Health Technology Update

CADTH

A newsletter on new and emerging health care technologies in Canada

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TECHNOLOGIES IN THIS ISSUE:

Artificial Intelligence Issue

This issue of *Health Technology Update* features brief summaries of information on a range of artificial intelligence technologies — from chatbots to systems for the detection of cognitive impairment and dementia. These technologies were identified through the CADTH Horizon Scanning Service as topics of potential interest to health care decision-makers in Canada.

FEEDBACK

Have you heard of a new health technology you think will have an impact on health care in Canada?

Please let us know!

Email: **HorizonScanning@cadth.ca.**

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About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

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Issue 22: Artificial Intelligence

Artificial intelligence (AI) is a branch of computer science concerned with developing programs to perform tasks that would usually require human intelligence.[1-4] Recent advances in computing power combined with declining costs have led to an expansion of AI research and applications, including in health care.[4,5] Common approaches to AI include: machine learning — training an algorithm to perform tasks by learning from patterns in data rather than performing a task it is explicitly programmed to do;[5] support vector machine — a type of machine learning often used in the diagnosis or disease prediction to classify the absence or presence of a condition;[6] artificial neural networks — a method of mimicking the way the human brain learns and is used for solving complex problems where relationships are unclear;[4,6] and deep learning — a more recent form of artificial neural network that has many hidden layers of decision-making between input and output.[6]

CADTH's publication *An Overview of Clinical Applications of Artificial Intelligence*[7] serves as a starting point for individuals seeking a better understanding of AI concepts and their emerging uses in health care.

In this issue of *Health Technology Update*, we present readers with five articles about new and emerging health technologies and clinical areas that use AI:

- IDx-DR, a diagnostic system designed to autonomously screen retinal images of people with diabetes for early detection of diabetic retinopathy
- chatbots, AI-powered conversational agents that attempt to mimic human therapists for people living with mental health disorders
- e-ASPECTS, an automated software enhanced with AI to assist physicians in identifying and interpreting the extent of brain damage in acute ischemic stroke patients from computed tomography, or CT, exams
- BrainFx, a tablet-based cognitive and neurofunction assessment tool that uses AI to detect early risk factors for mild to moderate brain dysfunction
- the many ways population and public health researchers are exploring how AI could impact disease surveillance, forecasting, and modelling.

Author: Jeff Mason

See references on page 21.

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Image courtesy of IDx LLC

IDx-DR: Automated Screening for Diabetic Retinopathy

Diabetic retinopathy is the most common cause of vision loss and blindness in adults, in Canada.[1-5] It occurs when high blood sugar levels damage blood vessels in the retina — the light-sensitive tissue located at the back of the eye.[3] Deep learning algorithms are being trained, using retinal images of varying disease severities, to autonomously identify early diabetic retinopathy and prevent vision loss.[1,2,6-8]

How It Works

IDx-DR (IDx, LLC, Coralville, Iowa) is an artificial intelligence (AI) diagnostic system designed to autonomously screen retinal images for signs of diabetic retinopathy.[9] IDx-DR is intended for the primary care diagnosis of moderate to severe diabetic retinopathy and macular edema in adults 22 years of age and older with diabetes and no previous diabetic retinopathy diagnosis.[9,10]

IDx-DR can provide screening decisions without the need for a clinician to interpret the images and results.[3] Clinic staff can be trained in four hours to operate IDx-DR, as the device provides guidance for image-taking.[11] IDx-DR is only to be used with the Topcon TRC-NW400 non-mydriatic retinal camera.[9] Two 45-degree field of view colour images of the retina per eye are taken by either clinical or non-clinical staff trained to operate the camera.[3,9] The camera images are then uploaded to the IDx-DR client user in the local computer and submitted to the IDx-DR analysis system located on a secure server.[3,9] IDx-DR uses deep learning detector algorithms to look for diabetic retinopathy-specific lesions in the images.[9] The algorithms evaluate each image for the disease and image quality.[9] If the image quality is insufficient, IDx-DR software will indicate that immediate reimaging is needed.[9]

The AI test results are provided in less than one minute and indicate if the images are negative for more than mild diabetic retinopathy (requiring retesting in 12 months), or positive for more than mild diabetic retinopathy.[9] Based on the results, the clinician determines if an individual requires a referral to an ophthalmologist for further evaluation and treatment.[9] An associated report is also produced, with care instructions for the provider.[12]

Automated systems have the potential to offset high demands for screening, and reduce rates of missed diagnoses and intra-expert variation in screening.[2,6,13] These systems may also reduce the screening workload because of efficient automated analysis of large numbers of retinal images, and could improve clinic-level workflow efficiency and coverage, allowing for increased patient interaction.[1,2,14]

Who Might Benefit?

