

## ***Supplementary Material***

### **Artificial Intelligence for Patient Support to Enhance Medication Adherence: A Focused Systematic Review**

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#### **Supplementary Information - Search Strategy**

**Search date:** 07/20/2024

##### **MEDLINE/PubMed (27 articles)**

(Patient OR Clients OR Client OR "Clinic Visits" OR "Clinic Visit") AND ("Intelligence, Artificial" OR "Computer Reasoning" OR "Reasoning, Computer" OR "Artificial Intelligence" OR "Machine Intelligence" OR "Intelligence, Machine" OR "Computational Intelligence" OR "Intelligence, Computational" OR "Learning, Machine" OR "Transfer Learning" OR "Learning, Transfer" OR "Language Processing, Natural" OR "Language Processings, Natural" OR "Natural Language Processings" OR "Processing, Natural Language" OR "Processings, Natural Language" OR "Machine Learning") AND ("Adherence, Medication" OR "Drug Adherence" OR "Adherence, Drug" OR "Medication Persistence" OR "Persistence, Medication" OR "Medication Nonadherence" OR "Nonadherence, Medication" OR "Medication Non-Adherence" OR "Medication Non Adherence" OR "Non-Adherence, Medication" OR "Medication Noncompliance" OR "Noncompliance, Medication" OR "Medication Compliance" OR "Compliance, Medication" OR "Drug Compliance" OR "Compliance, Drug" OR "Medication Non-Compliance" OR "Medication Non Compliance" OR "Non-Compliance, Medication" OR "Administration, Self" OR "Administrations, Self" OR "Self Administrations" OR "Therapeutic Adherence and Compliance" OR "Treatment Adherence" OR "Adherence, Treatment" OR "Therapeutic Adherence" OR "Adherence, Therapeutic" OR "Medication Adherence" OR "adherence monitoring" OR "adherence prediction") AND (Prescription OR Prescriptions OR "Electronic Prescribing" OR "Prescribing, Electronic")

### **COCHRANE LIBRARY (0)**

(Patient OR Clients OR Client OR "Clinic Visits" OR "Clinic Visit") AND ("Intelligence, Artificial" OR "Computer Reasoning" OR "Reasoning, Computer" OR "Artificial Intelligence" OR "Machine Intelligence" OR "Intelligence, Machine" OR "Computational Intelligence" OR "Intelligence, Computational" OR "Learning, Machine" OR "Transfer Learning" OR "Learning, Transfer" OR "Language Processing, Natural" OR "Language Processings, Natural" OR "Natural Language Processings" OR "Processing, Natural Language" OR "Processings, Natural Language" OR "Machine Learning") AND ("Adherence, Medication" OR "Drug Adherence" OR "Adherence, Drug" OR "Medication Persistence" OR "Persistence, Medication" OR "Medication Nonadherence" OR "Nonadherence, Medication" OR "Medication Non-Adherence" OR "Medication Non Adherence" OR "Non-Adherence, Medication" OR "Medication Noncompliance" OR "Noncompliance, Medication" OR "Medication Compliance" OR "Compliance, Medication" OR "Drug Compliance" OR "Compliance, Drug" OR "Medication Non-Compliance" OR "Medication Non Compliance" OR "Non-Compliance, Medication" OR "Administration, Self" OR "Administrations, Self" OR "Self Administrations" OR "Therapeutic Adherence and Compliance" OR "Treatment Adherence" OR "Adherence, Treatment" OR "Therapeutic Adherence" OR "Adherence, Therapeutic" OR "Medication Adherence" OR "adherence monitoring" OR "adherence prediction") AND (Prescription OR Prescriptions OR "Electronic Prescribing" OR "Prescribing, Electronic")

### **Embase (25 articles)**

(Patient OR Clients OR "patient participation" OR "Clinic Visits" OR "Clinic Visit") AND ("automated reasoning" OR "Artificial Intelligence" OR "Computational Intelligence" OR "machine learning" OR "Transfer of Learning" OR "Processing, Natural Language" OR "Machine Learning") AND ("Adherence, Medication" OR "medication compliance" OR "Medication Persistence" OR "Medication Nonadherence" OR "Compliance, Medication" OR "Drug Compliance" OR "Administration, Self" OR "Self Administrations" OR "Therapeutic Adherence and Compliance" OR "Treatment Adherence" OR "Adherence, Treatment" OR "Therapeutic Adherence" OR "Adherence, Therapeutic" OR "Medication Adherence") AND (Prescription OR Prescriptions)

### **SCOPUS (62 articles)**

(Patient OR Clients OR Client OR "Clinic Visits" OR "Clinic Visit") AND ("Intelligence, Artificial" OR "Computer Reasoning" OR "Reasoning, Computer" OR "Artificial Intelligence" OR "Machine Intelligence" OR "Intelligence, Machine" OR "Computational Intelligence" OR "Intelligence, Computational" OR "Learning, Machine" OR "Transfer Learning" OR "Learning, Transfer" OR "Language Processing, Natural" OR "Language Processings, Natural" OR "Natural Language Processings" OR "Processing, Natural Language" OR "Processings, Natural Language" OR "Machine Learning") AND ("Adherence, Medication" OR "Drug Adherence" OR "Adherence, Drug" OR "Medication Persistence" OR "Persistence, Medication" OR "Medication Nonadherence" OR "Nonadherence, Medication" OR "Medication Non-Adherence" OR

