Medication Adherence Prediction for Homecare Patients, Using Medication Delivery Data

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***Abstract*—This study aims to predict the risk of medication nonadherence for patients who are newly enrolled into a medication delivery homecare service – an insight that can underpin the design of more impactful patient support programs for patients with long term conditions. In the context of this study, we have defined a nonadherent patient as someone without any prescribed medication available across the month. This is calculated using medication delivery confirmation and prescription data. Convolutional Neural Networks (CNN) and Random Forest (RF) networks are used for this study, with the former shown to be our best-performing model, achieving an 82.8% Area Under the Curve (AUC) on a subset of the patient population who have been on service for 3 to 4 months. When testing the model on the entire patient population (regardless of how long they have been on service), and by using cross-validation, the AUC improves to 97.4%. The methodology that is applied in our study is novel based on three distinct factors: (1) prediction that is based on a novel visualization of 12 months of patient medication delivery data, (2) taking into consideration the temporal patient communications as well as the possibility of patient stockpiling of prescribed medication and (3) the service level i.e., level of nurse support received by the patient. We find that the inclusion of temporal patient communication data into our analysis improves both the AUC and the nonadherence prediction precision in the CNN model (0.7% and 19.4% respectively); a similar improvement in AUC and prediction precision is not seen in the RF model. The CNN model is therefore identified as the appropriate model for our use case. Furthermore, our results support the claim that temporal communication data are relevant datapoints for predicting adherence in a network that is better-suited to time-series data.**

Keywords- medication adherence; CNN; RF, healthcare; homecare; adherence prediction

I. INTRODUCTION

Medication adherence is a vital aspect of a patient's treatment journey, with adherence being linked to positive disease outcomes as well as lowering the burden on the healthcare provider. This is evidenced through global estimates of nonadherence causing 125,000 patient deaths per year, as well as $100 billion in preventable medical costs [1]. Machine Learning (ML) has been utilized effectively in predicting nonadherence, with the intent of providing these potentially nonadherent patients with the support necessary to keep them adherent – reducing risk to health, as well as future treatment cost [2]. It is however noted that different therapy areas and medications have different levels of burden, complexity, as well as different rates of nonadherence [3][4], and as such may require tailored interventions. In our study, the proposed use case for predicting adherent and nonadherent behavior is across a diverse range of therapy areas including, dermatology, gastroenterology, rheumatology and respiratory. The goal is to improve patient wellbeing across all therapy areas through predictive adherence, whilst acknowledging the role that a variety of clinical and non-clinical factors can play in influencing the chances that a patient will adhere to their prescribed therapy. Our study focuses on patients who are newly enrolled to the homecare delivery service.

This paper is structured into the following sections to provide insight into the work conducted. In "Background and related work", existing literature is reviewed for ML networks that have been previously used for adherence prediction, along with the data inputs and adherence metrics utilized. "Design decisions" explains why the identified approaches are most suitable for this study, along with any other modifications for our use case, "Data source and processing" delves into how these design decisions have been implemented with the data available to us. The "Methodology" section will explain our implementation of different ML models. In "Results", we will present our findings, followed by "Results comparison" to help contextualize our results against other studies. 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. Background and Related Work

The approaches for assessing and improving medication adherence differ greatly, with the main distinctions being the type of ML models that are utilized and the range of data types and/or adherence metrics incorporated into such models.

Adherence can be difficult to define, as different diagnoses have differing levels of repercussions for varying degrees of nonadherence [3][4]. However, the most used metrics for adherence tend to be the use of prescription refill data or a patient-reported adherence score, based on a questionnaire [5]–[11] . Both metrics typically use a binary label for whether a patient is adherent or not, with the prescription refill-based approach often defining a patient as adherent if they have a Proportion of Days Covered by medication (PDC) above 80% of the total predetermined timeframe [5][7][12]. However, it is important to note that this is an indirect measure of adherence, as it cannot be known whether the patient consumes their prescribed medication, only whether they have received it. The alternative patient-reported adherence score definition is typically based on a series of scored questions, and it is common for nonadherence to be defined as below 80%-85% of the maximum achievable score [6][9][10].

