The clinical and economic impact of a multicomponent digital therapeutic mobile app: a retrospective analysis

Part 1: Medication adherence

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1. INTRODUCTION

Medication adherence is defined as the process by which patients take the medication as prescribed incorporating initiation, implementation and discontinuation (1). With more than 50% of patients failing to adhere to their chronic medications (2, 3), effective interventions to address this prevalent problem are highly needed. Non-adherence has a significant negative impact leading to poor health outcomes, health complications, and increased use of healthcare resources (i.e. outpatient care, emergency department visits and hospitalisations). Moreover, it is estimated to be the cause of approximately 200,000 premature deaths in Europe every year (4). Particularly in Australia, it is estimated that up to 3% of hospitalisations are related to the inadequate use of medicines (including medication non adherence) (5), costing the health care system up to AUD$24,717 per patient per year. Medication non-adherence has been associated with an increase in cardiovascular events (6), worst glycaemic control on diabetic patients (7) and increased exacerbations and mortality in patients with COPD (8). A recent systematic review of the economic impact of medication non-adherence found that annual costs of non-adherence per person ranges from US$3,347 to US$19,472 for cardiovascular diseases, from US$3,232 to $19,363 for mental health conditions, from US$804 to US$36,259 for respiratory diseases and from US$949 to US$44,190 for other chronic conditions (9).

The literature shows that lack of adherence to medications is a complex problem of multifactorial origin, determined by the interplay of numerous factors (10) both intentional (i.e. patients decide not to take their medications due to perceptual barriers) or unintentional (i.e. patients have practical barriers that hinder the medication taking process) (11). One of the most important challenges faced in research and clinical practice today is the lack of evidence on the most effective strategies to manage medication adherence. A Cochrane review analysing medication adherence interventions concluded that most are either too complex or not very effective. However, a recent network meta-analysis analysing the comparative effectiveness of interventions to improve medication adherence found a combination of technical components (e.g. reminders, direct observation therapy, self-monitoring) in combination with rewards resulted in better improvement of medication adherence long term (≥10 months) (12).

With the increasing use of technology and access to mobile phones, mobile health (mHealth) apps (13) are increasingly being used to deliver interventions to manage health care and medication adherence (14). There are over 300,000 mHealth apps in the market with a growing focus on the management of chronic conditions through the

provision of tools to improve adherence to medications (15). While mobile apps with medication adherence components have been found to be beneficial for patients (16), further research is needed to determine the effectiveness on patient-specific outcomes (17). Another systematic review analysing the specific features of medication adherence apps found technical components, mostly targeting unintentional non-adherence, were the most common element used. However educational interventions, which may also target intentional non-adherence, were underutilised (17). Gamification was found to be another underutilised component identified in only 1.2% of the apps. Gamification in particular has been associated to increase intrinsic motivation and user engagement (18), which could impact on both unintentional and intentional medication non-adherence. Moreover, additional strategies such as rewards or incentives and social support seem promising strategies to promote health-related behavioural change (19).

Organizations such as to the International Society for Medication Adherence (ESPACOMP) have recognised that innovative approaches are needed to address the burden of medication non-adherence. In particular, the inclusion and analysis of Real-World Data (RWD) from “real-world” clinical practice has the potential to greatly improve this understanding. RWD can address existing knowledge gaps by collecting data from different sources and providing new insights into disease and adherence management. Data gathered from mobile apps is usually collected outside of clinical research settings and is an important source of RWD (20). The analysis of this data can provide an insight on the effect of mHealth interventions at improving patient’s outcomes. A previous retrospective analysis of RWD gathered through the Perx app involving educational, technical and gamification components demonstrated the ability to maintain optimal average medication adherence rates (adherence rates ≥ 80% (21)) after three and six months of follow-up (22). However, the effectiveness of this intervention considering specific therapeutic areas, high-risk populations and longer follow-up periods is still to be researched.

1.1 Objectives

General objective:

- To evaluate the effectiveness of Perx app on medication adherence in patients with chronic conditions.

Specific objectives:

- To evaluate the impact of the Perx app on medication adherence across different clinical conditions.
- To evaluate the impact of the Perx app based on the patient's number of clinical conditions and number of medications.
- To explore the association between medication adherence and health literacy.

2. METHODS

This was a retrospective observational study analysing RWD collected through the Perx app. De-identified user data included medication schedules, clinical conditions and clinical variables.

This study has been approved by the University of Technology Sydney Human Research Ethics Committee (HREC) (Application number: ETH21-5730).

2.1 Intervention

A medication adherence management intervention was provided through the digital Perx app. The Perx app supports individuals manage their chronic conditions and develop better health habits (i.e. medication adherence). A Perx program participant can download the app to their mobile phone or mobile device from a digital platform (i.e. Apple App Store or Google Play). Medication information (name, strength, dose and frequency), treatment schedules and physical health tasks can be recorded in the app. Clinical health measurements and doctor appointments can also be recorded and scheduled. Medication doses taken and mobile direct observation of therapy (MDOT) photo verification are recorded by the users. When it is time for a medication dose, games are offered to the individual to promote medication taking behaviour, receiving either a randomised reward or and/or “points” when a medication dose is taken on time. Points can also be earned by completing other daily tasks (e.g. exercise, appointments) or engaging with educational content (e.g. condition-specific education or tips for healthy living). Reaching a certain amount of gold points will cause the individual to “level-up”, unlock new potential rewards and improve their position on the leader board. Completion of all health tasks during the course of a day will provide participants with an in-app Heart badge and another gamified opportunity to earn a reward (e.g. gift card or charity donation). When Hearts are earned continuously over time they build into a Streak (representing how many days in a row a participant has achieved 100% adherence).

The Perx app involves technical components such as dose reminders (prompted from the patient’s scheduled doses for each medication) and visual feedback on medication adherence behaviour. It also includes self-serve educational content and resources (i.e. informative messages about the disease and the medications) and reward vouchers when accomplishing daily tasks.

2.2 Data Source

The Perx database was used as the data source. Data was de-identified and included app usage, health and medication data. Medication dosing data between November 2016 and September 2020 was analysed to determine medication adherence rates.

Cohort data was derived from Perx program participants recruited through existing programs.

Participants were included if they had medication dosing data during a timeframe of 6, 9 or 12 months, measured as the period of time between the first medication dose taken until the last medication dose taken. Participants were excluded if they did not have data recorded during any of the months during the specific timeframe.

Sub-analyses by clinical condition category, number of medications, number of clinical conditions and health literacy were conducted. The health literacy was measured with the short form health literacy questionnaire (HLS-SF12), containing 12 questions. Each question could be rated on 4-point Likert scales (1= very difficult, 2 = difficult, 3 = easy, and 4 = very easy), with a minimum score of 1 and highest of 4. The general score for the questionnaire was calculated based on the formula: *Score = (M-1) X (50/3)*, where M is the mean of the questions scores per user, 3 is the range of the mean and 50 is the maximum value chosen as the metric from previous validation (23).

Clinical conditions were classified in in five categories: respiratory, musculoskeletal and rheumatology, mental health, endocrine and cardiology. The selection of clinical conditions was based on the number of participants with these conditions with data available in the app. Clinical conditions were not mutually exclusive, as participants could have one or more clinical conditions.

2.3 Data Analysis

PostgreSQL database management system (Version 13), pgAdmin management tool (Version 4.26), Microsoft Excel 2019 (Microsoft Corporation) and SPSS 25 (SPSS Inc, Chicago, Illinois, USA) were utilized to organise the data and retrieve the results. Medication adherence was calculated as the number of medication doses taken (medication tasks completed in the app) over the total scheduled doses. The result was reported as a percentage. The analysis was conducted per time periods of 30 days. Mean (Standard Deviation: SD) and median (Interquartile: IQR) were used to summarise study variables. The normal distribution of adherence was verified using the Shapiro-

Wilk test. Due to the distribution of the data, the comparison of differences between adherence rates overtime was measured with the Friedman test. A *P* value <.05 was considered to indicate statistical significance. Linear regressions to explore associations between medication adherence rates and common predictors of non-adherence (i.e. number of medications, number of conditions, health literacy) were also conducted.

