Review

Drug/Regimen

Diabetes Metab J 2023;47:325-332
https://doi.org/10.4093/dmj.2022.0349
pISSN 2233-6079 · eISSN 2233-6087

DIABETES & METABOLISM JOURNAL

Machine Learning Approach to Drug Treatment Strategy for Diabetes Care

Kazuya Fujihara, Hirohito Sone

Department of Internal Medicine, Niigata University Faculty of Medicine, Niigata, Japan

Globally, the number of people with diabetes mellitus has quadrupled in the past three decades, and approximately one in 11 adults worldwide have diabetes mellitus. Since both microvascular and macrovascular diseases in patients with diabetes predispose them to a lower quality of life as well as higher rates of mortality, managing blood glucose levels is of clinical relevance in diabetes care. Many classes of antihyperglycemic drugs are currently approved to treat hyperglycemia in patients with type 2 diabetes mellitus, with several new drugs having been developed during the last decade. Diabetes-related complications have been reduced substantially worldwide. Prioritization of therapeutic agents varies according to national guidelines. However, since the characteristics of participants in clinical trials differ from patients in actual clinical practice, it is difficult to apply the results of such trials to clinical practice. Machine learning approaches became highly topical issues in medicine along with rapid technological innovations in the fields of information and communication in the 1990s. However, adopting these technologies to support decision-making regarding drug treatment strategies for diabetes care has been slow. This review summarizes data from recent studies on the choice of drugs for type 2 diabetes mellitus focusing on machine learning approaches.

Keywords: Artificial intelligence; Decision making; Diabetes mellitus, type 2; Hypoglycemic agents; Machine learning

INTRODUCTION

Globally, the number of people with diabetes mellitus has quadrupled in the past three decades, and approximately one in 11 adults worldwide now have diabetes mellitus [1]. Since both micro- and macrovascular diseases reduce the quality of life, avoiding micro/macro diabetes complications is clinically relevant [2]. Although comprehensive and intensive management of multiple cardiovascular risk factors in type 2 diabetes mellitus patients is recommended to reduce the risk of micro- and macrovascular disease events [3-8], a considerable number of patients still develop those conditions even under intensive management [9,10]. Multiple classes of antihyperglycemic drugs are currently approved for treatment of hyperglycemia in patients with type 2 diabetes mellitus [11], and diabetes-related complications have been reduced substantially worldwide [8,12]. However, along with early detection of such complications, the choice of drugs for initial treatment remains important. In addition, it is important to prevent hypoglycemia in clinical settings since severe hypoglycemia can provoke adverse cardiovascular outcomes such as myocardial ischemia or cardiac arrhythmia [13]. Machine learning, which is a type of artificial intelligence, can detect patterns and formulate decision rules from data and has been used in clinical practice [14-16]. So far, more than 100 medical devices using machine learning have been approved in the USA and Europe [17,18]. However, adopting these technologies to support decision-making with regard to drug treatment strategies for diabetes care has been slow. This review summarizes data from recent clinical studies using machine learning in the field of diabetes care focusing on decisions on the prescription of antihyperglycemic drugs.

Corresponding author: Kazuya Fujihara https://orcid.org/0000-0001-6725-4169
Department of Internal Medicine, Niigata University Faculty of Medicine, 1-754 Asahimachi, Niigata 951-8510, Japan
E-mail: kafujihara-dm@umin.ac.jp

