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An Artificial Neural Network Classification of Prescription Nonadherence

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ABSTRACT

This study investigates the use of artificial neural networks (ANNs) to classify reasons for medication nonadherence. A survey method is used to collect individual reasons for nonadherence to treatment plans. Seven reasons for nonadherence are identified from the survey. ANNs using backpropagation learning are trained and validated to produce a nonadherence classification model. Most patients identified multiple reasons for nonadherence. The ANN models were able to accurately predict almost 63 percent of the reasons identified for each patient. After removal of two highly common nonadherence reasons, new ANN models are able to identify 73 percent of the remaining nonadherence reasons. ANN models of nonadherence are validated as a reliable medical informatics tool for assisting healthcare providers in identifying the most likely reasons for treatment nonadherence. Physicians may use the identified nonadherence reasons to help overcome the causes of nonadherence for each patient.

KEYWORDS

Artificial Neural Network (ANN), Backpropagation, Drug, EHR, Medication, Medicine, Nigeria, Nonadherence, Pharmaceutical, Prescription

INTRODUCTION

Prescription (pharmaceutical) treatment plans require a specific pharmaceutical drug to be taken in specific amounts at specific intervals for a specific period of time. Nonadherence is the violation of any of these specified treatment requirements: not taking the correct dosage (too little or too much), missing or delaying scheduled administrations of the pharmaceutical, or not completing the treatment (Hugtenburg et al., 2013). Nonadherence to pharmaceutical treatment plans is a worldwide dilemma and prior research results examining the rate of nonadherence in 20 countries are shown in Table 1. As may be seen, documented nonadherence rates vary in different cultures, but range from 10% to 88%. Prescription nonadherence is a persistent problem in healthcare today (Lehane & McCarthy, 2007) and nonadherence through underuse of a medication is rising significantly in prevalence (Kirking et al., 2006).

Nonadherence, especially to antibiotics and antimalarials, causes increased risks to the population by enabling evolution of resistant strains of malaria and other diseases (Andrajati et al., 2016; Awad & Eltayeb, 2007; Okuboyejo, 2014; Pechère, 2001) and harms population health by promoting further spread of diseases due to resulting ineffective treatment (Andrajati et al., 2016; Awad & Eltayeb, 2007; Center for Disease Control, 2013; Gibson et al., 2011; Okuboyejo & Eyesan, 2014). The Center for Disease Control states that pharmaceutical treatment nonadherence leads to significant economic and well-being impacts with direct costs estimated at $289 billion annually and 125,000 deaths annually (Center for Disease Control, 2013).

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Table 1. Documented nonadherence rates from around the world

Country	Nonadherence rates	Reference
Australia/New Zealand	16.4%	(Hirth et al., 2012)
Belgium	12% 18%	(Hirth et al., 2012) (Pechère, 2001)
Canada	15%	(Hirth et al., 2012)
China	57-64%	(Zhu et al., 2016)
Columbia	41%	(Pechère, 2001)
France	12.3% 18%	(Hirth et al., 2012) (Pechère, 2001)
Germany	12.9%	(Hirth et al., 2012)
India	17%	(Agarwal, Yewale, & Dharmapalan, 2015)
Indonesia	43%	(Andrajati et al., 2016)
Italy	13.1% 35%	(Hirth et al., 2012) (Pechère, 2001)
Japan	10.9%	(Hirth et al., 2012)
Malaysia	29%	(Agarwal, Yewale, & Dharmapalan, 2015)
Morocco	38%	(Pechère, 2001)
Spain	12.7% 45%	(Hirth et al., 2012) (Pechère, 2001)
Sweden	11.8%	(Hirth et al., 2012)
Thailand	47%	(Pechère, 2001)
Turkey	30%	(Pechère, 2001)
United Kingdom	10% 13.2%	(Pechère, 2001) (Hirth et al., 2012)
United States	7% - 45% 18% 20 – 80% 38% 45% – 88% 50% 56.2%	(Kirking et al., 2006) (Hirth et al., 2012) (Gottlieb, 2000) (Au et al., 2014) (Gamble, 2009) (Buckalew & Sallis, 1986; Wapner, 2008) (Gibson et al., 2011)
Worldwide	0% - 95.4%	(DiMatteo, 2004)

Reasons for patient nonadherence with the pharmaceutical portion of their treatment plans vary. Self-medication is a rising worldwide problem (Agarwal, Yewale, & Dharmapalan, 2015) especially in regions of the world where antibiotics and other medications are available without prescription, and has been identified as a contributing factor to improper treatment including nonadherence to recommended treatment plans (Awad & Eltayeb, 2007; Grigoryan et al., 2006; Zhu et al., 2016). Other reasons for pharmaceutical nonadherence are: cost of medication (Center for Disease Control, 2013; Gibson et al., 2011; Hirth et al., 2012; Kirking et al., 2006), negative attitude toward drug or don't like taking drugs (Kirking et al., 2006; Okuboyejo, 2014; Urquhart, 2005), lack of time/employment/travel (Au et L., 2014; Okuboyejo, 2014), don't trust or other issues with physician (Okuboyejo, 2014, Zhu et al., 2016), lack of (Kirking et al., 2006; Urquhart, 2005), forgetfulness (Au et al., 2014), religious

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or cultural reasons (Urquhart, 2005), fear of side effects (Gottlieb, 2000; Kirking et al., 2006), and other personal reasons (Urquhart, 2005). It is important to note that each patient may have multiple reasons for being nonadherent (Okuboyejo, 2014; Urquhart, 2005).