It is therefore the chosen adherence metric that will determine what the model will predict, i.e., whether it predicts if the patient will have medication for 80% of the next month, or whether the patient will respond positively to adherence-related questions resulting in an adherence score above 80-85%.

The initial phase of our study entailed a review of previous research within the predictive adherence space. As part of this review process, data types used by the various predictive methods are broken down into groupings. These groupings are shown in Table 1.

Table 2 compares the data inputs across various research studies along with their use case and the prediction method that was used. The most common ML architectures used for adherence prediction tend to be decision-tree (DT) based, in particular, Random Forest (RF) and other decision-tree methodologies. Other methodologies have also been previously considered such as Long Short-Term Memory (LSTM), k-Nearest Neighbor (KNN), Logistic Regression (LR), Gradient Boosting (GB) and Artificial Neural Networks (ANN). None of the reviewed studies (Table 2) use Convolutional Neural Networks (CNNs) despite how commonplace they are in other areas [13][14]. Similarly, Long Short-Term Memory (LSTM) models appear to be unpopular in adherence prediction, despite having achieved better performance than RF models in some cases [2].

One benefit of the CNN and LSTM models is that they can easily accommodate windowed time-series data to the network in a way that RF cannot, as RF is reliant upon independent feature input [14]–[16]. This results in separate features in an RF network detailing characteristics, such as adherence on specific days, as opposed to a single sequential data input [5][17]. Thus, RF networks can be used successfully, but may be inferior to LSTMs and CNNs for time-series prediction tasks. CNNs have been used successfully for time-series forecasting and prediction, outperforming LSTMs, and other models [18]–[21]. Utilizing historical medication data for the prediction of adherence is a comparable use case, and another reason for the evaluation of CNNs in this field.

TABLE I. PREDICTIVE ADHERENCE DATA INPUT GROUPINGS

Patient Profile Data	Medication Supply Data	Communications Data
Demographics	Adherence levels	Communications with medication provider
Comorbidities	Medication complexity	
Service status	Medication supply	
	Prescription details	

Table 2 shows that patient profiling and medication delivery data are often used for adherence prediction, with some studies deeming the latter as having a stronger influence on such predictions [2].

To our knowledge, little research has been done to examine the extent to which time-series data, outside of medication stock, is relevant to adherence behavior. This is where the use of patient communications data as an additional variable in predicting adherence behavior is novel, as it provides information to the model regarding a patient's level of interaction with their prescriber and/or medication delivery service provider.

III. Design Decisions

The chosen adherence metric for our study is PDC, following the trend demonstrated by other studies in Table 2. There are several additional reasons for this, including, that the PDC metric has been advocated for by various bodies (e.g., the Pharmacy Quality Alliance (PQA)) as the preferred quality indicator for estimating adherence to therapies for chronic diseases [22].

Additionally, PDC captures the number of days the medication should last, rather than the number of days the medication is in a patient's possession. Hence it makes no difference if the patient collects the medication early. This capability means the metric lends itself well to the medication delivery data used in our study, as we can calculate the number of days that each prescription should last. Importantly however, unlike most of the studies included in our initial literature review, we deem 100% of days covered as adherent, and any value less than this as nonadherent. The

