VIETNAM NATIONAL UNIVERSITY - HO CHI MINH CITY
UNIVERSITY OF SCIENCE JOHN VON NEUMANN INSTITUTE

ASSOCIATIONS OF HYPERGLYCEMIA AND DYSLIPIDEMIA IN VIETNAMESE PATIENTS WITH TYPE 2 DIABETES

Presented by Nguyen Thanh Tung

Academic Supervisors:
Prof. Ho Tu Bao
MD. Nguyen Van Binh

December 31, 2022

Outline

Hyperglycemia

- Hyperglycemia means "Abnormally high blood glucose level" (PubMed)
- Complications of untreated or uncontrolled hyperglycemia over a prolonged period of time: Microvascular Complications (Retinopathy, Nephropathy, Neuropathy) and Macrovascular Complications (Coronary artery disease, Cerebrovascular disease, Peripheral vascular disease).

Dyslipidemia

- Dyslipidemia means "Abnormalities in the serum levels of LIPIDS, including overproduction or deficiency. Abnormal serum lipid profiles may include high total CHOLESTEROL, high TRIGLYCERIDES, low HIGH DENSITY LIPOPROTEIN CHOLESTEROL, and elevated LOW DENSITY LIPOPROTEIN CHOLESTEROL" (PubMed)
- The most significant complication for dyslipidemia is cardiovascular disease.

Problem Statement

- There are approximately 5.76 million people with diabetes currently living in Vietnam [1].
- Type 2 diabetes (Hyperglycemia) and serum lipid abnormalities (Dyslipidemia) often appear together, causing many serious complications for patients if they are not handled immediately.
- These patterns are immensely complicated and have not still been understood well [2], [3].

Problem Statement (cont)

- Relationships between hyperglycemia and dyslipidemia in type 2 diabetic patients in Vietnam may be hypothetically different with those in other countries.
- For example, Sone, Hirohito, et al. found that TG was a leading predictor of coronary heart disease (CHD), comparable to LDL-C in Japanese patients with type 2 diabetes, but in Western countries, TG was not a leading predictor of CHD in diabetic patients [4].

TG: Triglycerides
LDL-C: Low-Density Lipoprotein Cholesterol

Objective

The primary objective of this study was to investigate associations between hyperglycemia and dyslipidemia in Vietnamese patients with type 2 diabetes.

Contribution

- Extracted laboratory tests from Thong Nhat hospital's database consist of noisy, inconsistent, missing, unbalanced and high dimensional data because the data was unintentionally stored for scientific research purposes. Data preprocessing was proposed by the author and evaluated by the clinical expert to make it appropriate and suitable for algorithms.
- Association pattern mining was proposed as a new approach to investigate relationships between hyperglycemia and dyslipidemia in Vietnamese patients with type 2 diabetes.

Scope

- The scope of the study was to investigate associations between hyperglycemia and dyslipidemia in Vietnamese patients with type 2 diabetes utilizing association pattern mining.
- The data was extracted from Thong Nhat hospital's database between 2016 and 2018.
- The author used SPMF application which is an open-source software and data mining library written in Java, specialized in pattern mining to deploy data mining algorithms [5].

Laboratory Test Database

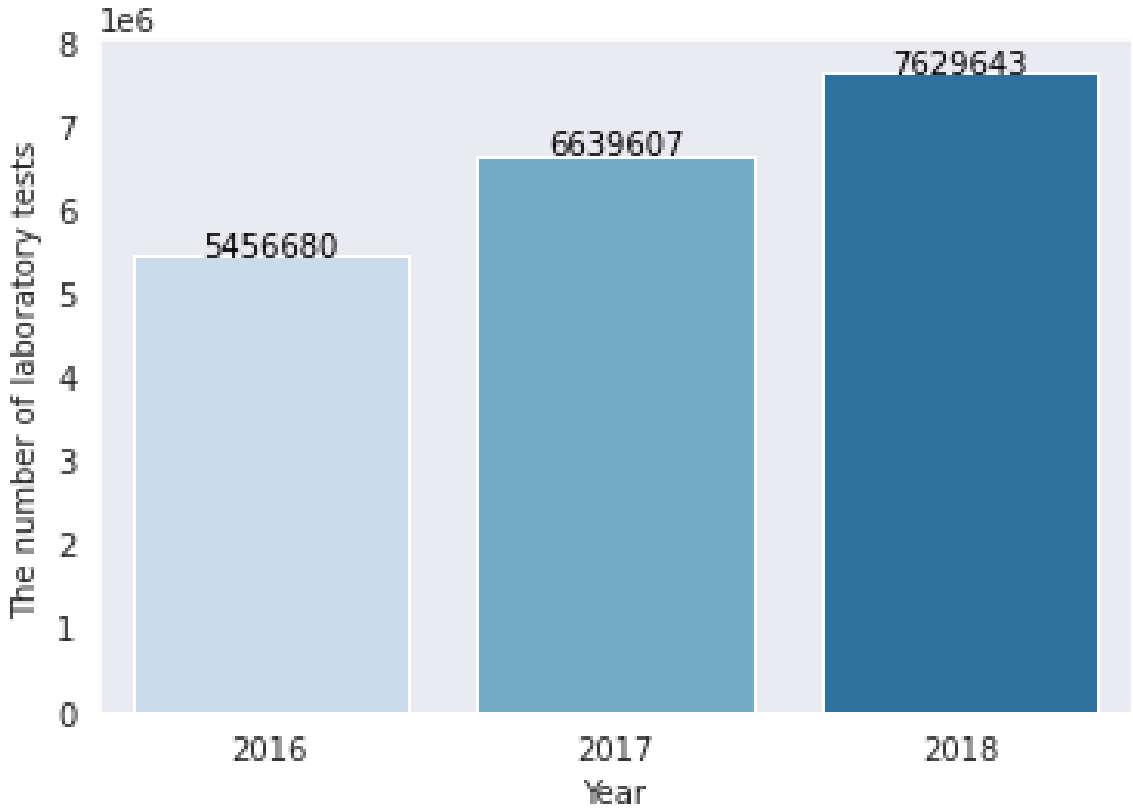
- Raw Data
- Laboratory Data Preprocessing
- Data Transformation