Various methods have been proposed to lessen nonadherence, including: better physician-patient communication (Agarwal, Yewale, & Dharmapalan, 2015; Buckalew & Sallis, 1986; Okuboyejo, 2014), other patient education (Oyelami, Okuboyejo, & Ebiye, 2013), and sending automatic reminders (Eyesan & Okuboyejo, 2013; Okuboyejo, Omoregbe, & Mbarika, 2012). Each of these proposed solutions is generic for a whole population of patients and typically addresses only a single reason for nonadherence. Identifying an individual patient's specific reasons for nonadherence would enable tailored individualized responses to address the reasons for nonadherence relevant to each patient. An artificial neural network (ANN) informatics tool to predict the nonadherence reasons for individual patients is developed based on Social Learning Theory. The ANN is tested for predicting individual nonadherence reasons on a population of patients in Nigeria.

BACKGROUND

Brief Background on Artificial Neural Networks

ANNs are nonparametric machine learning systems inspired by the human brain and composed of processing elements arranged in layers and highly interconnected (see Figure 1) (Caudill, 1987). Each connection is initially assigned a randomized value or weight. Input layer nodes receive raw numeric values representing the independent variables. Additional processing nodes are arranged into some number of hidden processing layers and finally an output layer, which represents the dependent variable(s). All hidden and output nodes receive the aggregation of the product of the incoming nodes and the associated connection weights, thus if summation is used as the aggregation function then a node's input value is equal to $\Sigma\, w_{ij} x_i$, where w_{ij} is the weight on the connection from node i to node j, coming from node x_i. Each processing element performs its own computation on this input value, known as a transfer function, before transmitting it along its outbound connections. Transfer and aggregation functions may be any function defined by the user, such as sum or average or maximum for the aggregation function and sigmoid or a hyperbolic tangent function for the transfer function.

The backpropagation learning algorithm, learns by propagating the error term of the output produced by a given set of input against the known values backwards through the network to adjust the connection weights. Backpropagation is known as a supervised learning system since it requires training records with known outcomes in order to calculate the correct output error.

One advantage of ANNs over other modeling paradigms is that since they are nonparametric they may work with any type of numeric input values and those values have no constraints as in other statistical models, such as requiring normal distribution or heteroskedastic error. Translating data into numeric representations for use in an ANN is easy to perform, such as representing a categorical variable with a corresponding number of input variables (one for each category) that are set to true or false. Second, since ANNs are learning systems, they are able to find optimal solution surfaces to model the given training data. This includes complex nonlinear solution surfaces. Additionally, once trained, ANNs are highly tolerant of noise in future input data. Disadvantages are that ANNs are sensitive to the independent variables selected, which must not be highly correlated, and the number of nodes in each hidden layer, which can cause poor out of sample performance due to memorization (Smith, 1993; Walczak & Cerpa, 1999). These disadvantages may be overcome by first testing desired independent variables with a correlation test, such as Pearson's Correlation Matrix, and by developing and testing multiple hidden node and layer architectures to find the optimal quantity of layers and processing nodes.

A more detailed explanation of ANNs is beyond the scope of this paper. Many tutorials exist and readers are encouraged to pursue these for additional explanation (see (Jain, Mao, & Mohiuddin, 1996; Rodvold, McLeod, & Brandt, 2001; Walczak & Cerpa, 1999; Zhang, 2007) for examples, guidelines, and further information on ANN development).

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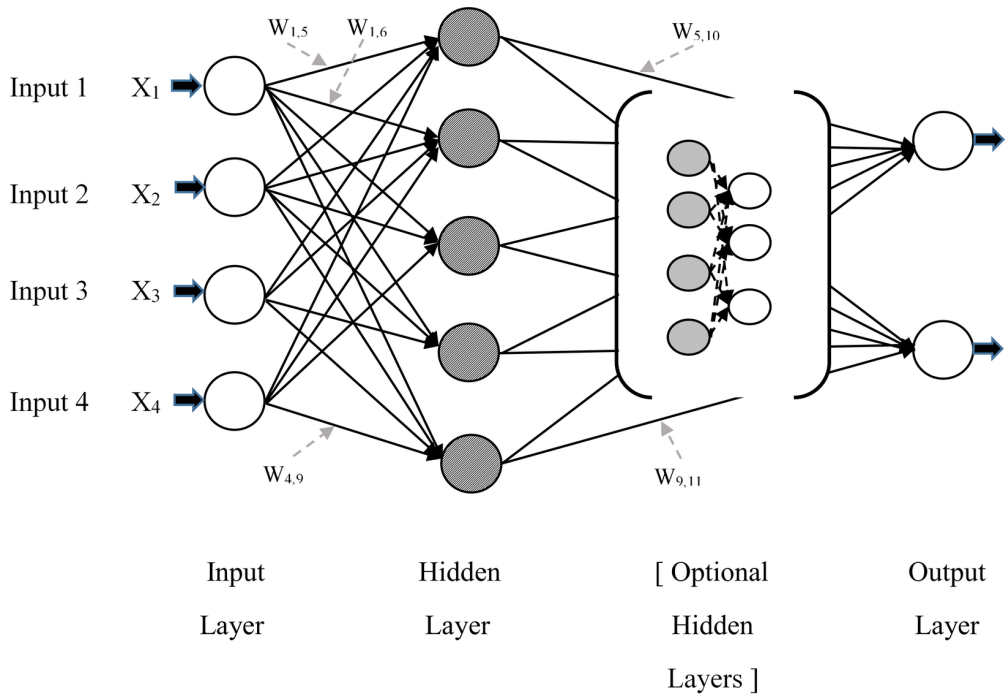
Figure 1. Artificial neural network architecture (only a few connection weights shown for clarity)



Prescription Nonadherence Research

As shown in Table 1, research on prescription nonadherence has been conducted that examines populations from around the world for at least the last sixty years (DiMatteo, 2004). Most of the reported research consists of empirical studies on specific populations for a single or small set of medical reasons (DiMatteo, 2004). Different theoretical models commonly used in prescription nonadherence research include: the Health Belief Model, Social Learning Theory, Theory of Planned Behavior, and the Transtheoretical Model (Bowen, Helmes, & Lease, 2001; DiMatteo & Martin, 2002).

