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Factors Influencing Drug Prescribing for Patients with Hospitalization History in Circulatory Disease: Patient Severity, Composite Adherence, and Physician-Patient Relationship - A Retrospective Cohort Study

2024年10月17日(木)

循環器疾患の入院歴のある患者に対する薬剤処方に影響を与える要因: 患者の重症度、複合アドヒアランス、医師と患者の関係 - 後ろ向きコホート研究

田倉 智之, 他

本日の構成

- 最初に
- 研究の概要、基本メッセージ
- 研究の結果：患者重症度（血圧、血糖、腎機能等）
- 研究の結果：医師患者の信頼関係、アドヒアランス
- まとめ



最初に...現在、In Press です



The screenshot shows the JMIR Publications website. At the top left, it says "JMIR Publications Advancing Digital Health & Open Science" with a "25 years" anniversary logo. A search bar is present with "Articles" and "Search articles" options. Navigation links include "Career Center", "Login", and "Register". Below this is a dark blue header with "JMIR Aging" and a dropdown menu containing "Journal Information", "Browse Journal", and "Submit Article". The main content area features the "JMIR Aging" title, a subtitle "Using technological innovations and data science to inform and improve health care services and health outcomes for older adults.", the Editor-in-Chief's name "Yun Jiang, PhD, MS, RN, FAMIA, University of Michigan School of Nursing, USA; and Jinjiao Wang, PhD, RN, MPhil, University of Rochester, USA", and metrics: "Impact Factor 5.0" and "CiteScore 6.5". A descriptive paragraph at the bottom states: "JMIR Aging (JA, ISSN 2561-7605, Journal Impact Factor™ 5.0, (Journal Citation Reports™ from Clarivate, 2024)) is an open-access journal that focuses on digital health, emerging technologies, health informatics applications, and patient education for preventative care, clinical care, home care, and self-management support for older adults. The journal als..."

JMIR Agingは、発刊25年以上でインパクトファクターが5.0の当該領域における上位の国際学会誌です。医療と看護に関する技術、医療機器、アプリ、エンジニアリング、情報科学アプリケーション、患者教育、高齢者の教育、予防的介入、臨床ケア/在宅ケアに焦点を当てたオープンアクセスジャーナルです。医療イノベーションと新興技術の設計と評価を報告する読みやすい応用科学に重点を置いています。



➤ 説明する内容は公表前につき、本スライド全体は【**転載禁止**】です。



研究の経緯 (AIによる先行研究)

- AIを応用した先行研究の結果、初期仮説として、薬剤選択は重症度、アドヒアランス（遵守）、信頼関係が影響を及ぼすと推察された。そのため本研究は、その検証を多変量解析にて実施した
- 以前の研究開発（ASHROスコア、長期予測モデル）では、AIによる指標等整理の過程において、**後発薬選択が経済負担のみならず臨床負担の軽減**に資すると示唆されていた
- 本研究は、**後発薬の選択要因と相互関係について**、多変量解析（ロジスティック回帰等）を用いつつ、探索的かつ予備的に**明らかに**することを標榜した（公表：JMIR Aging）

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BMC Medicine

RESEARCH ARTICLE

Open Access

Development of a predictive model for integrated medical and long-term care resource consumption based on health behaviour: application of healthcare big data of patients with circulatory diseases

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Abstract

Background: Medical costs and the burden associated with cardiovascular disease are on the rise. Therefore, to improve the overall economy and quality assessment of the healthcare system, we developed a predictive model of integrated healthcare resource consumption (Adherence Score for Healthcare Resource Outcome, ASHRO) that incorporates patient health behaviours, and examined its association with clinical outcomes.

Methods: This study used information from a large-scale database on health insurance claims, long-term care insurance, and health check-ups. Participants comprised patients who received inpatient medical care for diseases of the circulatory system (ICD-10 codes I00-I99). The predictive model used broadly defined composite adherence as the explanatory variable and medical and long-term care costs as the objective variable. Predictive models used random forest learning (AI: artificial intelligence) to adjust for predictors, and multiple regression analysis to construct ASHRO scores. The ability of discrimination and calibration of the prediction model were evaluated using the area under the curve and the Hosmer-Lemeshow test. We compared the overall mortality of the two ASHRO 50% cut-off groups adjusted for clinical risk factors by propensity score matching over a 48-month follow-up period.

Results: Overall, 48,456 patients were discharged from the hospital with cardiovascular disease (mean age, 68.3 ± 9.9 years; male, 61.9%). The broad adherence score classification, adjusted as an index of the predictive model by machine learning, was an index of eight: secondary prevention, rehabilitation intensity, guidance, proportion of days covered, overlapping outpatient visits/clinical laboratory and physiological tests, medical attendance, and generic drug rate. Multiple regression analysis showed an overall coefficient of determination of 0.313 ($p < 0.001$). Logistic regression analysis with cut-off values of 50% and 25%/75% for medical and long-term care costs showed that the overall coefficient of determination was statistically significant ($p < 0.001$). The score of ASHRO was associated with the incidence of all deaths between the two 50% cut-off groups (2% vs. 7%; $p < 0.001$).