Raw Data

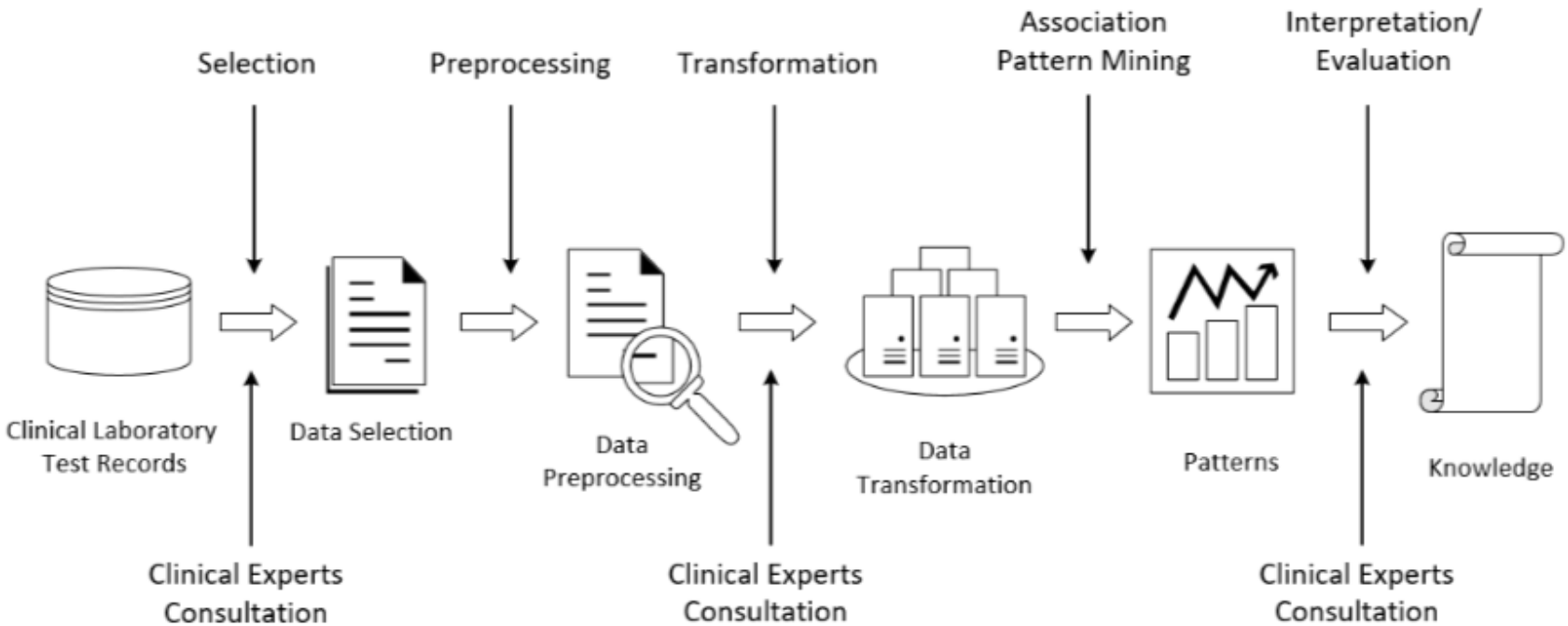
- 19,725,930 laboratory tests.
- 233 types of laboratory tests and 6 other attributes include of patient index, sex, birthday, test date, reference intervals for men and women.