Received: Oct. 7, 2022; Accepted: Nov. 30, 2022

ARTIFICIAL INTELLIGENCE AND MACHINE LEARNING

No clear definition of artificial intelligence has been established. Artificial intelligence is considered as a theory and requires the development of computer systems able to perform tasks or obtain information normally requiring human intelligence, such as visual perception, speech recognition, decision-making, and translation of languages. The first boom in artificial intelligence was in the late 1950s and the 1960s, and the second occurred in the 1980s, but during those periods there was no obvious increase in the number of medical papers reporting the use of artificial intelligence in PubMed, which is a free resource for searching and retrieving biomedical and life sciences literature (Fig. 1). In other words, during that time it was difficult to apply the technology to the medical field. However, rapid innovations in information and communications technology in the 1990s led to real-time processing and analysis of large amounts of data, and the third artificial intelligence boom took place in the early 2000s with the advent of deep learning. This led to a dramatic increase in the number of medical papers involving the use of this technology (Fig. 1). The number of papers that reported or discussed the use of artificial intelligence and machine learning in relation to diabetes reached 700 in 2021. Initially, artificial intelligence was introduced in the field of diagnostic imaging such as diabetic retinopathy and cancer, followed by its deployment in the fields of diagnosis and treatment. Machine learning, which is a subset of artificial intelligence and can learn patterns and decision rules from data [19-22], has been used in clinical practice. Applications of machine learning for the early detection of diabetic retinopathy and cancer, for which clear-cut diagnostic gold standards exist, have been evaluated [14,23-29]. In fact, the use of artificial intelligence-based medical devices could be of value in improving the quality of healthcare. There are various models for machine learning, including neural networks, support vector machines, naive Bayes, random forests, decision trees, K-Nearest Neighbors, etc. According to a review by Abhari et al. [21], support vector machines, artificial neural network, naive Bayes, decision tree, and random forest are commonly applied in the field of type 2 diabetes mellitus. However, some issues involving the nature of the machine learning algorithm, which is often referred to as a black box model [19-22], could be a barrier to the practice of evidence-based medicine. Thus far, due to the black box, which cannot easily explain the reasons for and background of results learned

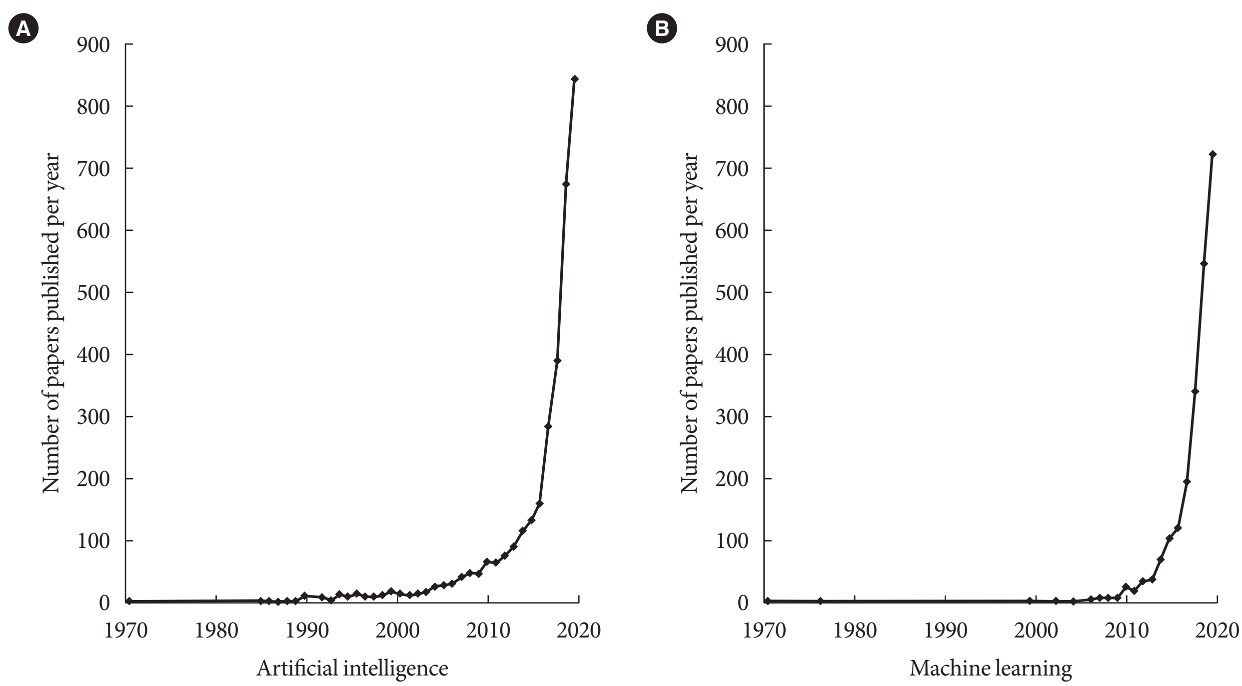

Fig. 1. Trends in the number of publications reporting the use of artificial intelligence or machine learning in the field of diabetes mellitus. (A) Artificial intelligence, (B) machine learning.

by the model, adopting artificial intelligence has been slow in some fields that require decisions and treatments to be dependent on evidence-based medicine such as diabetes [19-22]. Some models have attempted to solve the problem of this black box. For example, heterogeneous mixture learning technology is one method to automatically divide original data to increase the mining accuracy of patterns, trends, and rules in the data [30]. Even when it is difficult to know the number of splits or what clues to use for splitting, it is possible to conduct appropriate splits at high speed based on characteristics of new groups. Thus, this technology is expected to be superior to other machine learning models. In the field of diagnostic imaging, research is underway to explain the internal structure of complex black box machine learning models [31]. Machine learning technology has been modified for use in actual clinical practice.