(Continued on next page)



AIによる共変数（説明変数）の選択調整の過程において

後発薬選択



長期予後良

研究の目的

- ▶ 本研究は、「後発薬の選択は、患者重症度、医師信頼関係、アドヒアランスに関係するという」仮説の検証
- ◆ **背景:** 各国がジェネリック医薬品の処方を推進するにつれ、その普及は頭打ちになる可能性があり、医師と患者の視点など、この傾向に影響を与える要因についてさらに調査する必要があります。ジェネリック医薬品への切り替えを最大限に高め、医療システムの持続可能性を確保するには、低コスト以外の要因に焦点を当てた追加の戦略が必要になる場合があります。手頃な価格を強調し、他の処方法の考慮事項を明確にすることが不可欠です。
- ◆ **目的:** この研究は、患者の重症度、複合的なアドヒアランス、および医師と患者の関係がジェネリック医薬品の切り替えにどのように影響するかについて、最初の洞察を提供することを目的としました。
- ◆ **方法:** この研究では、全国医療データベースのデータを分析することにより、長期の遡及的コホート設計を使用しました。対象集団には、2014年4月から2018年3月までの4年間に心血管疾患 (CVD) (国際疾病分類第10版) による入院歴があり、一次から三次予防措置を必要としたすべての年齢層の患者 (主に高齢者) が含まれていました。臨床パラメータの時間的変動を独立変数として、ジェネリック医薬品への切り替えに焦点が当てられました。ライフスタイル要因 (喫煙と飲酒) も考慮されました。アドヒアランスは 11 の要素からなる複合スコアとして測定されました。医師と患者の関係は、医師の変更から処方までの間隔に基づいて確立されました。ロジスティック回帰分析と傾向スコアマッチング (PSM) が採用され、医師と患者の関係、服薬コンプライアンス (PDC) の層別化解析も行われました。