3. RESULTS

A total of 793, 207 and 246 users were included in the 6, 9 and 12 months analyses respectively. The majority of users were female (6 months: 50.06%, 9 months: 55.56%, 12 months: 64.63%). Most users were located in Australia. A descriptive of baseline characteristics is included on Table 1.

Table 1. Baseline demographic characteristics

Variable	6 months timeframe (n= 793)	9 months timeframe (n= 207)	12 months timeframe (n=246)
Age, years (SD)	41.12 (12.73)	47.67 (13.67)	49.71 (15.78)
Genre (%)			
- Female	50.06%	55.56%	64.63%
- Male	12.23%	22.71%	29.27%
- NULL	35.94%	21.26%	4.07%
- Undisclosed	1.77%	0.48%	2.03%
Location (%)			
- Africa	0.13%	0.00%	0.00%
- Asia	0.13%	0.00%	0.00%
- Auckland	0.13%	0.00%	0.00%
- Australia	65.83%	82.61%	99.19%
- Europe	0.00%	0.00%	0.00%
- NULL	1.77%	0.48%	0.81%
- USA	32.03%	16.91%	0.00%

3.1 Implementation adherence for all patients over different time periods

Adherence rates for the 6-month analysis are described in Figure 1 and the appendix.

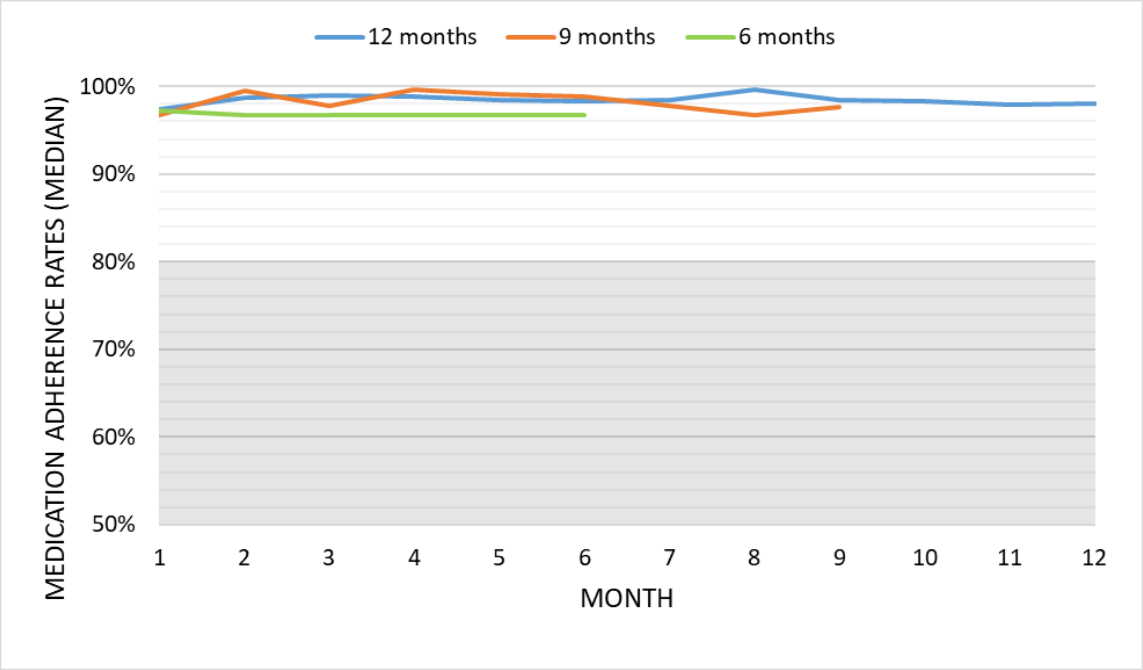
6-month analysis: Overall median adherence for the 6 months was 96.67% (IQR 85.0%-100%). Adherence at month 1 was 97.2% (IQR 90.0%-100%) and 96.70% (IQR 76.7%-100%) at month six. Differences in adherence rates over time were statistically significant (Fr(2)=110.914, *P*<.05) (Figure 1).

9-month analysis: Overall, median adherence rate was 98.33% (IQR 90.0%-100%) during the 9 months. At month 1, mean adherence rate was 96.7% (IQR 89.6%-100%). The final mean adherence rate was 97.6% (IQR 86.7%-100%). There was an increase in adherence rates across the 9 months and this was statistically significant (Fr(2)=27.769, *P*<.05).

12-month analysis: Overall median adherence rate was 98.45% (IQR 90.09%-100%) for the 12 months period. Median adherence rate was 97.4% (IQR 90.1%-100%) at month 1. At month 12, median medication adherence was 98.0%% (IQR 88.4%-100%). The

Friedman test revealed no significant differences on these differences overtime (Fr(2)=10.836, *P*=.458).

Figure 1. Medication adherence rates for patients across different timeframes



*The shadowed area represents suboptimal adherence (< 80%).

3.2 Impact of Perx in Complex High-Risk patients

3.2.1 Adherence across different categories of clinical conditions

6-month analysis: A total of 594 users were included in this sub-analysis corresponding to the following clinical conditions categories: Respiratory (n=117), Musculoskeletal and Rheumatology (n=113), Mental Health (n=297), Cardiology (n=103) and Endocrine (n=67). There was a decrease observed on mean adherence rates for all the categories during the six months. Results can be observed on Figure 2 and in the Appendix.

The overall median adherence rates were (98.2%, IQR 90.7%-100%) in the Musculoskeletal and Rheumatology group and (98.8%, IQR 92%-100%) in the Cardiology conditions group, (97.7%, IQR 87%-100%) Endocrine, (97.2%, IQR 88.3-100) Respiratory and (96.6%, IQR 83.3-100) Mental Health.

For the Musculoskeletal and Rheumatology conditions, median adherence at month 1 was 98.6% (IQR 91.5%-100%) and 97.8% (IQR 90.7%-100%) at month 6. The Friedman test revealed no significant differences on adherence rates overtime (Fr(2)=4.652, *P*=.460).

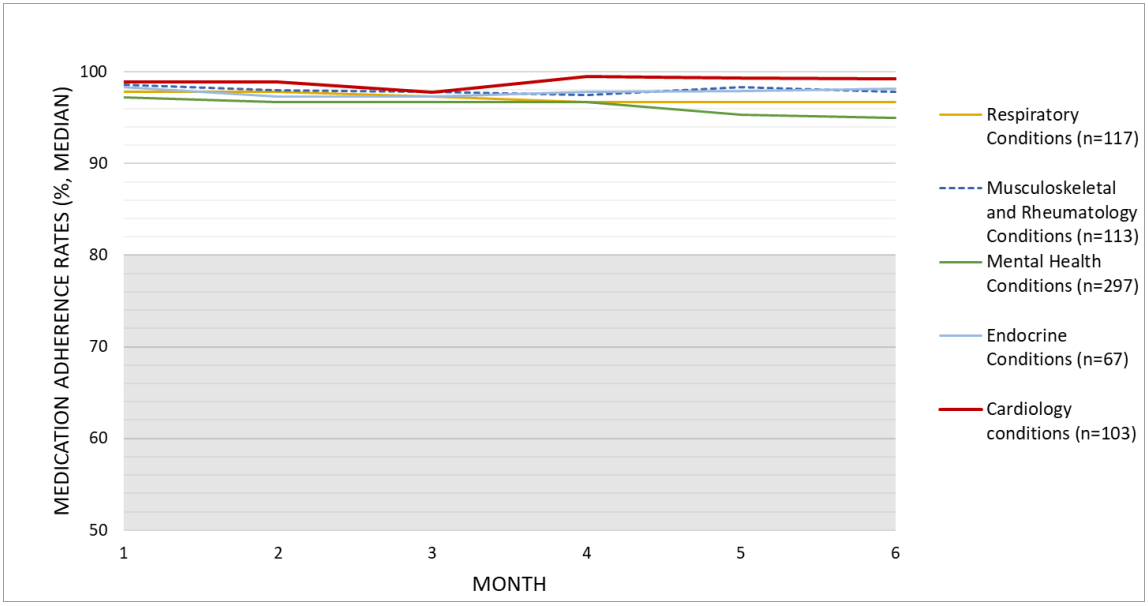
For the Cardiology conditions, median adherence was 98.9% (IQR 95%-100%) at month 1 and 99.2% (IQR 09%-100%) at month 6. The Friedman test revealed no significant differences on these differences overtime (Fr(2)=6.993, *P*=.221).