MACHINE LEARNING FOR DIABETES CARE

Use of machine learning for diabetes care has been mainly categorized into five parts: (1) early detection of diabetic retinopathy; (2) insulin treatment support (mainly continuous glucose monitoring); (3) patient self-management tools; (4) risk stratification; and (5) decision-making support tools for antihyperglycemic drug treatment for clinicians [32-34]. In this review, (1) to (4) will be briefly discussed and (5) will be discussed in detail.

The first category is automatically identifying diabetic retinopathy from fundus photographs. A meta-analysis showed that deep learning algorithms had high sensitivity and specificity for detecting referable diabetic retinopathy from retinal fundus photographs [35]. The pooled area under the curve (AUC) for diabetic retinopathy was 0.97 (95% confidence interval [CI], 0.95 to 0.98), sensitivity was 0.83 (95% CI, 0.83 to 0.83), and specificity was 0.92 (95% CI, 0.92 to 0.92). The U.S. Food and Drug Administration has already approved some technology involving artificial intelligence in medical devices which can be used in clinical practice. In fact, more than 100 artificial intelligence-based medical devices, including those devised for diabetic retinopathy, had been approved in the USA and Europe by 2020 [17].

The second category is insulin treatment support. Until the present, increasing or decreasing insulin doses were experience-based decisions by patients and clinicians. Recently, some medical instruments have been able to send information obtained by continuous glucose monitoring or self-monitoring blood glucose to a cloud server and use artificial intelligence to determine or suggest the appropriate insulin dose [22,36]. According to a review by Contreras and Vehi [22], artificial neural network approaches were the most widely applied. They clarified that many studies have already been published on the application of artificial intelligence to diabetes in a broad range of management domains. A randomized clinical trial revealed that use of an automated decision support tool for optimizing insulin pump settings was not inferior to intensive insulin titration provided by physicians from specialized academic diabetes centers [36]. On the other hand, severe hypoglycemia is a major barrier to achieving tight glycemic control in people with type 2 diabetes mellitus as well as type 1 diabetes mellitus. Combining machine learning-based decision support systems with the abundance of data generated by continuous glucose monitoring has the potential to identify hypoglycemia with greater accuracy. A recent meta-analysis conducted by Kodama et al. [37] showed that the positive likelihood and negative likelihood of machine learning algorithms for detecting hypoglycemia were 4.05 and 0.26, respectively. These estimates were almost unchanged throughout several sensitivity analyses limited to people with type 1 diabetes mellitus, suggesting that the current machine learning algorithms still had insufficient ability to detect hypoglycemia [37]. It is expected that improved machine learning methods will support the prevention of hypoglycemia.

The third category is patient self-management tools. Self-management is the key to the treatment of type 2 diabetes mellitus. Artificial intelligence technologies, such as web-based programs and mobile phone and smartphone applications, to support nutrition and physical activity behaviors in the context of diabetes self-management have been reported [38]. In people with type 1 diabetes mellitus, both the Guardian Connect with an Enlite sensor (Medtronic, Northridge, CA, USA) and the first-generation Freestyle Libre System (Abbott Diabetes Care, Witney, UK) devices are easy to use, educational, and useful in improving glycemic control [39]. A review by Krakauer et al. [40] showed that patients with type 2 diabetes mellitus who used a flash glucose monitoring system might expect to achieve a significant improvement in glycosylated hemoglobin (HbA1c) and glycemic parameters and several associated benefits. Also, a meta-analysis showed that starting the Freestyle Libre System as part of diabetes care resulted in a significant and sustained reduction in HbA1c for patients with type 2 diabetes mellitus [41]. These reports indicate that machine learning is widely used for self-management in clinical practice.