Prescription nonadherence research uses multiple direct and indirect methods in evaluating nonadherence (Farmer, 1999). Indirect methods include patient self-reporting and pill counting. The research reported in this article uses self-reporting. Direct methods involve urine or blood tests to detect the presence of the desired amount of the prescribed pharmaceutical.

Despite the plethora of research on prescription nonadherence, results have not been either cost effective or clinically effective in reducing nonadherence (Lehane & McCarthy, 2007). Several systematic studies have been performed over this large body of existing literature (DiMatteo, 2004; Hayes et al., 2002; McDonald, Garg, & Haynes, 2002) and commonly classify reasons for nonadherence as either intentional factors including physician-patient communication or unintentional factors such as forgetfulness (Lehane & McCarthy, 2007).

METHOD

Population and Data Collection

A survey based on Akers (1977) Social Learning Theory is designed using prior surveys examining pharmaceutical treatment nonadherence in Africa (Ekwunife, Udeogaranya, & Adibe, 2010; Erah & Arute, 2008; Ikechuwku, Obinna, & Ogochukwu, 2010; Uzochukwu et al., 2009). The survey

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contained five demographic questions (age, sex, marital status, education level, and payer) and 25 questions covering intentional and unintentional reasons for being nonadherent.

After obtaining informed consent and guaranteeing anonymity, the survey is given to 600 outpatients from university and government hospitals and clinics in southwest Nigeria who were taking any type of pharmaceutical as part of their prescribed treatment. A total of 474 responses are returned for a response rate of almost 79 percent.

Data Preparation and Independent Variable Definition

The anonymized raw data is then transcribed into a spreadsheet format for analysis and preparation to further format the data for the ANN. Ten of the responses are discarded because the respondents indicated they were not currently on a pharmaceutical treatment plan. Since respondents were instructed that they didn't have to answer any question which made them feel uncomfortable, numerous responses were missing values. Whether the missing values are due to discomfort or other reasons including laziness is unknown. Further preparation of the response data for use by the ANNs eliminates responses with too many missing values (Cherkassky & Lari-Najafi, 1992), leaving a total of 237 usable responses. The usable responses are divided into a training set of 137 responses and a validation set or hold-out sample of 100 responses. Three-fold cross validation is used to enable each response to serve as both a training and validation sample, but for different training instances of each ANN. The validation samples are never seen during the ANN training and can thus simulate real-world usage of the ANN for predicting individual patient reasons for nonadherence. Each response is only counted as a validation item a single time.

The survey specifies 23 specific reasons for nonadherence behavior and respondents are able to select as many as apply to them. These 23 individual reasons are further classified into seven distinct classifications of reasons for nonadherence which are: a lack of understanding or education, issues with the doctor (e.g., distrust or dislike), cost of the medication, religious objections, concern over side effects, lack of time or other time issues, and other personal reasons. Lack of understanding or education, time issues, and other personal reasons fall under unintentional reasons, while the remaining four categories of nonadherence reasons are intentional. These seven categories serve as output variables for the ANN.

ANN Design and Development

The demographic variables age, marital status, sex, education, and primary source of payment (self, family, work, insurance, charity, other) and 25 additional variables representing observational learning, differential association, differential reinforcement, medication adherence self-efficacy, outcome expectations, and personal attitudes towards adherence that are proposed influences on adherent behavior, as displayed in Figure 2. This creates a 34 variable input vector, since some of the demographic variables are treated as categorical variables.

Various training methods including radial basis function (RBF), traditional backpropagation or multi-layer perceptron, and backpropagation with two-layer forward connections are evaluated for classifying nonadherence reasons. The backpropagation with forward connections outperformed the other two learning methods and is the only one discussed for the remainder of this article. Backpropagation is the most common learning and training method used in ANNs and because of its robustness and ease of implementation and enabling easier comparison with future ANN research in nonadherence (Given, Given, & Simoni, 1978). Both single and two hidden layer architectures are investigated. The single layer architectures performed at least as well as the two hidden layer architectures and for simplicity (reducing the total number of connections in the ANN), the single hidden layer models were selected as the best performing architecture. The best performing ANN architecture had 34 input values, 42 hidden layer nodes in a single hidden layer, and seven output nodes. Using just a single hidden layer is informative as it indicates the solution surface is a hyperplane

