

Modelling Interactions between Multiple Causes of Death Using Causal Pies

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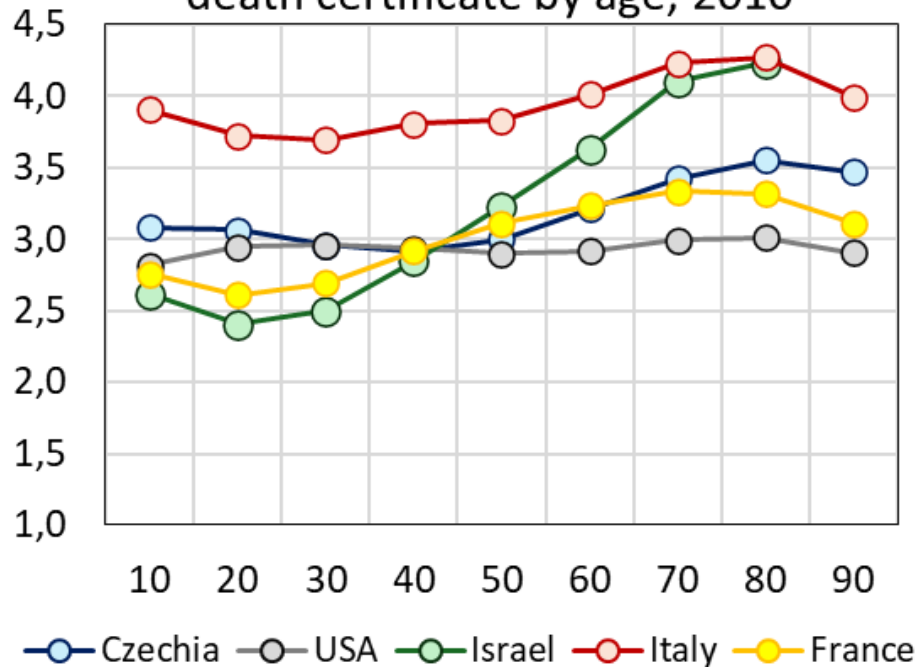
Are contributory causes of death recorded in Part 2 of the death certificate mediators of chains of morbid events leading to death?

Figure: Death certificate section to record causes of death

Administrative Data (can be further specified by country)																					
Sex			<input type="checkbox"/> Female				<input type="checkbox"/> Male			<input type="checkbox"/> Unknown											
Date of birth			D	D	M	M	Y	Y	Y	Y	Date of death			D	D	M	M	Y	Y	Y	Y
Frame A: Medical data: Part 1 and 2																					
1 Report disease or condition directly leading to death on line a Report chain of events in due to order (if applicable) State the underlying cause on the lowest used line		a	Cause of death						Time interval from onset to death												
		b	Due to: C																		
		c	Due to: B																		
		d	Due to: A																		
2 Other significant conditions contributing to death (time intervals can be included in brackets after the condition)					D																

Relevance

Average number of causes per death certificate by age, 2010



Number of multiple causes of death per death certificate (%), 2010

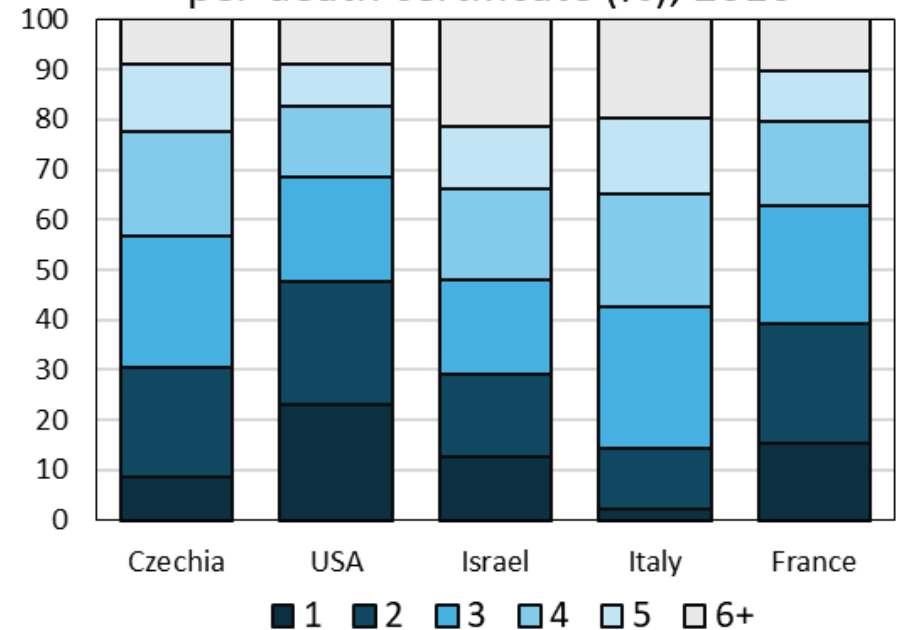


Table: Variation (in years) in life expectancy among individuals who died from leading underlying causes of death in the U.S. in 2019, by contributory causes and their combinations.