The fourth category is risk stratification. The use of machine learning to predict diabetes has been investigated. In a review by Nomura et al. [34], the accuracy of predictions of new onset diabetes within 1 to 5 years was around 0.71 to 0.87 for the AUC using random forest [42,43], logistic regression [44], and gradient boosting [29,43,45-47]. These values do not significantly exceed the results of conventional logistic regression analysis. However, the predictive ability may be improved by expanding the amount of data and incorporating psychological and social data in the future.

Fifth is a decision-making support tool for clinicians considering drug therapy. The choice of medication should depend on individual patient factors while strictly adhering to clinical guidelines [48]. However, approximately 35% to 40% of patients worldwide initiating the use of an oral antihyperglycemic drugs did not receive the recommended initial therapy [49-51]. Table 1 summarizes studies of the predictability of the use of antihyperglycemic medications using artificial intelligence [52-57]. Liu et al. [52] investigated prescriptions in 82 patients and reported that 80.2% of recommendations generated from guidelines coincided with the medication classes (metformin, insulin secretagogues or α-glucosidase inhibitors, thiazolidinediones, dipeptidyl peptidase-4 inhibitors [DPP-4I], insulin) from their real prescriptions by K-Nearest Neighbors. Wright et al. [53] evaluated sequential pattern mining of data on 161,497 patients and identified temporal relationships between medications ranging from 89.1% to 90.5% at the drug class level (α-glucosidase inhibitor, amylin analog, biguanide, bromocriptine, DPP-4I, glucagon-like peptide-1 receptor agonists [GLP-1RA], insulin, meglitinide, peroxisome proliferator-activated receptor γ [PPARγ] agonist, sulfonylurea). Mei et al. [54] proposed "Deep Diabetologist" using a recurrent neural network and a hierarchical recurrent neural network for electronic health records sequential data modeling to provide personalized predictions of antihyperglycemic medications

Table 1. Summary of studies that investigated the predictability of the use of antihyperglycemic medications using artificial intelligence

Study	Country	No. of participants	Type of drugs	Algorithms	Validation methods	Results
Liu et al. (2013) [52]	China	82	Metformin, insulin secretagogues or α-glucosidase inhibitors, thiazolidinediones, DPP-4I, insulin	K-Nearest Neighbor	ND	80.2% match with real prescriptions
Wright et al. (2015) [53]	USA	161,497	α-Glucosidase inhibitor, amylin analog, biguanide, bromocriptine, DPP-4I, GLP-1RA, insulin, meglitinide, PPARγ agonist, sulfonylurea	CSPADE algorithms	10-Fold cross validation	89.1%–90.5% at the drug class level
Mei et al. (2017) [54]	China	21,796	Biguanide, sulfonylurea, glinides, thiazolidinediones, a-glucosidase inhibitors, DPP-4I, insulin	Recurrent Neural Network	Trained on 80% of the cohort and validated on 10%	AUC 0.91–0.94
Tarumi et al. (2021) [55]	USA	27,904	Metformin, sulfonylurea, DPP-4I, SGLT2I, thiazolidinediones, GLP-1RA, long-acting insulin	Gradient Boosting Tree, Treatment Pathway Graph-based Estimation, Random Forest	5-Fold cross validation	ND
Fujihara et al. (2021) [56]	Japan	4,567	Insulin	Neural Network	5-Fold cross validation	AUC 0.67–0.74
Singla et al. (2022) [57]	India	4,974	Metformin, sulfonylurea, DPP-4I, SGLT2I, thiazolidinediones, pre-mix insulin, basal insulin	Random forest algorithms	ND	Accuracy 85%–99.4%

DPP-4I, dipeptidyl peptidase-4 inhibitor; ND, not described; GLP1-RA, glucagon-like peptide 1 receptor agonist; PPARγ, peroxisome proliferator-activated receptor γ; CSPADE, sequential pattern discovery using equivalence classes; AUC, area under the curve; SGLT2I, sodium-glucose co-transporter-2 inhibitor.