For the Endocrine conditions, median adherence rates were 98.3% (IQR 93.3%-100%) at month 1 and 98.2% (IQR 85.7%-100%) at month 6. The Friedman test revealed no significant differences on adherence rates overtime (Fr(2)=5.245, *P*=.387).

For the Respiratory conditions, adherence rates were 97.8% (IQR 91.6%-100%) at month 1 and 96.7% (IQR 82.2%-100%) at month 6. The Friedman test revealed significant differences on adherence rates overtime (Fr(2)=23.830, *P*<.05).

Finally, for the Mental Health conditions, median adherence rates were 97.2% (IQR 90%-100%) at month 1 and 95% (IQR 78.8%-100%) at month 6. The Friedman test revealed significant differences on adherence rates overtime (Fr(2)=62.954, *P*<.05).

Figure 2. Medication adherence rates across different clinical conditions categories – 6-month timeframe.



*The shadowed area represents suboptimal adherence (< 80%).

12-month analysis: 289 users were included in the 12-month analysis distributed across the following categories: Respiratory (n=58), Musculoskeletal and Rheumatology (n=43), Mental Health (n=79), Endocrine (n=45), Cardiology (n=64). Figure 3 describes median adherence rates for the 12-month analysis.

Overall median adherence rates were 99.8% (IQR 96.4%-100%) for Musculoskeletal and Rheumatology conditions, 100% (IQR 95.4%-100%) for Cardiology conditions, 100% (IQR 95.7%-100%) for Endocrine, 98.1% (IQR 88.8%-100%) for Respiratory and 98.9% (IQR 91.2%-100%) for Mental Health.

Median adherence rate was 98.5% (IQR 94.4%-100%) at month 1 for Musculoskeletal and Rheumatology category and 100.0% (IQR 95.6%-100%) at month 12. The Friedman test revealed no significant differences on adherence rates overtime (Fr(2)=6.278, *P*=.854).

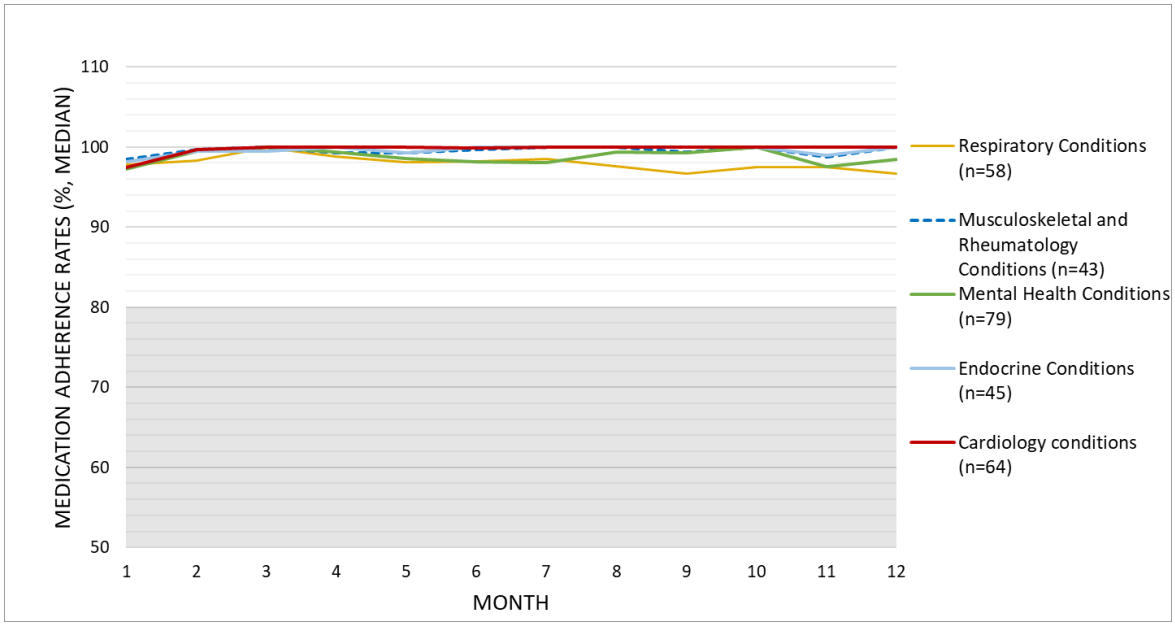
For the Cardiology conditions, median adherence rates increased from 97.4% (IQR 91.9%-100%) at month 1 to 100% (IQR 93.3%-100%) at month 12. The Friedman test revealed no significant differences on these rates overtime (Fr(2)=17.988, *P*=.082).

For the Endocrine conditions, median adherence rates were 98.1% (IQR 92.8%-100%) at month 1, and 100% (IQR 95.6%-100%) at month 12. The Friedman test revealed no significant differences on adherence rates overtime (Fr(2)=9.035, *P*=.619).

For the respiratory conditions, median adherence rate at month 1 was 97.8%, (IQR 86.9%-100%) and 96.7% (IQR 85.5%-100%) at month 12. The Friedman test revealed no significant differences on adherence rates overtime (Fr(2)=13.075, *P*=.288).

Finally, for the Mental Health conditions, median adherence rates were 97.2%, (IQR 90.1%-100%) and 98.5% (IQR 76.7%-100%) at month 12. The Friedman test revealed no significant differences on adherence rates overtime (Fr(2)=10.154, *P*=.517).

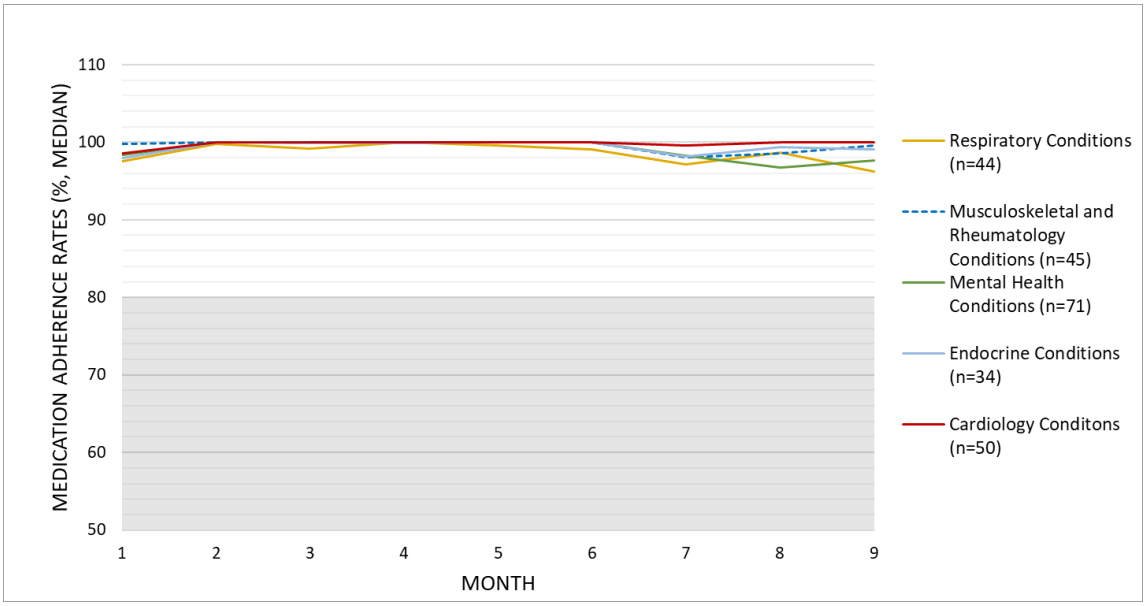
Figure 3. Medication adherence rates across different clinical conditions categories – 12 month timeframe.



