Approaches to Improving Medication Adherence Prediction in Chronic Disease Patients

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Abstract— **This study aims to identify the impact of a patient's treatment/ support service duration (LOS) on the ability of a machine learning model to predict their medication adherence. The insight generated from this study can support the adaptation of patient support interventions, based on the evolution of predicted adherence at different treatment or service durations. For adherence prediction, we use medication delivery data, driven by the patient's prescription, to calculate a patient's stock level at any given time during their participation in a homecare support service, whilst allowing for medication stockpiling. This data is visualized and inputted into a Convolutional Neural Network (CNN). To evaluate adherence for a range of LOS values, every patient's first x months on service are extracted, with the final month used as the target variable. To define nonadherence, we use Proportion of Days Covered (PDC) of 100% for this period, where if a patient does not have any medication during this month they will be classed as nonadherent. Using this approach, we found that as LOS changes, there is a variation in both the proportion of the population that are adherent as well as the prediction model's performance. Across the studied timeframe of 4-12 months LOS, proportion of the study population that are adherent varies between 54.6% and 66.1%, with an Area Under the Curve (AUC) varying from 88.1% to 98.6% for our best-performing model. We also found that additional variables linked with adherence such as: communications with the service provider, demographic data, socioeconomic data and diagnosis-specific average PDC, improve model performance. The model in this study achieves its highest AUC and adherence prediction accuracy of 98.6% and 92.8% respectively, at an LOS of 9 months. Additional evaluation was performed to identify variation across therapies offered through a Homecare service. The results from this evaluation show diversity across both adherence to these therapies as well as the accuracy to be expected from the adherence predictions. We conclude that this diversity is linked to medication delivery/prescription frequency, volume of medication stock prescribed as well as therapy-specific diagnosis differences.**

Keywords- medication adherence; CNN; healthcare; homecare; adherence prediction; length of service

I. INTRODUCTION

This study builds upon our previous research on adherence prediction, with aims of optimizing the network, whilst providing further analysis on the impact service duration has on predictive performance and adherence [1]. Tailored interventions that are deployed proactively or at treatment initiation have been championed by many as an impactful approach to tackling poor medication adherence [2][3]. The ability to identify/predict patients who are likely to become nonadherent at the beginning of their treatment journey and intervening early, when they are relatively more receptive to targeted interventions, should increase the chances of preventing the deterioration of poor medication adherence behavioral patterns later. Importantly, research has shown that the dynamic prediction of nonadherence risk can allow for the efficient deployment of interventions that are known to be effective in improving adherence [2][3].

Reducing nonadherence is directly linked to more favorable health outcomes as well as reduced financial burden [4][5]. Interventions influence adherent behavior differently, based upon when the intervention takes place [6]. Putting a priority on early identification of poor adherence, in addition to adaptation of these interventions can lead to greater overall adherence and more favorable health outcomes.

This also supports a more proactive and sustainable approach to healthcare delivery. To this end, and with a view to expanding on the findings of our previous study [1], the objective of this current study was to explore the extent to which several methodological and design approaches impact on the performance of a Machine Learning (ML) model in predicting poor medication adherence in patients who are newly enrolled in a Homecare Patient Support Program. The aforementioned methodological and design approaches include: (1) exploring the dynamics of patient adherence across differing treatment duration timeframes (2) increased granularity in the novel visualization of medication delivery data (3) Patient data selection that is based on the initial period on treatment (4) incorporating additional data to map

patient characteristics, including demographic and socioeconomic data (5) implementation of therapy-specific models.

Furthermore, we examined to what extent the area under the characteristic curve (AUC) and prediction accuracy can change as more data accrues and patients spend more time in a Homecare Patient Support Program. This will allow for more rigorous evaluation of the performance level that can be expected across patients who have been on the service for varying lengths of time. This is crucial as the dynamic interaction between the many factors that drive poor medication adherence can change over time, even with the same medication and the same patient [6]-[9]. Therefore, the continuous monitoring of the changing risk of poor medication adherence in a patient is key in implementing proactive interventions that are designed to tackle negative adherence behaviors. To our knowledge, this has not been studied in detail in existing literature - although some studies have demonstrated connections between treatment duration and adherence prediction, these studies have had a somewhat limited scope [1][8][10][11].

This paper is an extension to our previously conducted study on adherence prediction [1] and is structured into the following sections. In the "Literature review" section, existing literature is reviewed for variables that have benefited adherence prediction as well as the treatment duration timeframe applied for each study. "Data and preprocessing" discusses design decisions as well as the details of our study dataset. The "Methodology" section will explain our implementation of various strategies used to achieve the study objectives. In "Results", we will present our findings based on the discussed methodology. The "Discussion" section will provide our analysis of the results. Finally, the "Conclusion" will summarize these insights, as well as provide suggestions for future research.

