



UNIVERSITÀ DEGLI STUDI DI NAPOLI
FEDERICO II

itee^{PhD}
information technology
electrical engineering



Patrizia Quaranta

Causally-Driven Clinical Decision Support:
Interventions, Counterfactuals, and What-If
Scenarios from Real-World Data

Tutor: Roberto Pietrantuono

co-Tutor: Giuseppe Cascone

Cycle: XXXVIII

Year: 2025

Candidate's information

- MSc degree in Computer Engineering
- DIETI Research group: DESSERT
- PhD start date: 01/11/2022
- PhD end date: 31/10/2025
- Scholarship type: PNRR- DM 352
- Partner company: CML VESUVIO s.r.l.
 - 12 months
- Period abroad: University of Thessaly, Medical School, Laboratory of Hygiene and Epidemiology, Larisa, Greece
 - 6 months

Summary of study activities

PhD Year	Courses	Seminars	Research
1 st	35	6	24
2 nd	10	8.5	40.9
3 rd	-	2.9	57.1
Total	45	17.4	122

Conferences and workshops attended

- Conference IEEE 13th International Conference on Healthcare Informatics (ICHI 2025), Rende, IT presented paper.
- Conference 38th IEEE International Symposium on Computer-Based Medical Systems (CBMS 2025), Madrid, SP, presented a paper (poster session).

Research area: Causal Reasoning in Health Domain



Toward interpretable and
evidence-based clinical
decision support



Causal Discovery, Causal
inference with observational
healthcare data

Research results:

Causal Reasoning in Health Domain

- **Methods:**
 - Framework to construct, infer, and validate a causal model using observational data.
- **Application Domains:**
 - *Occupational Health*: understanding the causal relationships underlying *fitness for work*
 - *Public Health*: understanding the causal relationships underlying *diabetes*.
- **Results:** Consistent with real-world evidence

Research products

[P1]	<i>P. Quaranta, R. Pietrantuono and G. Cascone, "Correlation and Causal Analysis of Occupational Health Data in the Maritime Domain," 2025 IEEE 13th International Conference on Healthcare Informatics (ICHI), Rende, Italy, 2025, pp. 739-744, doi: 10.1109/ICHI64645.2025.00112.</i>
[P2]	<i>P. Quaranta and R. Pietrantuono, "Exploring Causal Modeling to Enhance Diabetes Prediction and Management," 2025 IEEE 38th International Symposium on Computer-Based Medical Systems (CBMS), Madrid, Spain, 2025, pp. 725-726, doi: 10.1109/CBMS65348.2025.00150.</i>

PhD thesis overview

*EHR &
Real-World
Data:*

*Rapid diffusion of Electronic Health Records-> Enables new opportunities to understand **causal relationships between factors***

Opportunity to study real-world patient outcomes

*Beyond
RCTs:*

*Randomized Controlled Trials are the **gold standard** for medical causal inference*