1	MSBN	NAMSINH	PHAI	CHANDOAN	TEN	KETQUA	DVT	CSBT_NAM	CSBT_NU	NGAY
2768	181319987	1952	0	Bệnh đái tháo đường không phụ thuộc insuline; Rối loạn chuyển hoá lipoprotein và tình trạng tăng lipid	ALT (GPT)	36	U/L - 37 °C	<= 40	<= 40	01-FEB-18
2769	181319987	1952	0	Bệnh đái tháo đường không phụ thuộc insuline; Rối loạn chuyển hoá lipoprotein và tình trạng tăng lipid	Na+	136	mmol/L	135 - 145	135 - 145	01-FEB-18
2770	181319987	1952	0	Bệnh đái tháo đường không phụ thuộc insuline; Rối loạn chuyển hoá lipoprotein và tình trạng tăng lipid	K+	3.7	mmol/L	3.5 - 5.0	3.5 - 5.0	01-FEB-18
2771	181319987	1952	0	Bệnh đái tháo đường không phụ thuộc insuline; Rối loạn chuyển hoá lipoprotein và tình trạng tăng lipid	Cl-	99	mmol/L	98 - 106	98 - 106	01-FEB-18
2772	181319987	1952	0	Bệnh đái tháo đường không phụ thuộc insuline; Rối loạn chuyển hoá lipoprotein và tình trạng tăng lipid	WBC	12.91	K/uL	4.01 - 11.42	4.01 - 11.42	01-FEB-18
2773	181319987	1952	0	Bệnh đái tháo đường không phụ thuộc insuline; Rối loạn chuyển hoá lipoprotein và tình trạng tăng lipid	MONO%	9.95	%	3.4 - 9.0	3.4 - 9.0	01-FEB-18
2774	181319987	1952	0	Bệnh đái tháo đường không phụ thuộc insuline; Rối loạn chuyển hoá lipoprotein và tình trạng tăng lipid	EOS%	1.00	%	0.0 - 7.0	0.0 - 7.0	01-FEB-18
2775	181319987	1952	0	Bệnh đái tháo đường không phụ thuộc insuline; Rối loạn chuyển hoá lipoprotein và tình trạng tăng lipid	LYM#	3.29	K/uL	1.2 - 4.0	1.2 - 4.0	01-FEB-18
2776	181319987	1952	0	Bệnh đái tháo đường không phụ thuộc insuline; Rối loạn chuyển hoá lipoprotein và tình trạng tăng lipid	MONO#	1.28	K/uL	0.2 - 0.8	0.2 - 0.8	01-FEB-18
2777	181319987	1952	0	Bệnh đái tháo đường không phụ thuộc insuline; Rối loạn chuyển hoá lipoprotein và tình trạng tăng lipid	RBC	4.84	M/uL	4.01 - 5.79	4.01 - 5.79	01-FEB-18
2778	181319987	1952	0	Bệnh đái tháo đường không phụ thuộc insuline; Rối loạn chuyển hoá lipoprotein và tình trạng tăng lipid	HCT	44.2	%	34.4 - 48.6	34.4 - 48.6	01-FEB-18
2779	181319987	1952	0	Bệnh đái tháo đường không phụ thuộc insuline; Rối loạn chuyển hoá lipoprotein và tình trạng tăng lipid	MCHC	33.2	g/dL	32 - 36	32 - 36	01-FEB-18
2780	181319987	1952	0	Bệnh đái tháo đường không phụ thuộc insuline; Rối loạn chuyển hoá lipoprotein và tình trạng tăng lipid	RDW	12.8	%	11.5 - 15.5	11.5 - 15.5	01-FEB-18
2781	181319987	1952	0	Bệnh đái tháo đường không phụ thuộc insuline; Rối loạn chuyển hoá lipoprotein và tình trạng tăng lipid	PLT	165	K/uL	150 - 450	150 - 450	01-FEB-18