F03	G30	I21	I25	J44	Other
4.1	4.0	15.3	16.1	11.2	17.4

In the U.S., life expectancy among those dying from ischemic heart disease varies by up to 16 years, depending on contributory causes.

Research questions and design

Are contributory causes of death recorded in Part 2 of the death certificate mediators of chains of morbid events leading to death?

Data: US Multiple

Cause of Death Data

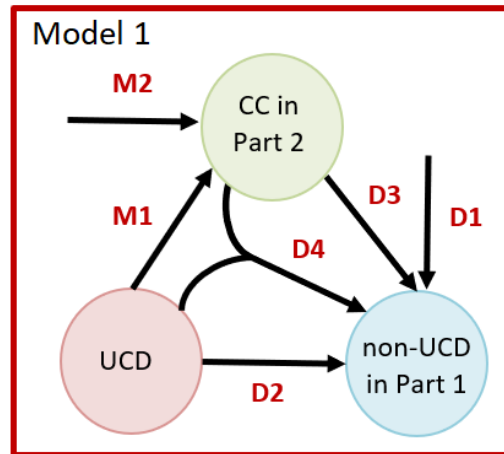
Year: 2019

Study population: Deaths aged 60–79 and 80+

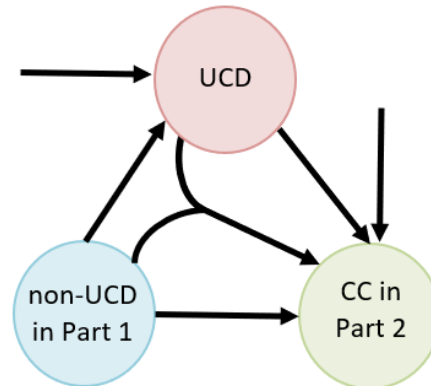
Methods: Causal pie models with mediators (Chen & Lee, 2018)

Disease selection: Top triads of causes of death on 3-digit ICD-10 level

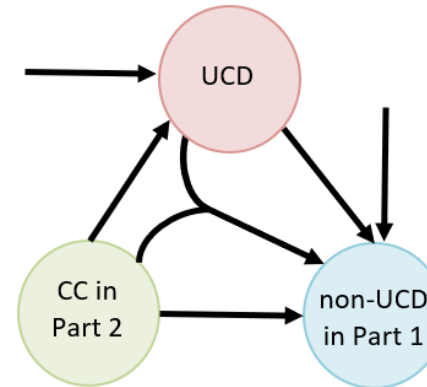
Figure: Causal pie models with mediators for different architecture of relations within triads of multiple causes of death