II. LITERATURE REVIEW

Adherence prediction using ML has been extensively studied [12][13]. In our previous work, we focused on adherence prediction model design considerations, particularly with respect to the choice of adherence metrics and the network architecture [1]. The scope of this paper is to extend upon this previous work, by exploring strategies implemented in other studies, to identify which of these strategies can further improve adherence prediction performance and accuracy. Furthermore, we sought to investigate the effectiveness of adherence prediction across a range of treatment durations for patients participating in a Homecare Support Program.

As an initial step in achieving these objectives, we reviewed published scientific literature with the aim of identifying a range of variables (e.g., demographics, treatment duration, disease burden etc.) that other studies within this field have utilized for their adherence prediction. Additionally, we reviewed the links between adherence metrics and the patient demographics they have been applied to. The most prevalent adherence metric is the Proportion of Days Covered by medication (PDC). The number following PDC denotes the percentage of days that the patient is required to have medication stock for to be deemed adherent.

Table I contains an overview of various relevant studies, showing the data that is utilized by the adherence prediction networks in each study. A patient's Length of time on Service (LOS), which is an indication of treatment duration, is considered a crucial measure in the context of our study. Additionally, a patient's LOS also influences the maximum quantity of data that is provided to the network for the patient. In other words, the longer the LOS, the more data is available. Adherence prediction is commonly applied to patients who are relatively new to their treatment, often starting from treatment naivety [8][11][14]. These studies also typically have a single LOS requirement for their patients, from which all testing is performed. As a result of this, little research has been conducted into the dynamics of patient adherence across a timeframe, or the impact of treatment duration on predictive adherence. Although, it has been shown that providing longer timeframes for naïve patient data to networks can improve performance, though this not been studied for longer treatment duration ranges [8][11].

Several studies have found that the inclusion of other types of variables other than medication delivery data, does improve predictive capabilities [14]-[16]. Findings from our previous study also support this point [1]. Most studies analyzed have included some form of patient demographics, most commonly age and gender, with performance gains or correlations with adherence being associated [13][15][17]. Similarly, a number of studies also incorporate a variable that represents the burden associated with specific diagnoses - often comorbidities, drug complexity or average PDC, with both variables having been shown to improve prediction performance or links with adherence [12][14][18][19].

Our previous work focused on predicting adherence for a patient's most recent month of service, for patients with 3-4 months LOS as well as for all patients regardless of LOS [1]. This approach allows for varied levels of patient experience with their medication from which adherence was predicted. However, this did not evaluate in detail the impact of LOS on adherence and adherence prediction. Due to the research gaps identified across our previous work as well as other studies, we are extending the scope of our previous study to address the relationship between treatment duration and adherence, as well as the further optimization of our network [1].

III. DATA AND PREPROCESSING

Patients included in our study are those diagnosed with long-term conditions and who have been receiving direct to home delivery of their medication as well as nurse support for medication self-administration at home from a clinical homecare provider (HealthNet Homecare Ltd). The study dataset contains, but is not limited to, demography, LOS, primary diagnosis, medication delivery confirmation, delivery communications and communication medium, and

Table I. Patient treatment duration and variable evaluation for adherence prediction

Author, year	Therapy Area	Patient treatment duration	Adherence metric duration	Input Variables	
				Patient demographics	Diagnosis/ medication burden
Franklin et al., 2015 [8]	Cardiovascular disease	Naïve to 3 months	PDC80 30 day	✓	✓
Lucas et al., 2017 [11]	Cardiovascular disease	Naïve to first prescription	PDC80 5 year	✓	✓
Kumamaru et al., 2018 [14]	Cardiovascular disease	Naïve to first prescription	PDC80 1 year	✓	✓
Haas et al., 2019 [20]	Fibromyalgia	Diverse	Self-reported adherence	✓	✓
Kim et al., 2019 [10]	Smoking addiction	Naïve to 4/16 weeks	Daily consumption	✓	
Galozy et al., 2020 [16]	Hypertension	2 years	PDC80 1 year	✓	✓
Gao et al., 2020 [15]	Hypertension	Various	PDC80 1 year	✓	
Koesmahargyo et al., 2020 [21]	Diverse – predominantly mental diagnoses	1-2 weeks	PDC80, 1 day and 1 week	✓	✓
Wang et al., 2020 [22]	Crohn's disease	6 months minimum, 36 months average	Self-reported adherence	✓	✓
Wu et al., 2020 [23]	Type 2 Diabetes	Diverse	PDC80 1 year	✓	
Gu et al., 2021 [24]	Diverse diagnoses	N/A - 1 Week of medication data used	Next medication consumption	✓	
Kharrazi et al., 2021 [18]	Diverse diagnoses	30-day prescription fill rate. 2 year PDC value provided	Hospitalizations same year/next year	✓	✓
Hsu et al., 2022 [25]	Cardiovascular disease	2 years observations	5 years PDC80	✓	✓
Malin et al., 2023 [1]	Diverse diagnoses – asthma, dermatitis, psoriasis and more	Up to 12 months	31 days PDC100/ PDC80		
(***Proposed work***)			31 days PDC100	✓	✓