*The shadowed area represents suboptimal adherence (< 80%).

Results for *9-month* analysis is observed on Figure 4 and the appendix. The Friedman test revealed significant differences on adherence rates overtime for Cardiology conditions (Fr(2)=21.134, *P*=.007), Endocrine Conditions (Fr(2)=21.984, *P*=.005), Mental Health Conditions (Fr(2)=32.725, *P*<.05), Musculoskeletal and Rheumatology Conditions (Fr(2)=17.926, *P*=.022), Respiratory Conditions (Fr(2)=19.332, *P*=.013).

Figure 4. Medication adherence rates across different clinical conditions categories – 9 month timeframe.



*The shadowed area represents suboptimal adherence (< 80%).

Adherence rates expressed in terms of mean (SD) for all the conditions analysed are reported in the appendix .

3.2.2 Adherence by number of clinical conditions managed by a patient

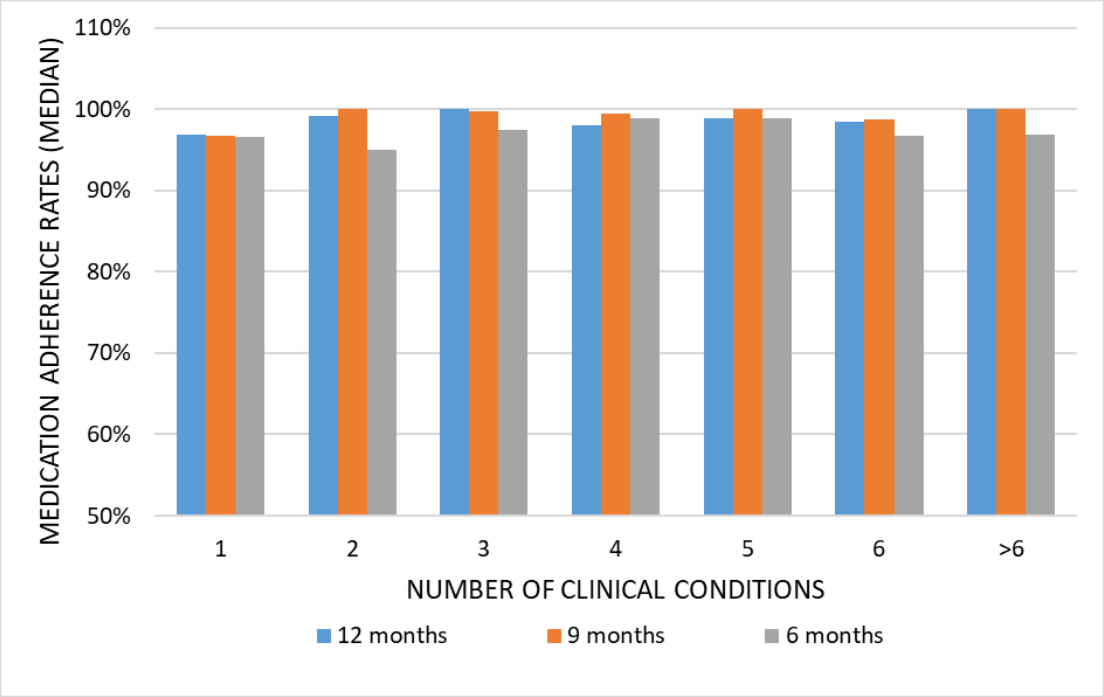
6-month analysis: Majority of users had 1 clinical condition (n=130), followed by users with more than 6 clinical conditions (n=91). Overall adherence rates were 96.6% (IQR 78.3%-100%) for users with 1 clinical condition, 95% (IQR 80.2%-100%) for 2 clinical conditions, 97.4% (IQR 88.6%-100%) for 3 clinical conditions, 98.9% (IQR 93.8%-100%) for 4 clinical conditions, 98.9% (IQR 86.7%-100%) for 5 clinical conditions, 96.7% (96%-100%) for 6 clinical conditions and 96.9% (IQR 87.5%-100%) for more than 6 clinical

conditions. The simple linear regression showed a significant association between the number of clinical conditions and adherence rates (R^2=0.014, *P*<.005).

9-month analysis: Majority of users had >6 clinical conditions (n=29), followed by users with 1 clinical condition (n=27). Overall adherence rates were 96.7% (IQR 80%-100%) for users with 1 clinical condition, 100% (IQR 93.6%-100%) for 2 clinical conditions, 99.8% (IQR 93.6%-100%) for 3 clinical conditions, 99.5% (IQR 88.1%-100%) for 4 clinical conditions, 100% (IQR 96.8%-100%) for 5 clinical conditions, 98.7% (IQR 90%-100%) for 6 clinical conditions and 100% (IQR 95.8%-100%) for more than 6 clinical conditions. The simple linear regression did not show a significant relationship between the number of clinical conditions and adherence rates (R^2=0.011, *P*=.113).

12-month analysis: Majority of users had 1 clinical condition (n=105), followed by users with 2 clinical conditions (n=29). Overall adherence rates were 96.8% (IQR 83.3%-100%) for users with 1 clinical condition, 99.2% (IQR 95.6%-100%) for 2 clinical conditions, 100% (IQR 93.9%-100%) for 3 clinical conditions, 98% (IQR 92.1%-100%) for 4 clinical conditions, 98.9% (IQR 93.3%-100%) for 5 clinical conditions, 98.5% (93.3%-100%) for 6 clinical conditions and 100% (IQR 98.6%-100%) for more than 6 clinical conditions. The simple linear regression showed a significant association between the number of clinical conditions and adherence rates (R^2=0.054, *P*<.005).

Figure 5. Medication adherence rates across number of clinical conditions



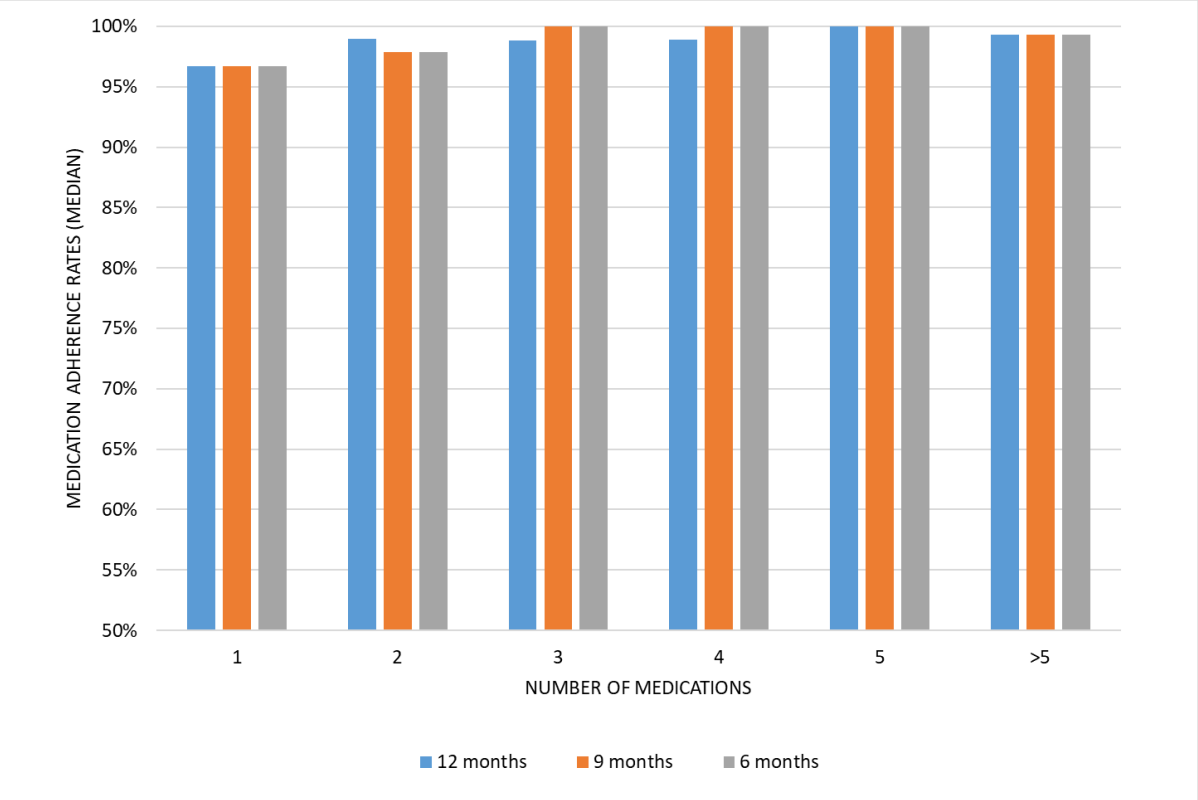
3.2.3 Adherence across patient's number of medications