In 2013-2014, approximately 3 million Canadians lived with diagnosed diabetes and about 200,000 were newly diagnosed with diabetes.[15] An estimated 11.4% of the Canadian population will be diagnosed with diabetes by 2025.[16]

All individuals with type 1 or type 2 diabetes are at risk for diabetic retinopathy.[17] In Canada, the disease affects about 500,000 people, and is more common in Indigenous populations.[4,17] In 2014, 66% of Canadians living with diabetes reported receiving an eye screening exam in the past year.[16]

IDx-DR is not intended to be used to screen individuals with laser eye treatment history; injections or surgery in the eye; floaters; blurred vision; persistent vision loss; severe non-proliferative, proliferative, or radiation retinopathy; retinal vein occlusion; previously diagnosed macular edema; or pregnant individuals with diabetes.[3]

Availability in Canada

IDx-DR is currently unavailable in Canada.[9]

The system received FDA clearance on April 11, 2018 under the De Novo premarket review pathway for novel low to moderate risk devices having no prior legally marketed devices.[3] IDx-DR is being used for patient care in the Diabetes and Endocrinology Centre at University of Iowa Health Care, and will be introduced into several other US health care systems in 2018.[18]

IDx-DR received the CE certification from the Underwriters Laboratory in 2013, and a Class IIa Medical Devices classification for sale in the European Union on April 23, 2016.[9] IDx has partnered with Medical Workshop in the Netherlands, and IBM

> "Deep learning algorithms are being trained, using retinal images of varying disease severities, to autonomously identify early diabetic retinopathy and prevent vision loss."

Watson Health for the rest of Europe, for device distribution.[9]

What Does It Cost?

The costs of purchasing and operating IDx-DR were not identified. In the Harris Health System (Texas, US), the cost of a similar automated screening system for diabetic retinopathy, without AI features — the Intelligent Retinal Imaging Systems (IRIS) — is approximately $55 US per person.[19]

Current Practice

The 2018 Diabetes Canada diabetic retinopathy guidelines recommend regular, comprehensive, dilated eye exams for the early detection of treatable diabetic retinopathy.[4] If retinopathy is not detected, annual screening is recommended for people with type 1 diabetes, and every one to two years for people with type 2 diabetes.[4]

Screening can be performed with stereoscopic-colour fundus photography, digital stereoscopic retinal photography, digital ophthalmoscopy, or optical coherence tomography by "qualified vision care professionals (ideally optometrists or ophthalmologists)."[2,4,6,8,20] Screening services based on trained human graders (non-ophthalmologic or ophthalmologic graders) are a suggested first-line assessment in order to reduce the number of people requiring further specialized ophthalmological assessment.[1] Telemedicine programs relying on fundus photography and ultra-wide field imaging are used widely in Canada to manually identify and triage people with diabetic retinopathy.[4]

In Canada, automated screening for diabetic retinopathy is not recommended by guidelines for clinical practice because of present limitations including technical failures in retinal vessel identification.[21]

Published Information

Published Studies

In a validation study in the Netherlands, retinal images from 1,371 people with diabetes in the Hoorn Diabetes Care System were graded by IDx-DR, and independently by three specialists, to determine the accuracy of automated retinopathy screening in primary care.[22] In a US observational study,[23] retinal images from 892 people (aged 22 to 84) with diabetes from 10 primary care clinics were evaluated to determine the accuracy of IDx-DR in detecting more than mild diabetic retinopathy.

Conference Abstracts

Results from the following studies are available within conference abstracts:

- A validation study in the US of 528 people with diabetes from five ophthalmologic centres compared the accuracy of IDx-DR to ophthalmologist examinations in detecting diabetic eye disease.[26]
- In a study in the Netherlands, 1,500 people with type 2 diabetes in the Diabetes Care System West-Friesland were screened for retinopathy using IDx-DR.[27] IDx-DR was evaluated for

accuracy in comparison to manual grading by three retinal specialists, and workflow changes resulting from the use of IDx-DR were measured.[27]

Registered Clinical Trials

A multi-centre observational study of 600 participants was reported as complete in 2014 but published results were not identified. The study compared the performance of IDx-DR to ophthalmologist-performed dilated eye examinations in its ability to distinguish between no or mild non-proliferative diabetic retinopathy without macular edema and more than mild non-proliferative diabetic retinopathy with or without macular edema.[28]