TABLE II. MACHINE LEARNING MODEL EVALUATION FOR ADHERENCE PREDICTION

Author, year	**Therapy Area**	**Adherence Metric**		**Architecture**	**Input Variables**		
					Patient Profile	**Medication Supply Data**	**Communications**
Franklin et al., 2015 [23]	Cardiovascular disease	Binary	>PDC 80 – Medication Dispensation Date	Group trajectory modelling	✓	✓	
Lucas et al., 2017 [24]	Cardiovascular disease	Binary	>PDC 80 – Medication Prescription Date	RF	✓	✓	
Kumamaru et al., 2018 [12]	Cardiovascular disease	Binary	>PDC 80 – Medication Dispensation Date	LR	✓	✓	
Haas et al., 2019 [6]	Fibromyalgia	Binary	Self-reported	RF	✓	✓	
Kim et al., 2019 [9]	Smoking addiction	Binary/ Tertiary	Patient estimated adherence	DT	✓	✓	
Galozy et al., 2020 [5]	Hypertension	Binary	>80% PDC – Medication Refill Date	RF, LR, GB, KNN	✓	✓	
Gao et al., 2020 [25]	Hypertension	Binary	>PDC 80 – Medication Prescription Date	DT	✓	✓	
Koesmahargyo et al., 2020 [17]	Diverse – predominantly mental diagnoses	Binary	>80% Recommended Daily Medication Consumption	GB	✓	✓	
Wang et al., 2020 [10]	Crohn's disease	Binary	Self-reported	SVM, LR	✓		
Wu et al., 2020 [11]	Type 2 Diabetes	Binary	>PDC 80 – Medication Prescription Date	SVM, KNN, DT, Ensemble	✓	✓	
Gu et al., 2021 [2]	Diverse diagnoses	Binary	Medicine taken on time	LSTM, RF, GB		✓	
Kharrazi et al., 2021 [8]	Diverse diagnoses	NA – predicting hospitalizations		LR	✓	✓	
Li et al., 2021 [26]	Hypertension	Binary	Medicine taken on time	LR, DT, ANN, RF	✓		
Hsu et al., 2022 [7]	Cardiovascular disease	Binary	>80% PDC – Dispensation Date	LSTM		✓	
(This Work, 2023)	Diverse diagnoses – asthma, dermatitis, psoriasis and more	Binary	100% PDC – Medication Delivery Date, >80% PDC – Medication Delivery Date	CNN	✓	✓	✓

motivation behind adopting this strict approach is the diversity of therapies prescribed to the patients included in our study and the variability in the ways that nonadherence can affect different patients and diagnoses [4][27].

The medication delivery frequency and stock level for the patients included in our study is driven by the patient's prescription and provides the recommended quantity of days of medication. It is important however, to note that patients who have their medications delivered direct to home can request more than their usual level of stock (for example just before a holiday), leading to a deviation in their standard delivery frequency. This behavior is commonplace for patients with a chronic disease [28][29]. It is therefore necessary to consider whether a patient has previously 'stockpiled' medication before they are deemed as nonadherent for failing to take delivery of their medication. While there are medication adherence studies based on prescription dispensing dates, to the best of our knowledge, ours is the first study predicting adherence using medication delivery confirmation data and taking into consideration the potential of stockpiling [23][19].

IV. DATA SOURCE 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 dataset contains, but is not limited to, demography, length of time on homecare service (LOS), primary diagnosis, medication delivery confirmation, nurse visit confirmation and whether the patient receives enhanced nurse support. Such enhanced nurse support is used to aid medication adherence.

Patients are excluded if they have finished their treatment, or if they have not had a medication delivery within the last 13 months. The medication delivery confirmation data contains the date-time at which each patient receives their medication, as well as the number of days that the delivered medication covers them for. Thus, any periods where the recommended medication delivery frequency is insufficient can be calculated. Additionally, periods where the patient received additional (i.e., extra) deliveries are accounted for, allowing for medication stockpiling, which is common in chronic disease management [29].

The medication delivery confirmation across each patient's latest month is calculated, and any period with a lapse of medication delivery confirmation frequency in this time period designates that patient as nonadherent. This label is used as the target variable for the model. The medication delivery confirmation data over the 12 months prior to the target variable month is used for model training and inference, as with this it is possible to determine whether the model accurately predicts nonadherence in the target variable month.