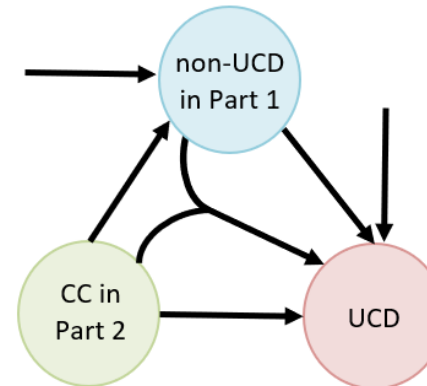
Model 4



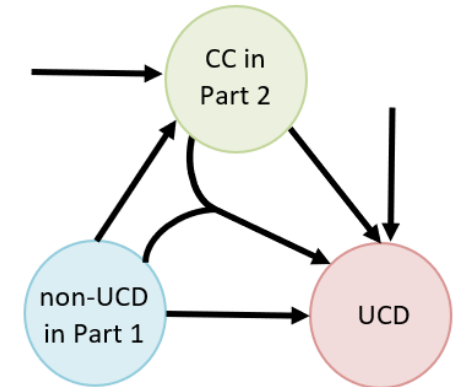
Model 2



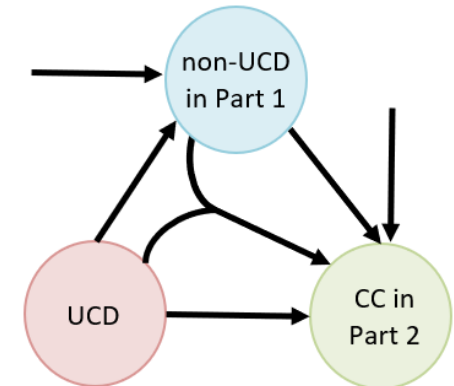
Model 5



Model 3



Model 6



Methods

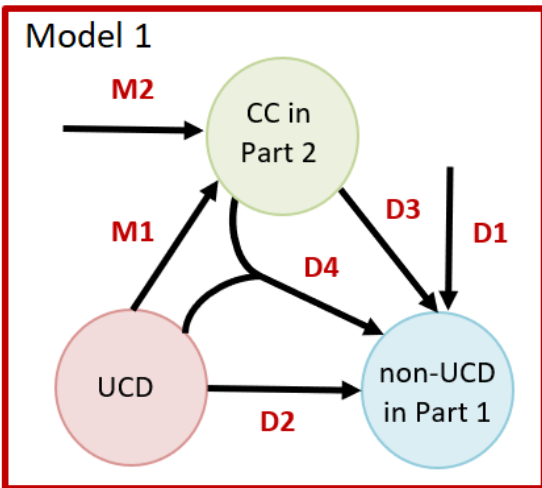


Figure: The pathways toward a terminating morbid state before death, Model 1

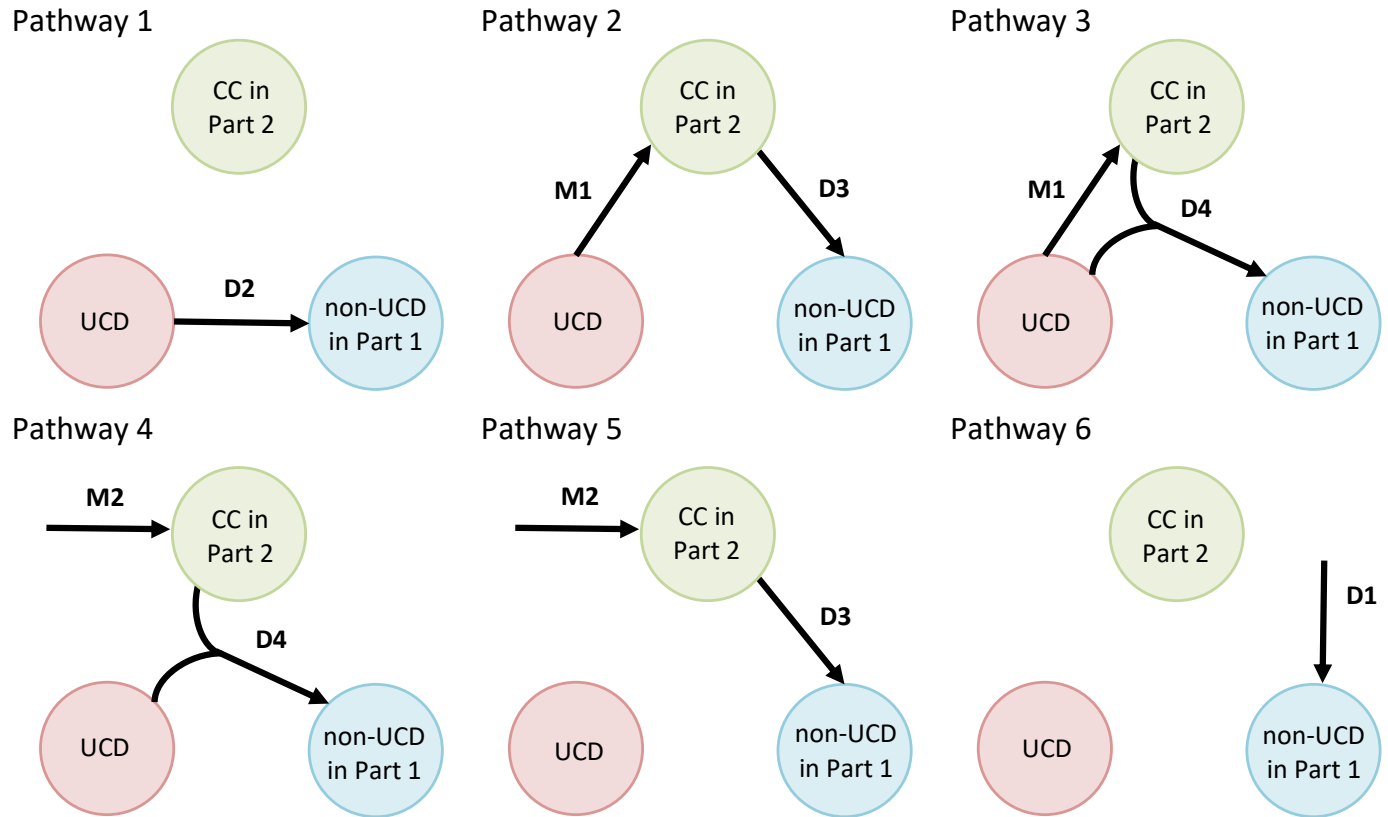


Table: Interpretation of pathways

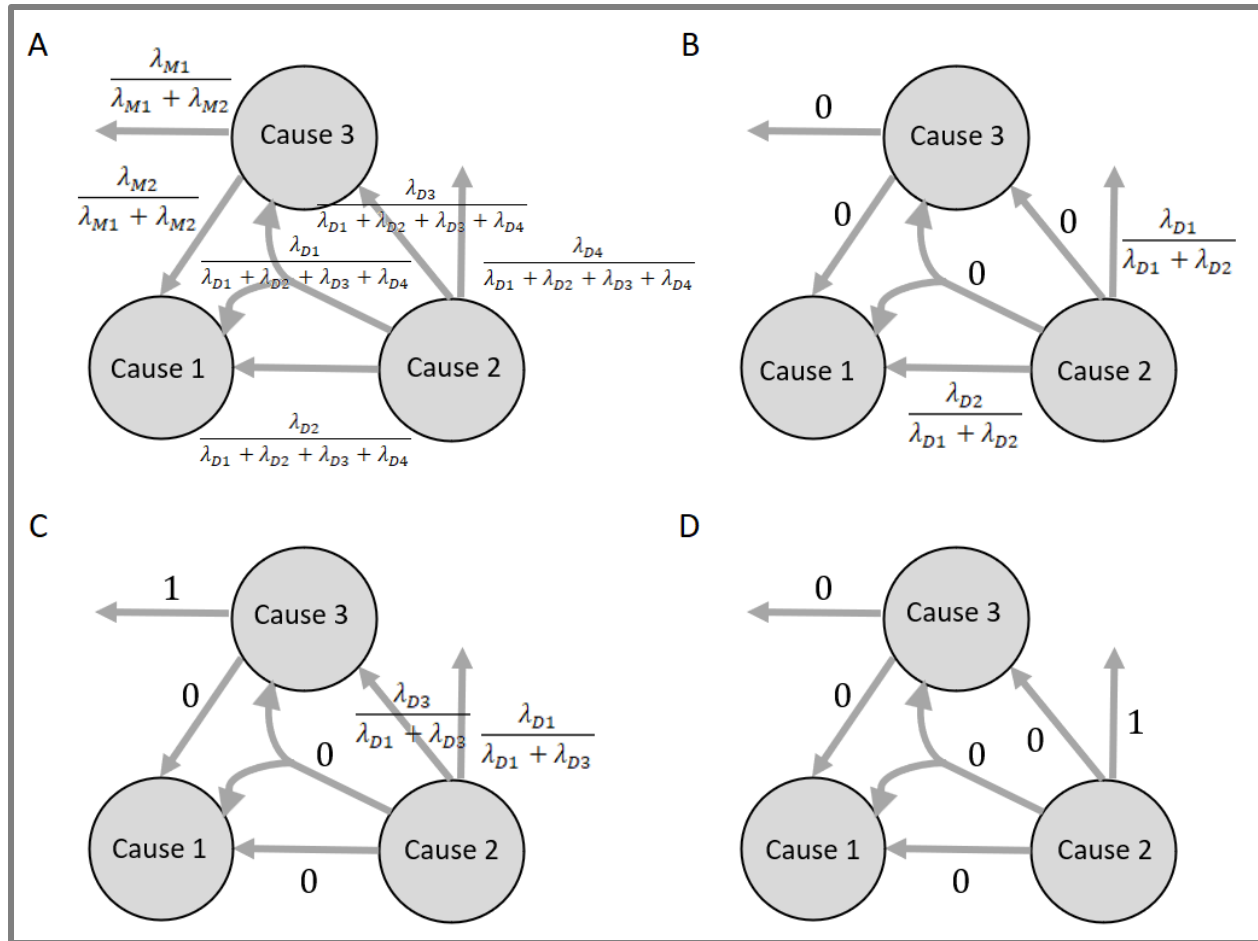
1. The UCD causes the non-UCD directly (path D2).
2. The UCD causes the CC, which in turn causes the non-UCD (path M1D3).
3. The UCD causes the CC, and then both interact to cause the non-UCD (path M1D4).
4. The UCD and an exogenous mediator interact to cause the non-UCD (path M2D4).
5. An exogenous mediator causes the non-UCD directly (path M2D3).
6. Neither the UCD nor the CC causes the non-UCD (path D1).

