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Sex-specific human, agent, and environment-related interactions in traumatic brain injury: Utility of the Haddon matrix

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DISCLOSURES

No financial or non-financial conflict(s) of interest relevant to this research

Funding:

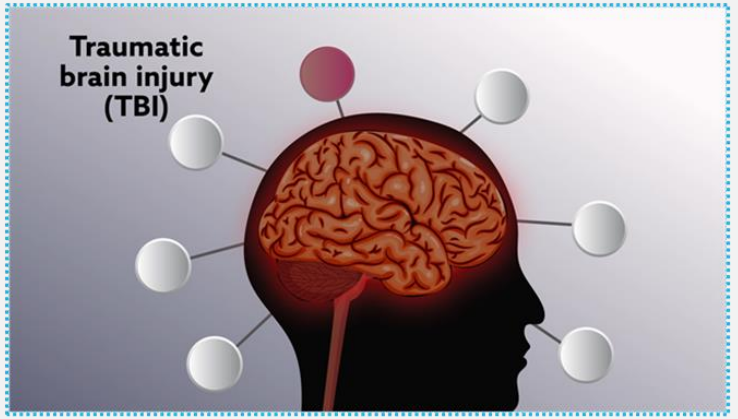
1. Eunice Kennedy Shriver National Institute of Child Health & Human Development of the National Institutes of Health **R21HD089106**
2. National Institute Of Neurological Disorders And Stroke of the National Institutes of Health **R01NS117921**
3. **Canada Research Chairs Program**

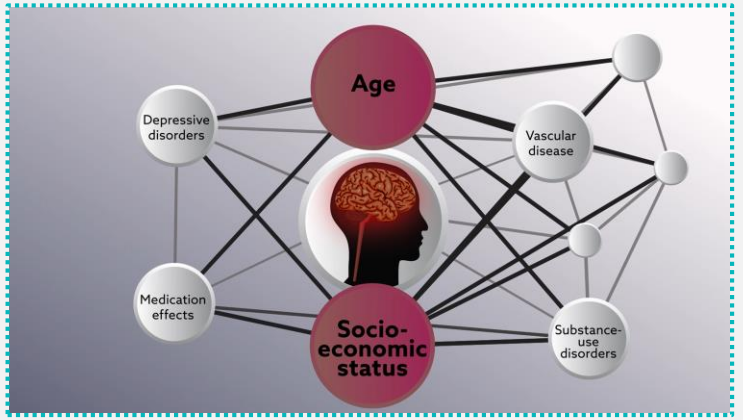
LEARNING OBJECTIVES ARE TO:

1. Recognize that the interplay of the Host, the Agent, and the Environment implicated in traumatic brain injury events is difficult to account for in hypothesis-driven research
2. Observe that data-driven approaches to the analysis of injury data may enable understanding of traumatic brain injury events in novel ways
3. Understand the differences uncovered between the sexes in the patterns of the Host, Agent, and Environment and consider how accounting for sex differences can promote more responsive prevention and care

Background

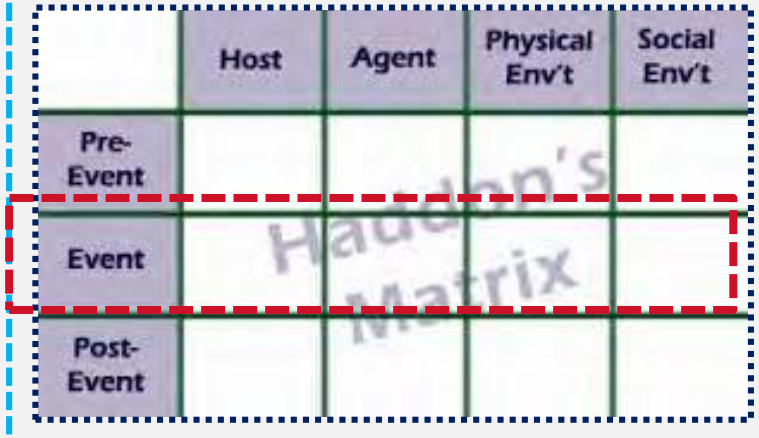
- Traumatic brain injury (TBI) has a big data problem
- National healthcare registries provide ***invaluable*** data about patients and the reasons why they visit clinics and hospitals
- Unfortunately, there's so much of data
- Little has been done to organize the data in a way that's meaningful for understanding TBI
- Computationally, however, the task is feasible