whether the patient receives enhanced nurse support (where enhanced nurse support is used to aid medication adherence).

The calculation of every patient's medication stock follows the methodology outlined in our previous study, with every medication delivery being converted into the number of days' worth of medication it provides [1]. Whilst taking into account, and allowing for, the stockpiling of this medication before it is fully depleted, a medication stock timeline is generated for every patient from when they joined the service until the current date. Using this medication stock history for patients, time periods can be extracted and processed into visualized time-series data. This preprocessing step follows the structure laid out in our previous work [1].

Most of the design decisions selected for this study have stayed consistent with the previous work, with the continued use of a PDC requirement of 100% across one month to define adherence. This month period is kept separate from the visualized time-series data and is the target variable, representing whether the patient did or did not possess

medication every day in that month. The network architecture remains a CNN with visualized medication stock data [1].

IV. METHODOLOGY

To achieve our objectives, as well as to cover areas of existing research gaps, the impact of varying treatment durations (i.e. LOS) on predicting adherence will be focused on in this study. Additionally, due to the desire for optimizing performance from the previous work, the implementation of patient demographics and disease burden will be evaluated, as these data points have shown utility or links to adherence within other studies [14]-[16][26].

A. Medication stock granularity

As discussed in detail in our previous study, the concept of representing numerical/time-series data into the visual data domain is a common preprocessing technique that is used in signal processing for the improvement of performance, and was inspiration for this work [27][28]. In our previous study, we apply similar techniques for the novel application of visualizing delivery data. However, in this study we only utilized four colors to represent patient medication delivery and possession information within a given period - this approach will be referred to as the block medication stock approach [1]. One drawback of this approach is the resulting loss of information with respect to the specific quantity of medication that each patient has at a given time. In view of this, we sought to test a more granular approach, by using a gradient of colors to represent the range of medication stock that each patient will have. For this purpose, a gradient of colors between red and green was created which is mapped to 0-31 days of medication stock i.e. 0 days is red, 31+ days is green, and every quantity in between has a unique shade which reflects the exact quantity of medication stock. Like with the previous approach, this new approach will use the color white to represent the period before a patient receives their first delivery. This allows for heterogeneous data to be inputted into the network – in other words, allowing the model to accommodate patients with varying treatment durations.

This new strategy will be referred to as the gradient medication stock approach. Figure 1 shows the new approach in comparison to the previous approach, for two patients. The theory behind this changed approach is that the additional granularity of data in the images should provide more information to the CNN from which to learn features that constitute adherent behavior.

B. Patient data selection

In our previous study the prediction model was tested using the most recent 12 months of medication stock data for every patient in the dataset [1]. Considering our objective of predicting adherence in the patients' first 3 – 4 months on treatment, the approach from our previous study has a risk of not being reflective of patient behavioral patterns that can occur during their first few months on a treatment. Moreover,

Figure 1a) Patient A.
Top: Gradient medication stock, Bottom: Block medication stock

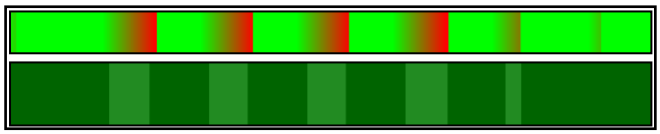

Figure 1b) Patient B.
Top: Gradient medication stock, Bottom: Block medication stock

Figure 1. Medication stock image representation comparison

training the network on the most recent 12 months of medication stock could be weighted towards longer LOS. To reduce this risk, we sought to evaluate whether the use of all patients' first 12 months on service would improve the prediction model's performance. Importantly, this new approach does not alter the testing dataset that is used, thus ensuring comparability across tests and studies. Furthermore, this change allows for features of naïve patients to be learned from when training the CNN model.