Figure 1 shows how the 12 months of medication delivery confirmation is visualized, with the horizontal axis representing time. The left-most point on the axis representing 13 months before the most recent dataset entry, and the right-most point representing one month before the most recent dataset entry – providing 12 months of patient medication timeline data. These areas are then colored based on the medication stock quantity that the patient should have on each day within this time period, and this representation can be seen in Figure 1a. Dark green represents sufficient medication stock of >31, light green is sufficient stock for 5-31 days, yellow is for 1-5 days, and red means the patient is not in possession of any medication stock. In instances where the patient has been on the service for less than 13 months, the period prior to beginning their treatment is color coded as white.

Additional information can also be encoded into these images, in the form of delivery communications and the patient's enhanced nursing support service status, merging temporal and non-temporal data into a single sample. This is illustrated in Figures 1b and 1c, where these data visualizations show different encoded information for the same patient.

Figure 1b represents a patient's enhanced service status as a solid line across the 12-month period, the color of which is blue for receiving enhanced services and black for not receiving enhanced services (not shown). Figure 1c encodes all delivery communications as colored dots, with the features of the dot representing the type of communication. The color and outline of the dots varies to reflect the medium used for communication as well as whether the communication was inbound or outbound. Thus, creating a unique color scheme for each communication type across our dataset. Where multiple communications occur on the same day, the subsequent dots are placed below the previous communications in chronological order.

V. METHODOLOGY

We implemented both RF and CNN models in this study. The RF network is intended to be used as a benchmark, due to its ubiquity for adherence prediction across other studies. The CNN on the other hand, was chosen given its capabilities in time-series prediction, as well as our desire to test its feasibility in adherence prediction whilst utilizing images produced with heterogeneous data [18][20].

Other studies have shown that CNNs can be effectively used on visually represented data that has been generated from both time-series data and tabular data, outperforming the use of the raw numerical data [18][19].

The approach 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 [30][31]. Taking inspiration from this domain and translating it to time-series patient data requires novel preprocessing, as techniques that are common in signal processing are incompatible with our data, such as Gramian Angular Summation/Difference Fields, Markov Transition Fields and spectrograms [30]–[32]. These images are automatically generated in a deterministic manner for each patient, using their medication stock level over time. Implementing a deep CNN architecture, Inception v3, on these data visualizations is straightforward and has the potential to learn features that the RF model cannot.

Each experiment is performed five times to reduce the influence of different random initializations. Additionally, 5-fold cross validation tests have been performed when there is