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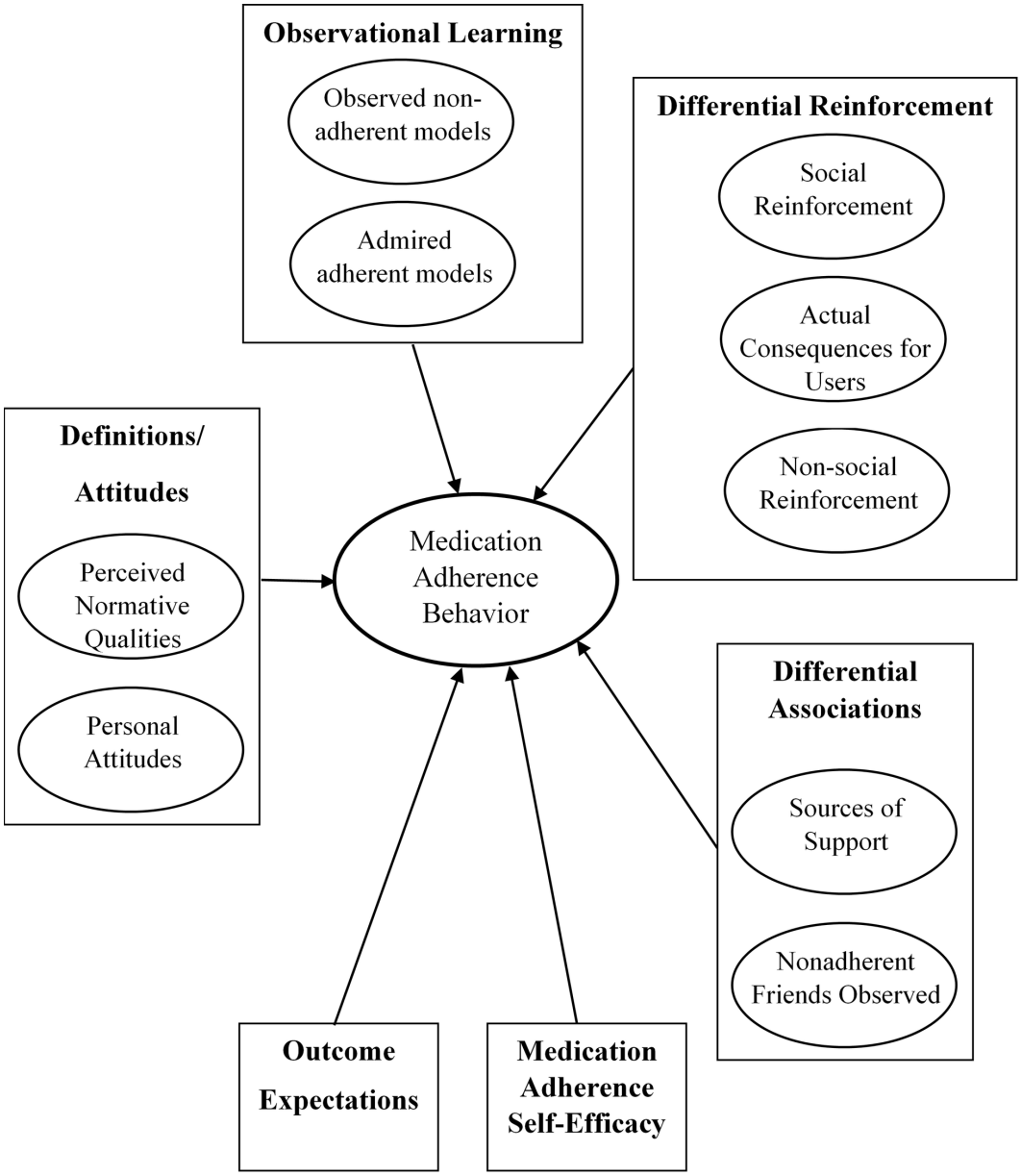
Figure 2. Factors influencing medication adherence



with a single concavity or convexity with no additional nonlinearities in the surface (Walczak & Cerpa, 1999).

After finding a single hidden layer ANN architecture that produced the best classification performance for likely nonadherence reasons for individual patients, further examination of the data revealed that less than three percent of individuals indicating cost was a reason had someone other than themselves or their family paying for the medication. Almost a third of those that self-paid had concerns about cost. Additionally, 85 percent of the respondents indicated that lack of education was a reason for nonadherence, but this answer may have been biased since a university was conducting

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the survey and this type of answer would seem desirable for a university research outcome. Therefore, if we assume that cost is usually an issue and that good communication between the physician and patient to educate them about the benefits of their medication is needed, then a new ANN model may be developed examining the remaining five nonadherence reasons for individual patients. Additionally, instead of using the 25 elements for the six factors influencing adherence shown in Figure 2, these are represented by the individual factors (two were used for attitudes and definitions). The best performing architecture for this new ANN is 13 input nodes, 11 hidden nodes in a single layer, and five output nodes as shown in Figure 3. This new ANN reduces the total number of connections in the best performing ANN from 1722 to 198 and thus reduces the chance for overfitting the data and consequent improvement to generalization of the results.

RESULTS

Population Demographic Results

Respondent age is captured in 10 year increments with a minimum of 18 (18-27) and a maximum of 67 (58-67). The median and mode for age are both the 28-37 year old group. Fifty percent of the respondents were married and 44.8 percent were single or divorced or widowed, with the remaining having a missing value. Males represented 46 percent and females 47 percent of the population with the remaining having a missing value. Three quarters were employed or self-employed, with 18.2 percent reporting unemployment and 6.8 percent unknown.