Methods

Procedure:

1. Estimate arrival rates across all six models.
2. Use these arrival rates to calculate attributable fractions.
3. Use attributable fractions to identify the leading pathways and mechanisms of synergy between diseases.

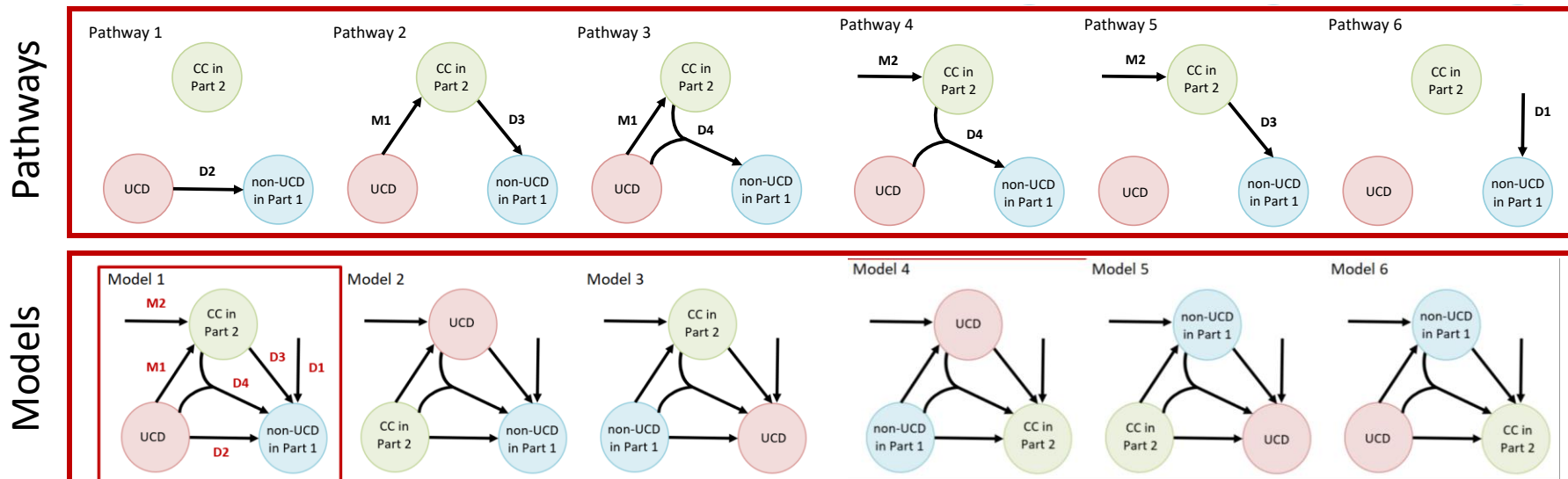
Figure: Attribution Process and Formulas for Attributable Fractions



Results

Table: Causal pie models and pathways with the highest attributable fractions (AF), females, 60–79

UCD	CC	non-UCD	Model	Pathway	AF	Diff. 1	Diff. 2
COPD	Hypertension	Respiratory failure	6	6	0.67	-0.50	-0.38
COPD	Congestive heart failure	Respiratory failure	3	4	0.57	-0.35	-0.33
Acute myocardial infarction	Hypertension	Ischemic heart disease	2	5	0.64	-0.33	-0.33
Ischemic heart disease	Hypertension	Cardiac arrest	3	4	0.51	-0.18	-0.15
Ischemic heart disease	Diabetes mellitus	Hypertensive heart disease	5	2	0.56	-0.33	-0.18
Ischemic heart disease	COPD	Congestive heart failure	3	4	0.53	-0.40	-0.19
Ischemic heart disease	Hypertension	Congestive heart failure	3	4	0.59	-0.42	-0.33
Ischemic heart disease	Chronic kidney disease	Congestive heart failure	1	4	0.57	-0.43	-0.31
Ischemic heart disease	Diabetes mellitus	Congestive heart failure	3	4	0.41	-0.15	-0.09
Acute myocardial infarction	Diabetes mellitus	Ischemic heart disease	3	4	0.71	-0.57	-0.41