Theory and research objectives

- This research was informed by **the epidemiologic triad in the Haddon Matrix**[1]
  - The Haddon Matrix consists of three columns (host, agent, and environment) and three rows (pre-event, event, post-event phases)
  - This study focused on the event phase
- **Research objectives were to:**
  1. Utilize computational approaches to sequence host, agent, and environment data at the injury event from ICD-10-CA codes
  2. Apply key concepts of host-agent-environment of the Haddon Matrix to comprehend the data of patients with a diagnosis of TBI through a sex lens **in the event phase**



https://www.npaihb.org/images/epicenter_docs/injuryprevention/HaddonMatrixBasics.pdf

[1]Haddon W Jr. (1980). Advances in the epidemiology of injuries as a basis for public policy. Public Health Rep. 95 (5): 411–21. PMC 1422748

Methods

- Research ethics boards approved the study (University Health Network and University of Toronto)
- **Study design:** A population-based retrospective cohort study of Ontarians, Canada
- **Data:** acquired from ICES; linked deterministically at the individual patient level through a unique, encoded identifier to other data based on name, sex, date of birth, and postal code
- **TBI:** ICD-10-CA codes S02.0, S02.1, S02.3, S02.7, S02.8, S02.9, S04.0, S07.1, and S06; published **severity classifications** to assign severity to every patient
- **External causes of injury:** established using CDC United States injury matrix; additionally identified sports-related injuries using Association of Public Health Epidemiologists in Ontario (APHEO) criteria

Methods, continue

Cohort #1 (TBI): Ontarians with TBI
Cohort #2 (Reference cohort): A 10% random sample of persons without TBI, individually matched to TBI persons by age, sex, income level, and place of residence

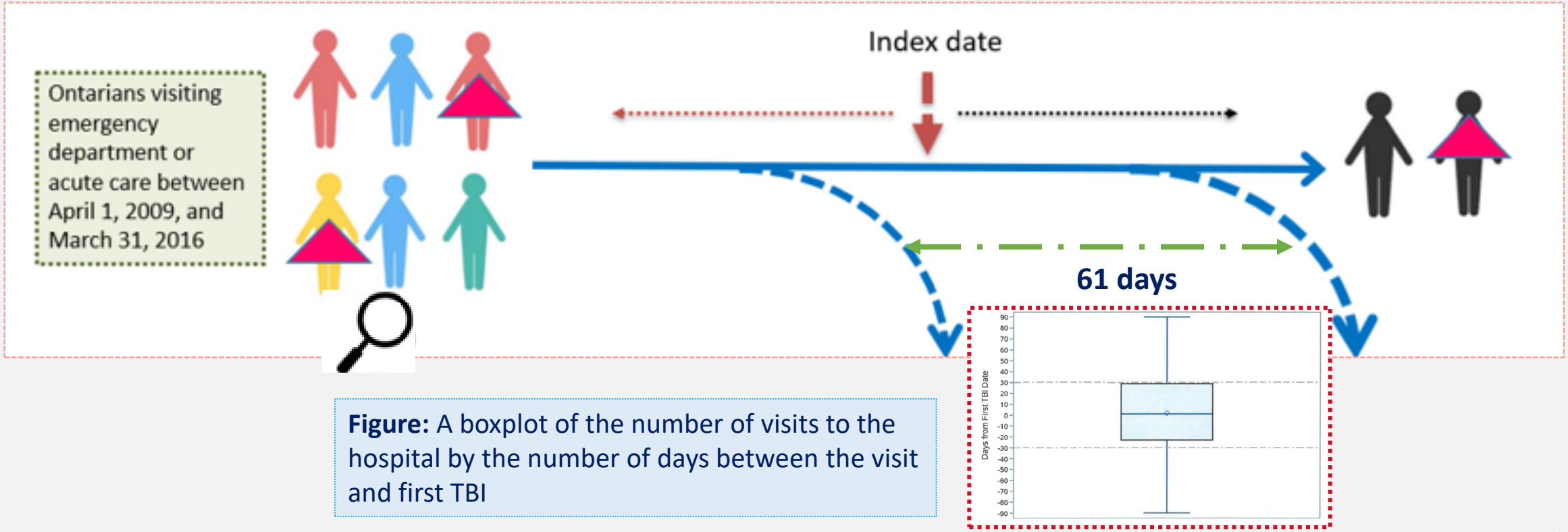


Figure: A boxplot of the number of visits to the hospital by the number of days between the visit and first TBI