"Medication Non Adherence" OR "Non-Adherence, Medication" OR "Medication Noncompliance" OR "Noncompliance, Medication" OR "Medication Compliance" OR "Compliance, Medication" OR "Drug Compliance" OR "Compliance, Drug" OR "Medication Non-Compliance" OR "Medication Non Compliance" OR "Non-Compliance, Medication" OR "Administration, Self" OR "Administrations, Self" OR "Self Administrations" OR "Therapeutic Adherence and Compliance" OR "Treatment Adherence" OR "Adherence, Treatment" OR "Therapeutic Adherence" OR "Adherence, Therapeutic" OR "Medication Adherence" OR "adherence monitoring" OR "adherence prediction") AND (Prescription OR Prescriptions OR "Electronic Prescribing" OR "Prescribing, Electronic")

### **Web of Science (26 articles)**

(Patient OR Clients OR "patient participation" OR "Clinic Visits" OR "Clinic Visit") AND ("automated reasoning" OR "Artificial Intelligence" OR "Computational Intelligence" OR "machine learning" OR "Transfer of Learning" OR "Processing, Natural Language" OR "Machine Learning") AND ("Adherence, Medication" OR "medication compliance" OR "Medication Persistence" OR "Medication Nonadherence" OR "Compliance, Medication" OR "Drug Compliance" OR "Administration, Self" OR "Self Administrations" OR "Therapeutic Adherence and Compliance" OR "Treatment Adherence" OR "Adherence, Treatment" OR "Therapeutic Adherence" OR "Adherence, Therapeutic" OR "Medication Adherence") AND (Prescription OR Prescriptions OR "Electronic Prescribing" OR "Prescribing, Electronic")

### **LILACS (19 articles)**

((Patient OR Clients OR Client OR "Clinic Visits" OR "Clinic Visit") AND ("Intelligence, Artificial" OR "Computer Reasoning" OR "Reasoning, Computer" OR "AI (Artificial Intelligence)" OR "Machine Intelligence" OR "Intelligence, Machine" OR "Computational Intelligence" OR "Intelligence, Computational" OR "Learning, Machine" OR "Transfer Learning" OR "Learning, Transfer" OR "Language Processing, Natural" OR "Language Processings, Natural" OR "Natural Language Processings" OR "Processing, Natural Language" OR "Processings, Natural Language" OR "Machine Learning") AND ("Adherence, Medication" OR "Drug Adherence" OR "Adherence, Drug" OR "Medication Persistence" OR "Persistence, Medication" OR "Medication Nonadherence" OR "Nonadherence, Medication" OR "Medication Non-Adherence" OR "Medication Non Adherence" OR "Non-Adherence, Medication" OR "Medication Noncompliance" OR "Noncompliance, Medication" OR "Medication Compliance" OR "Compliance, Medication" OR "Drug Compliance" OR "Compliance, Drug" OR "Medication Non-Compliance" OR "Medication Non Compliance" OR "Non-Compliance, Medication" OR "Administration, Self" OR "Administrations, Self" OR "Self Administrations" OR "Therapeutic Adherence and Compliance" OR "Treatment Adherence" OR "Adherence, Treatment" OR "Therapeutic Adherence" OR "Adherence, Therapeutic" OR "Medication Adherence" OR "adherence monitoring" OR "adherence prediction") AND (Prescription OR Prescriptions))