ANN Prediction Results

The resulting ANN system is called INReP (Individual Nonadherence Reason Predictor). Results for the INReP ANN predicting all 7 categories of nonadherence are shown in Table 2. The INReP ANN did best predicting when religious concerns were or were not a nonadherence reason. For every nonadherence reason, INReP was correct over 54 percent of the time. The results may be further analyzed with results to specificity and sensitivity. A total of 550 true positive predictions (where positive indicates the respondent indicated this was a reason for their nonadherence), 493 true negatives,

Figure 3. Backpropagation ANN architecture for predicting reasons for prescription nonadherence (not all connections shown)

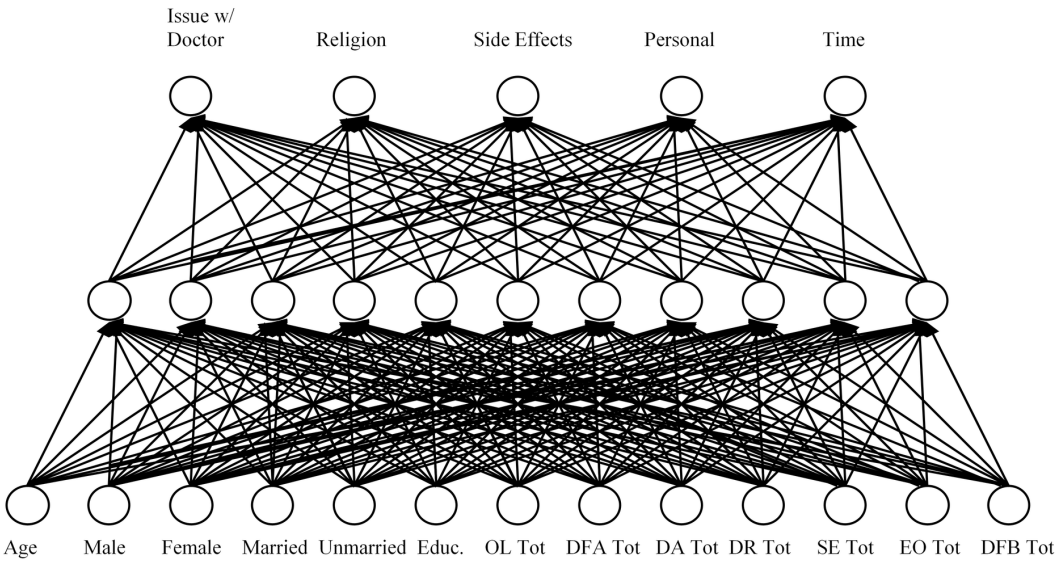

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Table 2. INReP ANN results for predicting up to seven possible reasons for nonadherence

Nonadherence Category	INReP ANN correct predictions* (N = 237)
Education/Understanding	175 (73.8%)
Issues with Doctor	135 (57.0%)
Cost	138 (58.2%)
Religion	183 (77.2%)
Concern over Side Effects	152 (64.1%)
Time	130 (54.9%)
Other Personal	130 (54.9%)
Total	1043 (62.9%)

*A prediction is considered correct if it was either a true positive or a true negative

132 false positives, and 128 false negatives resulted, producing a sensitivity to nonadherence reasons of 64.5 percent and a specificity to lack of nonadherence reasons of 61.2 percent.

The INReP ANN that predicted the 5 class subset of nonadherence reasons is shown in Table 3. A total of 479 true positive predictions, 384 true negatives, 197 false positives, and 125 false negatives resulted, producing a sensitivity to nonadherence reasons of 79.3 percent and a specificity to lack of nonadherence reasons of 66.1 percent.

DISCUSSION

As shown above, the two INReP ANN models both have reasonably high sensitivity for predicting the reasons a specific patient will become nonadherent and specificity for eliminating individual reasons of nonadherence. Naturally, assuming better education is always required and will improve medication adherence (Erah & Arute, 2008) and that cost is commonly an issue for self-payers, produces better prediction results, specifically an almost 23 percent improvement in sensitivity and an 8 percent improvement in specificity.

In addition to promoting increased patient communication with their physicians, other means may provide alternatives for patients to become better informed about their drugs and the need to complete treatment. The Internet is becoming much more widely used in Nigeria and provides a valuable resource for patient education (Oyelami, Okuboyejo, & Ebiye, 2013). Education can help address multiple nonadherence reasons beyond education or understanding, including concern over

Table 3. INReP ANN results for predicting only 5 reasons for nonadherence (minus education and cost)

Nonadherence Category	INReP ANN correct predictions* (N = 237)
Issues with Doctor	166 (70.0%)
Religion	197 (83.1%)
Concern over Side Effects	175 (73.8%)
Time	147 (62.0%)
Other Personal	178 (75.1%)
Total	863 (72.8%)

*A prediction is considered correct if it was either a true positive or a true negative

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side effects, overcoming observational learning and social reinforcement effects, and personal reasons associated with dislike of medicine or concerns over drug habits.

Methods for overcoming lack of time or the personal reason of forgetfulness have been recommended in the literature. These include placing automated telephone calls to patients (Eyesan & Okuboyejo, 2013) and sending text messages (Okuboyejo, Omoregbe, & Mbarika, 2012) to remind patients of current drug delivery times. Patients may also use or be provided alarm mechanisms (e.g., watch or cell phone) and carrying cases to assist them with remembering prescription administration time and enabling them to have their prescriptions readily available, though such mechanisms will increase the overall cost of care.

A need for future research to examine embedding ANN decision support into electronic heath records (EHRs) is still needed to make the results of the ANNs more readily available to physicians when getting ready to prescribe a pharmaceutical-based treatment plan. EHRs have been shown to improve patient safety within hospitals while enabling the improvement in the quality of care delivered in hospital setting (Bourgeois & Yaylacicegi, 2010). Patient safety and outcome concerns however, do not end at the hospital door. Patients being treated pharmacologically, are commonly monitored for adverse drug effects (Gupta et al., 2007), but this needs to be extended to assisting patients to follow and complete their prescription treatment courses to the fullest in order to obtain desired health outcomes.