2782	181319987	1952	0	Bệnh đái tháo đường không phụ thuộc insuline; Rối loạn chuyển hoá lipoprotein và tình trạng tăng lipid	LYM%	25.5	%	19 - 48	19 - 48	01-FEB-18
2783	181319987	1952	0	Bệnh đái tháo đường không phụ thuộc insuline; Rối loạn chuyển hoá lipoprotein và tình trạng tăng lipid	BASO%	0.10	%	0.0 - 1.5	0.0 - 1.5	01-FEB-18
2784	181319987	1952	0	Bệnh đái tháo đường không phụ thuộc insuline; Rối loạn chuyển hoá lipoprotein và tình trạng tăng lipid	NEO#	8.20	K/uL	1.7 - 7.5	1.7 - 7.5	01-FEB-18
2785	181319987	1952	0	Bệnh đái tháo đường không phụ thuộc insuline; Rối loạn chuyển hoá lipoprotein và tình trạng tăng lipid	EOS#	0.13	K/uL	0.0 - 0.6	0.0 - 0.6	01-FEB-18
2786	181319987	1952	0	Bệnh đái tháo đường không phụ thuộc insuline; Rối loạn chuyển hoá lipoprotein và tình trạng tăng lipid	BASO#	0.01	K/uL	0.0 - 0.1	0.0 - 0.1	01-FEB-18
2787	181319987	1952	0	Bệnh đái tháo đường không phụ thuộc insuline; Rối loạn chuyển hoá lipoprotein và tình trạng tăng lipid	MCV	91.5	fL	80 - 99	80 - 99	01-FEB-18
2788	181319987	1952	0	Bệnh đái tháo đường không phụ thuộc insuline; Rối loạn chuyển hoá lipoprotein và tình trạng tăng lipid	MCH	30.3	Pg	27 - 33	27 - 33	01-FEB-18
2789	181319987	1952	0	Bệnh đái tháo đường không phụ thuộc insuline; Rối loạn chuyển hoá lipoprotein và tình trạng tăng lipid	MPV	8.8	fL	7.4 - 10.9	7.4 - 10.9	01-FEB-18
2790	181319987	1952	0	Bệnh đái tháo đường không phụ thuộc insuline; Rối loạn chuyển hoá lipoprotein và tình trạng tăng lipid	NEU%	63.5	%	40 - 74	40 - 74	01-FEB-18
2791	181319987	1952	0	Bệnh đái tháo đường không phụ thuộc insuline; Rối loạn chuyển hoá lipoprotein và tình trạng tăng lipid	HGB	14.7	g/dL	11.5 - 15.0	11.5 - 15.0	01-FEB-18
2792	181319987	1952	0	Bệnh đái tháo đường không phụ thuộc insuline; Rối loạn chuyển hoá lipoprotein và tình trạng tăng lipid	Pro-BNP	60.92	pg/ml	< 125	< 125	01-FEB-18
2793	181319987	1952	0	Bệnh đái tháo đường không phụ thuộc insuline; Rối loạn chuyển hoá lipoprotein và tình trạng tăng lipid	URO	- 3.5umol/L	µmol/L	< 17.1	< 17.1	01-FEB-18
2794	181319987	1952	0	Bệnh đái tháo đường không phụ thuộc insuline; Rối loạn chuyển hoá lipoprotein và tình trạng tăng lipid	BIL	- neg	mmol/L	< 3,4	< 3,4	01-FEB-18
2795	181319987	1952	0	Bệnh đái tháo đường không phụ thuộc insuline; Rối loạn chuyển hoá lipoprotein và tình trạng tăng lipid	LEU	- neg	µL	<10	< 10	01-FEB-18
2796	181319987	1952	0	Bệnh đái tháo đường không phụ thuộc insuline; Rối loạn chuyển hoá lipoprotein và tình trạng tăng lipid	PRO	- neg	g/L	< 0.1	< 0,1	01-FEB-18