**Supplementary Table 1 - Reports screened studies by title and abstract,  
excluded with reasons**

| <b>N</b> | <b>Identification</b> | <b>Authors</b>                                   | <b>Year</b> | <b>No direct<br/>patient support<br/>for adherence</b> | <b>Support only<br/>for prescribers<br/>or systems</b> | <b>No answer to<br/>the research<br/>question<sup>#</sup></b> |
|----------|-----------------------|--------------------------------------------------|-------------|--------------------------------------------------------|--------------------------------------------------------|---------------------------------------------------------------|
| 1        | Search strategy       | Bayley, K.B. et al <sup>1</sup>                  | 2013        | X                                                      |                                                        | X                                                             |
| 2        | Search strategy       | Dixon, B.E .et al <sup>2</sup>                   | 2013        |                                                        | X                                                      | X                                                             |
| 3        | Search strategy       | Horsky, J. et al <sup>3</sup>                    | 2013        | X                                                      | X                                                      | X                                                             |
| 4        | Search strategy       | Ogallo, W. and Kanter, A. S. <sup>4</sup>        | 2016        | X                                                      |                                                        | X                                                             |
| 5        | Search strategy       | Lilih, S.et al <sup>5</sup>                      | 2017        |                                                        | X                                                      | X                                                             |
| 6        | Search strategy       | Bruce Guthrie <sup>6</sup>                       | 2019        | X                                                      |                                                        | X                                                             |
| 7        | Search strategy       | Appold, K. <sup>7</sup>                          | 2019        | X                                                      |                                                        | X                                                             |
| 8        | Search strategy       | Chaix, B. et al <sup>8</sup>                     | 2019        | X                                                      |                                                        | X                                                             |
| 9        | Search strategy       | Diaz Ochoa, J.G. and Weil, F. <sup>9</sup>       | 2019        | X                                                      |                                                        | X                                                             |
| 10       | Search strategy       | Godin, O. et al <sup>10</sup>                    | 2019        | X                                                      |                                                        | X                                                             |
| 11       | Search strategy       | Goh, MLI et al <sup>11</sup>                     | 2019        |                                                        |                                                        | X                                                             |
| 12       | Search strategy       | Hsieh CY <sup>12</sup>                           | 2019        | X                                                      |                                                        | X                                                             |
| 13       | Search strategy       | Rafiei, R. <sup>13</sup>                         | 2019        |                                                        |                                                        | X                                                             |
| 14       | Search strategy       | MacFarlane, A <sup>14</sup>                      | 2020        | X                                                      |                                                        | X                                                             |
| 15       | Search strategy       | Cheon, A. et al <sup>15</sup>                    | 2020        |                                                        |                                                        | X                                                             |
| 16       | Search strategy       | Lin, A. et al <sup>16</sup>                      | 2020        | X                                                      |                                                        | X                                                             |
| 17       | Search strategy       | Oakey-Neate, L. et al <sup>17</sup>              | 2020        |                                                        |                                                        | X                                                             |
| 18       | Search strategy       | Omboni, S. et al <sup>18</sup>                   | 2020        |                                                        | X                                                      | X                                                             |
| 19       | Search strategy       | Payne, N. et al <sup>19</sup>                    | 2020        |                                                        | X                                                      | X                                                             |
| 20       | Search strategy       | Rao, I et al <sup>20</sup>                       | 2020        |                                                        | X                                                      |                                                               |
| 21       | Search strategy       | Zhou, N. et al <sup>21</sup>                     | 2020        |                                                        |                                                        | X                                                             |
| 22       | Search strategy       | Bailly, S et al <sup>22</sup>                    | 2021        | X                                                      |                                                        | X                                                             |
| 23       | Search strategy       | Bulaj, G. et al <sup>23</sup>                    | 2021        | X                                                      |                                                        | X                                                             |
| 24       | Search strategy       | Gauthier, P. and Cardot, J.M. <sup>24</sup>      | 2021        | X                                                      |                                                        | X                                                             |
| 25       | Search strategy       | Hasan, M.M. et al <sup>25</sup>                  | 2021        |                                                        | X                                                      | X                                                             |
| 26       | Search strategy       | Donnenberg, N.S. et al <sup>26</sup>             | 2022        | X                                                      |                                                        | X                                                             |
| 27       | Search strategy       | Liu, E.S.et al <sup>27</sup>                     | 2022        | X                                                      |                                                        | X                                                             |
| 28       | Search strategy       | Oh, S.H. et al <sup>28</sup>                     | 2022        | X                                                      | X                                                      |                                                               |
| 29       | Search strategy       | Scarton, L. et al <sup>29</sup>                  | 2022        | X                                                      | X                                                      |                                                               |
| 30       | Search strategy       | Singla, R. et al <sup>30</sup>                   | 2022        | X                                                      | X                                                      |                                                               |
| 31       | Search strategy       | Tahseen, D. and Nambudiri,<br>V.E. <sup>31</sup> | 2022        | X                                                      |                                                        | X                                                             |
| 32       | Search strategy       | Tran, T.T. et al <sup>32</sup>                   | 2022        |                                                        |                                                        | X                                                             |
| 33       | Search strategy       | Zhu, Y. et al <sup>33</sup>                      | 2022        | X                                                      |                                                        | X                                                             |

|    |                 |                                             |      |   |   |   |
|----|-----------------|---------------------------------------------|------|---|---|---|
| 34 | Search strategy | Al Kuwaiti, A. et al <sup>34</sup>          | 2023 |   | X | X |
| 35 | Search strategy | Biehl, J et al <sup>35</sup>                | 2023 | X |   | X |
| 36 | Search strategy | Chen, J. et al <sup>36</sup>                | 2023 | X |   | X |
| 37 | Search strategy | Crespo, J. et al <sup>37</sup>              | 2023 | X |   | X |
| 38 | Search strategy | Crilly, P. <sup>38</sup>                    | 2023 |   | X | X |
| 39 | Search strategy | Garcia-Manau, P. et al <sup>39</sup>        | 2023 | X |   | X |
| 40 | Search strategy | Jeong, J. et al <sup>40</sup>               | 2023 | X | X |   |
| 41 | Search strategy | Kiemde, F. et al <sup>41</sup>              | 2023 |   | X | X |
| 42 | Search strategy | Machetanz, L et al <sup>42</sup>            | 2023 | X |   | X |
| 43 | Search strategy | Mucherino, S et al <sup>43</sup>            | 2023 | X |   | X |
| 44 | Search strategy | Narindrarangkura, P. et al <sup>44</sup>    | 2023 | X |   | X |
| 45 | Search strategy | Umar, A.K. et al <sup>45</sup>              | 2023 | X |   | X |
| 46 | Search strategy | Zhang, J.X. and Meltzer, D.O. <sup>46</sup> | 2023 | X |   | X |
| 47 | Search strategy | Zhang, L. et al <sup>47</sup>               | 2023 | X |   | X |
| 48 | Search strategy | Amiesimaka, O.I. et al <sup>48</sup>        | 2024 |   |   | X |
| 49 | Search strategy | Asano, M et al <sup>49</sup>                | 2024 | X |   | X |
| 50 | Search strategy | Chart-Pascual, JP et al <sup>50</sup>       | 2024 | X |   | X |
| 51 | Search strategy | Hoehns, J.D. et al <sup>51</sup>            | 2024 |   | X | X |
| 52 | Search strategy | Ke, Z. et al <sup>52</sup>                  | 2024 |   |   | X |
| 53 | Search strategy | Khartabil, N. et al <sup>53</sup>           | 2024 |   | X |   |
| 54 | Search strategy | Kostev, K. et al <sup>54</sup>              | 2024 |   |   | X |
| 55 | Search strategy | Martens, P.J. and Mathieu, C. <sup>55</sup> | 2024 |   |   | X |
| 56 | Search strategy | Mehta, S. <sup>56</sup>                     | 2024 |   |   | X |
| 57 | Search strategy | Rammal, D.S. et al <sup>57</sup>            | 2024 | X |   | X |
| 58 | Search strategy | Schliess, F. et al <sup>58</sup>            | 2024 | X |   | X |
| 59 | Search strategy | Zhang, H. et al <sup>59</sup>               | 2024 |   | X |   |