6-month analysis: Majority of users had one medication (n=367). Overall adherence rates were 96.7% (IQR 83.3%-100%) for users with 1 medication, 96.7% (83.3%-100%) for users with 2 medications, 96.7% (IQR 85.5%-100%) for users with 3 medications, 97.8% (IQR 86.3%-100%) for users with 4 medications, 97.8% (IQR 89.7%-100%) for users with 5 medications and 98.6% (IQR 92%-100%) for users with more than 5 medications. The simple linear regression showed a significant association between the number of medications and adherence rates (R^2=0.009, *P*=.006).

9-month analysis: Majority of users had one medication (n=69). Overall adherence rates were 96.7% (IQR 86.7%-100%) for users with 1 medication, 97.9% (IQR 88.3%-100%) for users with 2 medications, 100% 86.9%-100%) for users with 3 medications, 100% (96.7%-100%) for users with 4 medications, 100% (IQR 93.7%-100%) for users with 5 medications and 99.3% (IQR 92.9%-100%) for users with more than 5 medications. The simple linear regression did not show a not significant association between the number of medications and adherence rates (R^2=0.011, *P*=.072).

12-month analysis: Majority of users had one medication (n=58). Overall adherence rates were 96.7% (IQR 90%-100%) for users with 1 medication, 99% (IQR 90%-100%) for users with 2 medications, 98.8% (IQR 90.2%-100%) for users with 3 medications, 98.9% (IQR 92.5%-100%) for users with 4 medications, 100% (96.7%-100%) for users with 5 medications and 99.3% (IQR 94.7%-100%) for users with more than 5 medications. The simple linear regression did not show a significant relationship between the number of medications and adherence rates (R^2=0.009, *P*=.095)

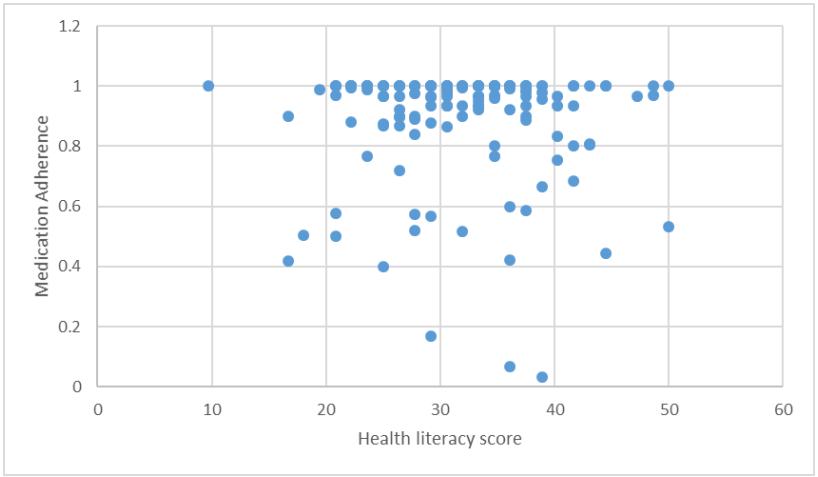
Figure 6. Medication adherence rates across number of medications



3.2.4 Adherence and health literacy

A total of 157 patients had data for the health literacy questionnaire (HLS-SF12). 26 patients had a score <25 and 131 patients (83%) had a score ≥25. There was no correlation between adherence and health literacy (Pearson coefficient = 0.67).

Figure 7. Correlation between health literacy and medication adherence rates



Discussion

The results of this retrospective analysis highlight the positive impact of the Perx app, a multicomponent medication adherence mHealth intervention, across different chronic conditions, time periods of analysis and patient attributes.

Medication adherence rates remained stable across most of the timeframes analysed and well above 80%, which is usually considered threshold for optimal adherence (21). These results align with those reported by Wiecek et al. reporting a retrospective analysis of six month medication data of the Perx app, in which median medication adherence rates were over 85% (22). These rates are also higher than those found in previous analysis of dispensing data in Australia, where medication adherence rates (measured using the Proportion of Days Covered) in patients with different chronic conditions remained between 50% and 70% during a 2 year follow-up period (24). The decrease on medication adherence rates over time in patients with chronic conditions is a common phenomenon and has previously been observed in retrospective analyses in Australia (23, 24). Blaschke et al. identified the same trend of decreasing medication adherence when analysing electronically monitored drug dosing histories across different conditions (3). These findings highlight the need of continuous monitoring and management of medication adherence for the maintenance of optimal adherence. The Perx app is an effective strategy to achieve this objective. The positive impact of the Perx app observed on medication adherence may be due to the combination of the different intervention components used, including adherence visual feedback or self-monitoring, which have been found to be effective at changing health-related behaviour (25). Some other features like reminders and the possibility of monitoring other health information have found to be highly proffered by users (26).

Interestingly, users included in the 6-month analysis had an overall adherence lower than those included in the 9-month and 12-month analyses. It could hypothesised that a longer exposition to the intervention (use of the Perx app), increases the likelihood of having a better adherence behaviour over time. The analysis of medication adherence rates across clinical conditions showed high median adherence rates across all time periods, with no significant decreases over time. Positive trends were observed in respiratory conditions, musculoskeletal and rheumatology diseases and Mental Health conditions. Although mHealth tools have been found to have a positive impact on patients with cardiovascular diseases, there is limited evidence on the long-term impact (27). This analysis provides an insight on the effect of a mHealth app on long-term (>6

months) adherence. The lower adherence rates observed in the respiratory conditions may be associated to the complexity of these conditions, as not only medication adherence but also symptoms control need to be targeted in order to achieve self-management (28).

To evaluate the impact of the intervention on the different groups of high-risk patients, an analysis was conducted looking at well-known predictors of poor adherence (i.e. number of medications, number of clinical conditions, health literacy).

Between 50% and 80% of the participants analysed in this study had more than one clinical condition across all the timeframes. Patients managing multiple clinical conditions ("polychronic" patients) have been associated with increased use of more expensive healthcare services like emergency room visits, hospitalizations, re-admissions and post-acute care (29). However, our results show a positive association between medication adherence and the number of clinical conditions, suggesting the positive impact of the Perx app on patients managing multiple conditions. This strategy could, therefore, be successfully implemented to target more complex, polychronic patients in the future.

Patients managing more than one medication ("polypharmacy") has been associated with medication non-adherence in previous adherence research (30). However, when analysing Perx participant adherence rates based on the number of medications, significant associations were not found between medication adherence and the number of medications when analysing more than 6 months data. This suggests the positive impact of the Perx app on patients managing multiple medications. This strategy could, therefore, be successfully implemented to target more polypharmacy patients in the future.

Health literacy has previously been positively correlated with adherence to medical treatment in chronic and acute illness and has been previously reported as a strong predictor of medication adherence (31, 32). However, when analysing Perx participant data, no association was found between health literacy and medication adherence. Nevertheless, regardless of the score, participants had adherence rates above 80%. This strategy could, therefore, be successfully implemented to target more low health literacy patients in the future.