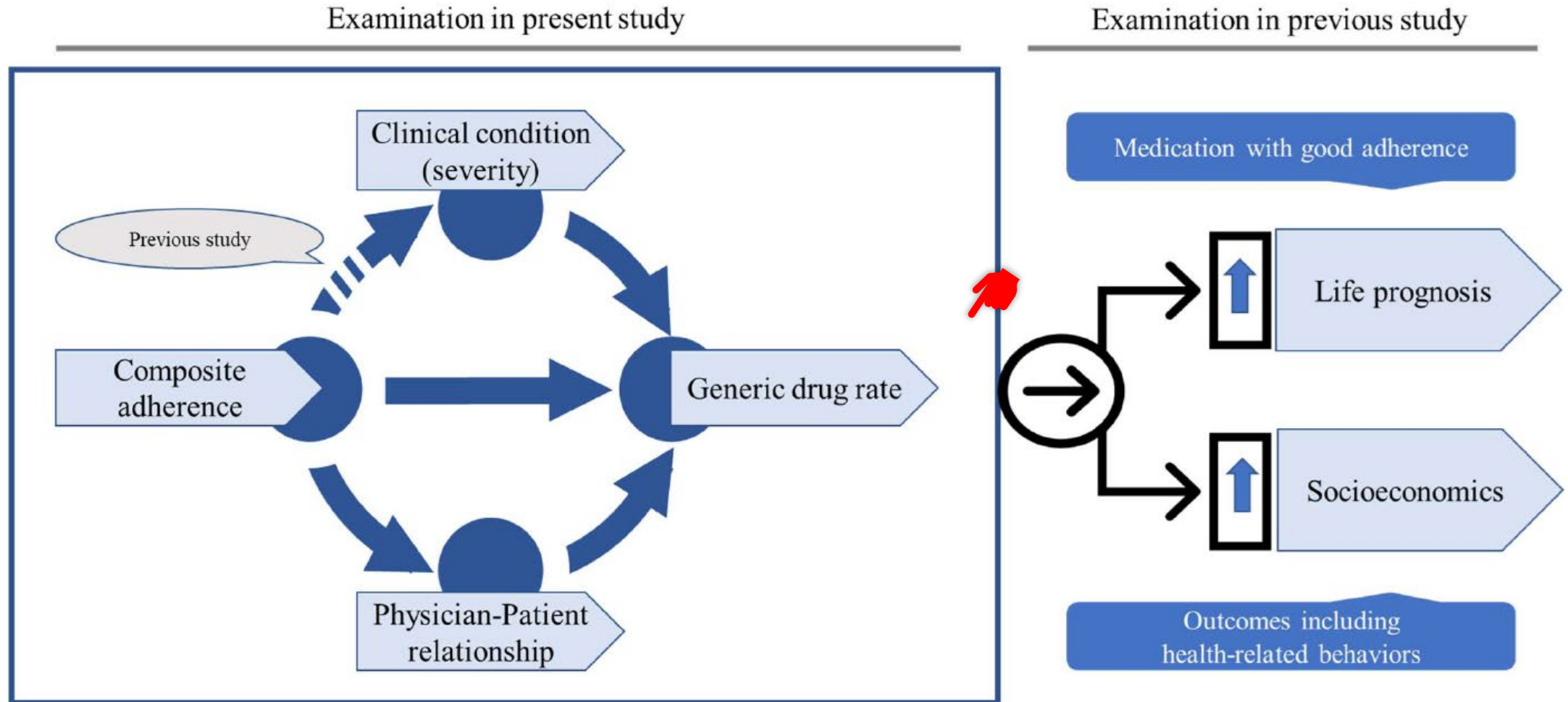
研究の結果

➤ 後発薬の選択は、患者重症度、医師信頼関係、アドヒアランス等に関係する傾向が明らかに

- ◆ **結果:** この研究には 48,456 人の患者が含まれ、平均追跡期間は 36.1 ± 8.8 か月でした。平均年齢は 68.3 ± 9.9 歳、BMIは 23.4 ± 3.4 kg/m²、収縮期血圧は 131.2 ± 15.0 mmHg、低密度リポタンパク質コレステロール (LDL-C) は 116.6 ± 29.3 mg/dL、ヘモグロビンA1c (HbA1c) は $5.9\% \pm 0.8\%$ 、血清クレアチニンは 0.9 ± 0.8 mg/dLであった。ロジスティック回帰分析により、ジェネリック医薬品への切り替えと収縮期血圧 (オッズ比 [OR]、0.996、95% 信頼区間 [CI] : 0.993~0.999)、血清クレアチニン値 (OR、0.837、95% CI : 0.729~0.962)、グルタミン酸オキサロ酢酸トランスアミナーゼ値 (OR、0.994、95% CI : 0.990~0.997)、PDC スコア (OR、0.959、95% CI : 0.948~0.970)、およびアドヒアランス・スコア (OR、0.910、95% CI : 0.875~0.947) との間に有意な関連があることが明らかになりました。さらに、HbA1c レベル帯および喫煙レベルの改善とともに、ジェネリック医薬品の割合が増加しました ($P < .01$ 、 $P < .001$)。PSM 後の医師と患者の関係が優れていたグループ ($51.6 \pm 15.2\%$) は、劣っていたグループ ($47.7 \pm 17.7\%$) よりもジェネリック医薬品の処方率が有意に高かった ($P < .001$)。
- ◆ **結論:** 医師の理解はジェネリック医薬品の選択に影響しますが、患者の状態 (重症度) とアドヒアランスの水準もこの決定に影響します。たとえば、クレアチニン値の改善はジェネリック医薬品の選択と関連しており、医師と患者の関係が強固であることはジェネリック医薬品の利用率の高さと相関しています。これらの知見は、ジェネリック医薬品の政策的普及が鈍化し始めた場合、医薬品の適切な処方に貢献する可能性があります。したがって、信頼を築きながら重篤な病気を予防することは、臨床上の利益と社会経済的な成果の向上につながる可能性があります。

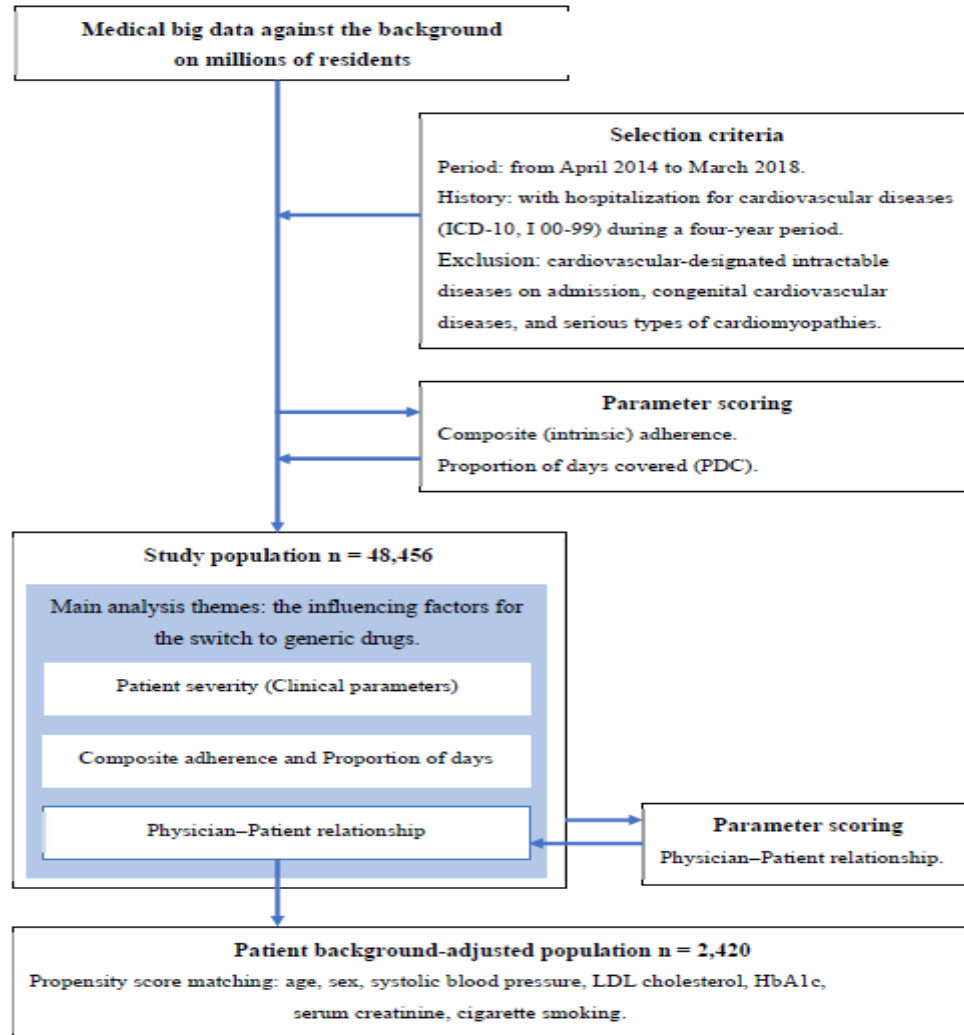
研究の基本メッセージ

- ▶ 後発薬の選択は、患者重症度、医師信頼関係、アドヒアランスの影響を受け、生命予後と医療費用に影響を及ぼす。すなわち、後発薬選択の状況で、臨床経済的な予後を論じることが潜在的に可能