\*No AI-based tools for medication adherence or mitigating self-administration errors

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55. Martens, P.-J. & Mathieu, C. Type 1 diabetes mellitus: a brave new world. *Nat. Rev. Endocrinol.* **20**, 71–72 (2024).
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59. Zhang, H. *et al.* Design and rationale of the Comprehensive intelligent Hypertension managEment SyStem (CHESS) evaluation study: A cluster randomized controlled trial for hypertension management in primary care. *Am. Heart J.* **273**, 90–101 (2024).

**Supplementary Table 2 - Reports accessible for eligibility and excluded studies  
with reasons after full reading**

| N  | Identification  | Authors                                      | Year | No direct patient support | Support only for prescribers or systems | Editorials and reviews <sup>#</sup> |
|----|-----------------|----------------------------------------------|------|---------------------------|-----------------------------------------|-------------------------------------|
| 1  | Manual          | Lee, S..K. et al <sup>1</sup>                | 2013 | X                         |                                         |                                     |
| 2  | Search strategy | Lo-Ciganic, W. H. et al <sup>2</sup>         | 2015 | X                         |                                         |                                     |
| 3  | Search strategy | Nousias, S. et al <sup>3</sup>               | 2016 | X                         |                                         |                                     |
| 4  | Search strategy | Waljee, K. et al <sup>4</sup>                | 2017 | X                         |                                         |                                     |
| 5  | Search strategy | Brown, K. J. and Gaggin, H. K. <sup>5</sup>  | 2019 |                           |                                         | X                                   |
| 6  | Search strategy | Haas, K. et al <sup>6</sup>                  | 2019 | X                         |                                         |                                     |
| 7  | Search strategy | Galozy, A. and Nowaczyk, S. <sup>7</sup>     | 2020 | X                         |                                         |                                     |
| 8  | Search strategy | Aziz, F. et al <sup>8</sup>                  | 2020 | X                         |                                         |                                     |
| 9  | Manual          | Wang, L. et al <sup>9</sup>                  | 2020 | X                         |                                         |                                     |
| 10 | Search strategy | Gosselin, L et al <sup>10</sup>              | 2021 |                           |                                         | X                                   |
| 11 | Search strategy | Curto, M. et al <sup>11</sup>                | 2021 |                           |                                         | X                                   |
| 12 | Manual          | Gu, Yiing at al                              | 2021 | X                         |                                         |                                     |
| 13 | Search strategy | Warren, D. et al <sup>12</sup>               | 2022 | X                         |                                         |                                     |
| 14 | Search strategy | Ru, X. Y. et al <sup>13</sup>                | 2022 |                           | X                                       |                                     |
| 15 | Search strategy | Alarifi, M. et al <sup>14</sup>              | 2022 | X                         |                                         |                                     |
| 16 | Search strategy | Salgado Garcia, F. I. et al <sup>15</sup>    | 2022 | X                         |                                         |                                     |
| 17 | Search strategy | Sarraj, A. et al <sup>16</sup>               | 2023 | X                         |                                         |                                     |
| 18 | Search strategy | Al Faysal, J. et al <sup>17</sup>            | 2023 | X                         |                                         |                                     |
| 19 | Search strategy | Earla, J. R. et al <sup>18</sup>             | 2023 | X                         |                                         |                                     |
| 20 | Search strategy | Iyo, M. et al <sup>19</sup>                  | 2023 | X                         |                                         |                                     |
| 21 | Search strategy | Bakken, S. <sup>20</sup>                     | 2023 |                           |                                         | X                                   |
| 22 | Search strategy | Liu, P.-S. et al <sup>21</sup>               | 2024 |                           | X                                       |                                     |
| 23 | Search strategy | Adhikari, S. et al <sup>22</sup>             | 2023 | X                         |                                         |                                     |
| 24 | Search strategy | Kanyongo, W. and Ezugwu, A. E. <sup>23</sup> | 2023 |                           |                                         | X                                   |
| 25 | Search strategy | Chen, Y.-L. et al <sup>24</sup>              | 2024 | X                         |                                         |                                     |

<sup>#</sup> Reviews used only for citation searching

1. Lee, S. K., Kang, B.-Y., Kim, H.-G. & Son, Y.-J. Predictors of Medication Adherence in Elderly Patients with Chronic Diseases Using Support Vector Machine Models. *Healthc. Inform. Res.* **19**, 33 (2013).
2. Lo-Ciganic, W.-H. *et al.* Using Machine Learning to Examine Medication Adherence Thresholds and Risk of Hospitalization. *Med. Care* **53**, 720–728 (2015).
3. Nousias, S. *et al.* Monitoring asthma medication adherence through content based audio classification. in *2016 IEEE Symposium Series on Computational Intelligence (SSCI)* 1–5 (IEEE, Athens, Greece, 2016). doi:10.1109/SSCI.2016.7849898.

