Text mining to identify potential mechanisms linking sedentary behaviour to disease outcomes

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Sedentary Behaviour Council
ISPAH satellite workshop
Cambridge
13 October 2018

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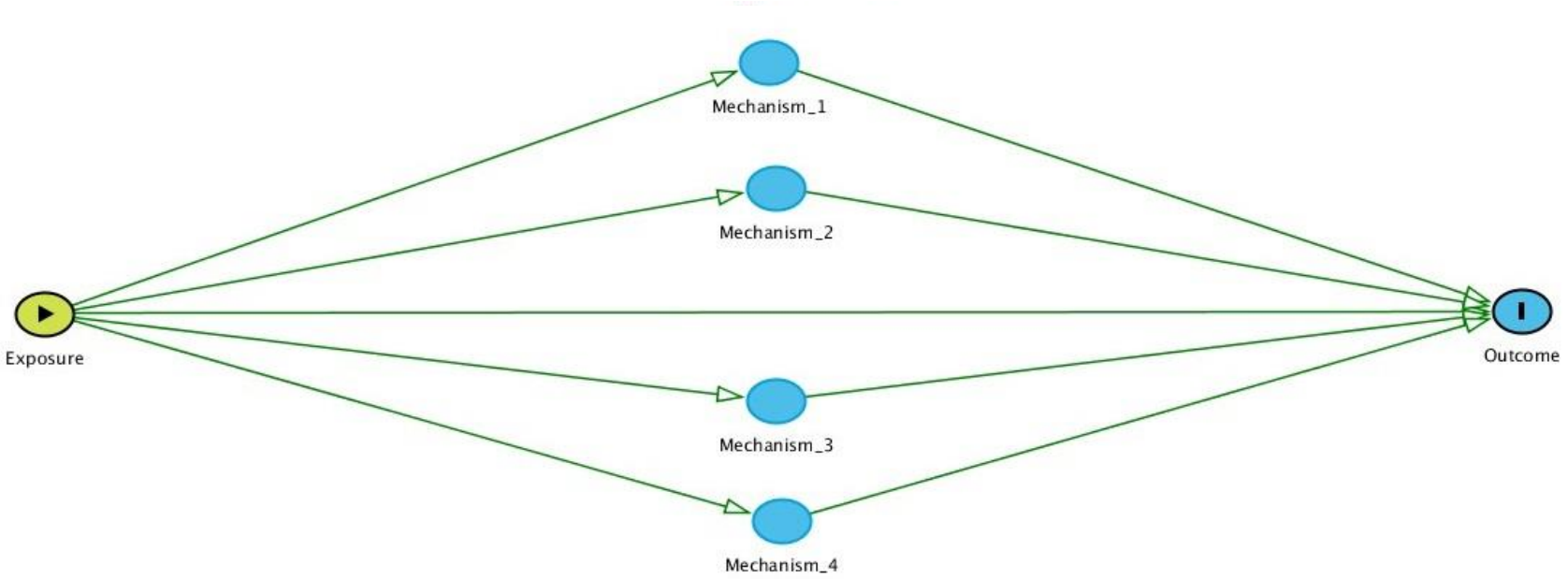
Understanding mechanisms



- Improve causal inference
- Easier/more effective to intervene on mediator
- Alter exposure in way to maximise mediation effect

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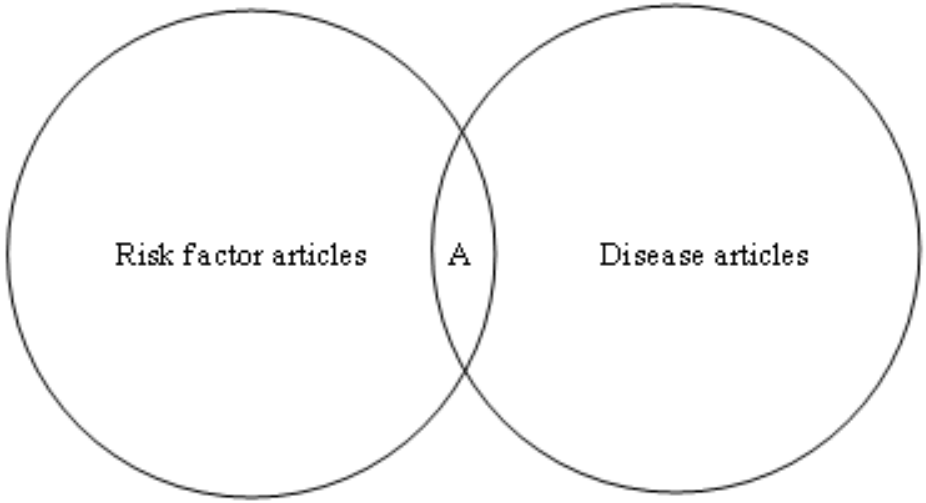
How to identify plausible mechanisms?