Results

- The dataset consisted of 235,003 unique patients who had a TBI-related visit to either an ED or acute care hospital over the study period and same number of reference patients; split randomly into testing (25%; n = 58,516), validation (25%; n = 58,798), and training (50%; n = 117,689)

Table 1 Characteristics of patients with a first traumatic brain injury-related visit in the emergency department or acute care and matched reference patients

Variables	Patients with TBI ($n = 58,516$)		Reference patients ($n = 58,516$)	
	Female ($n = 25,137$; 43%)	Male ($n = 33,379$; 57%)	Female ($n = 25,137$; 43%)	Male ($n = 33,379$; 57%)
Sociodemographic characteristics				
Age at injury (years)	39.41 (26.3)	33.84 (24.3)	39.41 (26.3)	33.85 (24.3)
Income quintile				
Q1 (lowest)	4868 (19)	6597 (20)	4868 (19)	6597 (20)
Q2	4895 (19)	6645 (20)	4895 (19)	6645 (20)
Q3	4956 (20)	6538 (20)	4956 (20)	6538 (20)
Q4	5269 (21)	6913 (21)	5269 (21)	6913 (21)
Q5 (highest)	5149 (20)	6686 (20)	5149 (20)	6686 (20)
Rurality (yes)	3842 (15)	5242 (16)	3842 (15)	5242 (16)
TBI-related characteristics				
TBI main diagnosis	22,163 (88)	29,542 (89)	NA	NA
Injury severity				
Unspecified	12,075 (48)	12,961 (39)	NA	NA
Mild	8260 (33)	12,201 (37)	NA	NA
Moderate	682 (3)	1484 (4)	NA	NA
Severe	4120 (16)	6733 (20)	NA	NA

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External causes of injury, by CDC[a]				
Sports injury	4668 (19)	9804 (29)	NA	NA
Assault	928 (4)	3431 (10)	NA	NA
Falls	13,080 (52)	13,400 (40)	NA	NA
Motor vehicle collisions	2587 (10)	3221 (10)	NA	NA
Struck by/against	7475 (30)	13,370 (40)	NA	NA
Other	2519 (10)	4272 (13)	NA	NA
Missing	44 (0)	122 (0)	NA	NA

Results, continue

- From 2600 codes classifying the TBI and reference patients' health conditions on which matched McNemar tests were performed, 273 had an odds ratioo greater than one after Benjamini Yekutieli correction; 226 (83%) were internally validated
  - Of the 226 codes included in the factor analysis, 164 (73%) unique codes met the factor loading cut-off of 0.2
  - 34 factors were selected based on their interpretability and the breakpoints on the scree plots from further analyses

Factor number	Description	Category	ICD-10-CA Codes	Frequency in cohorts		OR [95% CI]
				TBI	Reference	
Factor 1	Multitrauma$^{H/A}$	Traumatology/Human–product interaction	S36, S27, S37, T06, T79, S42, S26, S72	2,535	749	3.49 [3.21-3.79]
Factor 2	Heart & Metabolic Disorders^{H}	Cardiology	E78, I10, I48, Z95, I50, Z92, E03, E11	6,095	3,787	1.97 [1.88-2.07]
Factor 3	Alzheimer's & Dementia^{H}	Neurology	F00, G30	267	79	3.41 [2.65-4.39]
Factor 4	Endocrine, Metabolic & Elderly Emerg^{H}	Emergency medicine/ Geriatrics	I10, E87, E83, E22, F05, Z75, N17, F06, B96, I95, R41	6,338	2,873	2.85 [2.70-3.00]
Factor 5	Complications & Resp Emerg^{E}	Emergency medicine	J95, Y84, J15	638	204	3.14 [2.68-3.68]
Factor 6	Elderly Disorders, Neoplasms & Falls$^{H/A}$	Geriatrics, External Cause of Injury	S72, F05, Z75, R41, F03, Z51, R29, W05, R26, W19, C79, Z74, W06	10,793	2,275	6.92 [6.54-7.31]

Color coding:

Designation	Colour	Factors
Host		2; 3; 4; 7; 8; 10; 11; 14; 17; 19; 23; 24; 27
Agent		18; 21; 22; 30; 31; 32; 33
Environment		5; 9; 12; 13; 15
Host-Agent linked		1; 6; 16; 26; 29; 34
Host-Environment linked		20; 25; 28