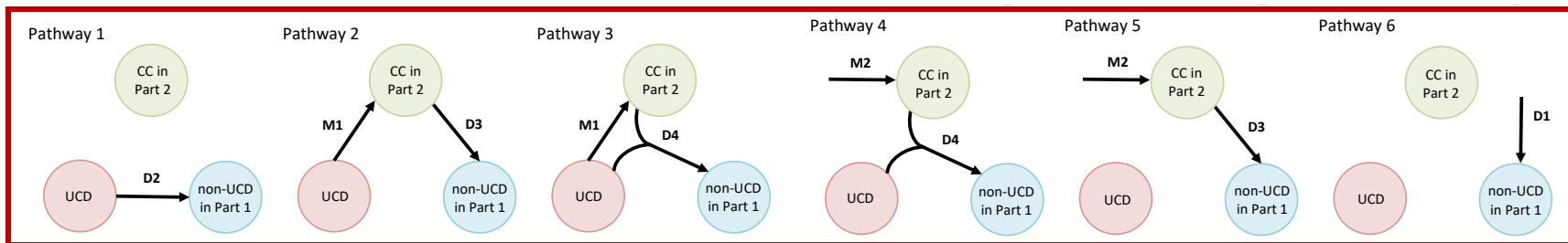


Results

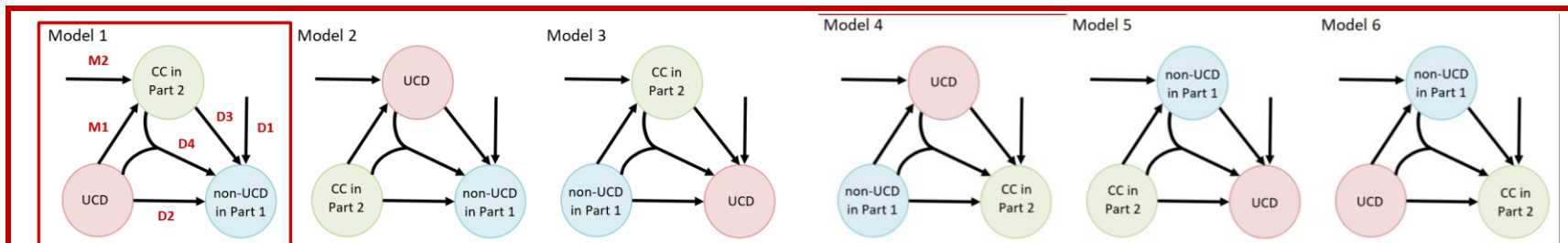
Table: Causal pie models and pathways with the highest attributable fractions (AF), males, 60–79

UCD	CC	non-UCD	Model	Pathway	AF	Diff. 1	Diff. 2
Acute myocardial infarction	Hypertension	Ischemic heart disease	2	5	0.60	-0.34	-0.29
Ischemic heart disease	Diabetes mellitus	Hypertensive heart disease	5	2	0.52	-0.05	-0.20
Ischemic heart disease	Hypertension	Cardiac arrest	1	6	0.63	-0.28	-0.03
Ischemic heart disease	Chronic kidney disease	Congestive heart failure	1	4	0.59	-0.46	-0.32
Ischemic heart disease	Hypertension	Congestive heart failure	2	5	0.59	-0.33	-0.02
Ischemic heart disease	COPD	Congestive heart failure	1	4	0.56	-0.42	-0.19
Acute myocardial infarction	Diabetes mellitus	Ischemic heart disease	4	5	0.96	-0.92	-0.60
Ischemic heart disease	Diabetes mellitus	Congestive heart failure	5	5	0.70	-0.43	-0.37
Ischemic heart disease	Diabetes mellitus	Cardiac arrest	5	5	0.70	-0.41	-0.40
Ischemic heart disease	Atrial fibrillation & flutter	Congestive heart failure	1	4	0.69	-0.54	-0.42