(biguanide, sulfonylurea, glinides, thiazolidinediones, α-glucoidase inhibitors, DPP-4I, insulin) needed based on clinical indicators for diabetic patients. Using a cohort of 21,796 patients from an electronic health records repository in China, the AUC for drug classes ranged from 0.91 to 0.94 [54]. In Japan, Tarumi et al. [55] investigated a dataset on 27,904 patients with diabetes focusing on changes in HbA1c levels during treatment transition. Artificial intelligence-driven clinical decision support systems (treatment pathway graph-based estimation) were found to outperform baseline machine learning models using gradient boosting tree and random forest methods. While oral antihyperglycemic agents are indicated for many patients with type 2 diabetes mellitus, some patients require insulin injections in the advanced stages of diabetes. Thus, a physician's misjudgment sometimes results in a hyperglycemic coma or another serious condition. Diabetes specialists, defined as board-certified diabetologists, can be expected to choose antihyperglycemic drugs, including insulin therapy, based on their perception of the existence of complex conditions in their patients. We recently elucidated the ability of machine learning models and determined whether artificial intelligence might assist clinicians in deciding on the initial insulin therapy for type 2 diabetes mellitus in clinical practice. We recruited 4,860 participants who received initial monotherapy by diabetes specialists [56,58]. We found no superiority of performance of machine learning over logistic regression. The AUCs for prediction of the need for insulin were 0.89 to 0.90 for logistic regression and 0.67 to 0.74 for machine learning. However, the accuracy of machine learning was higher than that by general physicians [56]. Although further study is needed before machine learning-based decision support systems can be used for initiation of insulin in clinical practice, these findings suggest that machine learning may support such decisions by general physicians.

LIMITATIONS OF MACHINE LEARNING

There are several concerns regarding the use of machine learning in clinical practice. First, a review showed that evidence was lacking to support the claim that clinical prediction models based on machine learning led to better AUCs than those based on logistic regression [59]. Stylianou et al. [60] revealed that an established logistic regression model performed as well as more complex machine learning methods in predictions of mortality from burns. Machine learning, represented as neural networks, is capable of reproducing human judgments that can't be derived from traditional regression analysis. However, the AUC is influenced by specific strong factors, so the advantages of machine learning may not be reflected in the results. Thus, further study is needed before using machine learning decision support tools in clinical practice since the neural network model lacks explainability. A black box model, system, or program that allows visualizing input and output gives no view of the processes and workings between input and output. Recently [31], research has been underway to explain the internal structure of complex black box machine learning models. Thus, it will not be long before explainable artificial intelligence can be implemented. Second, many ethical questions remain unanswered since there are no absolute criteria for use of each antihyperglycemic drug in clinical settings. Third, there is concern over the lack of quality data. For example, consider the data used to train an algorithm to predict the suitability of an antihyperglycemic drug among Japanese. In that case, the model trained on that dataset might be biased in a way that produces inaccurate predictions for other ethnicities.

FUTURE PERSPECTIVES

The most common method utilizing machine learning is to predict use of the need for prescription drugs based on age, sex, body weight, and laboratory values such as those on renal and liver function. However, it is possible to build a model that suggests personalized treatment strategies by training artificial intelligence using natural language. Lyell et al. [18] investigated bridging the gap between machine learning algorithms and how they are used in clinical practice. They concluded that leveraging the benefits of machine learning algorithms to support clinicians while mitigating risks requires a solid relationship between clinicians and machine learning-based devices [18]. Machine learning algorithms provide the diagnosis and judgment, but the final decision is left to clinicians. Thus, solid relationship between clinicians and machine learning-based devices is needed for reducing risk and increasing efficiency. Such relationships need to be carefully designed, considering how the algorithm will be integrated into the devices.

CONCLUSIONS

This review summarizes data from recent clinical studies using machine learning in the field of diabetes care focusing on decisions on antihyperglycemic drug prescription. Although further study is needed before machine learning-based decision support systems can be used for drug choices in clinical practice, there is a possibility that machine learning may support such decisions by general physicians. Ultimately, it will be necessary to certify whether the use of artificial intelligence improves patient outcomes. We also need to develop flexible practices among clinicians to maintain the quality of care when artificial intelligence cannot be used.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

ORCID

Kazuya Fujihara *https://orcid.org/0000-0001-6725-4169*

FUNDING

None

ACKNOWLEDGMENTS

This work is supported by the Japan Society for the Promotion of Science. No potential conflicts of interest relevant to this article were reported. The sponsor had no role in the design and conduct of the study. The authors also thank Mami Haga and Kimiko Sato, Niigata University Faculty of Medicine, for excellent secretarial assistance.