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Results, continue

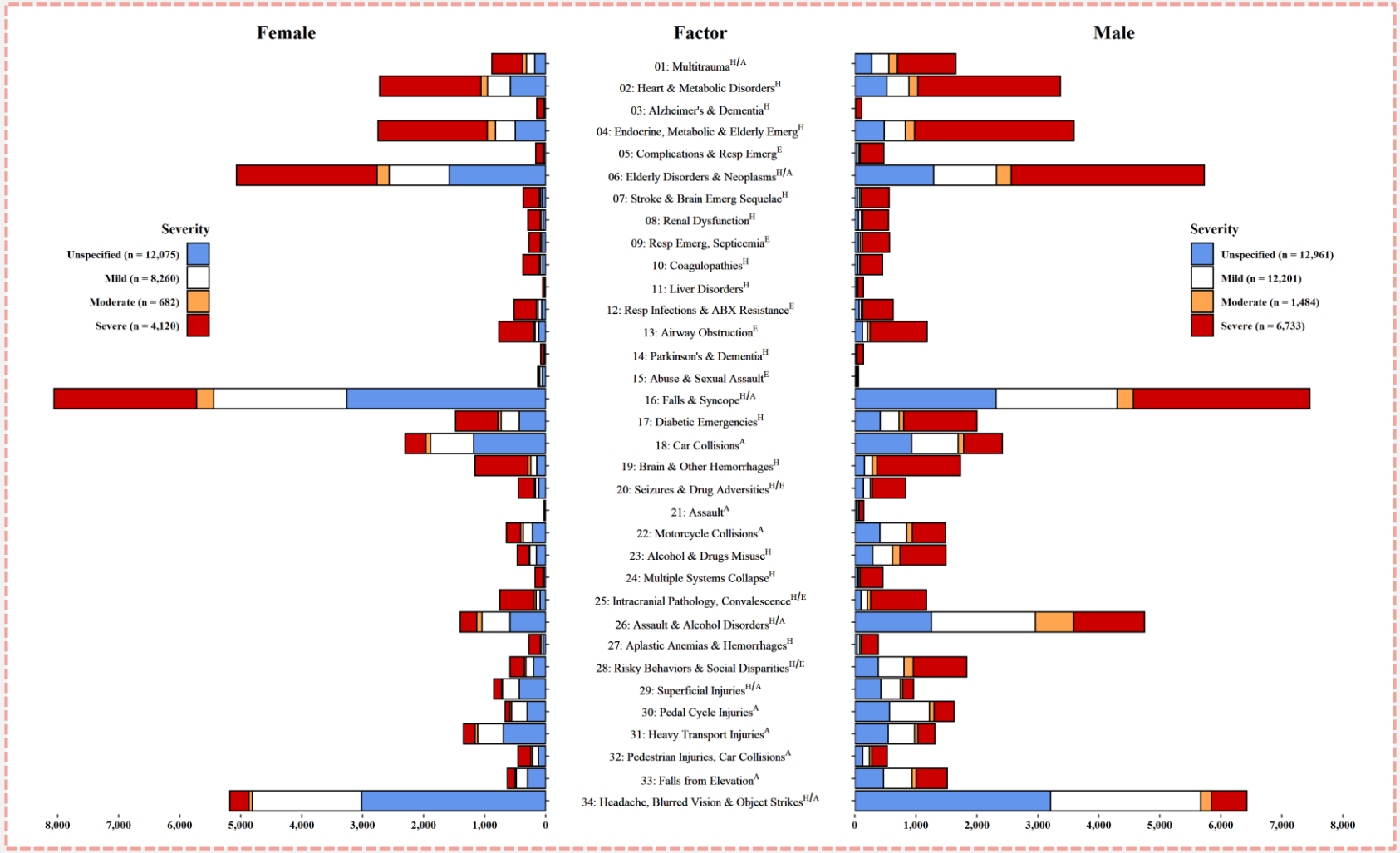

Figure: Host (H), agent (A), environment (E) and intertwined (H/A and H/E) factors in male and female patients with TBI in Ontario, Canada. Data are shown by injury severity

