mediated was lower if only active decayed surfaces were considered (23.7%) and higher if only cavitated lesions (ICDAS 3–6) (30.1%) were considered. ***Conclusion:*** The effect of parental LoC on child OHRQoL was mediated in part through the development of dental caries.

THANK YOU.