REFERENCES

1. Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. Nat Rev Endocrinol 2018;14:88-98.
2. Japan Diabetes Society. Treatment Guide for Diabetes 2022-2023. Tokyo: Japan Diabetes Society; 2022.
3. UK Prospective Diabetes Study (UKPDS) Group. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). Lancet 1998;352:854-65.
4. UK Prospective Diabetes Study Group. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. BMJ 1998;317:703-13.
5. Shichiri M, Kishikawa H, Ohkubo Y, Wake N. Long-term results of the Kumamoto Study on optimal diabetes control in type 2 diabetic patients. Diabetes Care 2000;23 Suppl 2:B21-9.
6. Sone H, Tanaka S, Iimuro S, Tanaka S, Oida K, Yamasaki Y, et al. Long-term lifestyle intervention lowers the incidence of stroke in Japanese patients with type 2 diabetes: a nationwide multicentre randomised controlled trial (the Japan Diabetes Complications Study). Diabetologia 2010;53:419-28.
7. Yamada-Harada M, Fujihara K, Osawa T, Yamamoto M, Kaneko M, Kitazawa M, et al. Relationship between number of multiple risk factors and coronary artery disease risk with and without diabetes mellitus. J Clin Endocrinol Metab 2019;104:5084-90.
8. Ueki K, Sasako T, Okazaki Y, Kato M, Okahata S, Katsuyama H, et al. Effect of an intensified multifactorial intervention on cardiovascular outcomes and mortality in type 2 diabetes (J-DOIT3): an open-label, randomised controlled trial. Lancet Diabetes Endocrinol 2017;5:951-64.
9. Centers for Disease Control and Prevention. Diabetes Fact Sheet. Available from: https://www.cdc.gov/diabetes/basics/quick-facts.html (cited 2023 Jan 2).
10. Fujihara K, Sone H. Cardiovascular disease in Japanese patients with type 2 diabetes mellitus. Ann Vasc Dis 2018;11:2-14.
11. American Diabetes Association Professional Practice Committee, Draznin B, Aroda VR, Bakris G, Benson G, Brown FM, et al. 9. Pharmacologic approaches to glycemic treatment: standards of medical care in diabetes-2022. Diabetes Care 2022;45 (Suppl 1):S125-43.
12. Gregg EW, Li Y, Wang J, Burrows NR, Ali MK, Rolka D, et al. Changes in diabetes-related complications in the United States, 1990-2010. N Engl J Med 2014;370:1514-23.
13. Desouza CV, Bolli GB, Fonseca V. Hypoglycemia, diabetes, and cardiovascular events. Diabetes Care 2010;33:1389-94.
14. Rajkomar A, Dean J, Kohane I. Machine learning in medicine. N Engl J Med 2019;380:1347-58.
15. Yu KH, Beam AL, Kohane IS. Artificial intelligence in healthcare. Nat Biomed Eng 2018;2:719-31.
16. Perakakis N, Yazdani A, Karniadakis GE, Mantzoros C. Omics, big data and machine learning as tools to propel understanding of biological mechanisms and to discover novel diagnostics and therapeutics. Metabolism 2018;87:A1-9.
17. Muehlematter UJ, Daniore P, Vokinger KN. Approval of artificial intelligence and machine learning-based medical devices