研究の集団

▶ 対象集団は、循環器系のリスクのある48,456人

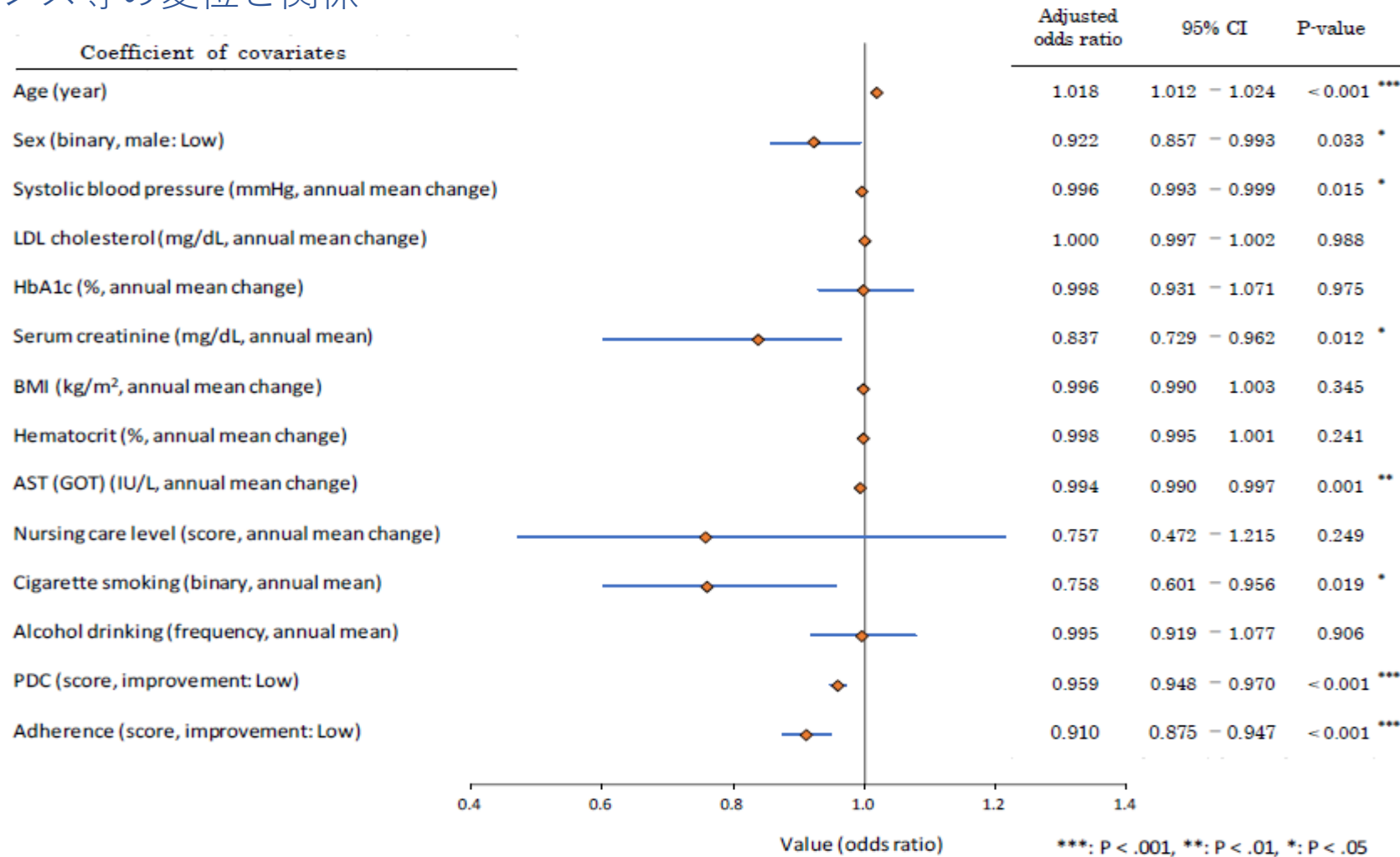


Parameter	Mean ± SD ^g	Median	IQR ^h
Sample			
Patients, n	48,456		
Health check-up examination			
Age, years	68.3 ± 9.9	69.0	65.0 - 73.0
Male sex, n (%)	29,994 (61.9)		
Physical examination			
Height, cm	160 ± 8.8	160.3	153.4 - 166.6
Weight, kg	60.0 ± 11.3	59.5	52.1 - 67.1
BMI ^a , kg/m ²	23.4 ± 3.4	23.2	21.1 - 25.3
Waist, cm	84.4 ± 9.3	84.2	78.5 - 90.0
Systolic BP ^b , mmHg	131.2 ± 15.0	130.5	121.8 - 140.0
Diastolic BP ^b , mmHg	75.7 ± 10.3	75.3	69.3 - 81.8
Lipid profile			
Triglycerides, mg/dL	120.8 ± 75.2	103.3	76.0 - 143.5
HDL ^c cholesterol, mg/dL	59.4 ± 15.9	57.5	48.0 - 68.8
LDL ^d cholesterol, mg/dL	116.6 ± 29.3	116.0	97.0 - 134.5
Kidney function			
Serum creatinine, mg/dL	0.9 ± 0.8	0.8	0.6 - 0.9
Serum uric acid, mg/dL	5.4 ± 1.4	5.4	4.5 - 6.3
eGFR ^e , mL/min/1.73m ²	69.2 ± 17.1	69.6	60.2 - 79.1
Blood sugar			
HbA1c ^f (%)	5.9 ± 0.8	5.7	5.5 - 6.1
Follow-up period, months			
	36.1 ± 8.8	44.0	

^a BMI: body mass index, ^b BP: blood pressure, ^c HDL: high-density lipoprotein, ^d LDL: low-density lipoprotein, ^e GFR: glomerular filtration rate, ^f HbA1c: hemoglobin A 1c, ^g SD: Standard Deviation, ^h IQR: Interquartile range
Values are expressed as mean ± SD, n (%)