Decision support regarding dangerous drug interactions already exist in EHRs (Helmons et al., 2015) and including the INReP ANN prediction of nonadherence reasons along with other drug related decision support should be a simple extension to existing EHRs (Kuperman et al., 2007). Research has shown that when EHRs are available 65 percent of physicians use them to examine drug interactions and to get recommendations when prescribing pharmaceuticals (DeMello & Deshpande, 2012). With the INReP predictions embedded in the EHR utilized by a healthcare practice or hospital, physicians can optimize patient outcomes by including education, reminders, or other initiatives to overcome individual patients' reasons for nonadherence, thus improving outcomes not only for the individual patient, but for the population health as well.

Another area for further research, but outside of the scope of information systems research is that of response bias. Recall that while the survey had a reasonable response rate of 79 percent, only half of these responses could be used in the ANN research due to missing values. Missing data values increases the uncertainty related to the data and nay cause to decrease the subsequent reliability of various modeling paradigms, including ANNs. Further research should investigate the reasons why respondent elect to not answer all of the questions, especially values critical to the research, in medically oriented domains to determine if further explanation or guarantees of anonymity could alleviate this problem.

A short questionnaire provided to patients during check-in or triage would produce the values needed by the ANN clinical decision support informatics tool for predicting nonadherence reasons for individual patients. These values would then be directed to the ANN, which would also access the patient's EHR to determine desired demographic values for the ANN's input vector. The ANN prediction of nonadherence reasons would then be written directly to the EHR so the physician would have this information available should a pharmaceutical treatment plan be diagnosed and enable the physician to direct the patient to various resources to overcome their potential nonadherence. Figure 4 represents the ANN clinical informatics tool relative to other resources.

CONCLUSION

An ANN method for predicting individual patient reasons for nonadherence to treatment has been presented and shown to be able to identify reasons, including multiple reasons, for nonadherence for 64 to 79 percent of the individual patients. Once incorporated into the EHR workflow, physicians will readily have this information available. Physicians or other clinical staff can then use these medical

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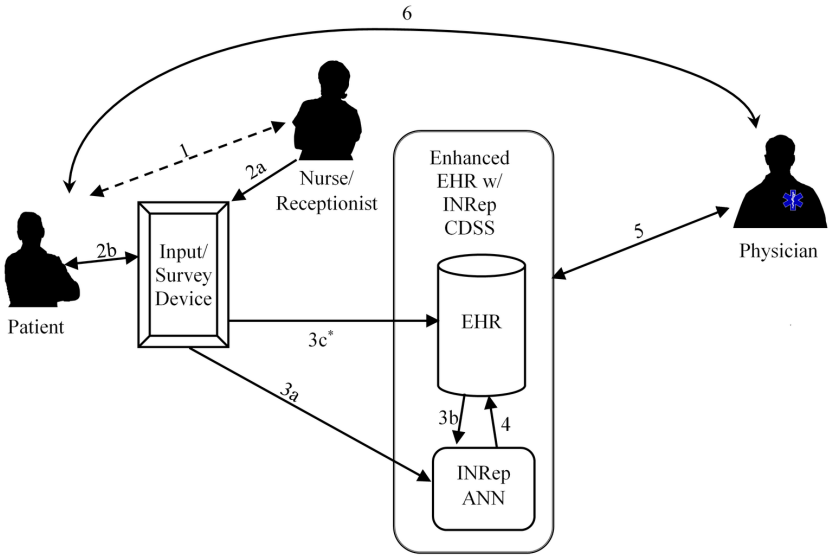
Figure 4. ANN clinical informatics tool in healthcare



*The patient survey device may also be used for check in and will then communicate via the office network with the EHR in addition to the INRep ANN

informatics classifications as recommendations on how to plan for ways to overcome their patients' nonadherence and consequently improve medical outcomes and a healthy lifestyle for these patients. Improving the health outcomes for pharmaceutically treatable conditions may also further promote a healthier population at large through decreased spread of the respective illnesses.

Future research may address how to facilitate incorporation of new features into EHRs and the clinician's natural workflow to enable identification of nonadherence or other dangerous behaviors of patients related to their treatments. Early identification of causes for non-optimal healthcare outcomes will enable education and other efforts, such as automated notifications or reminders, to improve healthcare outcomes.

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REFERENCES

Agarwal, S., Yewale, V. N., & Dharmapalan, D. (2015). Antibiotics Use and Misuse in Children: A Knowledge, Attitude and Practice Survey of Parents in India. *Journal of Clinical and Diagnostic Research*, *9*(11), SC21–SC24. PMID:26674397

Akers, R. L. (1977). *Deviant Behavior: A Social Learning Approach*. Belmont, CA: Wadsworth.