in the USA and Europe (2015-20): a comparative analysis. Lancet Digit Health 2021;3:e195-203.
18. Lyell D, Coiera E, Chen J, Shah P, Magrabi F. How machine learning is embedded to support clinician decision making: an analysis of FDA-approved medical devices. BMJ Health Care Inform 2021;28:e100301.
19. Cabitza F, Rasoini R, Gensini GF. Unintended consequences of machine learning in medicine. JAMA 2017;318:517-8.
20. Kavakiotis I, Tsave O, Salifoglou A, Maglaveras N, Vlahavas I, Chouvarda I. Machine learning and data mining methods in diabetes research. Comput Struct Biotechnol J 2017;15:104-16.
21. Abhari S, Niakan Kalhori SR, Ebrahimi M, Hasannejadasl H, Garavand A. Artificial intelligence applications in type 2 diabetes mellitus care: focus on machine learning methods. Healthc Inform Res 2019;25:248-61.
22. Contreras I, Vehi J. Artificial intelligence for diabetes management and decision support: literature review. J Med Internet Res 2018;20:e10775.
23. Verbraak FD, Abramoff MD, Bausch GC, Klaver C, Nijpels G, Schlingemann RO, et al. Diagnostic accuracy of a device for the automated detection of diabetic retinopathy in a primary care setting. Diabetes Care 2019;42:651-6.
24. Haenssle HA, Fink C, Schneiderbauer R, Toberer F, Buhl T, Blum A, et al. Man against machine: diagnostic performance of a deep learning convolutional neural network for dermoscopic melanoma recognition in comparison to 58 dermatologists. Ann Oncol 2018;29:1836-42.
25. Schmidt-Erfurth U, Sadeghipour A, Gerendas BS, Waldstein SM, Bogunovic H. Artificial intelligence in retina. Prog Retin Eye Res 2018;67:1-29.
26. Ting DSW, Pasquale LR, Peng L, Campbell JP, Lee AY, Raman R, et al. Artificial intelligence and deep learning in ophthalmology. Br J Ophthalmol 2019;103:167-75.
27. Munir K, Elahi H, Ayub A, Frezza F, Rizzi A. Cancer diagnosis using deep learning: a bibliographic review. Cancers (Basel) 2019;11:1235.
28. Burt JR, Torosdagli N, Khosravan N, RaviPrakash H, Mortazi A, Tissavirasingham F, et al. Deep learning beyond cats and dogs: recent advances in diagnosing breast cancer with deep neural networks. Br J Radiol 2018;91:20170545.
29. Ravaut M, Harish V, Sadeghi H, Leung KK, Volkovs M, Kornas K, et al. Development and validation of a machine learning model using administrative health data to predict onset of type 2 diabetes. JAMA Netw Open 2021;4:e2111315.
30. Fujimaki R, Morinaga S. Factorized asymptotic Bayesian inference for mixture modeling. Proc Mach Learn Res 2012;22:400-8.
31. Savage N. Breaking into the black box of artificial intelligence. Nature 2022 Mar 29 [Epub]. https://doi.org/10.1038/d41586-022-00858-1.
32. Ellahham S. Artificial intelligence: the future for diabetes care. Am J Med 2020;133:895-900.
33. Gautier T, Ziegler LB, Gerber MS, Campos-Nanez E, Patek SD. Artificial intelligence and diabetes technology: a review. Metabolism 2021;124:154872.
34. Nomura A, Noguchi M, Kometani M, Furukawa K, Yoneda T. Artificial intelligence in current diabetes management and prediction. Curr Diab Rep 2021;21:61.
35. Islam MM, Yang HC, Poly TN, Jian WS, Jack Li YC. Deep learning algorithms for detection of diabetic retinopathy in retinal fundus photographs: a systematic review and meta-analysis. Comput Methods Programs Biomed 2020;191:105320.
36. Nimri R, Battelino T, Laffel LM, Slover RH, Schatz D, Weinzimer SA, et al. Insulin dose optimization using an automated artificial intelligence-based decision support system in youths with type 1 diabetes. Nat Med 2020;26:1380-4.
37. Kodama S, Fujihara K, Shiozaki H, Horikawa C, Yamada MH, Sato T, et al. Ability of current machine learning algorithms to predict and detect hypoglycemia in patients with diabetes mellitus: meta-analysis. JMIR Diabetes 2021;6:e22458.
38. Rollo ME, Aguiar EJ, Williams RL, Wynne K, Kriss M, Callister R, et al. eHealth technologies to support nutrition and physical activity behaviors in diabetes self-management. Diabetes Metab Syndr Obes 2016;9:381-90.
39. Yeoh E, Png D, Khoo J, Chee YJ, Sharda P, Low S, et al. A head-to-head comparison between Guardian Connect and FreeStyle Libre systems and an evaluation of user acceptability of sensors in patients with type 1 diabetes. Diabetes Metab Res Rev 2022;38:e3560.
40. Krakauer M, Botero JF, Lavalle-Gonzalez FJ, Proietti A, Barbieri DE. A review of flash glucose monitoring in type 2 diabetes. Diabetol Metab Syndr 2021;13:42.
41. Evans M, Welsh Z, Ells S, Seibold A. The impact of flash glucose monitoring on glycaemic control as measured by HbA1c: a meta-analysis of clinical trials and real-world observational studies. Diabetes Ther 2020;11:83-95.
42. Zou Q, Qu K, Luo Y, Yin D, Ju Y, Tang H. Predicting diabetes mellitus with machine learning techniques. Front Genet 2018;9:515.