Raw Data (cont)



Laboratory Data Preprocessing



Laboratory Data Preprocessing (cont)

- Data Integration
- Data Structure
- Invalid Values Removal
- Data Selection
- Feature Selection
- Outlier Removal
- Missing Values Imputation

Data Transformation

- The author used the reference range based approach because reference intervals have been widely used by clinicians or physicians to interpret laboratory test results.
- For example, TC has three reference ranges [1.3-5.18), [5.18-6.18] and (6.18-8.7] with the minimum and maximum values in the laboratory test data after preprocessing are 1.3 and 8.7 respectively.

Proposed Solution

- Association Pattern
- Association Pattern Mining

Association Pattern

- Association patterns are "IF-THEN" statements.
- An association pattern has two parts: the left side is the antecedent (IF) and the right side is the consequent (THEN).

Table: An example of an association pattern.

Antecedent	Consequent
FPG = [8.6-10.2] AND TG = (2.2-5.6] AND Age = [65-87] AND Sex = Women	HDL-C = [0.6-1.3)

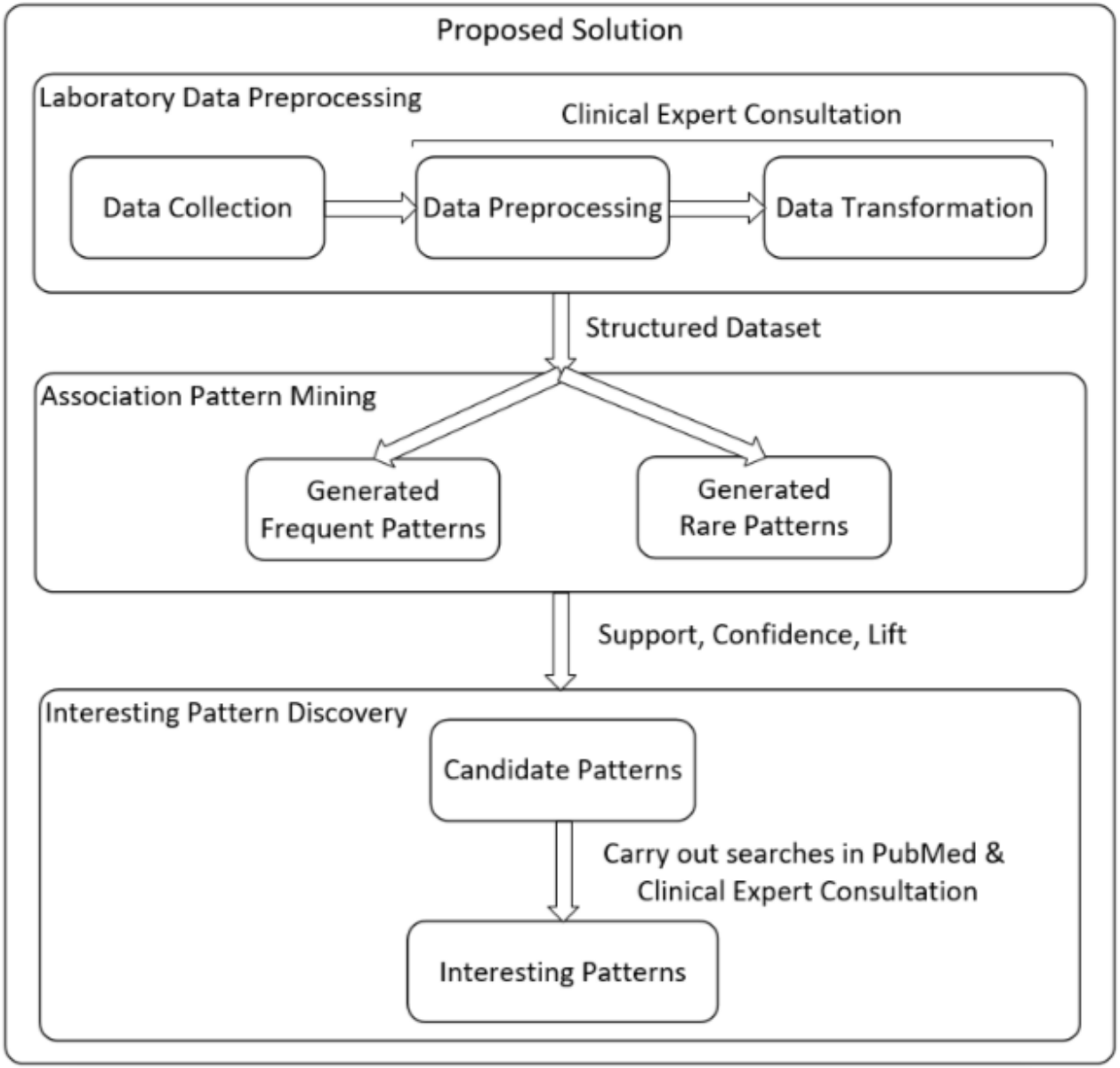
FPG: Fasting Plasma Glucose
TG: Triglycerides
HDL-C: High-Density Lipoprotein Cholesterol

Association Pattern Mining

Pattern Mining	Base Algorithm	Item Type	Generated Itemsets
FP-Growth	FP-Tree	Frequent items	Frequent Itemsets
CFP-Growth++	FP-Growth	Rare and Frequent Items	Frequent and Rare Itemsets
RP-Tree	FP-Growth	Rare and Frequent Items	Rare Itemsets
Apriori-Inverse	Apriori	Rare Items	Rare Itemsets

FP-Growth: Frequent Pattern Growth
CFP-Growth++: Conditional Frequent Pattern Growth++
RP-Tree: Rare Pattern Tree

Proposed Solution



Experiments and Results

- Findings compared with clinical observations
- Findings which are different clinical observations

Candidate patterns vs Selected candidate patterns

- The author extracted candidate patterns for interesting pattern discovery by eliminating patterns which did not contain FPG.
- From candidate patterns, concerning relations between hyperglycemia and dyslipidemia in type 2 diabetic patients were selected with respect to two below conditions:
  - The consequent of pattern contains one of the laboratory tests such as FPG, TC, HDL-C, LDL-C and TG.
  - The values of the laboratory tests are in abnormal levels.