Andrajati, R., Tilaqza, A., & Supardi, S. (2016). Factors related to rational antibiotic prescriptions in community health centers in Depok City, Indonesia. *Journal of Infection and Public Health*. Retrieved from http://www.jiph.org/article/S1876-0341(16)00037-X/pdf

Au, L. E., Harris, S. S., Jacques, P. F., Dwyer, J. T., & Sacheck, J. M. (2014). Adherence to a Vitamin D Supplement Intervention in Urban Schoolchildren. *Journal of the Academy of Nutrition and Dietetics*, *114*(1), 86–90. doi:10.1016/j.jand.2013.06.350 PMID:23999277

Awad, A. I., & Eltayeb, I. B. (2007). Self-medication practices with antibiotics and antimalarials among Sudanese undergraduate university students. *The Annals of Pharmacotherapy*, *41*(7-8), 1249–1255. doi:10.1345/aph.1K068 PMID:17565044

Bourgeois, S., & Yaylacicegi, U. (2010). Electronic Health Records: Improving Patient Safety and Quality of Care in Texas Acute Care Hospitals. *International Journal of Healthcare Information Systems and Informatics*, *5*(3), 1–13. doi:10.4018/jhisi.2010070101

Bowen, D. J., Helmes, A., & Lease, E. (2001). Predicting Compliance: How Are We Doing? In L. Burke & I. Ockene (Eds.), *Compliance in Healthcare and Research*. New York: Wiley.

Buckalew, L. W., & Sallis, R. E. (1986). Patient Compliance and Medication Perception. *Journal of Clinical Psychology*, *42*(1), 49–53. doi:10.1002/1097-4679(198601)42:1<49::AID-JCLP2270420107>3.0.CO;2-F PMID:3950014

Caudill, M. (1987). Neural Networks Primer, Part I. *AI Expert*, *2*(12), 46–52.

Center for Disease Control. (2013). Medication Adherence. Retrieved from https://www.cdc.gov/primarycare/materials/medication/docs/medication-adherence-01ccd.pdf

Cherkassky, V., & Lari-Najafi, H. (1992). Data representation for diagnostic neural networks. *IEEE Expert*, *7*(5), 43–53. doi:10.1109/64.163672

DeMello, J. P., & Deshpande, S. P. (2012). Factors impacting use of information technology by physicians in private practice. *International Journal of Healthcare Information Systems and Informatics*, *7*(2), 17–28. doi:10.4018/jhisi.2012040102

DiMatteo, M. R. (2004). Variations in patients adherence to medical recommendations: A quantitative review of 50 years of research. *Medical Care*, *42*(3), 200–209. doi:10.1097/01.mlr.0000114908.90348.f9 PMID:15076819

DiMatteo, M. R., & Martin, L. R. (2002). *Health Psychology*. Boston: Allyn & Bacon.

Ekwunife, O. I., Udeogaranya, P. O., & Adibe, M. O. (2010). Predictors of self reported adherence to Antihypertensive Medication in a Nigerian population. *Journal of Basic and Clinical Pharmacy*, *1*, 133–138. PMID:24825980

Erah, P. O., & Arute, J. E. (2008). Adherence of HIV/AIDS patients to antiretroviral therapy in a tertiary health facility in Benin City. *African Journal of Pharmacy and Pharmacology*, *2*(7), 145–152.

Eyesan, O. L., & Okuboyejo, S. R. (2013). Design and implementation of a voice-based medical alert system for medication adherence. *Procedia Technology, 2013*(9), 1033-1040.

Farmer, K. C. (1999). Methods for measuring and monitoring medication regimen adherence in clinical trials and clinical practice. *Clinical Therapeutics*, *21*(6), 1074–1090. doi:10.1016/S0149-2918(99)80026-5 PMID:10440628

Gamble, J., Stevenson, M., McClean, E., & Heaney, L. G. (2009). The Prevalence of Nonadherence in Difficult Asthma. *American Journal of Respiratory and Critical Care Medicine*, *180*(9), 817–822. doi:10.1164/rccm.200902-0166OC PMID:19644048

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Gibson, T. B., Landrum, M. B., Batata, A., Fendrick, A. M., Wang, S., & Chernew, M. (2011). Regional Variation in Medication Adherence. *Forum Health Econ Policy, 14*(2).

Given, C. W., Given, B. A., & Simoni, L. E. (1978). The association of knowledge and perception of medications with compliance and health states among hypertension patients: A prospective study. *Research in Nursing & Health*, *1*(2), 76–84. doi:10.1002/nur.4770010205 PMID:248835

Gottlieb, H. (2000). Medication Nonadherence: Finding Solutions to a Costly Medical Problem. *Drug Benefit Trends*, *12*(6), 57–62.

Grigoryan, L., Haaijer-Ruskamp, F. M., Burgerhof, J. G., Mechtler, R., Deschepper, R., Tambic-Andrasevic, A., & Edelsein, H. et al. (2006). Self-medication with antimicrobial drugs in Europe. *Emerging Infectious Diseases*, *12*(3), 452–460. doi:10.3201/eid1203.050992 PMID:16704784

Gupta, A., Woosley, R., Crk, I., & Sarnikar, S. (2007). An Information Technology Architecture for Drug Effectiveness Reporting and Post-Marketing Surveillance. *International Journal of Healthcare Information Systems and Informatics*, *2*(3), 65–80. doi:10.4018/jhisi.2007070106

Hayes, R. B., McDonald, H., Garg, A. X., & Montagne, P. (2002). Interventions for helping patients to follow prescriptions for medications. *The Cochrane Library*, *2*, 1–50.