C. Treatment Duration (Length of time on service)

It is common within medication adherence studies for adherence prediction to be applied to patients who are relatively new to their treatment, often starting from a point of treatment naivety [8][11][14]. Crucially however, most studies in this area typically have a single LOS or treatment duration requirement for their study participants, from which all prediction model testing is performed [8][11][14]. To our knowledge therefore, little research has been conducted into the dynamics of patient adherence across varying treatment duration timeframe, or the impact of treatment duration on the prediction of adherence. Notably, it has been shown that providing longer timeframes of patient data, beginning from naivety, into an adherence prediction network can improve performance. However, this has not been studied for longer treatment duration ranges [8][11].

In our previous study, we focused on predicting adherence in two different patient scenarios: (1) for a patient's most recent month on a Homecare Support Program and (2) for patients with LOS of 3-4 months [1]. Although this approach allows for varied levels of patient experience with their medication to be taken into consideration when predicting adherence, it did not evaluate in detail the impact of LOS (and varying treatment durations) on adherence and adherence prediction. This is what we intend to evaluate in this study.

As previously stated, one of the major objectives of this study is to evaluate adherence across varying LOS. To achieve this, every patient has their full medication stock timeline extracted. The specific LOS (or treatment duration) that is being evaluated dictates where the patient medication stock data is cut-off. For example, if a patient has 15 months of medication data and we are evaluating adherence for an

LOS of <6 months then their first 6 months are taken and used for training; this process will occur for every patient.

This strategy ensures that every available patient is utilized, and that their data is processed in a way to capture their medication delivery and possession timeline from when they were at a specific LOS. This allows for more rigorous testing as the effective dataset size is far larger. It also allows for the use of cross-validation testing, as the whole dataset is now homogeneous with the evaluation criteria.

D. Incorporating additional patient variables

As demonstrated in our previous study, adherence prediction performance improved when additional relevant data such as enhanced service status and delivery communications are incorporated into the model [1]. Against this backdrop, we elected to identify further data variables that could potentially enhance the model performance even more. additional variables were selected on the basis of their potential to reflect patient behavior, and provided that they have already been collected as a part of our study dataset. It is important to note that the inclusion of a variable in the dataset means that such variables can either be routinely collected, in whole or in part, by virtue of a patient participating in a Homecare Support Program or that such variable can be collected/calculated from available and verifiable healthcare or population datasets.

In this study, two additional variables have been derived from data that is collected. These variables are average PDC and IMD (Index of Multiple Deprivation). The average PDC variable has been created for every diagnosis that is supported by the HealthNet Homecare Patient Support Program. For our study, diagnosis-specific average PDC has been used in our study as a proxy for disease severity. Other studies have shown correlation between the severity of disease and adherence, as well as direct links between an average PDC variable and predictive adherence performance [14][26][29].

IMD is used as another proxy for patient behavior, as several studies have shown that there is a correlation between deprivation/economic status and medication adherence [30][31].

To calculate an IMD value for each patient, the open-source IMD percentiles for the UK can be used, which correlate to specific Lower Layer Super Output Areas (LSOA) [32]. This can be mapped to partial postcode data, and the median IMD for that region is used. This gives a rough measure of deprivation for any given patient within the dataset. In addition to these derived variables, age, gender, enhanced service status and delivery communications with the patient are also evaluated due to noted benefits within other studies [1][14][15][16].

Our previous CNN tests that have implemented similar variables have visually appended this data to the images that are used for training and testing [1]. However, this approach is less feasible with more complex data, such as the average PDC and IMD, which are numeric data. To implement this data into a CNN the architecture must be modified to allow for numeric and categorical data in addition to the image-based data that has previously been utilized. To input this data, for each patient their numeric and categorical variables are processed and concatenated into the network before the final dense layer – fusing heterogeneous data into a single network, with the aim of enhancing the level of information provided by each data point. This strategy has proven effective in other domains [33][34]. However, delivery communications continue to be visually appended to the medication stock timeline image.

E. Therapy specific training

There are four separate therapies (with different indications) represented in our study dataset. The therapy areas covered by the therapies included in our study are respiratory disease, dermatology, rheumatology, and gastroenterology. The included therapies have different features associated with them, with varying quantities of medication delivered as well as differing levels of disease severity and drug complexity. Table II shows the quartiles of how much medication is delivered to a patient in one delivery cycle.

It has been shown that a patient who is supplied with more medication, more regularly is likely to have different adherence patterns to a patient who receives larger deliveries less frequently [16][35]. As the four therapies within our study dataset cover a diverse range of diagnoses as well as varied prescription size, it is likely that there will be different behaviors associated with these therapies, which we wish to identify.