Safety

The letter issued by the FDA following a De Novo classification of the system identified risks to health with using IDx-DR including false-positive results, which lead to additional unnecessary medical procedures; false-negative results, which delay further evaluations and treatments as a result of diagnostic algorithm or software failure; and operator failure in providing images meeting input quality specifications.[10]

Issues to Consider

The ability of deep learning algorithms to detect referable diabetic retinopathy and reduce incorrect readings depends on the amount and quality of data available for training.[2,14] Automated systems may produce incorrect diagnoses when algorithms are unable to detect lesions because of variations in image lighting, contrast, clarity, background texture, and fundus camera quality.[14,29,30]

The cybersecurity of medical images is a growing concern, particularly with image-sharing over networks and storage in electronic databases.[31] Digital watermarking can be used to hide patient identity in medical images; however, it can make slight computational changes to the retinal images, which may affect automated diagnosis.[31] New algorithms are being developed to ensure that embedded watermarks maintain an individual's health information without causing information loss or compromising diagnostic accuracy.[31]

IDx-DR accepts most image formats and uses common output formats for compatibility with electronic medical record systems and software.[9]

Related Developments

AI Diagnosis of Eye Disease

Additional pilot studies for the IDx-DR software are pending in Finland, the Czech Republic, and Italy. IDx-DR plans to conduct trials to expand its indication for use with other camera manufacturers (Laura Shoemaker, Director of Marketing Communications, IDx, LLC, Coralville, Iowa: personal communication, 2018 Jun 28).

IDx, LLC is developing algorithms for detecting disease across multiple imaging tools, with a focus on fundus imaging and optical coherence tomography.[9] Algorithms are being developed for detecting stroke risk, cardiovascular disease, Alzheimer disease, signs of age-related macular degeneration (IDx-AMD), and glaucoma (IDx-G) indicators from retinal images.[9]

Other automated diagnostic systems for diabetic retinopathy screening include EyeCheck, iGradingM (Medalytix (Group) Ltd., Manchester, UK), EyeArt and EyeApp (Eyenuk, Woodland Hills, CA), and Retmarker (Retmarker, SA, Taveiro, Portugal).[1,7,32]

Automated teleretinal systems for diabetic retinopathy screening include the cloud-based SELENA automated software, and IRIS.[7,30]

DeepMind (Alphabet Inc.) has developed and is testing an automated deep learning algorithm designed to detect 50 eye diseases (including diabetic retinopathy) using optimal coherence tomography scans.[33]

Looking Ahead

In Canada, in 2007, the estimated cost to the health care system for vision loss due to diabetic retinopathy was $205 million.[34]

There is interest in enhancing the precision of automated retinal screening by combining algorithms from multiple imaging tools, and by developing deep learning algorithms that could infer disease progression patterns, determine reliable predictors of diabetic retinopathy, and combine image data with other health data for more comprehensive information, including risk of systemic disease.[8,35] Using deep learning algorithms for screening could also contribute to the universal standardization of retinal image grading across multiple populations.[8]

AI may also be used for teleretinal screening programs, which may help overcome geographical barriers and wait times to increase access to screening.[30,35]

Because IDx-DR is currently unavailable in Canada, the impact of this technology on human resources for diabetic retinopathy screening in the Canadian health care system is unclear.

Author: Humaira Nakhuda

See references on page 21.

Photo: iStock/NicoElNino

Chatbots: AI-Based Delivery of Therapy or Coaching for Mental Health Conditions

Chatbot technologies — artificial intelligence (AI)-based conversational agents — marry mobile and Internet-based therapies with simulated human conversation to help address mental health problems. Available 24/7 and to anyone with an Internet connection, chatbots are positioned as an adjunct to conventional therapy, and as a way of increasing access to therapeutic education for individuals in need.

How It Works

Conversational agents are a form of AI that mimic real-life human interactions through a conversational approach, much like talking with a therapist or friend.[1] This software is activated by natural language input (text, speech, or both) and uses a pattern-matching algorithm to link user words with topic categories. It then executes goal-directed commands through these topic-linked inputs.

One type of conversational agent, chatbots, are commonly employed in customer service or social media interactions. Another, embodied conversational agent (ECA), is like a chatbot but with the addition of a virtual avatar that embodies the AI computer system.[1] All modern chatbots trace their origins to ELIZA — the original chatbot created by a psychotherapist — and have now broadened out to a variety of different applications and uses. Chatbots can deliver psychological techniques modelled on real psychotherapy, such as cognitive behavioural therapy (CBT) or positive psychology, through this conversational interface. Although some chatbots may mimic human interaction, they are generally not intended as a replacement for human-led therapy. Chatbots provide responses that can lead patients to videos, mood tracking, and core concepts in psychological interventions.[2] Chatbots may also have machine learning, which allows them to adapt to new information.