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Appendix

Number of patients per number of clinical conditions included in the analysis.

Number of Clinical Conditions	12 month timeframe	9 month timeframe	6 month timeframe
1	105	27	130
2	29	23	82
3	22	21	58
4	19	14	44
5	8	13	48
6	13	13	33
>6	21	29	91

Number of patients per number of medications included in the analysis.

Number of Clinical Conditions	12 month timeframe	9 month timeframe	6 month timeframe
1	58	69	367
2	30	38	108
3	24	12	74
4	29	19	62
5	18	20	39
>5	45	45	107

Adherence rates across timeframes (all values expressed in percentages).

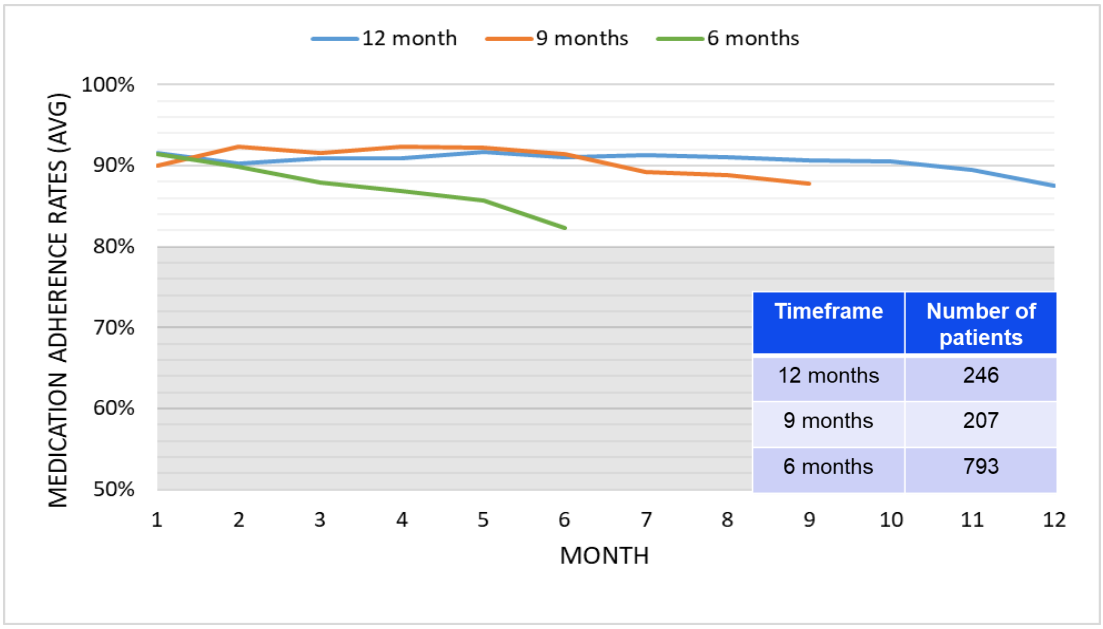
Month	12 month timeframe, Mean (SD)	12 month timeframe, Median (IQR)	9 month timeframe, Mean (SD)	9 month timeframe, Median (IQR)	6 month timeframe, Mean (SD)	6 month timeframe, Median (IQR)
1	91.6 (15.5)	97.4 (90.1-100.0)	90.0 (17.6)	96.7 (89.6-100.0)	91.5 (14.8)	97.2 (90.0-100.0)
2	90.3 (17.7)	98.7 (90.0-100.0)	92.3 (16.1)	99.5 (90.3-100.0)	89.8 (17.5)	96.7 (88.3-100.0)
3	90.9 (17.3)	99.0 (90.5-100.0)	91.5 (15.8)	97.8 (91.1-100.0)	87.9 (19.8)	96.7 (86.5-100.0)
4	90.9 (17.9)	98.9 (93.0-100.0)	92.4 (14.6)	99.6 (93.3-100.0)	86.8 (21.0)	96.7 (83.3-100.0)
5	91.7 (15.8)	98.5 (90.2-100.0)	92.2 (16.1)	99.1 (93.3-100.0)	85.7 (21.9)	96.7 (81.4-100.0)
6	91.0 (18.4)	98.3 (93.1-100.0)	91.4 (17.0)	98.9 (93.3-100.0)	82.2 (26.0)	96.7 (76.7-100.0)
7	91.4 (17.0)	98.4 (90.0-100.0)	89.2 (19.9)	97.8 (86.8-100.0)	NA	NA
8	91.0 (17.3)	99.6 (91.6-100.0)	88.9 (18.9)	96.7 (86.7-100.0)	NA	NA
9	90.7 (17.2)	98.5 (89.9-100.0)	87.7 (22.3)	97.6 (86.7-100.0)	NA	NA
10	90.5 (18.3)	98.3 (90.3-100.0)	NA	NA	NA	NA
11	89.5 (20.5)	97.9 (90.2-100.0)	NA	NA	NA	NA
12	87.5 (23.6)	98.0 (88.4-100.0)	NA	NA	NA	NA

Adherence clinical conditions categories (all values expressed in percentages).