Search for common terms (potential mechanisms) in literature using PubMed®



A overlapping terms identified by Boolean operator 'and'

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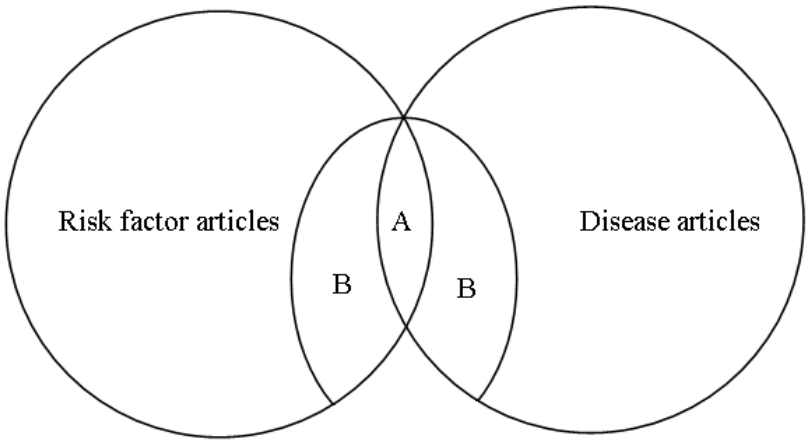
How to identify plausible mechanisms?

Search for common terms (potential mechanisms) in literature using text mining



A overlapping articles (with common terms)

B non-overlapping articles (with common terms) associated with both risk factor and disease

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Example - BDNF

- Protein expressed by hypothalamus
- Also excreted by skeletal muscle during exercise
- Exercise and cognitive function research (humans)
- Mouse models have shown upregulation of BDNF reduces tumour burden (various cancers)

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Text-mining tools

University of BRISTOL

MRC Integrative Epidemiology Unit

Current students Current staff Alumni

search

Integrative Cancer Epidemiology Programme

- Research themes
- **Research outputs**
  - ↳ Publications
  - ↳ Grants
  - ↳ **Data and analysis tools**
- People
- Collaborations
- Impact and engagement
- Contacts

Data and analysis tools

MR Base

MR Base enables online Mendelian randomization analysis using a comprehensive manually curated database of GWAS studies.

MELODI

MELODI is a literature mining platform to identify potential mechanistic pathways between exposures and disease outcomes.

"MR Base has transformed the ability of researchers world-wide to run rapid two-sample Mendelian randomization analyses, which can form the basis for in-depth analyses of many important questions regarding possible prevention or treatment of disease"

— PROF GEORGE DAVEY SMITH

TeMMPo

TeMMPo is a literature search tool to quantify the literature for specific disease mechanism.

LD Hub

LD Hub supports online LD score regression analysis using a comprehensive manually curated database of GWAS studies.

TeMMPo tool

- Text Mining for Mechanism Priorisation
- Uses Medical Subject Headings (MeSH) system
- Identifies co-ocurrence of MeSH headings in publications
  → Link ‘mechanism’ to exposure and/or outcome
- Targeted approach: specify *a priori* potential mechanism terms

https://www.temmpo.org.uk/

TeMMPo

TEXT MINING FOR MECHANISM PRIORITISATION

World Cancer Research Fund

University of BRISTOL

MRC Integrative Epidemiology Unit

Cancer Council Victoria

MELODI

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Software Application Profile

Software Application Profile

MELODI: Mining Enriched Literature Objects to Derive Intermediates

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MELODI

- A text mining platform designed to identify and prioritise intermediates between two datasets.
- Uses PubMed to create datasets (exposure and outcome).
- MELODI looks for overlapping
  - MeSH terms
  - Single SemMedDB concepts
  - SemMedDB ‘triples’ (subject – predicate – object) datasets.
- Enrichment step – compares frequency of terms within datasets to background frequency in PubMed.

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MELODI

- Enrichment using OR and two-tailed FET.
- P-values corrected for multiple testing using the Benjamini/Hochberg (non-negative) correction with a cutoff of $p<1e-5$.
- The results (corrected p-value and OR) used to filter results.
- Also uses frequency of predicate term (SemMedDB Triple) and minimum position in the MeSH hierarchy (MesH method).

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- Visualisation of results via Sankey plot.
- SemMedDB Triples method also shows directed network diagram.
- These graphs are ‘live’ and change as filters applied.
- Once spurious intermediates removed and filters applied need to manually curate results.

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Search results are retained if they represent a biological marker that could plausibly be associated with both the exposure and outcome. Two independent extractions!

Exclusion criteria for intermediates:

- synonyms, antonyms or similar terms for the exposure or outcome
- scientific methods, diagnostic tests, therapies (including drugs), anatomical or physiological nomenclature, comorbid conditions.

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Example application

Identifying known and novel mechanisms underpinning association between sedentary behaviour and breast cancer risk

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Strengths and limitations

- Strengths:
  - Sophisticated text-mining techniques
  - Mechanism discovery
  - Combining literature from different fields

- Limitations:
  - Co-occurrence in article → not necessarily association
  - Multiple intermediates in pathway:
    Not really possible to combine

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Thank you

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http://www.bristol.ac.uk/integrative-epidemiology/faciliitiesresources/software/

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Further enquiry