Due to this level of variability between patients within the study dataset, it is worth evaluating whether the network is over-generalising to the adherent behaviours for patients of specific therapies where there is a higher proportion of samples.

To evaluate the influence of this therapy imbalance, the use of a patient's therapy to create sub-groups for training specialised models was tested. If the overall performance improves then this would indicate that there is relevant information gained through using smaller, therapy specific networks. These results will be compared to models trained on all therapies, and both methodologies will be evaluated for their therapy-specific performance as well.

Table II. Quantity of medication delivered per therapy

Therapy	Q1 Medication Stock Days	Median Medication Stock Days	Q3 Medication Stock Days	Percentage of total patients
A	56	56	56	43.4
B	28	28	84	35.9
C	56	56	56	13.5
D	56	84	84	7.2

V. RESULTS

A. Medication stock granularity

Following the methodology discussed previously, the use of gradient medication stock images have been evaluated against block medication stock images. Examples of these images can be seen in Figure 1. The results of this testing can be seen in Table III, where all results have been averaged across five runs.

The use of the new gradient methodology improves the capability of the network to generalize across both adherence and nonadherence. This is shown by a 0.9% AUC increase, and a 20.7% increase in overall accuracy. Due to this performance increase, this methodology will be utilized for all future testing and optimization.

B. Patient data selection

Initial results compare the performance of training using all patient's first 12 months of data, against the use of their most recent 12 months on the service, whilst testing on a separate 3-4 month test set, as detailed in our previous work [1]. These results can be seen in Table IV. Through using the first months of data for every patient, the AUC increases by 2.17%, and the accuracy increases by 2.70%. These results validate the use of the first months of a patient's medication stock data instead of their most recent months, when training a network to predict adherence for low LOS patients. This is likely due to the greater compatibility between patient behaviors, resulting from similar levels of naivety across the training and testing sets.

C. Treatment duration (length of time on service)

Table V shows the results of 5-fold cross-validation testing across various LOS categories for all patients. Following the 4th month, all patients should have received two deliveries, and this is when performance improves, which is corroborated in the literature where adherence prediction performance has increased following a prescription refill [8][11].

Table III. Medication supply visualization comparison

Experiment	Accuracy (%)	AUC (%)
Block medication image	54.19	82.12
Gradient medication image	74.92	82.99

Table IV. Evaluation of patient medication period used for training

Experiment	Accuracy (%)	AUC (%)
Naïve - 12 months patient data	77.62	85.16
Latest 12 months patient data	74.92	82.99

Table V. Predictive adherence comparison across a range of target months

Adherence prediction month	Accuracy (%)	AUC (%)	Adherent Population (%)
4	73.30	85.25	54.6
5	92.19	98.11	66.0
6	84.54	94.28	65.5
7	89.96	96.82	66.0
8	88.63	96.24	64.9
9	**92.63**	**98.36**	66.1
10	88.24	96.07	61.1
11	90.68	96.70	62.3
12	89.56	97.52	60.9
Average	87.75	95.48	63.0

Additionally, it is worth noting that AUC does not linearly increase as more patient medication delivery data is provided. Instead, it appears to rise and fall cyclically. This can be explained through the medication delivery cycles that correspond to specific LOS months. This is shown in Figure 2 where the mean medication delivery and possession data is plotted across the first year of treatment for all patients. The weakest performance is seen in months 4 and 6 - it is during these months that a large portion of patients receive a medication delivery. This is indicated by the rise in mean medication stock days in Figure 2, as well as from Table II showing that all patients are expected to receive a delivery during month 6 (the 3rd delivery for therapies A and B and the 2nd delivery for therapies C and D). These factors likely contribute to weaker performance, as before an expected delivery the medication stock in a patient's possession will be lowest, leading to greater uncertainty for the network.

Disparities between the balance of adherent and nonadherent patients across the LOS months can also be linked to these performance variations, as the worst AUC was seen in the model with the least adherent population, and the best AUC was reached by the model with the most adherent population.

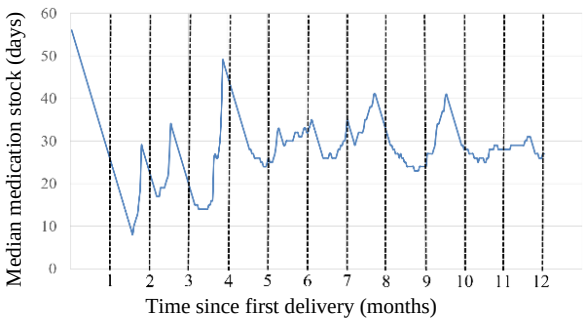

Figure 2. Median medication stock across every patient's first year of treatment

Generally, AUC improves as more patient data is supplied. This can be hypothesized to be due to patient behaviors becoming more stable as their treatment duration increases, as well as the network receiving more data with which to identify adherence patterns for patients. The best performing network was predicting the adherence for the 9th month across all patients, with 92.6% of predictions correct, with an AUC of 98.4%.