Pathways



Models

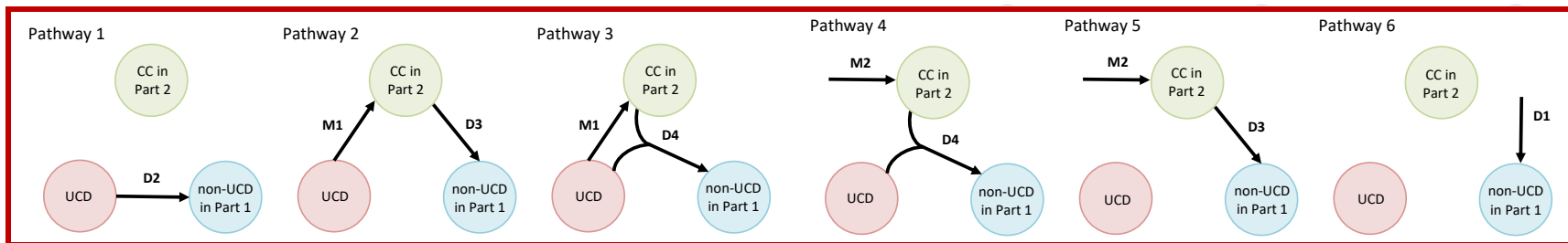


Results

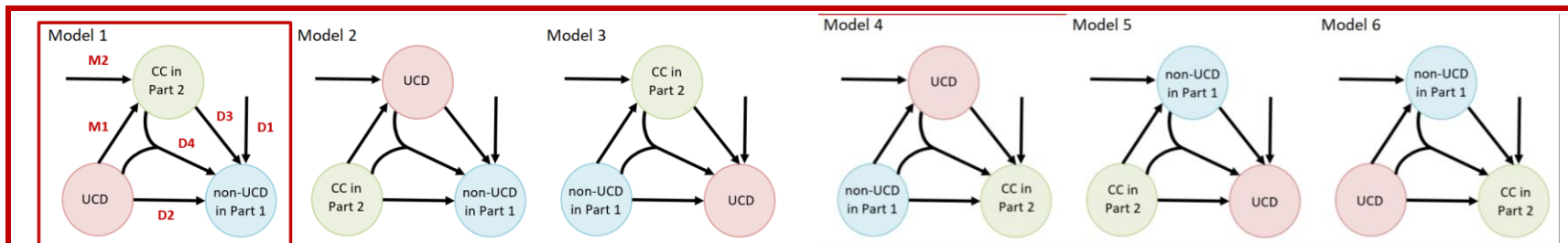
Table: Causal pie models and pathways with the highest attributable fractions (AF), females, 80+

UCD	CC	non-UCD	Model	Pathway	AF	Diff. 1	Diff. 2
Ischemic heart disease	Hypertension	Congestive heart failure	3	4	0.61	-0.43	-0.34
Ischemic heart disease	Atrial fibrillation & flutter	Congestive heart failure	1	4	0.60	-0.45	-0.32
Ischemic heart disease	Chronic kidney disease	Congestive heart failure	1	4	0.57	-0.40	-0.32
Ischemic heart disease	Hypertension	Cardiac arrest	2	5	0.64	-0.33	-0.04
Acute myocardial infarction	Hypertension	Ischemic heart disease	2	5	0.70	-0.41	-0.35
Ischemic heart disease	COPD	Congestive heart failure	1	4	0.51	-0.38	-0.22
Atrial fibrillation and flutter	Hypertension	Congestive heart failure	3	4	0.75	-0.60	-0.39
Ischemic heart disease	Dementia	Cardiac arrest	6	6	0.59	-0.21	-0.22
Ischemic heart disease	Dementia	Congestive heart failure	2	5	0.74	-0.54	-0.42
COPD	Congestive heart failure	Respiratory failure	3	4	0.55	-0.37	-0.30