4. Waljee, A. K. *et al.* Machine Learning Algorithms for Objective Remission and Clinical Outcomes with Thiopurines. *J. Crohns Colitis* **11**, 801–810 (2017).
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6. Haas, K., Ben Miled, Z. & Mahoui, M. Medication Adherence Prediction Through Online Social Forums: A Case Study of Fibromyalgia. *JMIR Med. Inform.* **7**, e12561 (2019).
7. Galozy, A. & Nowaczyk, S. Prediction and pattern analysis of medication refill adherence through electronic health records and dispensation data. *J. Biomed. Inform.* **112**, 100075 (2020).
8. Aziz, F. *et al.* Determining hypertensive patients’ beliefs towards medication and associations with medication adherence using machine learning methods. *PeerJ* **8**, e8286 (2020).
9. Wang, L. *et al.* Applying Machine Learning Models to Predict Medication Nonadherence in Crohn’s Disease Maintenance Therapy. *Patient Prefer. Adherence* **Volume 14**, 917–926 (2020).
10. Gosselin, L., Thibault, M., Lebel, D. & Bussi eres, J.-F. Utilisation de l’intelligence artificielle en pharmacie : une revue narrative. *Can. J. Hosp. Pharm.* **74**, 135–143 (2021).
11. Curto, M. *et al.* Improving adherence to pharmacological treatment for schizophrenia: a systematic assessment. *Expert Opin. Pharmacother.* **22**, 1143–1155 (2021).
12. Gu, Y. *et al.* Predicting medication adherence using ensemble learning and deep learning models with large scale healthcare data. *Sci. Rep.* **11**, 18961 (2021).
13. Warren, D. *et al.* Using machine learning to study the effect of medication adherence in Opioid Use Disorder. *PLOS ONE* **17**, e0278988 (2022).
14. Ru, X., Zhu, L., Ma, Y., Wang, T. & Pan, Z. Effect of an artificial intelligence-assisted tool on non-valvular atrial fibrillation anticoagulation management in primary care: protocol for a cluster randomized controlled trial. *Trials* **23**, 316 (2022).
15. Alarifi, M., Jabour, A., Foy, D. M. & Zolnoori, M. Identifying the underlying factors associated with antidepressant drug discontinuation: content analysis of patients’ drug reviews. *Inform. Health Soc. Care* **47**, 414–423 (2022).
16. Salgado Garc a, F. I. *et al.* Using wearable technology to detect prescription opioid self-administration. *Pain* **163**, e357–e367 (2022).
17. Sarraju, A. *et al.* Identifying Reasons for Statin Nonuse in Patients With Diabetes Using Deep Learning of Electronic Health Records. *J. Am. Heart Assoc.* **12**, e028120 (2023).
18. Al Faysal, J. *et al.* An explainable machine learning framework for predicting the risk of buprenorphine treatment discontinuation for opioid use disorder among commercially insured individuals. *Comput. Biol. Med.* **177**, 108493 (2024).
19. Earla, J. R., Li, J., Hutton, G. J., Johnson, M. L. & Aparasu, R. R. Comparative adherence trajectories of oral disease-modifying agents in multiple sclerosis. *Pharmacother. J. Hum. Pharmacol. Drug Ther.* **43**, 473–484 (2023).
20. Iyo, M., Akiyoshi, H., Sekine, D., Shibasaki, Y. & Mamiya, N. An exploratory database study of factors influencing the continuation of brexpiprazole treatment (prescription) in patients with schizophrenia using information from psychiatric electronic medical records processed with natural language processing. *Schizophr. Res.* **255**, 122–131 (2023).
21. Bakken, S. Innovative informatics interventions to improve health and health care. *J. Am. Med. Inform. Assoc.* **30**, 409–410 (2023).
22. Liu, P.-S. *et al.* Optimizing methadone dose adjustment in patients with opioid use disorder. *Front. Psychiatry* **14**, 1258029 (2024).
23. Adhikari, S. *et al.* Cohort profile: a large EHR-based cohort with linked pharmacy refill and neighbourhood social determinants of health data to assess heart failure medication adherence. *BMJ Open* **13**, e076812 (2023).
24. Kanyongo, W. & Ezugwu, A. E. Machine learning approaches to medication adherence amongst NCD patients: A systematic literature review. *Inform. Med. Unlocked* **38**, 101210 (2023).
25. Chen, Y.-L. *et al.* Machine learning-based prediction of medication refill adherence among first-time

insulin users with type 2 diabetes. *Diabetes Res. Clin. Pract.* **207**, 111033 (2024).