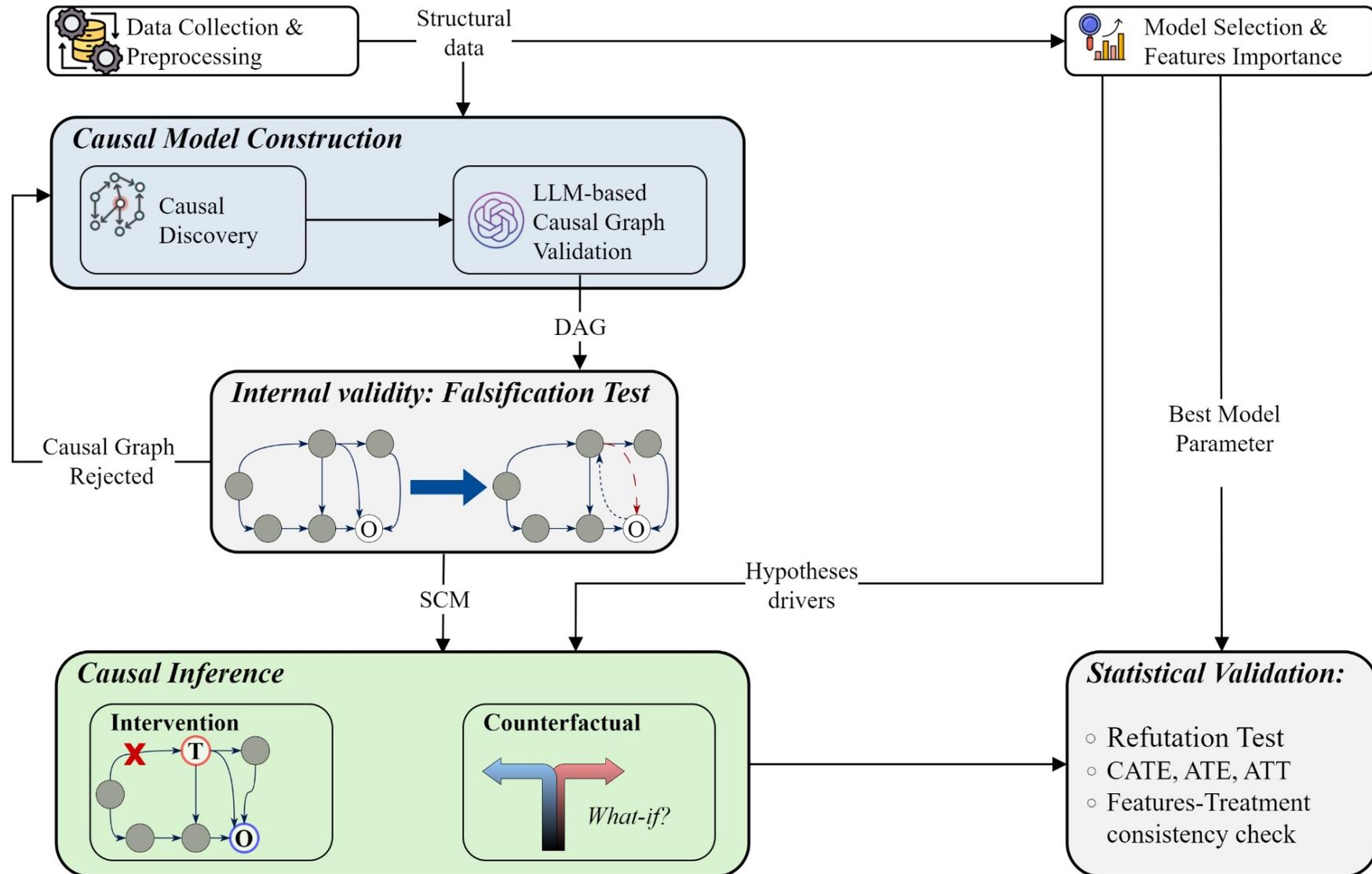
Costly, time- consuming, limited in scope

Often unfeasible or unethical

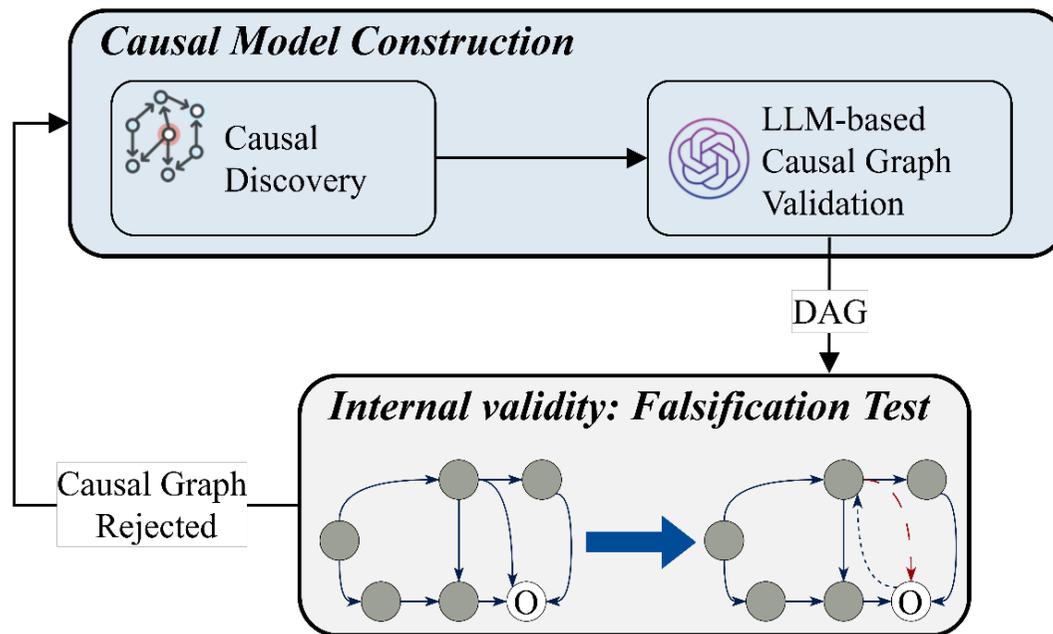
Objective:

Hybrid strategy that combines the advantages of RCT and observational study

PhD thesis: the proposed framework



PhD thesis: Causal Model Construction



- Extraction of DAG from data
- LLM- based validation :
 - Prompt to validate the causal relation
- Statistical Validation of the DAG via Falsification test:
 - *“Is the model empirically plausible?”*

PhD thesis: LLM-based Validation

You are an expert in causal inference and graphical models. I will provide you with a causal graph in DOT format.

Important instructions:

- Only use the information from the DOT graph and the provided domain description.
- If something is unclear or missing, explicitly say "I don't know" instead of guessing.
- For every answer, give a confidence score (0–100%).
- Use structured outputs (bullet points or tables where possible).

Your task is to audit the DOT graph step by step following this checklist:

1. Global order validation

- Extract a topological order of the variables from the DOT graph.
- Is this order plausible given the domain [insert domain description]?
- Explicitly report any variable that appears isolated (i.e., has no incoming edges) and discuss whether this is plausible in the given domain.
- Point out up to 3 variable pairs that may be incorrectly ordered.
- Provide an overall confidence score.

2. Local edge validation

- For each edge $X \rightarrow Y$ in the DOT graph:
- Is the effect plausibly direct, mediated, or implausible?
- Answer in the format: [direct / mediated / implausible] + short explanation + confidence.

3. Cycle check

- Identify if any cycles exist in the DOT graph.
- If cycles exist, are they plausible in a causal model?
- Suggest which edge(s) should be removed or reversed to restore acyclicity, with justification.

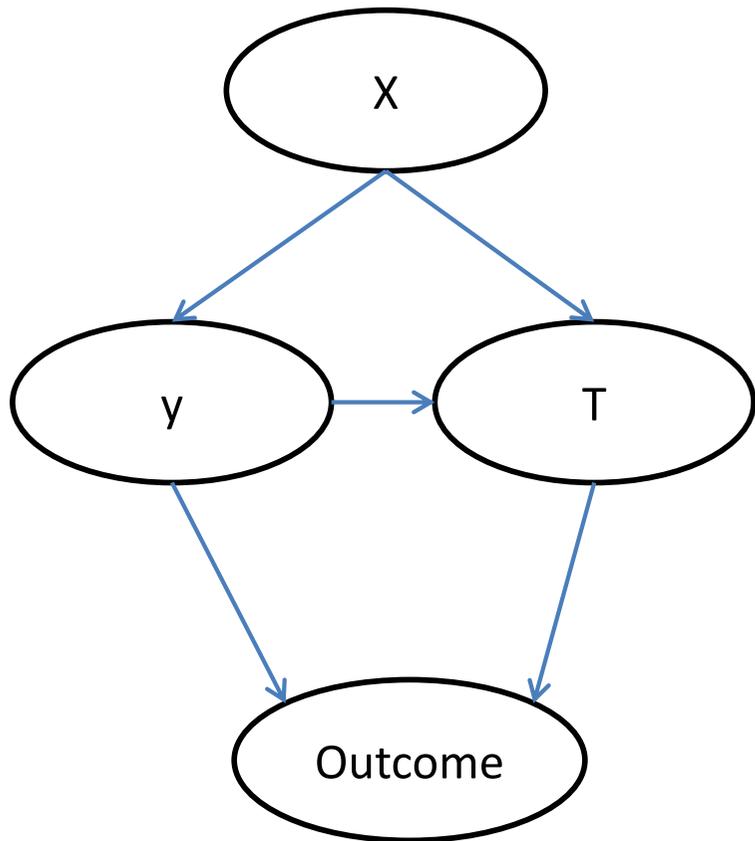
4. Adjustment set validation

- Suppose we want to estimate the causal effect of T (treatment) on Y (outcome).
- What is the minimal valid adjustment set to block all backdoor paths?
- Is this set plausible in the domain [insert domain description]?
- If not, suggest corrections (variables to remove/add) with reasoning.