D. Incorporating additional patient variables

As shown in our previous study, and other studies, including a wide range of heterogeneous patient data can improve performance [1][21][24]. As determined by the literature review conducted, we have incorporated additional patient demographic data into the network following the trends shown in these studies. The additional data variables incorporated includes: age, gender, IMD and whether the patient receives enhanced nurse support. These variables have been grouped together under the column demographic data. The average PDC for each diagnosis is also trialed, attempting to capture the level of disease burden for each patient.

Additionally, medication delivery communications with patients have been visually appended to the medication delivery and possession images as they were previously shown to improve performance [1]. The results of this experimental testing can be seen below in Table VI. When delivery communications are incorporated there is an overall increase in AUC across most LOS months, as the networks with this variable had the highest average AUCs. This corroborates the findings in our previous study. However, most network configurations attain comparable performance, suggesting that the influence of the additional variables are not fundamental to adherence prediction, but do provide some benefit. This is most notable at 4 months, which should be the hardest predictive task due to limited prescription data [8][11], where integration of delivery communications increases both accuracy and AUC by 2-3%. As more patient data is included into the network, these performance differences diminish, but still convey utility.

E. Therapy specific training and evaluation

Correlation has been found between disease severity, drug complexity and prescription duration with respect to adherence [14][26][29][35]. All these features are directly linked to the therapy that a patient is on. As a result, we have performed tests on networks that have been trained and tested exclusively on specific therapies, using five-fold cross-validation testing. This will be referred to as the therapy specific approach, whilst the previous methodology that has been used will be referred to as the therapy agnostic approach. In this new therapy specific approach, the entire study dataset is segmented by therapy to create four smaller, therapy specific datasets, from which cross-validation testing is performed. Table VII compares the performance achieved by both approaches across the entire dataset, with therapy specific results being averaged across therapies. Additionally, Table VIII has been created which breaks down the performance per therapy. For the therapy agnostic approach, these results have been segmented by therapy after cross-validation testing was performed. The performance of therapy specific models was weaker than that found with the therapy agnostic models, but performance was closest when training and testing on the therapies with the most samples (therapies A and B). The explanation for this weaker performance is likely due to fewer training samples, which can result in overfitting. A further explanation is the difference in patient characteristics between therapies are potentially less significant than hypothesized. The therapies within our study dataset all have comparable drug complexity, which could be limiting the utility of this approach. It is plausible however, that as more data accrues for each therapy, there comes a point where the therapy specific models have enough samples to reliably outperform the agnostic models.

Despite the therapy specific models being outperformed by the therapy agnostic models, the segmentation of performance by therapy provides additional insight into the variations associated with predicting adherence for specific therapies. Patients associated with therapy D have the highest

Table VI. Predictive adherence comparison across a range of target months and incorporated variables

Variables				Maximum LOS months																		Average	
				4		5		6		7		8		9		10		11		12			
Medication supply	Delivery comms.	Disease severity	Demographic	Accuracy (%)	AUC (%)	Accuracy (%)	AUC (%)	Accuracy (%)	AUC (%)	Accuracy (%)	AUC (%)	Accuracy (%)	AUC (%)	Accuracy (%)	AUC (%)	Accuracy (%)	AUC (%)	Accuracy (%)	AUC (%)	Accuracy (%)	AUC (%)	Accuracy (%)	AUC (%)
✓				73.3	85.3	92.2	98.1	84.5	94.3	**90.0**	**96.8**	88.6	96.2	92.6	98.4	88.2	96.1	90.7	96.7	89.6	**97.5**	87.7	95.5
✓	✓			**76.3**	87.3	92.3	**98.3**	85.7	94.3	89.9	96.2	84.2	95.9	88.9	97.5	88.5	96.2	**91.7**	**97.7**	**91.7**	97.4	87.7	95.7
✓		✓	✓	73.6	85.9	92.0	98.0	84.7	93.6	89.0	96.7	88.3	96.3	92.6	98.4	88.0	96.3	89.4	97.5	90.7	97.3	87.6	95.6
✓	✓	✓	✓	76.0	**88.1**	**92.5**	98.2	**86.3**	**95.0**	89.8	96.4	**89.3**	**96.8**	**92.8**	**98.6**	**89.3**	**96.6**	86.3	95.2	90.4	97.5	**88.1**	**95.8**