Helmons, P. J., Suijkerbuijk, B. O., Panday, P. V. N., & Kosterink, J. G. (2015). Drug-drug interaction checking assisted by clinical decision support: A return on investment analysis. *Journal of the American Medical Informatics Association*, *22*(4), 764–772. doi:10.1093/jamia/ocu010 PMID:25670751

Hirth, R. A., Greer, S. L., Albert, J. M., Young, E. W., & Piette, J. D. (2008). Out-of-pocket spending and medication adherence among dialysis patients in twelve countries. *Health Affairs*, *27*(1), 89–102. doi:10.1377/hlthaff.27.1.89 PMID:18180483

Hugtenburg, J. G., Timmers, L., Elders, P. J., Vervloet, M., & van Dijk, L. (2013). Definitions, variants, and causes of nonadherence with medication: A challenge for tailored interventions. *Patient Prefer Adherence*, *7*, 675–682. doi:10.2147/PPA.S29549 PMID:23874088

Ikechuwku, E. O., Obinna, U. P., & Ogochukwu, A. M. (2010). Predictors of Self Reported Adherence to Antihypertensive Medication in a Nigerian Population. *Journal of Basic and Clinical Pharmacy*, *1*(2), 133–138. PMID:24825980

Jain, A. K., Mao, J., & Mohiuddin, K. M. (1996). Artificial Neural Networks: A Tutorial. *Computer*, *29*(3), 31–44. doi:10.1109/2.485891

Kirking, D. M., Lee, J. A., Ellis, J. J., Briesacher, B., & Mckercher, P. L. (2006). Patient-reported underuse of prescription medications: A comparison of nine surveys. *Medical Care Research and Review*, *63*(4), 427–446. doi:10.1177/1077558706288845 PMID:16847072

Kuperman, G. J., Bobb, A., Payne, T. H., Avery, A. J., Gandhi, T. K., Burns, G., & Bates, D. W. et al. (2007). Medication-related clinical decision support in computerized provider order entry systems: A review. *Journal of the American Medical Informatics Association*, *14*(1), 29–40. doi:10.1197/jamia.M2170 PMID:17068355

Lehane, E., & McCarthy, G. (2007). Intentional and unintentional medication non-adherence: A comprehensive framework for clinical research and practice? A discussion paper. *International Journal of Nursing Studies*, *44*(8), 1468–1477. doi:10.1016/j.ijnurstu.2006.07.010 PMID:16973166

McDonald, H. P., Garg, A. X., & Haynes, R. B. (2002). Interventions to enhance patient adherence to medication prescriptions: Scientific review. *Journal of the American Medical Association*, *288*(22), 2868–2879. doi:10.1001/jama.288.22.2868 PMID:12472329

Okuboyejo, S. (2014). Non-Adherence to Medication in Outpatient Setting in Nigeria: The Effect of Employment Status. *Global Journal of Health Science*, *6*(3), 37–44. doi:10.5539/gjhs.v6n3p37 PMID:24762344

Okuboyejo, S., & Eyesan, O. (2014). mHealth: Using mobile technology to support healthcare. *Online Journal of Public Health Informatics*, *5*(3), 233–242. doi:10.5210/ojphi.v5i3.4865 PMID:24678384

Okuboyejo, S., Omoregbe, N. A., & Mbarika, V. (2012). A Framework for the Design of a Mobile-Based Alert System for Outpatient Adherence in Nigeria. *African Journal of Computing & ICT*, *5*(5), 151–158.

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Oyelami, O. M., Okuboyejo, S., & Ebiye, V. (2013). Awareness and usage of Internet-based health information for self-care in Lagos State, Nigeria: Implications for healthcare improvement. *Journal of Health Informatics in Developing Countries*, *7*(2), 165–177.

Pechère, J. C. (2001). Patients interviews and misuse of antibiotics. *Clinical Infectious Diseases*, *33*(Suppl. 3), S170–S173. doi:10.1086/321844 PMID:11524715

Rodvold, D. M., McLeod, D. G., Brandt, J. M., Snow, P. B., & Murphy, G. P. (2001). Introduction to artificial neural networks for physicians: Taking the lid off the black box. *The Prostate*, *46*(1), 39–44. doi:10.1002/1097-0045(200101)46:1<39::AID-PROS1006>3.0.CO;2-M PMID:11170130

Smith, M. (1993). *Neural Networks for Statistical Modeling*. New York: Van Nostrand Reinhold.

Urquhart, E. (2005). Challenging perceptions of long-acting injectable antipsychotic medications. *Mental Health Practice*, *8*(10), 14–18. doi:10.7748/mhp2005.07.8.10.14.c1872

Uzochukwu, B. S. C., Onwujekwe, O. E., Onoka, A. C., Okoli, C., Uguru, N. P., & Chukwuogo, O. I. (2009). Determinants of Non-Adherence to Subsidized Anti-Retroviral Treatment in Southeast Nigeria. *Health Policy and Planning*, *24*(3), 189–196. doi:10.1093/heapol/czp006 PMID:19276155

Walczak, S., & Cerpa, N. (1999). Heuristic Principles for the Design of Artificial Neural Networks. *Information and Software Technology*, *41*(2), 107–117. doi:10.1016/S0950-5849(98)00116-5

Wapner, J. (2008). Doctors Without Orders The Mystery of Patients Who Fail to Follow Prescriptions. *Medical Examiner*. Retrieved from http://www.slate.com/articles/health_and_science/medical_examiner/2008/03/doctors_without_orders.html

Zhang, G. P. (2007). Avoiding pitfalls in neural network research. *IEEE Transactions on Systems, Man and Cybernetics. Part C, Applications and Reviews*, *37*(1), 3–16. doi:10.1109/TSMCC.2006.876059

Zhu, X., Pan, H., Yang, Z., Cui, B., Zhang, D., & Ba-Thein, W. (2016). Self-medication practices with antibiotics among Chinese university students. *Public Health*, *130*, 78–83. doi:10.1016/j.puhe.2015.04.005 PMID:26008209

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