43. Kopitar L, Kocbek P, Cilar L, Sheikh A, Stiglic G. Early detection of type 2 diabetes mellitus using machine learning-based prediction models. Sci Rep 2020;10:11981.
44. Choi BG, Rha SW, Kim SW, Kang JH, Park JY, Noh YK. Machine learning for the prediction of new-onset diabetes mellitus during 5-year follow-up in non-diabetic patients with cardiovascular risks. Yonsei Med J 2019;60:191-9.
45. Lai H, Huang H, Keshavjee K, Guergachi A, Gao X. Predictive models for diabetes mellitus using machine learning techniques. BMC Endocr Disord 2019;19:101.
46. Zhang L, Wang Y, Niu M, Wang C, Wang Z. Machine learning for characterizing risk of type 2 diabetes mellitus in a rural Chinese population: the Henan Rural Cohort Study. Sci Rep 2020;10:4406.
47. Nomura A, Yamamoto S, Hayakawa Y, Taniguchi K, Higashitani T, Aono D, et al. SAT-LB121 development of a machine-learning method for predicting new onset of diabetes mellitus: a retrospective analysis of 509,153 annual specific health checkup records. J Endocr Soc 2020;4(Supplement_1):SAT-LB121.
48. American Diabetes Association. Standards of medical care in diabetes-2022 abridged for primary care providers. Clin Diabetes 2022;40:10-38.
49. Desai NR, Shrank WH, Fischer MA, Avorn J, Liberman JN, Schneeweiss S, et al. Patterns of medication initiation in newly diagnosed diabetes mellitus: quality and cost implications. Am J Med 2012;125:302.
50. Filion KB, Joseph L, Boivin JF, Suissa S, Brophy JM. Trends in the prescription of anti-diabetic medications in the United Kingdom: a population-based analysis. Pharmacoepidemiol Drug Saf 2009;18:973-6.
51. Berkowitz SA, Krumme AA, Avorn J, Brennan T, Matlin OS, Spettell CM, et al. Initial choice of oral glucose-lowering medication for diabetes mellitus: a patient-centered comparative effectiveness study. JAMA Intern Med 2014;174:1955-62.
52. Liu H, Xie G, Mei J, Shen W, Sun W, Li X. An efficacy driven approach for medication recommendation in type 2 diabetes treatment using data mining techniques. Stud Health Technol Inform 2013;192:1071.
53. Wright AP, Wright AT, McCoy AB, Sittig DF. The use of sequential pattern mining to predict next prescribed medications. J Biomed Inform 2015;53:73-80.
54. Mei J, Zhao S, Jin F, Zhang L, Liu H, Li X, et al. Deep diabetologist: learning to prescribe hypoglycemic medications with recurrent neural networks. Stud Health Technol Inform 2017;245:1277.
55. Tarumi S, Takeuchi W, Chalkidis G, Rodriguez-Loya S, Kuwata J, Flynn M, et al. Leveraging artificial intelligence to improve chronic disease care: methods and application to pharmacotherapy decision support for type-2 diabetes mellitus. Methods Inf Med 2021;60(S 01):e32-43.
56. Fujihara K, Matsubayashi Y, Harada Yamada M, Yamamoto M, Iizuka T, Miyamura K, et al. Machine learning approach to decision making for insulin initiation in Japanese patients with type 2 diabetes (JDDM 58): model development and validation study. JMIR Med Inform 2021;9:e22148.
57. Singla R, Aggarwal S, Bindra J, Garg A, Singla A. Developing clinical decision support system using machine learning methods for type 2 diabetes drug management. Indian J Endocrinol Metab 2022;26:44-9.
58. Fujihara K, Igarashi R, Matsunaga S, Matsubayashi Y, Yamada T, Yokoyama H, et al. Comparison of baseline characteristics and clinical course in Japanese patients with type 2 diabetes among whom different types of oral hypoglycemic agents were chosen by diabetes specialists as initial monotherapy (JDDM 42). Medicine (Baltimore) 2017;96:e6122.
59. Christodoulou E, Ma J, Collins GS, Steyerberg EW, Verbakel JY, Van Calster B. A systematic review shows no performance benefit of machine learning over logistic regression for clinical prediction models. J Clin Epidemiol 2019;110:12-22.
60. Stylianou N, Akbarov A, Kontopantelis E, Buchan I, Dunn KW. Mortality risk prediction in burn injury: comparison of logistic regression with machine learning approaches. Burns 2015;41:925-34.