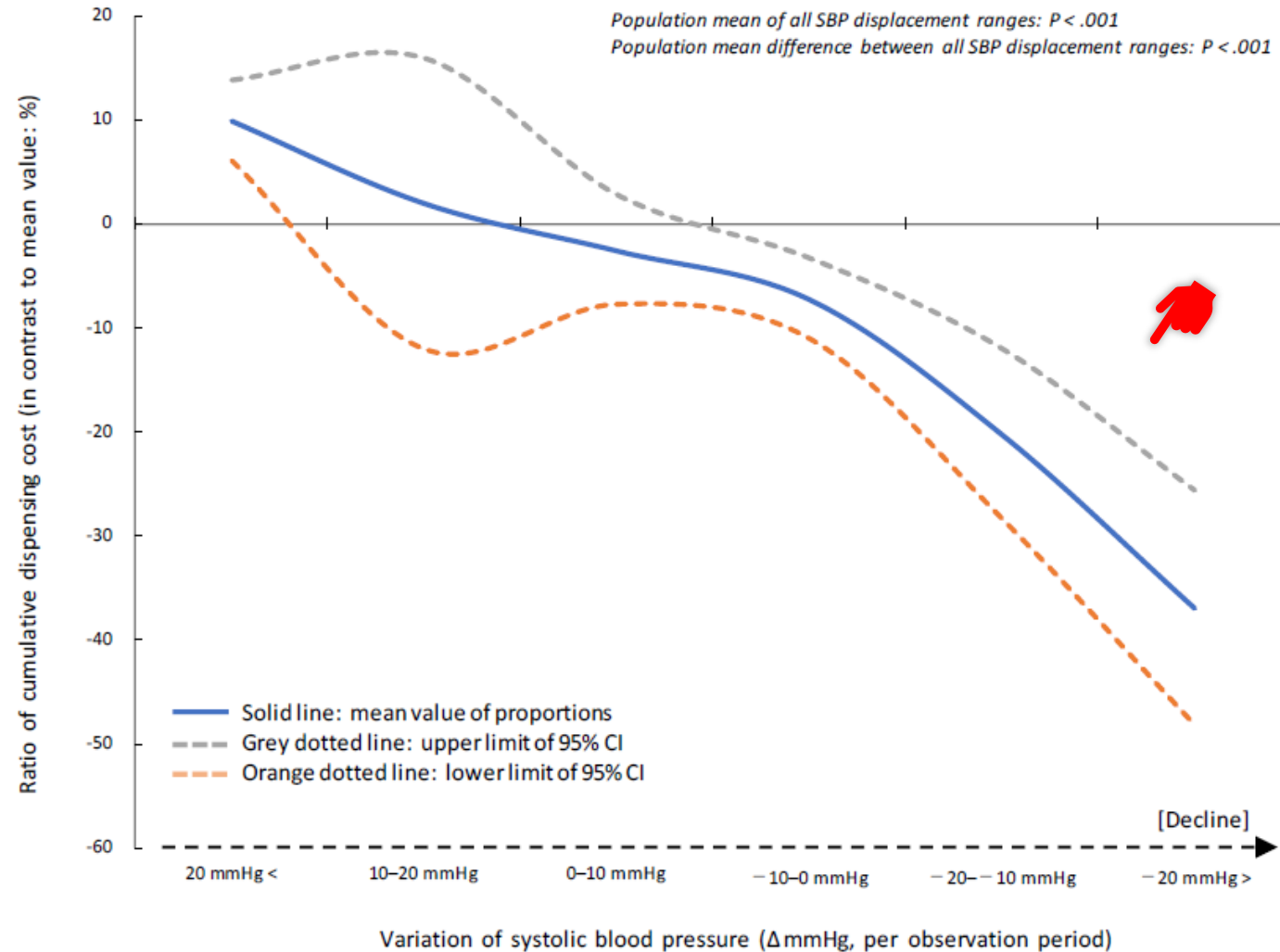
患者重症度と後発薬選択

- 後発薬選択は、年齢、性、収縮期血圧、血清クレアチニン、AST（肝機能、心機能等）、喫煙、アドヒアランス等の変位と関係



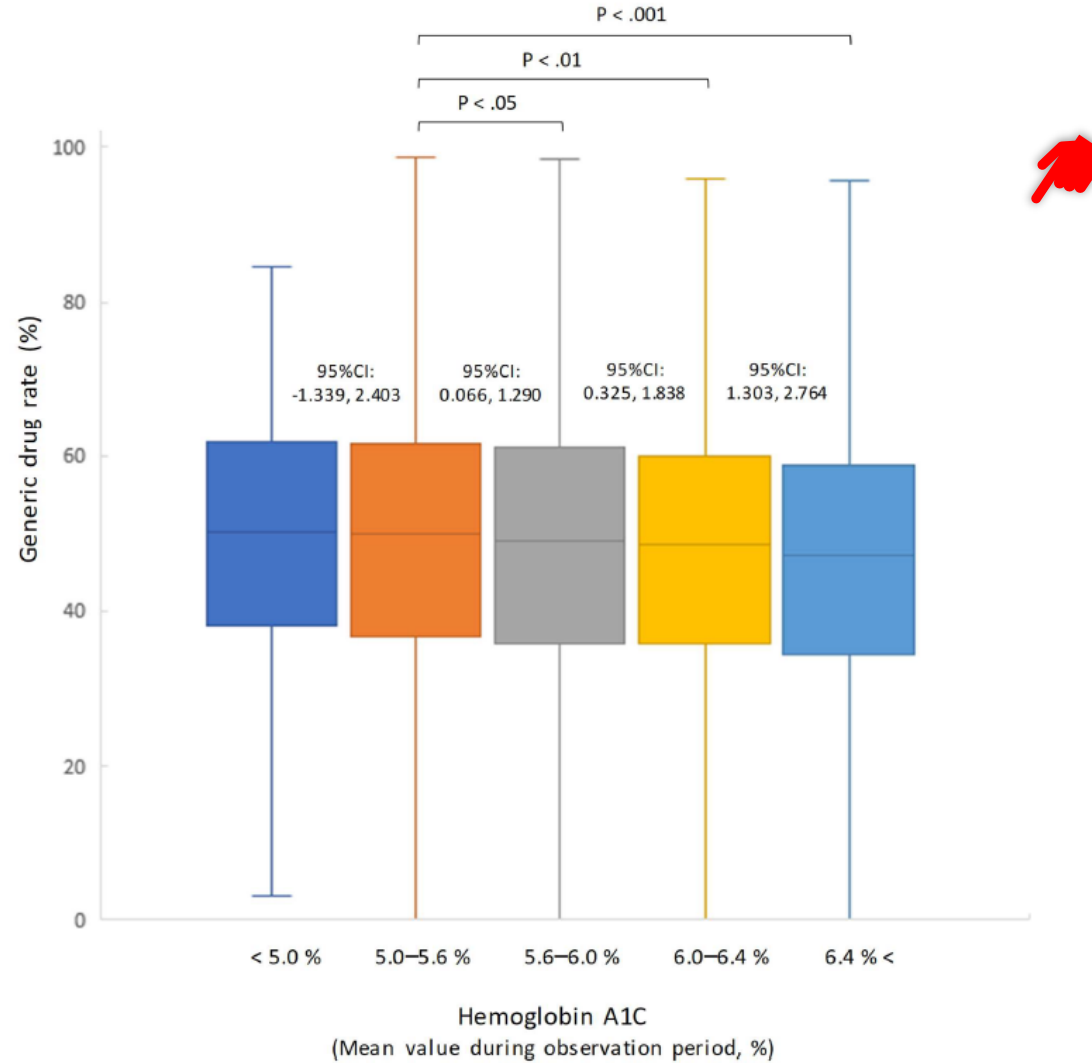