Table VII. Predictive adherence comparison across a range of target months for therapy-specific and agnostic models

Experiment	Months																Average	
	4		5		6		7		8		9		10		11		12			
	Accuracy (%)	AUC (%)	Accuracy (%)	AUC (%)	Accuracy (%)	AUC (%)	Accuracy (%)	AUC (%)	Accuracy (%)	AUC (%)	Accuracy (%)	AUC (%)	Accuracy (%)	AUC (%)	Accuracy (%)	AUC (%)	Accuracy (%)	AUC (%)	Accuracy (%)	AUC (%)
Therapy agnostic	**73.3**	**85.3**	**92.2**	**98.1**	**84.5**	**94.3**	**90.0**	**96.8**	**88.6**	**96.2**	**92.6**	**98.4**	**88.2**	**96.1**	**90.7**	**96.7**	**89.6**	**97.5**	**87.7**	**95.5**
Therapy specific	68.5	76.9	88.2	94.5	78.0	87.5	84.0	90.9	85.1	90.6	87.1	87.9	82.1	86.0	87.6	93.6	87.0	93.7	83.1	89.1

Table VIII. Predictive adherence comparison across a range of target months and therapies

Months	Adherence (%)	Therapy A				Adherence (%)	Therapy B				Adherence (%)	Therapy C				Adherence (%)	Therapy D			
		Therapy agnostic		Therapy specific			Therapy agnostic		Therapy specific			Therapy agnostic		Therapy specific			Therapy agnostic		Therapy specific	
		Accuracy (%)	AUC (%)	Accuracy (%)	AUC (%)		Accuracy (%)	AUC (%)	Accuracy (%)	AUC (%)		Accuracy (%)	AUC (%)	Accuracy (%)	AUC (%)		Accuracy (%)	AUC (%)	Accuracy (%)	AUC (%)
4	**75.9**	**86.5**	71.7	81.5	**68.9**	**81.5**	62.6	75.6	71.2	78.6	**75.5**	**85.3**	**92.7**	**98.1**	72.4	79.0	**75.9**	**86.5**	71.7	81.5
5	**92.8**	**98.1**	92.0	97.7	**90.9**	**97.2**	85.9	96.1	93.1	**97.7**	85.7	85.3	**97.3**	**99.4**	88.7	83.2	**92.8**	**98.1**	92.0	97.7
6	**79.5**	90.5	76.1	**91.2**	**92.7**	**98.1**	83.1	92.7	**75.8**	**80.5**	71.7	64.9	**70.3**	**81.6**	68.7	62.2	**79.5**	90.5	76.1	**91.2**
7	**93.0**	**98.5**	85.7	94.1	**85.7**	92.6	85.1	**93.4**	**93.0**	**97.4**	89.2	89.8	**96.0**	**99.4**	93.4	86.9	**93.0**	**98.5**	85.7	94.1
8	86.6	95.2	**87.2**	**95.4**	**91.2**	**97.4**	86.5	93.7	**80.8**	**84.6**	73.0	73.7	**95.4**	**98.9**	82.0	74.9	86.6	95.2	**87.2**	**95.4**
9	91.5	**98.0**	**92.0**	97.9	**94.4**	**98.7**	86.6	90.6	**94.1**	**97.4**	84.5	84.8	**84.8**	**92.6**	79.1	85.9	91.5	**98.0**	**92.0**	97.9
10	**89.1**	**96.9**	82.8	89.4	**87.1**	**95.1**	85.4	94.3	**85.6**	**91.7**	73.4	83.1	**94.1**	**97.7**	86.2	69.7	**89.1**	**96.9**	82.8	89.4
11	89.1	96.0	**89.5**	**97.1**	**93.0**	**97.6**	92.0	97.3	**87.4**	**91.1**	79.4	63.3	**88.4**	**92.4**	78.9	66.2	89.1	96.0	**89.5**	**97.1**
12	**89.2**	**97.2**	85.9	92.0	**90.4**	**97.3**	86.3	90.3	87.0	95.7	**90.4**	**95.8**	**89.0**	**97.1**	86.0	92.5	**89.2**	**97.2**	85.9	92.0
Avg.	87.4	95.2	84.8	92.9	88.3	95.1	83.7	91.5	85.3	90.5	80.3	80.7	89.8	95.2	81.7	77.8	87.4	95.2	84.8	92.9

average accuracy of 89.8% and an AUC of 95.3% across all treatment duration timeframes. This is despite the relatively smaller number of training samples for this therapy.