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Results, continue

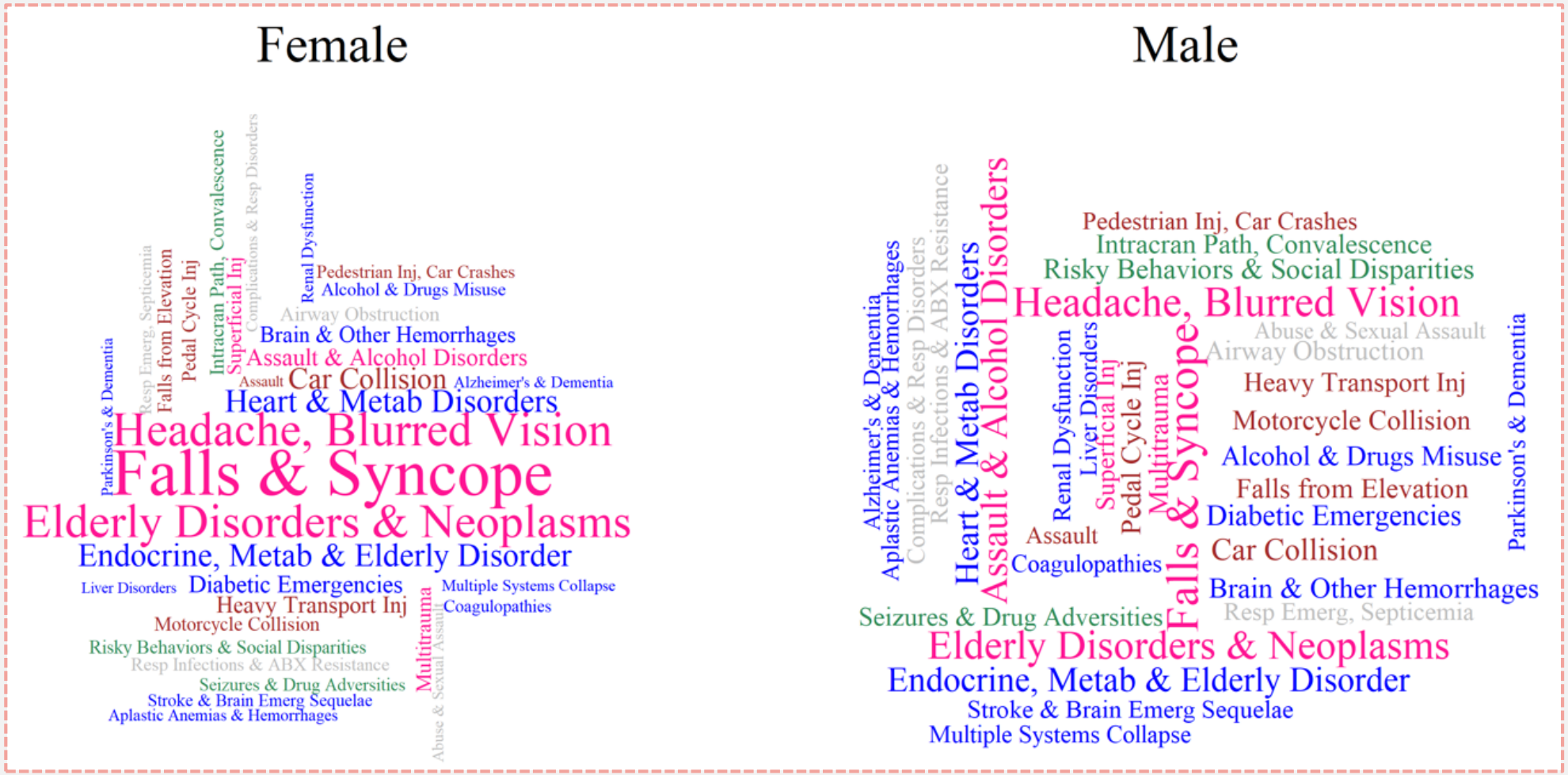

Figure. Wordcloud of factors, by proportion, in male and female patients.