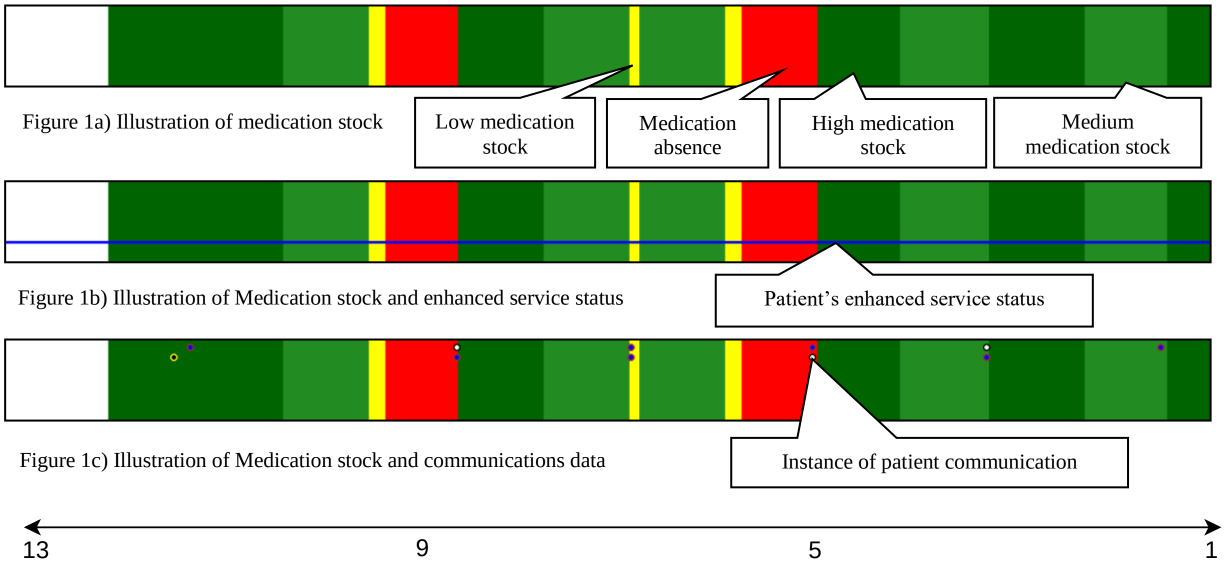

Figure 1 Patient timeline images

no predetermined test set – iterating through which patients are included into the training and testing sets. This validation strategy is commonplace for adherence prediction [7][24]. CNN training was performed using 50 epochs per run with the Adam optimizer.

Additionally, undersampling was trialed for every test, due to the imbalance between the majority and minority class. When undersampling yielded the best result this has been stated. Undersampling is the process of data reduction to distribute the data quantity between two classes more evenly, with the aim of reducing the likelihood of misclassifying the minority class [33]. In our case, this will refer to removal of adherent samples, which comprise approximately 80% of all samples. Multiple studies have successfully used this balancing technique to improve their performance [5][26]. Oversampling is another technique that could be utilized for reducing class imbalance and has been used for adherence prediction previously, though it is out of scope for this study [26].

VI. MODEL RESULTS

Initial comparative testing was conducted using both RF and CNN architectures. These tests were performed using the entire patient population data (i.e., regardless of how long they have been on the homecare service), using 5-fold cross-validation to determine which patients comprise the test set. For the RF network, each patient's data is inputted as 365 features with each feature containing the number of days' worth of medication stock they should have in their possession. When delivery communications data is utilized, these features are inputted using one-hot encoding to the network, with a feature for each day. The enhanced services feature is a single feature that denotes a binary variable. The data input for the CNN is image-based and Figure 1 is representative of the data variants used for this test. These results can be seen below in Table 3. The RF network attains comparable AUC, but with superior nonadherent precision. Additionally, the CNN attains its best performance through the inclusion of delivery communications data and enhanced service status information, unlike the RF which peaks with just medication delivery confirmation data and enhanced service status information. This could be due to the RF network's inability to process time-dependencies across features, unlike a CNN where our inclusion of delivery communications marginally improves AUC but provides a significant gain to nonadherent precision.

However, the primary objective of this study is to predict the risk of non-adherence for patients who are new to the homecare delivery service. The main reason behind this is that we wish to identify potential nonadherence before it occurs, so that targeted interventions can be initiated. As well as the need to make accurate predictions for patients without requiring them to have been on the service for a long time – during which they may have benefited from greater support.

To achieve this primary objective, a test set was created exclusively of patients within the first 3-4 months Length Of Service (LOS) range. Patients with an LOS under 3 months are excluded due to there being limited data for each patient, after the removal of one month for use as the target variable. None of the same patients/patient data were included in both the training and testing data sets. The training set uses data from patients who had joined the service earlier than (i.e., before) the patients whose data was used for testing. This allows for training samples that are comparable to the testing samples, in terms of LOS, without the inclusion of testing data. Once again, both RF and CNN model architectures were implemented in order to identify the optimal network as well as the optimal data. These results can be seen below in Table 4.