収縮期血圧と医薬品費用

- 収縮期血圧の改善は、指数関数的に医薬品費用を低下させ社会経済に貢献（後発薬選択にも関係）



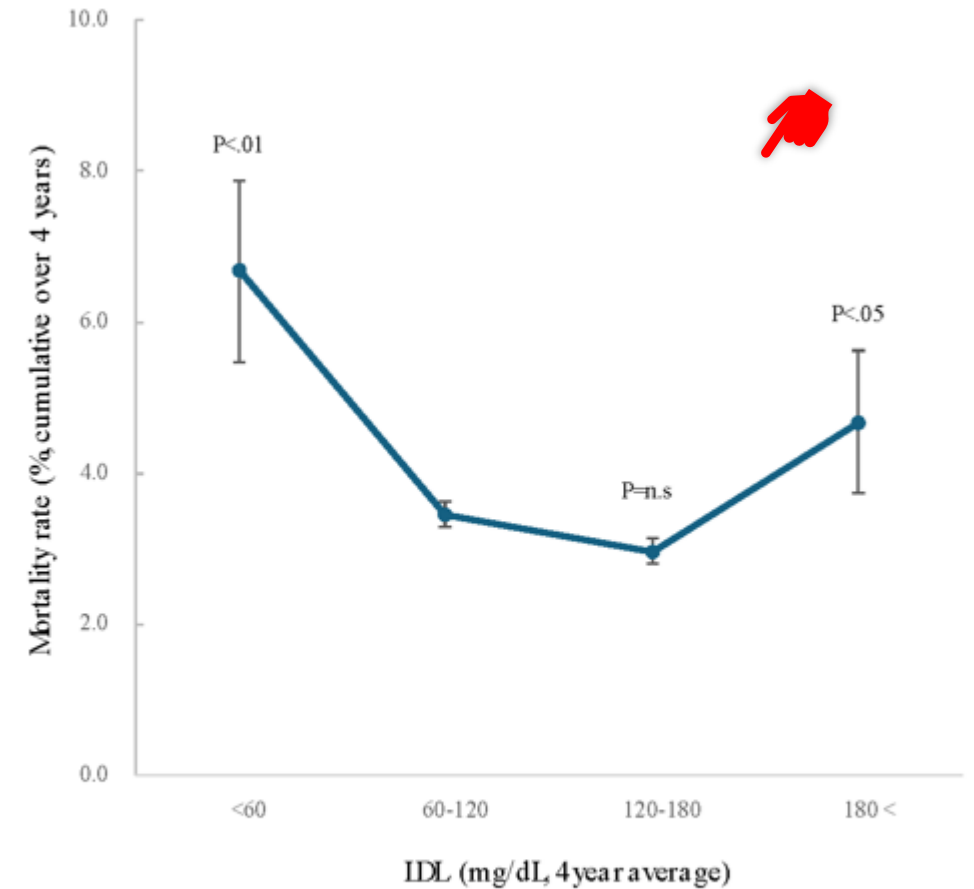
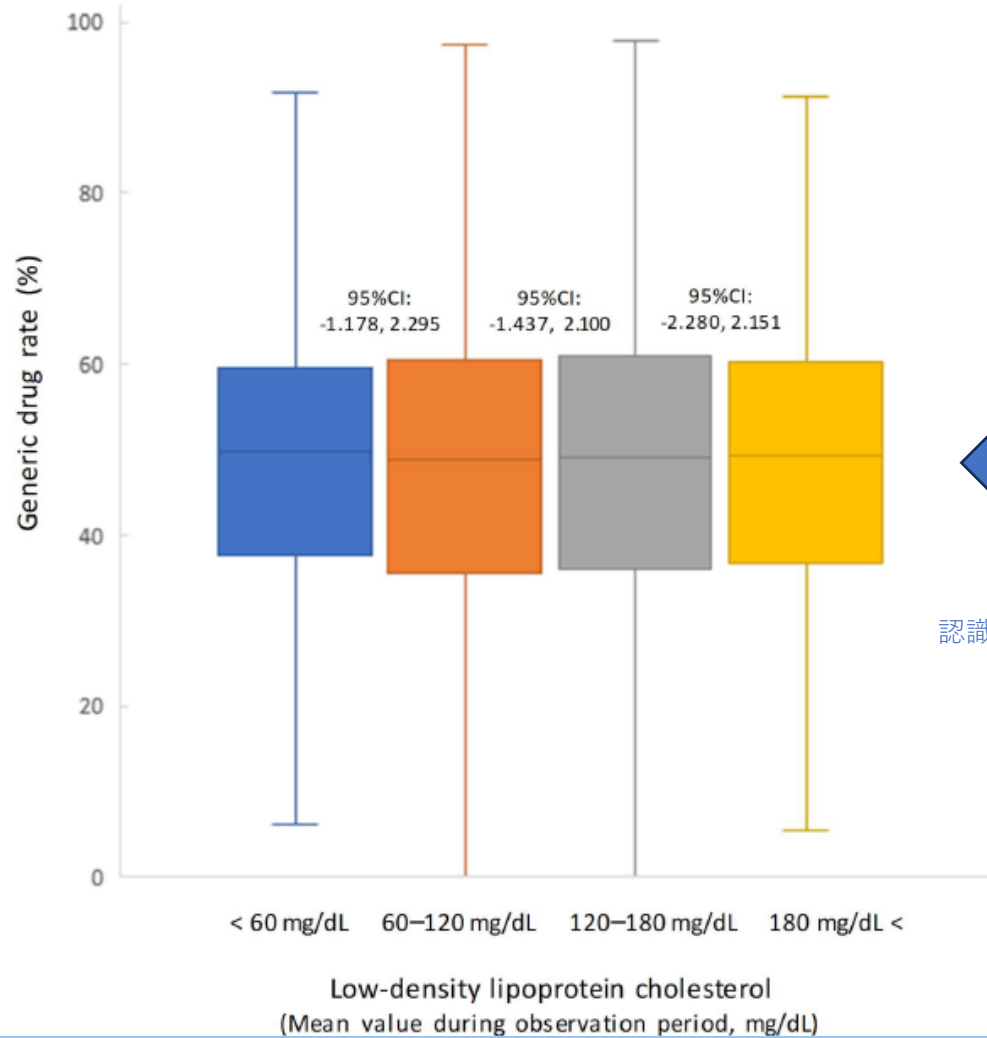
血糖値水準と後発薬選択