**Supplementary Table 3. Details of AI-based tools**

|                                  | <b>Solutions</b>                                           | <b>Facial recognition</b> | <b>Alerts</b> | <b>IoT or Wi-Fi</b> | <b>Real-time data tracking</b> | <b>Live calls</b> | <b>Messaging &amp; Notifications</b> | <b>Video recording of patients</b> | <b>Voice-based interactions</b> |
|----------------------------------|------------------------------------------------------------|---------------------------|---------------|---------------------|--------------------------------|-------------------|--------------------------------------|------------------------------------|---------------------------------|
| Bain EE, et al. 2017 (23)        | The AI mobile app (AiCure)                                 | YES                       | YES           | YES                 | YES                            | NO                | YES                                  | YES                                | NO                              |
| Gracey, B et al., 2018 (25)      | Call center / AllazoEngine (proprietary)                   | NO                        | NO            | YES                 | NO                             | YES               | NO                                   | NO                                 | NO                              |
| Da Silva, et al., 2019(27)(*)    | Intelligente integrated system with IoT and smart sensors. | NO                        | YES           | YES                 | YES                            | NO                | YES                                  | YES                                | NO                              |
| Koesmahargyo et al., 2020(26)    | The AI mobile app (AiCure)                                 | NO                        | NO            | YES                 | YES                            | NO                | NO                                   | YES                                | NO                              |
| Julius, M.S et al., 2021 (29)(*) | ML framework to personalized interventions                 | NO                        | NO            | ?                   | YES                            | NO                | NO                                   | ?                                  | NO                              |
| Nayak, A. et AL., 2023 (24)      | Voice-based conversational AI application                  | NO                        | NO            | YES                 | YES                            | NO                | YES                                  | NO                                 | YES                             |
| Aparna, R. et al., 2023(28)(*)   | IoT-based system, wireless networks, and ML                | NO                        | YES           | YES                 | YES                            | NO                | YES                                  | YES                                | NO                              |

(\*)Not implemented. (?) Undefined. ML: Machine learning.

23. Bain EE, Shafner L, Walling DP, Othman AA, Chuang-Stein C, Hinkle J, et al. Use of a Novel Artificial Intelligence Platform on Mobile Devices to Assess Dosing Compliance in a Phase 2 Clinical Trial in Subjects With Schizophrenia. JMIR MHealth UHealth. 21 de fevereiro de 2017;5(2):e18.

24. Nayak A, Vakili S, Nayak K, Nikolov M, Chiu M, Sosseinheimer P, et al. Use of Voice-Based Conversational Artificial Intelligence for Basal Insulin Prescription Management Among Patients With Type 2 Diabetes: A Randomized Clinical Trial. JAMA Netw Open. 1º de dezembro de 2023;6(12):e2340232.

25. Gracey, B., Jones, C. A., Cho, D., Conner, S., & Greene, E. Improving medication adherence by better targeting interventions using artificial intelligence-a randomized control study. Value Health. 2018;21:S76.

26. Koesmahargyo V, Abbas A, Zhang L, Guan L, Feng S, Yadav V, et al. Accuracy of machine learning-based prediction of medication adherence in clinical research. Psychiatry Res. dezembro de 2020;294:113558.

27. João Da Silva V, Da Silva Souza V, Guimarães Da Cruz R, Mesquita Vidal Martínez De Lucena J, Jazdi N, Ferreira De Lucena Junior V. Commercial Devices-Based System Designed to Improve the Treatment Adherence of Hypertensive Patients. Sensors. 18 de outubro de 2019;19(20):4539.

28. Aparna R, Aravinda Kashyap KS, K R S, R B S, Rao JE, M S. MediSync: An IoT and ML-Powered Medication Adherence Solution. Em: 2023 7th International Conference on Computation System and Information Technology for Sustainable Solutions (CSITSS) [Internet]. Bangalore, India: IEEE; 2023 [citado 18 de outubro de 2024]. p. 1–6. Disponível em: <https://ieeexplore.ieee.org/document/10334070/>

29. Sunday Julius M, Rita Alo U, Uchenna Onu F, Ihuoma Akobundu C. Machine Learning Framework to Predict Patient Non-Adherence to Medication using Non-Clinical Data: A Prognosis Approach. Em: Proceedings of the 9th International Conference on Computer and Communications Management [Internet]. Singapore Singapore: ACM; 2021 [citado 18 de outubro de 2024]. p. 98–103. Disponível em: <https://dl.acm.org/doi/10.1145/3479162.3479177>

## **Supplementary Information - Extracted data**

|                                                                                                                                                                                                               |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Title                                                                                                                                                                                                         |
| Authors                                                                                                                                                                                                       |
| Year                                                                                                                                                                                                          |
| Authors                                                                                                                                                                                                       |
| Abstract                                                                                                                                                                                                      |
| Status/Selection                                                                                                                                                                                              |
| Status/Extraction                                                                                                                                                                                             |
| Reading Priority                                                                                                                                                                                              |
| Score                                                                                                                                                                                                         |
| Journal                                                                                                                                                                                                       |
| Keywords                                                                                                                                                                                                      |
| Type                                                                                                                                                                                                          |
| comment                                                                                                                                                                                                       |
| URL                                                                                                                                                                                                           |
| Volume                                                                                                                                                                                                        |
| Pages                                                                                                                                                                                                         |
| DOI                                                                                                                                                                                                           |
| ISSN/ISBN                                                                                                                                                                                                     |
| Importation Date                                                                                                                                                                                              |
| (I) Patients with prescribed medication by an authorized professional                                                                                                                                         |
| (I) Prescribed medication for self-administration                                                                                                                                                             |
| (I) Approaches based on Artificial Intelligence tools                                                                                                                                                         |
| (I) Medication adherence or self-administration errors                                                                                                                                                        |
| (E) Artificial Intelligence is used to exclusively avoid prescribers' errors as alert on drug interaction or polypharmacy, to the prescriber's support on dosage, administration route, and frequency of use. |
| (E) Inaccessible full publication                                                                                                                                                                             |
| (E) Study that does not answer the research question                                                                                                                                                          |
| (E) Digital technology, even using AI, to exclusively remember patients their medication schedule                                                                                                             |
| (E) Editorial, opinião, carta ao editor                                                                                                                                                                       |
| (E) System to avoid errors during prescription                                                                                                                                                                |
| (E) System to retrospectively predict medicine adherence without patient support                                                                                                                              |
| (E) Others                                                                                                                                                                                                    |
| (E) Reviews and editorials                                                                                                                                                                                    |
| Country of study (scenario)                                                                                                                                                                                   |
| Main objective                                                                                                                                                                                                |