Now here is the DOT graph to audit.

- 4 key points:
 1. Order validation
 2. Local validation
 3. Cycle check
 4. Adjustment set validation
- Avoids hallucination
- Identification of isolated nodes

PhD thesis: Causal Inference

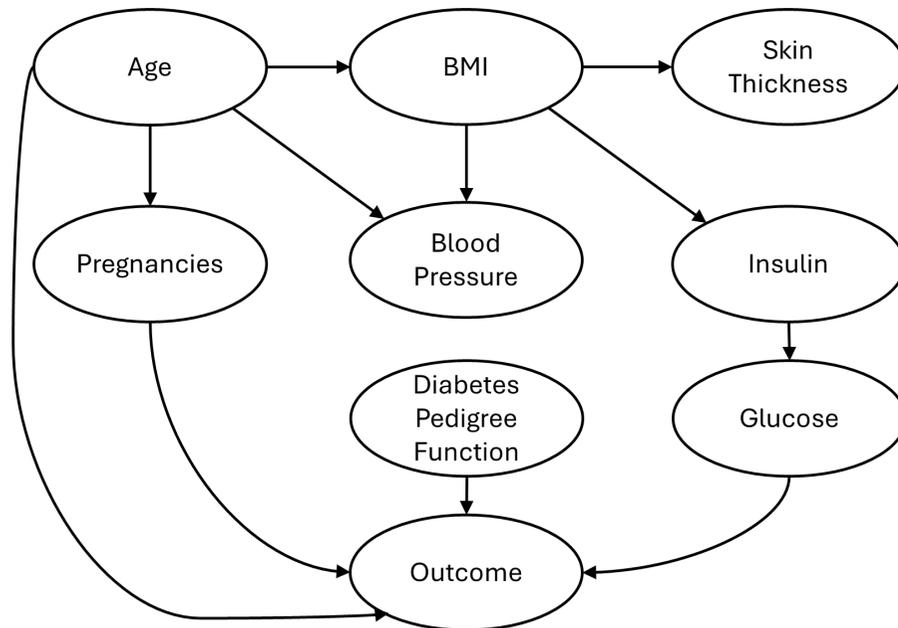


- ~~Contextual~~ **Interventional**
 - ~~Active sets \bar{a}~~
 - ~~What happens to the subject if in the past $T=t$?~~
 - Graphically deletes the relation with the Parent nodes.

PhD thesis: Statistical Validation

- Robustness of the model was assessed with Refutation Test:
 - 4 tests
 - *"Do our causal conclusions remain stable when the model or data are perturbed?"*
- Heterogeneity of the model was assessed with Conditional Average Treatment Effect:
 - *"Do the heterogeneous treatment effects we estimate reflect true causal differences?"*

PhD thesis: Diabetes Application



- Evaluate the effects of healthy life-style on diabetes management.
- Treatment: BMI = 22

PhD thesis: Diabetes Application Results

Intervention

Id	Characteristic	IGlucose-PIGlucose	95% CI
I1	BMI = 25.2	-1.43	-62.80, 34.21
I2	BMI = 32.9	13.58	-49.12, 48.76
I3	BMI = 35.9	23.28	-40.06, 58.70
I4	BMI = 40.6	41.93	-19.52, 77.00
S1	Age = [20-29]	-15.62	-18.89, -12.30
S2	Age = [30-39]	0.3	-5.04, 6.12
S3	Age = [40-49]	10.5	2.61, 17.89
S4	Age ≥ 50	42.25	33.16, 50.74