➤ HbA1cが増悪するにつれて、後発薬選択率が低下（後発薬選択率は糖尿病リスクのサロゲートに）



コレステロールと後発薬選択の関係

➤ LDL-Cは、死亡率等のリスクに対して指数的(U字型)関係にあり、より複雑な機序が影響する傾向

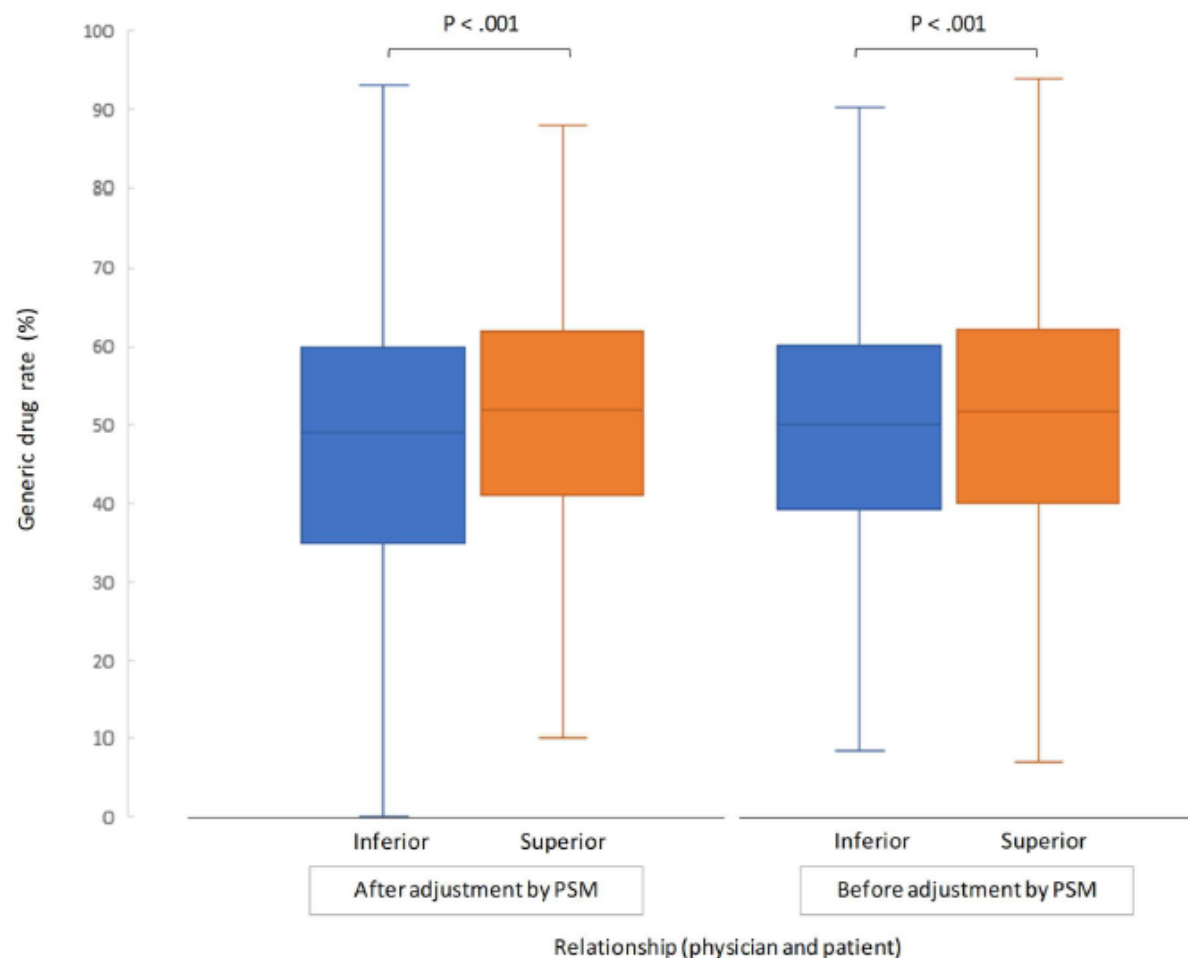
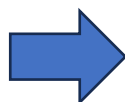


Abbreviations: LDL, Low-density Lipoprotein Cholesterol
Test: Spearman's rank correlation coefficient