Month	Respiratory		Musculoskeletal and Rheumatology		Mental Health		Endocrine		Cardiology	
6 month timeframe										
	Mean (SD)	**Median (IQR)**	**Mean (SD)**	**Median (IQR)**	**Mean (SD)**	**Median (IQR)**	**Mean (SD)**	**Median (IQR)**	**Mean (SD)**	**Median (IQR)**
1	93.3 (11.5)	97.8 (91.6-100.0)	93.5 (11.9)	98.6 (91.5-100.0)	92.1 (12.9)	97.2 (90.0-100.0)	93.8 (11.4)	98.3 (93.3-100.0)	93.2 (15.2)	98.9 (95.0-100.0)
2	90.2 (18.2)	97.8 (89.4-100.0)	92.6 (15.7)	98.0 (93.3-100.0)	89.1 (18.4)	96.7 (86.7-100.0)	92.3 (10.6)	97.3 (86.7-100.0)	92.4 (16.6)	98.9 (93.3-100.0)
3	89.2 (20.7)	97.3 (90.6-100.0)	92.1 (13.6)	97.8 (91.2-100.0)	86.9 (21.5)	96.7 (85.0-100.0)	89.8 (18.5)	97.3 (88.4-100.0)	89.9 (18.7)	97.8 (90.0-100.0)
4	86.4 (22.9)	96.7 (84.7-100.0)	91.4 (15.4)	97.5 (90.1-100.0)	86.0 (21.7)	96.7 (81.9-100.0)	88.6 (22.4)	97.8 (93.3-100.0)	90.5 (19.5)	99.5 (93.3-100.0)
5	85.7 (23.9)	96.7 (81.3-100.0)	90.6 (16.1)	98.3 (87.8-100.0)	83.4 (23.4)	95.3 (76.7-100.0)	87.1 (21.4)	97.9 (83.2-100.0)	88.1 (23.4)	99.3 (88.6-100.0)
6	83.4 (27.1)	96.7 (82.2-100.0)	90.1 (19.5)	97.8 (90.7-100.0)	82.5 (26.1)	95.0 (78.8-100.0)	87.5 (22.6)	98.2 (85.7-100.0)	88.9 (22.6)	99.2 (90.0-100.0)
9 month timeframe, Median (IQR)										
	Mean (SD)	**Median (IQR)**	**Mean (SD)**	**Median (IQR)**	**Mean (SD)**	**Median (IQR)**	**Mean (SD)**	**Median (IQR)**	**Mean (SD)**	**Median (IQR)**
1	90.7 (17.5)	97.5 (91.2-100.0)	93.3 (12.3)	99.8 (93.5-100.0)	92.3 (14.7)	98.4 (92.2-100.0)	89.0 (20.0)	97.9 (83.7-100.0)	91.9 (13.6)	98.6 (90.0-100.0)
2	94.7 (9.6)	99.8 (92.9-100.0)	95.9 (8.8)	100.0 (96.7-100.0)	94.7 (11.4)	100.0 (96.7-100.0)	95.4 (8.1)	100.0 (91.7-100.0)	95.5 (11.3)	100.0 (97.3-100.0)
3	94.4 (10.9)	99.2 (95.7-100.0)	96.3 (6.9)	100.0 (96.6-100.0)	93.8 (12.9)	100.0 (96.7-100.0)	94.4 (11.0)	99.9 (96.4-100.0)	94.8 (9.8)	100.0 (96.7-100.0)
4	93.9 (12.3)	100.0 (95.7-100.0)	96.7 (8.2)	100.0 (97.6-100.0)	94.5 (12.6)	100.0 (96.7-100.0)	96.4 (7.1)	99.9 (95.8-100.0)	95.9 (10.4)	100.0 (96.7-100.0)
5	93.5 (15.1)	99.6 (96.6-100.0)	95.3 (12.9)	100.0 (96.6-100.0)	94.1 (14.7)	100.0 (96.7-100.0)	95.9 (8.9)	100.0 (96.6-100.0)	95.5 (13.2)	100.0 (97.6-100.0)
6	94.2 (11.1)	99.1 (93.4-100.0)	93.1 (15.2)	100.0 (93.5-100.0)	92.5 (15.5)	100.0 (93.3-100.0)	91.1 (20.5)	100.0 (95.9-100.0)	94.7 (14.4)	100.0 (98.3-100.0)
7	91.4 (13.3)	97.1 (87.2-100.0)	88.5 (21.6)	98.0 (89.0-100.0)	88.9 (20.7)	98.3 (88.3-100.0)	89.0 (21.1)	98.2 (92.7-100.0)	90.7 (19.1)	99.6 (93.3-100.0)
8	88.2 (19.5)	98.7 (83.8-100.0)	90.9 (14.9)	98.6 (88.3-100.0)	88.9 (16.9)	96.7 (83.3-100.0)	87.2 (22.0)	99.4 (82.7-100.0)	91.7 (18.7)	100.0 (94.4-100.0)
9	83.4 (24.7)	96.2 (73.1-100.0)	91.0 (16.5)	99.6 (90.0-100.0)	87.0 (21.7)	97.6 (83.3-100.0)	85.2 (28.2)	99.1 (88.8-100.0)	89.2 (22.8)	100.0 (93.8-100.0)
12 month timeframe, Median (IQR)										
	Mean (SD)	**Median (IQR)**	**Mean (SD)**	**Median (IQR)**	**Mean (SD)**	**Median (IQR)**	**Mean (SD)**	**Median (IQR)**	**Mean (SD)**	**Median (IQR)**
1	90.5 (16.6)	97.8 (86.9-100.0)	95.2 (8.6)	98.5 (94.4-100.0)	93.6 (10.5)	97.2 (90.1-100.0)	91.4 (16.4)	98.1 (92.8-100.0)	92.6 (14.9)	97.4 (91.9-100.0)
2	88.1 (18.6)	98.3 (80.0-100.0)	96.5 (8.1)	99.7 (96.7-100.0)	93.3 (12.8)	99.5 (94.8-100.0)	92.3 (17.5)	99.5 (95.1-100.0)	93.3 (15.9)	99.7 (95.8-100.0)
3	90.9 (17.8)	99.9 (92.5-100.0)	94.8 (13.0)	100.0 (97.0-100.0)	93.5 (14.0)	100.0 (94.2-100.0)	93.7 (14.3)	99.5 (95.1-100.0)	94.1 (12.3)	100.0 (93.0-100.0)
4	90.3 (19.1)	98.8 (93.1-100.0)	94.8 (15.8)	99.3 (96.7-100.0)	92.6 (15.7)	99.4 (93.3-100.0)	91.9 (19.2)	100.0 (94.0-100.0)	94.3 (14.4)	100.0 (93.9-100.0)
5	91.5 (15.5)	98.1 (90.0-100.0)	95.2 (9.6)	99.3 (94.4-100.0)	92.3 (15.0)	98.6 (90.0-100.0)	94.0 (12.7)	99.3 (96.7-100.0)	94.8 (10.4)	100.0 (95.7-100.0)

Month	Respiratory		Musculoskeletal and Rheumatology		Mental Health		Endocrine		Cardiology	
6	91.0 (17.6)	98.2 (92.5-100.0)	96.8 (6.0)	99.7 (96.7-100.0)	91.5 (17.0)	98.1 (93.3-100.0)	93.6 (13.4)	100.0 (94.9-100.0)	94.9 (13.0)	99.9 (93.8-100.0)
7	90.9 (17.7)	98.5 (91.2-100.0)	96.9 (5.9)	100.0 (96.7-100.0)	90.9 (15.7)	98.0 (87.1-100.0)	93.4 (17.3)	100.0 (97.1-100.0)	97.3 (5.3)	100.0 (97.4-100.0)
8	87.4 (21.0)	97.6 (83.2-100.0)	95.9 (8.7)	100.0 (96.7-100.0)	90.9 (17.6)	99.4 (93.3-100.0)	93.1 (15.2)	100.0 (92.7-100.0)	95.8 (8.9)	100.0 (96.7-100.0)
9	86.6 (21.3)	96.7 (78.6-100.0)	97.2 (5.1)	99.4 (96.7-100.0)	91.9 (15.2)	99.3 (89.2-100.0)	93.8 (14.2)	100.0 (96.9-100.0)	96.2 (8.1)	100.0 (96.7-100.0)
10	88.2 (21.2)	97.5 (88.9-100.0)	93.5 (17.0)	100.0 (94.7-100.0)	90.4 (20.3)	100.0 (90.0-100.0)	93.4 (15.0)	100.0 (96.3-100.0)	96.1 (8.6)	100.0 (96.7-100.0)
11	88.8 (20.7)	97.5 (87.7-100.0)	93.3 (17.9)	98.8 (92.7-100.0)	90.5 (18.3)	97.5 (90.8-100.0)	93.6 (14.4)	99.0 (93.5-100.0)	93.0 (19.2)	100.0 (93.2-100.0)
12	85.3 (27.0)	96.7 (85.5-100.0)	94.7 (15.1)	100.0 (95.6-100.0)	86.3 (25.3)	98.5 (76.7-100.0)	92.7 (17.7)	100.0 (95.6-100.0)	95.2 (10.2)	100.0 (93.3-100.0)

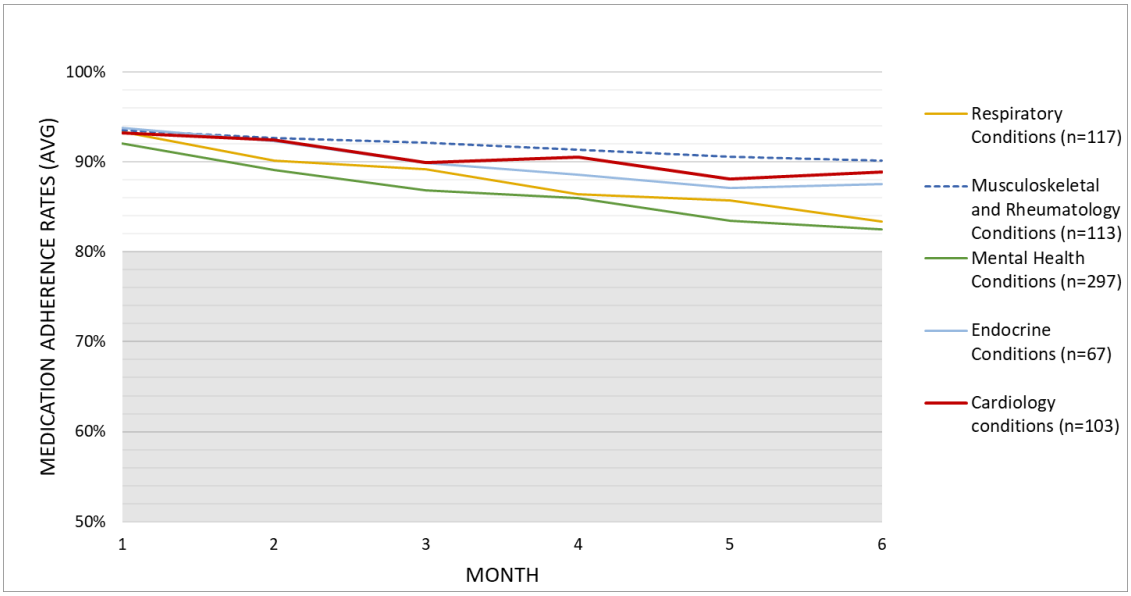
Medication adherence mean rates for patients across different timeframes.



