ADHERENCE THRESHOLDS FOR PCSK9is IN TERMS OF CLINICAL OUTCOMES AND HEALTHCARE UTILIZATION

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INTRODUCTION

- Adherence patterns to lipid-lowering therapy (LLT), and particularly Proprotein Convertase Subtilisin/Kexin Type 9 inhibitors (PCSK9is), have been studied.
- Little is known about the optimal adherence threshold leading to improvement in cardiovascular (CV) outcomes and healthcare utilization (HCU).

OBJECTIVE

To identify this threshold in terms of low-density lipoprotein cholesterol (LDL-c) change and to analyze its association with CV-related outcomes and HCU.

METHODS

- A retrospective cohort study among adult Leumit Health Care Services' enrollees, who initiated PCSK9is in January 2021-June 2023 (n=470).
- Adherence ranges, measured by proportion of days covered (PDC), with the lowest variability in LDL-c change were defined using hierarchical clustering analysis.
- A multivariable linear model, logistic models and generalized linear models were specified to evaluate the determinants associated with LDL-c change, newly diagnosed CV disease and HCU, respectively, at 12-month follow-up.
- The core independent variable was the optimal adherence cluster.

RESULTS

Figure 1. Density heatmap illustrating the rate of change in LDL-c across varying levels of medication adherence, shows gradually increasing density of LDL-c decrease among individuals with PDC levels of above 50%.

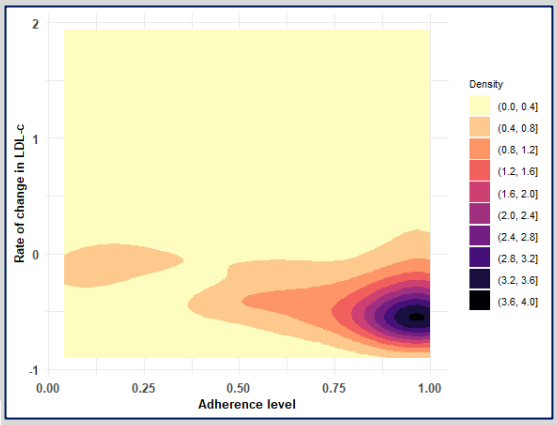

Table 1. Laboratory results, HCU and newly diagnosed CV disease at 12 months follow-up, by PCSK9i adherence.

Variable	PCSK9is adherence<67%	PCSK9is adherence≥67%	P-value
n (%)	166 (35.3%)	304 (64.7%)	
LDL-c (mg/dL)	115.0±60.9 (108,91)	74.2±34.8 (68,43)	<0.001[b]
LDL-c below 70mg/dL (%)	28.9	51.7	<0.001[a]
Rate of change in LDL-c	-0.13±0.45 (-0.18,0.47)	-0.39±0.33 (-0.48,0.35)	<0.001[b]
Total Cholesterol (mg/dL)	197.0±70.7 (194,102)	150.0±43.7 (146,55)	<0.001[b]
Neurologist visits	0.4±1.0 (0,0)	0.3±0.8 (0,0)	0.028[b]
Cardiac Rehabilitation care	0.7±6.6 (0,0)	0.8±3.8 (0,0)	0.022[b]
CeVD (%)	2.9	0.4	0.039[a]

Values are mean ± SD (median, IQR) else otherwise stated.
[a] Chi-square test, [b] Mann-Whitney U test.

Table 2. Multivariable analysis of CV-related health outcomes at 12-month follow-up.

Variable		PDC≥0.67 (vs. others)	N	R^2 or McFadden's R^2
LDL change[a]	β	-0.285***	403	0.271
	95% CI	-0.355 – -0.214		
Neurologist visits[b]	RR	0.61*	448	0.038
	95% CI	0.38 - 0.99		
Cardiac Rehabilitation[b]	RR	3.90*	448	0.056
	95% CI	1.22 - 12.48		
New CeVD[c]	OR	0.52	448	0.038
	95% CI	0.13 - 2.18		

[a] Linear regression model, [b] Generalized linear model assuming negative binomial distribution and log link function, [c] Logistic model.
* p<0.05, **p<0.01, ***p<0.001

LIMITATIONS

- A prescription refill does not necessarily mean medication uptake.
- HCU estimates may not be generalizable to other healthcare systems, as practice patterns may differ.
- Our analyses are based on a relatively small cohort.

CONCLUSIONS

- A substantial decrease in LDL-c was observed even at an adherence level of PDC≥67%, which is lower than the widely used threshold of PDC≥80%, seen in literature.
- These findings may enable the development of support programs emphasizing the advantages even at partial adherence.
- Most of CV-related diagnoses and HCU did not improve at this optimal level of adherence in 12-month follow-up.
- Further research is required to validate these findings through long-term follow-up and in larger populations.

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