TABLE III. CNN AND RF PRELIMINARY DATA INPUT EVALUATION

Medication Availability	Enhanced Services	Delivery Communications	Mean AUC		Mean Nonadherent Precision	
			RF	CNN	RF	CNN
✓			95.36%	95.70%	88.64%	80.02%
✓	✓		95.40%	95.14%	88.49%	81.31%
✓		✓	94.90%	96.26%	88.13%	87.69%
✓	✓	✓	94.92%	97.40%	88.53%	90.10%

Testing on the predetermined set of patients with 3-4 months LOS results in a substantial decrease in performance, compared to testing against the full population. However, for this use-case, the CNN, compared to the RF model, provides better AUC and nonadherent prediction precision. As is the case when the model utilized the entire patient population data, the CNN with the highest AUC incorporates both enhanced service status data and delivery communications data, whilst the best RF model does not use delivery communications data.

VII. RESULTS COMPARISON

For greater comparability with other studies, a PDC of 80% was used in addition to a PDC of 100%, as this is the most common medication availability adherence measure [8][9][14]. Additionally, 5-fold cross-validation was used to evaluate the dataset – with each patient's sample providing 12 months of data. These results can be seen below in Table 5, where our best-performing CNN and RF models are shown. However, the other studies shown in this table do not define medication availability through delivery data, instead this data is provided through in-person prescription refills. Additionally, the other studies have not factored in medication stockpiling which will impact the adherence dynamics. These distinctions, along with the fact that alternative cohorts of patients likely have different demographics and behaviors, do separate the studies from one another. However, comparisons between the studies can be drawn with these caveats, to compare the use of differing data inputs.

The model with the best AUC in our tests was an undersampled CNN which made predictions by utilizing medication delivery confirmation data, enhanced services status information, and delivery communications data, all formatted into an image, as shown in Figure 1. This model attained the highest AUC when predicting both, whether a patient would have a PDC>80% or PDC of 100% in their latest month. The CNN benefited from the use of random undersampling, whereas the RF network performed worse when undersampled. Additionally, the RF network shown in Table 5 does not utilize delivery communications as this data input led to an AUC reduction.

VIII. DISCUSSION

We investigated various methodologies for predicting nonadherence of patients, across both CNN and RF networks. The methods trialed incorporated differing levels of medication delivery confirmation data, timestamped patient communications and a binary variable representing the level of service that a patient receives. This testing was done on a predefined test set of patients with LOS ranging from 3-4 months, in line with the overarching project objective. It was found that the best-performing model utilized all the available encoded data, giving an AUC of 82.8%, with a PDC requirement of 100%. For the CNN, the greatest performance improvements were attained through the inclusion of both the enhanced services status data, as well as the delivery communications data – in addition to medication delivery confirmation data. These features, when encoded into the images, improved AUC by 0.7% and nonadherent prediction precision by 19.4% from the model without these features, thus supporting the claim that these are relevant datapoints for predicting nonadherence. The RF network attained its best performance without the inclusion of delivery communications data, likely due to RF networks being unable to process time-dependencies across features.

TABLE IV. CNN AND RF 3-4 MONTH LOS TEST SET EVALUATION

Medication Supply	Enhanced Services	Delivery Communications	Mean AUC		Mean Nonadherent Precision	
			RF	CNN	RF	CNN
✓			55.44%	82.12%	38.74%	19.13%
✓	✓		53.64%	68.49%	37.81%	80.33%
✓		✓	54.47%	80.05%	37.01%	40.07%
✓	✓	✓	54.81%	82.84%	37.99%	38.54%