Counterfactual

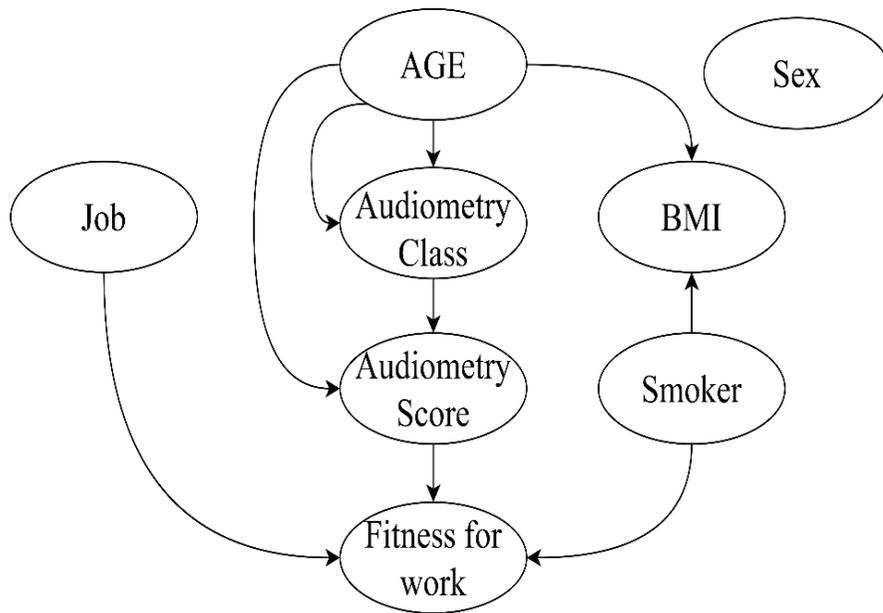
Id	#Diabetic	#Healthy	95% CI
I2	1	0	0, 0
I3	1	0	0, 0
S1	48	5	5, 5
S2	35	13	13, 13
S3	26	11	11, 11
S4	21	7	7, 7

Statistical Validation Results:

- **Refutation Test:** The model was stable from perturbation
- **CATE:** The model captured well all the heterogeneity.

PhD thesis: Real World Case

Occupational Health Application



- Understanding the factors most involved in Fitness for work validation.
- Treatment: Audiometry Score = 0

PhD thesis: Real World Case Occupational Health Application

Intervention

Job	FFW	Median of instance	95% CI	Δ Variation vs. Ground Truth
DO	Fit	103 [99, 107]		42.40%
DO	Fit with condition	22 [18, 26]		-40.80%
DO	Unfit	-	-	-1.60%
ED	Fit	698 [687, 709]		19.80%
ED	Fit with condition	69 [63, 89]		-19.60%
ED	Unfit	-	-	-0.30%
EP	Fit	624 [610, 636]		8.90%
EP	Fit with condition	75 [63, 89]		-8.60%
EP	Unfit	-	-	-0.30%
PCC	Fit	275 [269, 282]		29.00%
PCC	Fit with condition	53 [46, 59]		-28.40%
PCC	Unfit	-	-	-0.60%
SJ	Fit	77 [71, 82]		12.00%
SJ	Fit with condition	15 [10, 21]		-10.90%
SJ	Unfit	-	-	-1.10%

PhD thesis: Real World Case

Occupational Health Application

Counterfactual

Job	FFW	Median of instance	95% CI	Δ Variation vs. Ground Truth
DO	Fit	82	[70, 88]	24.60%
DO	Fit with condition	39	[29, 46]	-24.70%
DO	Unfit	4	[0, 5]	0.10%
ED	Fit	650	[616, 671]	16.10%
ED	Fit with condition	115	[85, 125]	-16.10%
ED	Unfit	2	[0, 4]	0.00%
EP	Fit	577	[543, 588]	6.50%
EP	Fit with condition	119	[93, 135]	-6.50%
EP	Unfit	3	[0, 5]	0.00%
PCC	Fit	190	[165, 206]	4.20%
PCC	Fit with condition	133	[108, 147]	-5.20%
PCC	Unfit	5	[2, 9]	1.00%
SJ	Fit	75	[60, 90]	13.30%
SJ	Fit with condition	15	[6, 16]	-13.40%

PhD thesis: Real World Case Occupational Health Application

Statistical Validation Results

- **Refutation Test:** The model was stable from perturbation
- **CATE:** The model did not capture well all the heterogeneity.

PhD thesis: Conclusion

Advantages

- It's possible to verify the effect of treatment or risk exposure before testing it on the patient
- It's cheaper and more ethical than RCTs

Limitation

- Necessity of prior knowledge and domain expertise
- Affected by bias of the data
- Presence of unobserved factors that have an effect on the causal structure.

Thanks for the attention