|                                                                                                           |
|-----------------------------------------------------------------------------------------------------------|
| Study design: Prospective (cohort                                                                         |
| Study design: clinical trial                                                                              |
| Study design: experimental)                                                                               |
| Study design: Cross-sectional                                                                             |
| Study design: Retrospective                                                                               |
| Study design: database analysis                                                                           |
| Study design: Review                                                                                      |
| Study design: Simulation}                                                                                 |
| Participants (n)                                                                                          |
| Scenario : Outpatient                                                                                     |
| Scenario : Discharge instructions                                                                         |
| Scenario : Inpatient                                                                                      |
| Scenario : Undefined                                                                                      |
| Scenario : Other                                                                                          |
| Disease or condition                                                                                      |
| Age of patients, when specific                                                                            |
| Prescribing system : Private system                                                                       |
| Prescribing system : Public system                                                                        |
| Prescribing system : Undefined                                                                            |
| Prescribing system : No-applicable}                                                                       |
| System coverage : National                                                                                |
| System coverage : Multinational                                                                           |
| System coverage : Regional                                                                                |
| System coverage : Local (city or specific healthcare units)                                               |
| System coverage : Undefined                                                                               |
| System coverage : Non-applicable}                                                                         |
| Artificial Intelligence tools                                                                             |
| AI approach (stage of development) : Development only (train and test in the same sample)                 |
| AI approach (stage of development) : Development with external validation (validation in other geographic |
| AI approach (stage of development) : temporal or different database)                                      |
| AI approach (stage of development) : External validation only                                             |
| AI approach (stage of development) : Post-market analysis                                                 |
| AI approach (stage of development) : No-applicable}                                                       |
| Model performance of IA approach (accuracy, F1, etc)                                                      |
| Outcome: Medication adherence metrics (quantitative or qualitative indicators)                            |
| Outcome: Self-administration errors (quantitative or qualitative indicators)                              |



**Supplementary Table 4 - Adherence measurement quality according to Emerge checklist**

|                                        | <b>Operational definition</b>                                                                                                                                                                            | <b>Phases of medication adherence</b>                                                                                                                                     | <b>Measurement</b>                                                                                                                                                                                                                                                                                                                                            | <b>Results</b>                                                                                                                                                                                                              |
|----------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Recommendation according to EMERGE(22) | Yes.<br>A precise operational/working definition for each phase of medication adherence studied)                                                                                                         | Phase(s) of medication adherence studied: initiation, implementation, and persistence) and justify, where possible, the reasons the study focuses on this/these phase(s). | Yes.<br>Methods of measuring medication adherence (e.g., self-report, claims data, blood sampling, electronic monitoring). Consider each phase studied (i.e., initiation, implementation, and persistence), with details on the performance of the measures (e.g., validity, reliability, and potential bias).                                                | Describe the results of the analysis appropriate to each phase of medication adherence studied (i.e., initiation, implementation, and persistence).                                                                         |
| Bain EE, et al. 2017 (23)              | Yes.<br>Number of doses captured by the AI platform/number of planned doses.<br><br>Pharmacokinetic sample by drug concentration.                                                                        | Implementation.                                                                                                                                                           | Yes.<br>Computer vision to verify drug ingestion).<br>Plasma drug levels<br>Self-reported adherence via an app or phone call.                                                                                                                                                                                                                                 | AI-based tool ability to detect non-adherence patterns.                                                                                                                                                                     |
| Gracey, B et al., 2018 (25)            | Yes.<br>Intention-to-treat approach on year-end proportion of days covered (PDC) greater than 80%, calculated by Medicare Star Rating methodology using pharmacy claims.                                 | Implementation.                                                                                                                                                           | Yes.<br>Pharmacy claims data.<br>Difference-in-differences (DiD) analysis: Compared adherence changes between intervention and control groups over two consecutive years.<br>AI-targeted intervention effectiveness: whether patients in the AI group had a significantly higher likelihood of achieving adherence compared to traditional or control groups. | Patients in the AI Group were 6.1% more likely to be adherent than those in the Control Group (p=0.04).<br><br>AI-targeted interventions increased adherence likelihood by 7.8% compared to the Traditional Group (p=0.08). |
| Da Silva, et al., 2019(27)(*)          | Yes<br>Sensor-detected medication retrieval and intake actions, and wireless technology inform a gateway of dates, times, and locations of medication intake while monitoring the ingestion by a camera. | Initiation, prototype.                                                                                                                                                    | No adherence behaviors were measured in a clinical or home setting.                                                                                                                                                                                                                                                                                           | The AI-based tools successfully identified non-adherence behaviors in a simulated environment.                                                                                                                              |
| Koesmahargyo et al., 2020(26)          | Yes<br>Proportion medication doses confirmed as ingested using AI-based                                                                                                                                  | Implementation.                                                                                                                                                           | Yes.<br>Smartphone app with facial recognition and AI-driven image processing to verify                                                                                                                                                                                                                                                                       | The ML prediction improves adherence assessment, offering an opportunity for direct                                                                                                                                         |