FPG: Fasting Plasma Glucose
TC: Total Cholesterol TG: Triglycerides
HDL-C: High-Density Lipoprotein Cholesterol
LDL-C: Low-Density Lipoprotein Cholesterol

Experimental Results

Pattern mining	Parameters	Generated itemsets	Generated patterns	Candidate patterns	Selected candidate patterns
FPGrowth	minsup=0.5% minconf=70% lift=1.5	4,444	2,128	1,131	76
CFPGrowth++	$\alpha = 10$ minconf=70% lift=1.5	3,104	1,395	624	63
RP-Tree	minraresup=0.5% minfreqsup=15% minconf=70% lift=1.5	2,069	1,575	917	72
Apriori-Inverse	minsup=0.5% maxsup=60% minconf=70% lift=1.5	2,973	1,534	766	99

Interesting Pattern

To verify the selected candidate patterns with existing medical knowledge in order to determine those that may be novel, they were searched in PubMed by combining selected candidate of MeSH terms and AND operator. The author used filters to narrow research results by

- The journal MEDLINE (it contains citations to journal articles in the life sciences with a concentration on biomedicine)
- Abstract
- Sex (female, male)
- Age (adult: 19-44 years; middle aged: 45-64 years; aged: 65+ years)

Interesting Pattern (cont)

Pattern mining	Medical knowledge		
Algorithm	"established"	"less well known"	"unknown"
FPGrowth	36%	25%	39%
CFPGrowth++	40%	25%	35%
RPTree	40%	37%	23%
Apriori-Inverse	30%	34%	36%

Definitions:

- "Established" medical knowledge: four or more citations found in PubMed.
- "Less well known" medical knowledge: one to three citations found in PubMed.
- "Unknown" medical knowledge: zero citation found in PubMed.

Findings compared with clinical observations

- Several association patterns abstracted by the dataset that appear to be reflections of "established" and "less well known" with medical knowledge.
- These patterns conform to the reported medical knowledge.
- Several patterns illustrate that the relationships of hyperglycemia and dyslipidemia are formed in type 2 diabetic patients who are in two age groups (Age = [45-64], Age = [65-87]) and both sexes.
- More importantly, the patterns provide quantitative information on clinical observations which assist physicians interpret the diagnosis.

Association between FPG and TC

- The patterns between $R2_{FPGrowth}$ and $R23_{FPGrowth}$, between $R41_{FPGrowth}$ and $R44_{FPGrowth}$ (also between $R5_{CFPGrowth++}$ and $R36_{CFPGrowth++}$, between $R29_{RPTree}$ and $R56_{RPTree}$, between $R33_{AprioriInverse}$ and $R66_{AprioriInverse}$) illustrate that there has the correlation between FPG and TC.
- For instance, the pattern $R17_{FPGrowth}$ illustrates that the elevated FPG (FPG = [7.0-8.6)) and elevated LDL-C (LDL-C = (4.1-4.9]) have relations with elevated TC (TC = (6.18-8.7]) in type 2 diabetic patients.

> $R17_{FPGrowth}$: FPG = [7.0-8.6) LDL-C = (4.1-4.9] Age = [45-64] Sex = Men ⇒ TC = (6.18-8.7]

- This was confirmed by the study [6] which showed that FPG had the positive correlation with TC.

FPG: Fasting Plasma Glucose TC: Total Cholesterol TG: Triglycerides
HDL-C: High-Density Lipoprotein Cholesterol LDL-C: Low-Density Lipoprotein Cholesterol

Association between FPG and HDL-C

- The patterns between $R24_{FPGrowth}$ and $R40_{FPGrowth}$, between $R63_{FPGrowth}$ and $R67_{FPGrowth}$ (also between $R37_{CFPGrowth++}$ and $R47_{CFPGrowth++}$, between $R1_{RPTree}$ and $R28_{RPTree}$, between $R1_{AprioriInverse}$ and $R32_{AprioriInverse}$) illustrate that there has the correlation between FPG and HDL-C.
- For instance, the pattern $R45_{CFPGrowth++}$ illustrates that the elevated FPG (FPG = [8.6-10.2]) and elevated TG (TG = (2.2-5.6]) have relations with elevated HDL-C (HDL-C = [0.6-1.3)) in type 2 diabetic patients.

> $R45_{CFPGrowth++}$: FPG = [8.6-10.2] TG = (2.2-5.6] Age = [65-87] Sex = Women $\Rightarrow$ HDL-C = [0.6-1.3)

- This was also confirmed by the study [7] which found that low HDL-C level had the contribution to the pathophysiology of type 2 diabetes through direct effects on glucose levels.