TABLE V. PREDICTIVE ADHERENCE COMPARISON USING PDC

Author, year	Adherence Metric	Input Variables			Validation strategy	AUC	Training Samples	Test Samples
		Patient Profile	Medication Availability Data	Communications				
Lucas et al., 2017 [24]	PDC >80%	✓	✓		30-fold cross-validation	73.60% - 81.00%	134,107	4,624
Kumamaru et al., 2018 [12]	PDC >80%	✓	✓		Logistic Regression	Up to 69.60%	49,745	49,745
Galozy et al., 2020 [5]	PDC >80%	✓	✓		Stratified random split *(undersampled)*	80.30% - 80.70%	15,794	2,787
Gao et al., 2020 [25]	PDC >80%	✓	✓		10-fold random seed	81.00%	5,730	1,908
Wu et al., 2020 [11]	PDC >80%	✓	✓		10-fold random seed	57.70% - 86.60%	401	40
Hsu et al., 2022 [7]	PDC >80%		✓		5-fold cross-validation *(predetermined test set)*	80.50%	90,000	10,096
(This work, 2023)	PDC >80% CNN	✓	✓	✓	5-fold cross-validation *(undersampled)*	97.89%	5,359	1,972
(This work, 2023)	PDC >80% RF		✓		5-fold cross-validation	95.37%	22,596	5,649
(This work, 2023)	PDC = 100% CNN	✓	✓	✓	5-fold cross-validation *(undersampled)*	97.40%	6,338	3,142
(This work, 2023)	PDC = 100% RF	✓	✓		5-fold cross-validation	95.40%	22,596	5,649

When migrating this methodology to testing on the entire patient population (i.e., regardless of how long they have been on service), using 5-fold cross-validation, the AUC increases to 97.4% with a nonadherence prediction precision of 90.1% for the CNN; the RF network attained an AUC of 95.4% and a nonadherent prediction precision of 88.5%. This performance difference signifies that nonadherence prediction is more challenging on patients with lower LOS, this could be explained through different behavior for new patients, as well as the reduction in data quantity. Whilst nonadherence prediction for new patients is our primary focus, performance across the full dataset is still relevant, as it is also important to be able to identify any patients across the cohort who may subsequently become nonadherent and would benefit from ongoing additional support.

When the PDC requirement is lowered to 80%, the AUC of the CNN improves marginally to 97.9% with a nonadherence precision of 87.3%. Whilst the RF network attains the same AUC and a marginal nonadherence precision improvement to 88.6%. These results are more comparable to those found in other studies due to the same PDC requirements being used.

The results of this study, particularly when considered in the context of other similar studies, highlights the need for further research with respect to clearer impact of patient demographics and behavioral patterns on adherence prediction. We acknowledge that the demographics and behaviors of the patients included in all the studies reviewed, and our study, may differ. Similarly, we acknowledge that our study may differ from the other studies that were reviewed, in terms of differing patient diagnosis and their use of a less strict PDC metric.

Our design decision to consider the use of medication stockpiling for our calculation of medication availability is an approach that was rarely seen in other studies and so should be considered when comparing the results. Importantly however, due to the prevalence of medication stockpiling within chronic disease patients, we believe this methodology is more suitable for defining adherence and adds value to this study [29].

IX. CONCLUSION

This study set out to predict nonadherence for patients that are new to a homecare delivery service, where new patients were defined as having been on the service between 3 and 4 months. Our best-performing model achieved an AUC of 82.8% when predicting whether these patients would run out of medication in the next month (by failing to confirm the delivery of their prescribed medication). When adapting this methodology to predict nonadherence for the full cohort of patients within the dataset (using a PDC of 80%, so that more comparable evaluation against other studies could be made), an AUC of 97.9% was achieved. Both CNN and RF networks were evaluated for their capability at this task. The CNN tests were conducted using a novel form of data encoding, producing visually represented medication stock timelines for patients with various additional information encoded within them. This outperformed the RF network by 2% AUC. The results have also shown a performance gain through the inclusion of temporal communication information into the network in addition to medication delivery confirmation data.

Future work by the authors includes additional visualization approaches for the benefit of clinicians, as well as testing these visualizations for adherence prediction. Additionally, more comprehensive experimental testing using a PDC of 80% and cross-validation as well as different strategies for further encoding the temporal delivery communications data within the RF network will be explored. Finally, the use of data oversampling instead of undersampling is a technique that has the potential to further improve performance whilst mitigating class imbalance and would be worth evaluating.

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