Timeframe	Number of patients
12 months	246
9 months	207
6 months	793

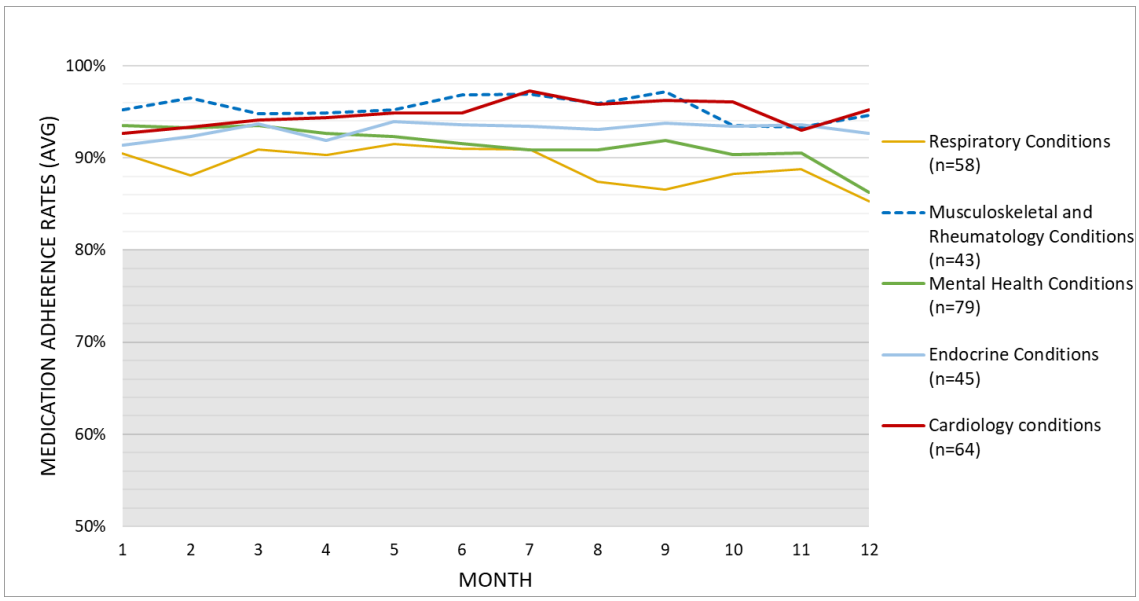
*The shadowed area represents suboptimal adherence (< 80%).

Medication adherence mean rates across different clinical conditions categories – 6-month timeframe.



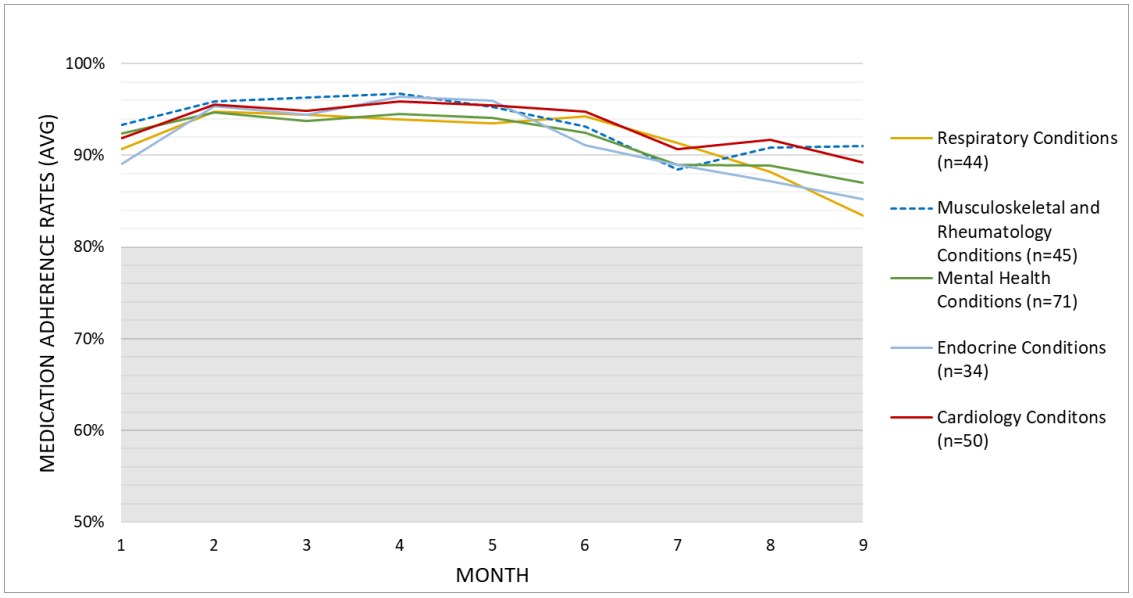
*The shadowed area represents suboptimal adherence (< 80%).

Medication adherence mean rates across different clinical conditions categories – 12 month timeframe.



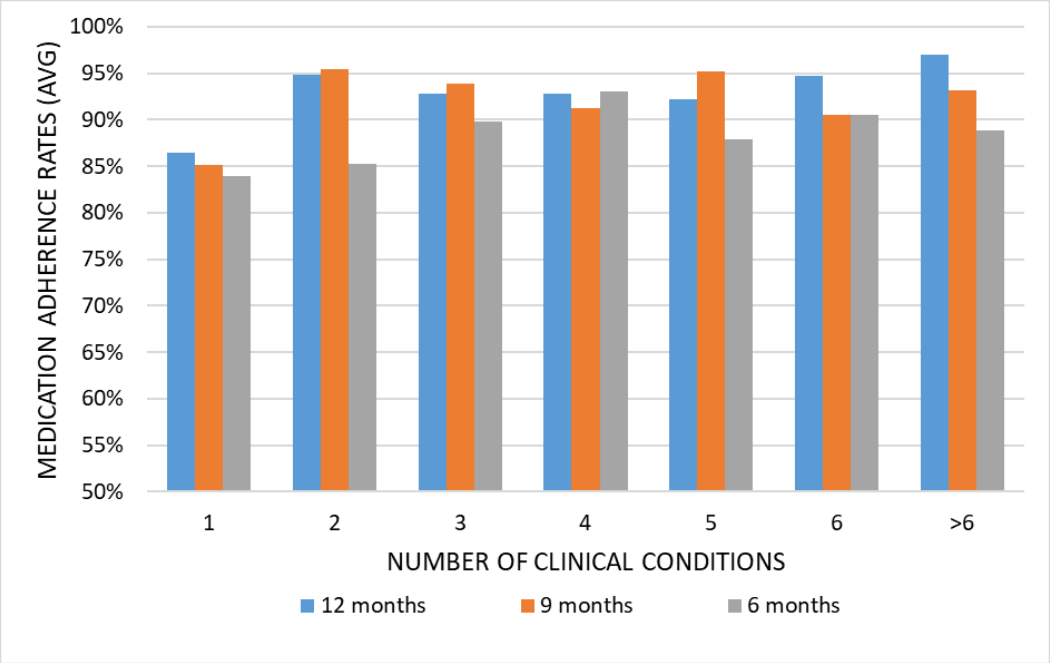
*The shadowed area represents suboptimal adherence (< 80%).

Medication adherence mean rates across different clinical conditions categories – 9 month timeframe.



*The shadowed area represents suboptimal adherence (< 80%).

Medication adherence mean rates across number of clinical conditions



Medication adherence mean rates across number of medications