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Results, continue

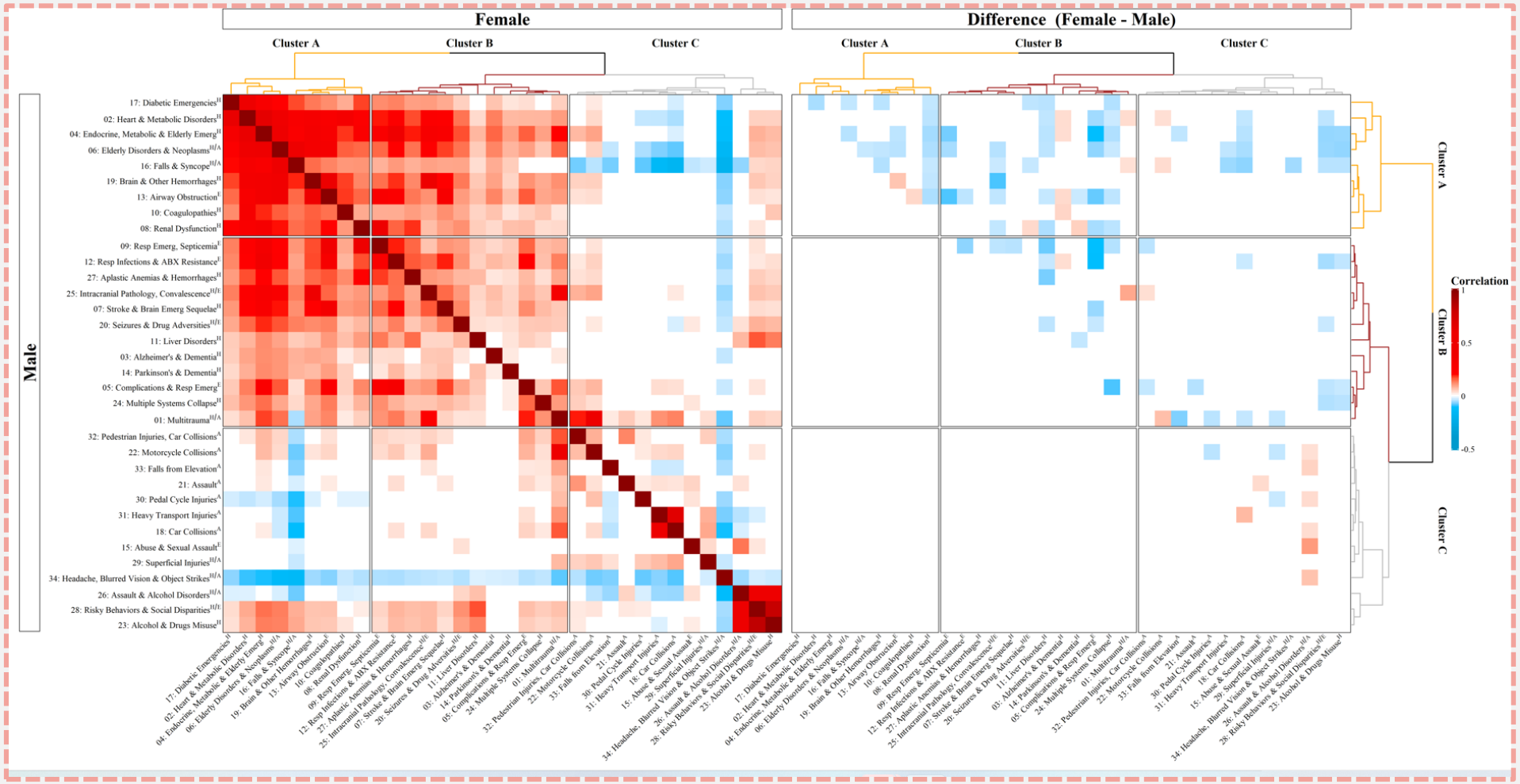

Figure. The Host, agent, and environment factors correlations **(a)** and differences between the sexes (female-male) **(b)**.

Highlights

- The interplay of Host, Agent, and Environment implicated in traumatic brain injury events is difficult to account for in hypotheses-driven research
- Data-driven approaches to the analysis of injury data may enable understanding of these events in novel ways
- Meaningful differences between the sexes in the patterns of Host, Agent, and Environment were uncovered; the results were internally validated
- The study findings support the benefit of data-driven analysis in examining sex-specific patterns within the Haddon matrix

Implications for prevention

- The goal of prevention is to protect, promote, and maintain health and well-being and to prevent disease, disability, and death
  - **Primary:** circumvents injury before it occurs
  - **Secondary:** recognizes pathology at its earliest stages, to stop its progression
  - **Tertiary and quaternary:** treatment directed to prevent complications and minimize disability
- Results suggest need for
  - Balance training and addressing cardiovascular syncope in the elderly to prevent TBI sustained in falls (**Cluster A:** Advanced Age-related Brain Pathology)
  - Regulating environment through government action on road planning, traffic laws, protective equipment, airbags and seatbelts (**Cluster B:** Multiple Body System Pathology)
  - Education about alcohol intoxication to prevent assault related TBI (**Cluster C:** Young Age-related Concerns)

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For more information, please refer to

Mollayeva *et al.*
BMC Medical Research Methodology (2022) 22:30
https://doi.org/10.1186/s12874-021-01493-6

RESEARCH Open Access

Sex-specific analysis of traumatic brain injury events: applying computational and data visualization techniques to inform prevention and management

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