FPG: Fasting Plasma Glucose TC: Total Cholesterol TG: Triglycerides
HDL-C: High-Density Lipoprotein Cholesterol LDL-C: Low-Density Lipoprotein Cholesterol

Association between FPG and TG

- The patterns between $R45_{FPGrowth}$ and $R62_{FPGrowth}$ (also between $R48_{CFPGrowth++}$ and $R57_{CFPGrowth++}$, between $R57_{RPTree}$ and $R72_{RPTree}$, between $R67_{AprioriInverse}$ and $R98_{AprioriInverse}$) illustrate that there has the correlation between FPG and TG.
- For instance, the pattern $R67_{RPTree}$ illustrates that the elevated FPG (FPG = [7.0-8.6)), elevated TC (TC = (6.18-8.7]) and HDL-C (HDL-C = [0.6-1.3)) have relations with elevated TG (TG = (2.2-5.6]) in type 2 diabetic patients.

$R67_{RPTree}$: TC = (6.18-8.7] FPG = [7.0-8.6) HDL-C = [0.6-1.3) $\Rightarrow$ TG = (2.2-5.6]

- This conforms to the reported medical knowledge that elevated TG is the characteristic of diabetic dyslipidemia [8].

FPG: Fasting Plasma Glucose TC: Total Cholesterol TG: Triglycerides
HDL-C: High-Density Lipoprotein Cholesterol LDL-C: Low-Density Lipoprotein Cholesterol

Association between FPG and LDL-C

- The patterns between $R68_{FPGrowth}$ and $R76_{FPGrowth}$ (also between $R59_{CFPGrowth++}$ and $R63_{CFPGrowth++}$, $R99_{AprioriInverse}$) illustrate that there has the correlation between FPG and LDL-C.
- For instance, the pattern $R99_{AprioriInverse}$ illustrates that the elevated FPG (FPG = [7.0-8.6)) and elevated TC (TC = [5.18-6.18]) have relations with elevated LDL-C (LDL-C = (3.3-4.1]) in type 2 diabetic patients.

> $R99_{AprioriInverse}$: TC = [5.18-6.18] FPG = [7.0-8.6) TG = [0.3-1.7) $\Rightarrow$ LDL-C = (3.3-4.1]

- This conforms to the reported medical knowledge that elevated LDL-C is the characteristic of diabetic dyslipidemia [8].

FPG: Fasting Plasma Glucose TC: Total Cholesterol TG: Triglycerides
HDL-C: High-Density Lipoprotein Cholesterol LDL-C: Low-Density Lipoprotein Cholesterol

Findings which are different clinical observations

- Pattern suggests that lipid components can be a marker for diabetes prediction.
- Patterns which classified as "unknown" medical knowledge may suggest that type 2 diabetic dyslipidemia may be characterized by various patterns which are a complex combination of TC, TG, HDL-C, LDL-C.
- Patterns in which FPG plays the role of a consequent are not generated by the algorithms suggesting that elevated FPG may not be a consequence of dyslipidemia in type 2 diabetic patients. For example, $R58_{FPGrowth}$, $R46_{RPTree}$, $R30_{AprioriInverse}$

$R58_{FPGrowth}$: TC = (6.18-8.7] FPG = [8.6-10.2] LDL-C = (3.3-4.1] Age = [45-64] $\Rightarrow$ TG = (2.2-5.6]

$R46_{RPTree}$: FPG = [8.6-10.2] LDL-C = (4.1-4.9] TG = (2.2-5.6] $\Rightarrow$ TC = (6.18-8.7]

$R30_{AprioriInverse}$: TC = [5.18-6.18] FPG = [8.6-10.2] TG = (2.2-5.6] Age = [65- 87] Sex = Women $\Rightarrow$ HDL-C = [0.6-1.3)

Findings which are different clinical observations (cont)

Hypercholesterolemia has been not frequently observed in type 2 diabetic patients in the medical research, but patterns such as between $R20_{FPGrowth}$ and $R23_{FPGrowth}$, between $R25_{CFPGrowth++}$ and $R30_{CFPGrowth++}$, between $R45_{RPTree}$ and $R47_{RPTree}$, between $R37_{AprioriInverse}$ and $R39_{AprioriInverse}$ show that TC can be hypothetically a marker of type 2 diabetes.