医師患者の信頼関係は影響するのか

➤ 医師と患者の信頼関係が高いと、後発薬率の選択率も高くなる傾向（PSMで背景を揃えて解析）

Parameter	Inferior group	Superior Group	P-value
Sample (n)	1,210	1,210	
Age (year)	70.2 ± 6.6	70.2 ± 6.8	0.444
Sex ^a (male: n, %)	816 (67.4%)	836 (69.1%)	0.407
Systolic blood pressure (mmHg, mean change per observation period)	8.9 ± 5.6	8.5 ± 5.5	0.143
LDL ^b cholesterol (mg/dL, mean change per observation period)	7.8 ± 5.3	7.4 ± 5.1	0.086
HbA1c ^c (% , mean change per observation period)	0.3 ± 0.2	0.3 ± 0.2	0.284
Serum creatinine (mg/dL, mean per observation period)	0.6 ± 0.8	0.7 ± 1.1	0.126
Cigarette smoking ^d (binary, mean per observation period)	0.2 ± 0.3	0.2 ± 0.3	0.732



^a Sex: binary (male; 1, female; 2), ^b LDL: low-density lipoprotein, ^c HbA1c: hemoglobin A 1c, ^d Cigarette smoking: binary (presence; 0, existence; 1)

医師患者の信頼関係に影響する要因

➤ 年齢、性別、アドヒアランスの要因は、医師患者の信頼関係に影響

Parameter	Standard partial regression coefficient	Standard error	Odds ratio	95% CI (Partial regression coefficient)	P-value
Age (year)	-0.064	0.002	0.982	0.977 - 0.986	< 0.001
Sex (binarization) ^b	0.024	0.044	1.145	1.050 - 1.249	0.002
Adherence (score, improvement: Low)	0.104	0.002	1.025	1.021 - 1.029	< 0.001

Model (Logistic regression, Dependent variable: Relationship^a): P < .001

^a Relationship: binary (Superior; 0, Inferior; 1), ^b Sex: binary (male; 1, female; 2)

本日のまとめ

- ▶ 患者重症度、医師信頼関係、アドヒアランスが、後発薬率の選択に影響を及ぼす因子
- ▶ 収縮期血圧、血糖値(HbA1c)、血清クレアチンのみならず、喫煙等の生活習慣も関係要因
- ▶ 後発薬の選択状況は、長期的な生命予後／経済予後のサロゲート指標になりえる可能性



信頼を築きながら重篤な病気を予防することは、臨床上の利益と社会経済的な成果の向上につながる



ご清聴、ありがとうございました

ご質問や意見があれば遠慮なくお願いします。



以上

Original Paper

Factors Influencing Drug Prescribing for Patients with Hospitalization History in Circulatory Disease: Patient Severity, Composite Adherence, and Physician-Patient Relationship - A Retrospective Cohort Study

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Abstract

Background: With countries promoting generic drug prescribing, their growth may plateau, warranting further investigation into the factors influencing this trend, including physician and patient perspectives. Additional strategies may be needed to maximize the switch to generic drugs while ensuring healthcare system sustainability, focusing on factors beyond mere low cost. Emphasizing affordability and clarifying other prescription considerations are essential.

Objective: This study aimed to provide initial insights into how patient severity, composite adherence, and physician-patient relationships impact generic switching.

Methods: This study utilized a long-term retrospective cohort design by analyzing data from a national healthcare database. The population included patients of all ages, primarily older adults, who required primary-to-tertiary preventive actions with a history of hospitalization for cardiovascular diseases (CVDs) (International Classification of Diseases, Tenth Revision) during April 2014 to March 2018 (4 years). We focused on switching to generic drugs, with temporal variations in clinical parameters as independent variables. Lifestyle factors (smoking and drinking) were also considered. Adherence was measured as a composite score comprising 11 elements. The physician-patient relationship was established based on the interval between physician change and prescription. Logistic regression analysis and propensity score matching (PSM) were employed, along with complementary analysis of physician-patient relationships, proportion of days covered (PDC), and adherence for a subset of the population.

Results: The study included 48,456 patients with an average follow-up of 36.1±8.8 months. The mean age was 68.3 ± 9.9 years, body mass index was 23.4 ± 3.4 kg/m², systolic blood pressure was 131.2 ± 15.0 mmHg, low-density lipoprotein cholesterol (LDL-C) was 116.6 ± 29.3 mg/dL, hemoglobin A1c (HbA1c) was 5.9% ± 0.8%, and serum creatinine was 0.9 ± 0.8 mg/dL. Logistic regression analysis revealed significant associations between generic switching and systolic blood pressure (odds ratio [OR], 0.996, 95% confidence interval [CI]: 0.993–0.999), serum creatinine levels (OR, 0.837, 95% CI: 0.729–0.962), glutamic oxaloacetic transaminase levels (OR, 0.994, 95% CI: 0.990–0.997), PDC score (OR, 0.959, 95% CI: 0.948–0.970), and adherence score (OR, 0.910, 95% CI: 0.875–0.947). Additionally, generic drug rates increased with improvements in the HbA1c level band and smoking level (P<.01, P<.001). The group with a superior physician-patient relationship after PSM had a significantly higher rate of generic drug prescribing (51.6±15.2%) than the inferior relationship group (47.7±17.7%) (P<.001).

Conclusions: Although physicians' understanding influences the choice of generic drugs, patient condition (severity) and adherence also impact this decision. For example, improved creatinine levels are associated with generic drug choice, while

stronger physician-patient relationships correlate with higher rates of generic drug utilization. These findings may contribute to the appropriate prescription of pharmaceuticals if the policy diffusion of generic drugs begins to slow down. Thus, preventing serious illness while building trust may result in clinical benefits and positive socio-economic outcomes.

(*JMIR Aging* 2024;0:e0) doi: [10.2196/59234](https://doi.org/10.2196/59234)

KEYWORDS

Medication adherence; Drug prescription switch; Generic drug; Logistic model; Long-term longitudinal study; Patient severity; Systolic blood pressure; Serum creatinine; Aging; big data

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