Pathways



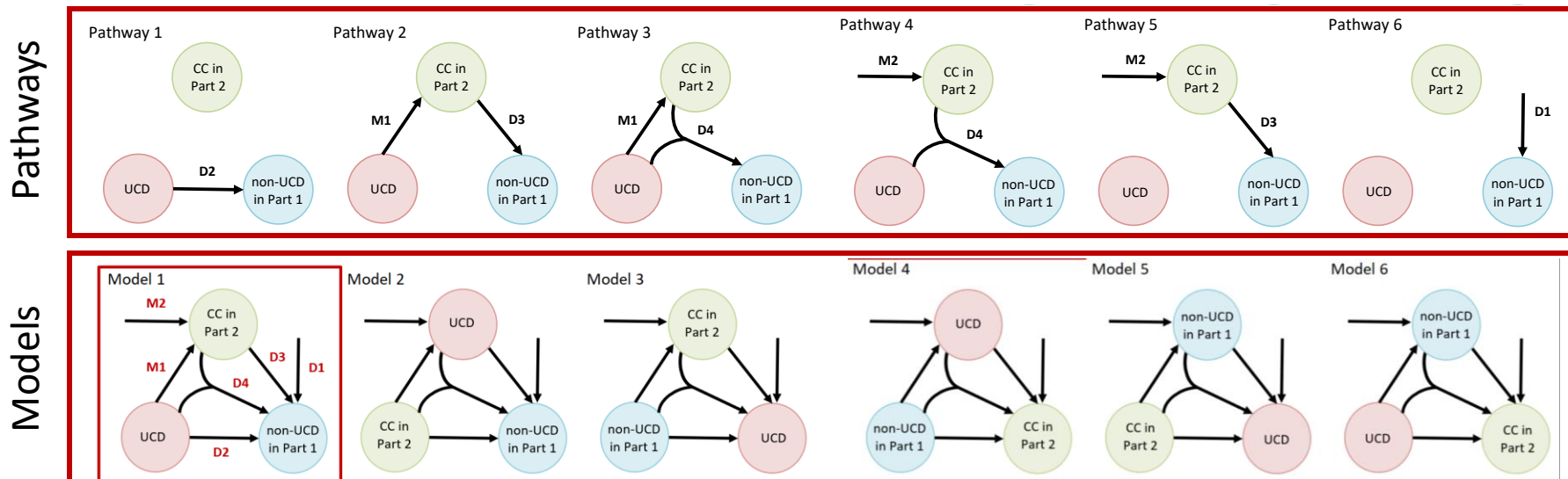
Models



Results

Table: Causal pie models and pathways with the highest attributable fractions (AF), males, 80+

UCD	CC	non-UCD	Model	Pathway	AF	Diff. 1	Diff. 2
Ischemic heart disease	Atrial fibrillation & flutter	Congestive heart failure	1	4	0.54	-0.40	-0.19
Ischemic heart disease	Chronic kidney disease	Congestive heart failure	1	4	0.49	-0.34	-0.22
Ischemic heart disease	Hypertension	Congestive heart failure	2	5	0.63	-0.39	-0.06
Ischemic heart disease	COPD	Congestive heart failure	1	4	0.47	-0.29	-0.10
Ischemic heart disease	Hypertension	Cardiac arrest	2	5	0.57	-0.26	-0.09
Acute myocardial infarction	Hypertension	Ischemic heart disease	2	5	0.65	-0.32	-0.31
Ischemic heart disease	Diabetes mellitus	Congestive heart failure	2	5	0.66	-0.51	-0.35
Ischemic heart disease	Atrial fibrillation & flutter	Cardiac arrest	2	5	0.62	-0.28	-0.19
Ischemic heart disease	Dementia	Congestive heart failure	2	5	0.84	-0.69	-0.53
COPD	Congestive heart failure	Respiratory failure	3	4	0.57	-0.39	-0.31



Conclusion

Three broader categories of roles that CCs in Part 2 can play in the lethal process can be distinguished:

1. Some act as mediators in the chain of morbid events leading to death (atrial fibrillation and flutter, heart failure, COPD, chronic kidney disease)
2. Others do not exhibit any interaction with the conditions listed in Part 1 (dementia).
3. Additionally, as demonstrated by several models involving contributory diabetes, they can even play a role in the development of UCDs.

Exploring synergy between diseases? Exploring quality of death certification?

Key contribution:

1. Moving beyond pairwise associations, focus on mechanisms;
2. Findings highlight the substantial heterogeneity in deaths that are otherwise hidden behind a single UCD;
3. Differentiating multiple causes by the roles they played in death process.

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1. Some act as mediators in the chain of morbid events leading to death (atrial fibrillation and flutter, heart failure, COPD, chronic kidney disease)
2. Others do not exhibit any interaction with the conditions listed in Part 1 (dementia).
3. Additionally, as demonstrated by several models involving contributory diabetes, they can even play a role in the development of UCDs.

Thank you!

Key contribution:

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2. Findings highlight the substantial heterogeneity in deaths that are otherwise hidden behind a single UCD;
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