Furthermore, Figure 3 has been created to demonstrate the variation in delivery cycles across therapies, providing further insight into these results. This shows that the 6th month correlates with expected deliveries for therapies A, C and D and a large portion of patients within these therapies having low medication stock at the end of month 5. This can largely explain the drop in AUC seen in month 6.

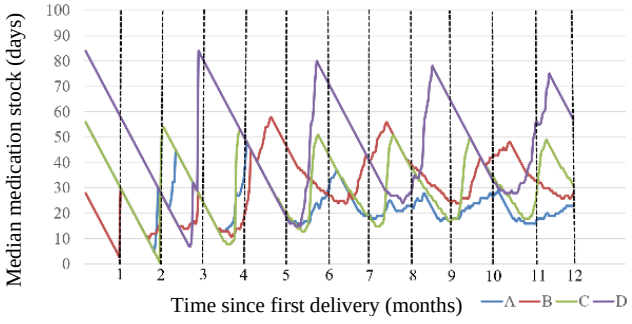

Figure 3. Median medication stock across every patient's first year of treatment per therapy

The variation in the model performance between different treatment durations and therapies indicates that there is utility in this information. Due to these distinct results attained by different therapies, using the patient LOS and their therapy can lead to more precise performance estimates in a real-world environment.

VI. Discussion

Compared to our previous study, the prediction performance for patients with a 3-4 month LOS has improved, demonstrated by the AUC which increased from 82.12% to 85.16%. This improvement was driven by the more thorough analysis in this study, varying the granularity of medication stock data as well as the timeframe of patient data used for training. In addition to this, the treatment duration timeframe that adherence is predicted for was systematically evaluated. This approach allowed for analysis into the expected performance that can be achieved for specific points in a patient's length of service.

We found that our model's performance is strongest at the 9 months LOS range, with an accuracy of 92.8% and an AUC of 98.6%. The variations in model performance observed across the different LOS's performance is likely due to the variation in medication delivery cycles, with there being significant trends in quantity of medication stock in a patient's possession with their time on service. This best-performing model utilized delivery communications, age, gender, IMD, diagnosis-specific average PDC, a variable detailing the presence of additional nurse support and the application of visualized medication possession time-series data. This corroborates with previous studies that have shown the benefit for adherence prediction when data relating to diagnosis, demographics, and communications are incorporated into the model [1][14][15][21][24]. As well as demonstrating how data can be enhanced through heterogeneity.

Additionally, through analysis into the predictions across the therapies included in this study, we found distinct differences in performance for specific therapies at certain months. This is linked to medication delivery cycle trends and can be used to further inform our level of confidence for classifications.

The results achieved in this study are crucial because tackling the issue of poor medication adherence requires the ability to accurately identify which patients have the greatest risk of poor adherence very early on in the patient's treatment journey and before negative adherence behaviors have set in or deteriorated. Needless to say, tailored interventions would be more impactful if implemented earlier, when patients are still relatively better engaged and subsequent interventions can also be amended accordingly as patients' poor adherence risks changes with the passage of time.

VII. Conclusion

This study set out to evaluate the difference in adherence prediction performance across varying patient treatment durations, as well as to optimize AUC achieved through our previous study [1]. The use of naïve patient data and more granular image data improved the AUC by 3.0% on a subset of patients with LOS between 3-4 months. Further analysis was conducted across a range of patient LOS values, finding the highest AUC reached when predicting the adherence during the 9th month, with an AUC of 98.6% We find utility in the inclusion of delivery communications, improving AUC by approximately 0.2% when compared to comparable models without this variable. Likewise, the use of demographic data improves AUC by approximately 0.1%, with our best-performing model utilizing all of these variables. Though, there is scope for further modification of the CNN architecture to process these variables, as CNNs are novel within this domain and there are many approaches that can be taken.

When gathering all results attained through 5-fold cross-validation and averaging across treatment durations, we have identified disparity between the adherence of patients, as well as the prediction results, across the therapies offered. When averaged across all studied months, there is a 5% difference in AUC between the best performing therapy and the worst, indicating therapy specific characteristics linked to adherence. Through our analysis across therapies and LOS, greater specificity can be attained with regards to expected performance for patients in real-world situations.

The ability to predict the risk of poor medication adherence offers immense value to healthcare providers and to patients. However, intervening accordingly (with the appropriate intervention delivered through the appropriate channel for each patient) in response to such predicted risk is of equal importance. To this end, an area of further study includes the prediction of how patients' preferences in terms of the type, format and channel of interventions could change over time.

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