|                                     |                                                                                                                                                                                                                                                                                                                               |                        |                                                                                                                                                                                                  |                                                                                                                                                              |
|-------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                     | <p>video monitoring.<br/>Daily adherence value =<br/>n medications expected /<br/>n medications are taken<br/>with AiCure.<br/>Human review:<br/>Daily adjusted adherence<br/>value = (n medications<br/>expected – n medications<br/>with red or orange alerts)<br/>/ n medications taken<br/>with AiCure.</p>               |                        | <p>medication intake in real-<br/>time.<br/>AI-based monitoring.<br/>Human review.</p>                                                                                                           | support to the patient.                                                                                                                                      |
| Julius, M.S et al.,<br>2021 (29)(*) | Not declared.                                                                                                                                                                                                                                                                                                                 | Initiation, framework. | No real medication intake<br>tracking occurred.                                                                                                                                                  | The study proposed a<br>novel prognosis-based<br>approach, aiming to<br>provide early intervention<br>strategies for high-risk<br>patients of non-adherence. |
| Nayak, A. et AL.,<br>2023 (24)      | <p>Yes.<br/>Mean insulin adherence<br/>based on logged data and<br/>change in the composite<br/>scores of the 3 surveys<br/>measuring attitudes<br/>toward diabetes, health<br/>technology, and<br/>medication adherence.</p>                                                                                                 | Implementation.        | <p>Yes.<br/>Self-reported insulin<br/>administration using the<br/>voice-based conversational<br/>AI application.</p>                                                                            | AI-based tool provided<br>significant improvements<br>in adherence, dose<br>titration frequency, and<br>glycemic control.                                    |
| Aparna, R. et al.,<br>2023(28)(*)   | <p>Yes.<br/>Number of pills in the<br/>pill bottle and alert<br/>the user when the<br/>quantity falls below a<br/>predefined threshold<br/>level, prompting them to<br/>refill the bottle.<br/>The IoT component will<br/>employ pill recognition<br/>technology to identify<br/>the specific pill inside<br/>the bottle.</p> | Initiation, prototype. | <p>Yes.<br/>Successful intake of pills as<br/>detected by an IoT-enabled<br/>smart pillbox, using a<br/>weight sensor (200g load<br/>cell with HX711) to track<br/>changes in pill quantity.</p> | The IoT-based system<br>successfully tracked<br>simulated medication<br>intake.                                                                              |

(\*)Not implemented. AI: artificial intelligence. ML: machine learning.

23. Bain EE, Shafner L, Walling DP, Othman AA, Chuang-Stein C, Hinkle J, et al. Use of a Novel Artificial Intelligence Platform on Mobile Devices to Assess Dosing Compliance in a Phase 2 Clinical Trial in Subjects With Schizophrenia. JMIR MHealth UHealth. 21 de fevereiro de 2017;5(2):e18.
24. Nayak A, Vakili S, Nayak K, Nikolov M, Chiu M, Sosseinheimer P, et al. Use of Voice-Based Conversational Artificial Intelligence for Basal Insulin Prescription Management Among Patients With Type 2 Diabetes: A Randomized Clinical Trial. JAMA Netw Open. 1º de dezembro de 2023;6(12):e2340232.
25. Gracey, B., Jones, C. A., Cho, D., Conner, S., & Greene, E. Improving medication adherence by better targeting interventions using artificial intelligence-a randomized control study. Value Health. 2018;21:S76.
26. Koesmahargyo V, Abbas A, Zhang L, Guan L, Feng S, Yadav V, et al. Accuracy of machine learning-based prediction of medication adherence in clinical research. Psychiatry Res. dezembro de 2020;294:113558.
27. João Da Silva V, Da Silva Souza V, Guimarães Da Cruz R, Mesquita Vidal Martínez De Lucena J, Jazdi N, Ferreira De Lucena Junior V. Commercial Devices-Based System Designed to Improve the Treatment Adherence of Hypertensive Patients. Sensors. 18 de outubro de 2019;19(20):4539.

28. Aparna R, Aravinda Kashyap KS, K R S, R B S, Rao JE, M S. MediSync: An IoT and ML-Powered Medication Adherence Solution. Em: 2023 7th International Conference on Computation System and Information Technology for Sustainable Solutions (CSITSS) [Internet]. Bangalore, India: IEEE; 2023 [citado 18 de outubro de 2024]. p. 1–6. Disponível em: <https://ieeexplore.ieee.org/document/10334070/>
29. Sunday Julius M, Rita Alo U, Uchenna Onu F, Ihuoma Akobundu C. Machine Learning Framework to Predict Patient Non-Adherence to Medication using Non-Clinical Data: A Prognosis Approach. Em: Proceedings of the 9th International Conference on Computer and Communications Management [Internet]. Singapore Singapore: ACM; 2021 [citado 18 de outubro de 2024]. p. 98–103. Disponível em: <https://dl.acm.org/doi/10.1145/3479162.3479177>