$R20_{FPGrowth}$: FPG = [7.0-8.6) LDL-C = (4.1-4.9] TG = (2.2-5.6] $\Rightarrow$ TC = (6.18-8.7]

$R30_{CFPGrowth++}$: FPG = [7.0-8.6) LDL-C = (4.9-6.01] TG = (2.2-5.6] Sex = Women $\Rightarrow$ TC = (6.18-8.7]

$R47_{RPTree}$: FPG = [7.0-8.6) LDL-C = (4.1-4.9] TG = (2.2-5.6] Age = [45-64] $\Rightarrow$ TC = (6.18-8.7]

$R39_{AprioriInverse}$: FPG = [8.6-10.2] LDL-C = (4.1-4.9] TG = (2.2-5.6] $\Rightarrow$ TC = (6.18-8.7]

Findings which are different clinical observations (cont)

- The "unknown" diagnosis patterns suggest that TC, HDL-C, LDL-C and TG should be focused on the process of type 2 diabetes management in Vietnam.
- This is inconsistent with the work [9, 10] that merely lowering LDL-C or addressing LDL-C, HDL-C and TG should be taken into consideration as the combination therapy for type 2 diabetic patients.

Conclusion

- A majority of generated patterns which were classified as "established" and "less well known" medical knowledge can be directly confirmed with references to the biomedical literature.
- Discovered patterns were marked as "unknown" can potentially represent hypotheses and experimentation for medical research. The "unknown" patterns may reveal complex relations between hyperglycemia and dyslipidemias in type 2 diabetic patients because they tend to be the combination of more "antecedent" compared with frequent ones which mostly show well known medical knowledge.
- These findings highlight applications of pattern mining in health care and medical research.

Limitation

- An analytical cross-sectional design.
- Features were only selected based on the clinical expert judgment rather than feature selection algorithms because the lack of medical knowledge poses limitations on the scope of feature selection for data scientists.
- The CFPGrowth++, RPTree and Apriori-Inverse have been proved to be highly efficient due to the avoidance of expensive pruning steps, but they failed to generate the complete set of rare itemsets.
- The author discussed the feasibility and performance of association pattern mining in type 2 diabetes, but not its prospective practical implementation.

Future Work

- For feature selection, the author may use algorithms to select the features automati- cally without additional burden on physicians or clinicians.
- For data transformation, the author may use unsupervised methods such as equal width, equal frequency, and k-means to discretize the continuous values instead of using merely the reference range based approach.
- The author may deploy different association mining algorithms which have different approaches. For example, Maximum Constraint based Conditional Frequent Pattern Growth (MCCFP) algorithm, Automated Apriori Rare, Inverse FP-Tree
- Moreover, to investigate the cause and effect of the relationship between lipids and glucose in type 2 diabetes in Vietnam, longitudinal studies may be conducted by clinical experts.

References I

[1] Nguyen Bich Ngoc, Zhou Lu Lin, and Waqas Ahmed. "Diabetes: what challenges lie ahead for Vietnam?" In: *Annals of global health* 86.1 (2020).

[2] Klaus G Parhofer. "Interaction between glucose and lipid metabolism: more than diabetic dyslipidemia". In: *Diabetes & metabolism journal* 39.5 (2015), pp. 353–362.

[3] Guenther Boden and Markku Laakso. "Lipids and glucose in type 2 diabetes: what is the cause and effect?" In: *Diabetes care* 27.9 (2004), pp. 2253–2259.

[4] Hirohito Sone et al. "Serum level of triglycerides is a potent risk factor comparable to LDL cholesterol for coronary heart disease in Japanese patients with type 2 diabetes: subanalysis of the Japan Diabetes Complications Study (JDCS)". In: *The Journal of Clinical Endocrinology & Metabolism* 96.11 (2011), pp. 3448–3456.

References II

[5] Philippe Fournier-Viger et al. "The SPMF open-source data mining library version 2". In: *Joint European conference on machine learning and knowledge discovery in databases*. Springer. 2016, pp. 36–40.

[6] Nahid Yeasmin et al. "Serum Triglycerides and Total Cholesterol levels and its Relation with type 2 148 Diabetes mellitus". In: *Journal of Dhaka Medical College* 27.2 (2018), pp. 148–154.

[7] Brian G Drew et al. "The emerging role of HDL in glucose metabolism". In: *Nature Reviews Endocrinology* 8.4 (2012), p. 237.

[8] Liya Wu and Klaus G Parhofer. "Diabetic dyslipidemia". In: *Metabolism* 63.12 (2014), pp. 1469–1479.

References III

[9] Shukang Wang et al. "Relationship between lipid profiles and glycemic control among patients with type 2 diabetes in Qingdao, China". In: *International Journal of Environmental Research and Public Health* 17.15 (2020), p. 5317.

[10] HA Khan, SH Sobki, and SA Khan. "Association between glycaemic control and serum lipids profile in type 2 diabetic patients: HbA 1c predicts dyslipidaemia". In: *Clinical and experimental medicine* 7.1 (2007), pp. 24–29.

The End