Some chatbot technologies have security systems to help prevent breach of data. For example, Woebot attempts to eliminate security issues with user data by encryption, compliance with data privacy legislation, and informed consent (Dr. Athena Robinson, Chief Clinical Officer, Woebot, San Francisco, CA: personal communication, 20184 Jun 4).

Who Might Benefit?

Individuals with mental health disorders or individuals experiencing distress could potentially benefit from chatbots. Mental health conditions are common: one in three Canadians will meet the criteria for having a mental health disorder during their lifetime.[3] There is also a high societal, economic burden of mental illness through absenteeism, unemployment, loss of productivity, and medical expenses.[3]

Accessing psychological services can be challenging — issues such as stigma,[2] limited infrastructure,[4] and lack of access often prevent people from seeking help.[4,5] Mental health chatbots may help bridge these issues. Online interventions also provide patients with immediate access to resources and information.[6]

It has been reported that individuals interact with chatbots as they would a human therapist, and are more likely to share information on sensitive topics (such as mental health) than with human counterparts.[2,7-9] Online interventions also provide anonymity for users.[6] It has been reported that anonymity and rapport are important in interviews, as they lead to greater disclosure from patients.[7]

Availability in Canada

A number of chatbots are available in Canada for use. Some chatbots for mental health are available through a downloadable mobile app, or through Facebook Messenger. Some chatbots or ECAs are available through specific websites and do not require an account or sign-up to access.[5]

Internet-delivered interventions, AI or otherwise, are unique when compared to regular therapy in that they are continuously available to individuals who have access to the Internet or to a mobile phone.[10] According to the Canadian Internet Registration Authority and the International Telecommunication Union, in 2016, 90% of Canadians had Internet access, although some individuals in remote regions did not, and those with access may not have had sufficient speed and quality, or access in a private home.[11]

"Accessing psychological services can be challenging — issues such as stigma, limited infrastructure, and lack of access often prevent people from seeking help. Mental health chatbots may help bridge these issues."

Health Canada is currently looking into the regulation process for digital health, including AI and other mobile medical applications.[12] Health Canada cannot make a blanket statement regarding the regulatory classification of AI in the health care field because it is largely dependent on the characteristics of the specific application; however, so far Health Canada has not licensed any chatbots (Medical Devices Bureau, Therapeutic Products Directorate, Health Products and Food Branch, Health Canada, Ottawa, ON: personal communication, 2018 Jul 4).

What Does It Cost?

Many chatbots appear not to have a paywall.[2,5,13] Some chatbots have a monthly paywall, such as Tess, which has a platform fee of US$50 per month and a patient fee of US$1 per month.[14] Wysa currently has a premium product, in addition to its free AI chat, called "Wysa Coach" (US$30 per month) in which a user can talk to a trained mental health professional and share content gathered from conversations with the AI chatbot to build mental resilience skills (Ramakant Vempati, Co-founder, Wysa Ltd., Bangalore, India: personal communication, 2018 Jun 4).

In comparison, a 50-minute individual therapy session is suggested to cost between $120 in British Columbia (2016)[15] and $200 in Alberta (2018).[16]

Current Practice

Currently, Canadian guidelines recommend CBT, interpersonal therapy, and behavioural action as non-pharmacological treatments for mood disorders such as depression.[17] Second-line therapies include telephone-, Internet-, and computer-assisted therapy (none of the interventions studied appearing to include an AI chatbot component).[17] For anxiety disorders, CBT is often recommended as a non-pharmacological treatment.[18]

Published Studies

Three randomized controlled trials were identified in the literature that assessed AI chatbots and mental health-related outcomes.[2,19,20] The studies compared Woebot to information-only control,[2] iPhone-based Shim to wait list control,[19] and MYLO to ELIZA.[20] Not all participants had a diagnosed mental health condition, and no studies were performed in a Canadian population.

Safety

One potential safety issue is the unintended side effects of intelligent agents. For example, if the programmer inputs provided to an AI are flawed or biased, the output the patient receives will be inherently flawed or biased.[21] This possible violation of the therapeutic process can be attenuated through the inclusion of trained clinicians to help develop and design the chatbots.[2] Additionally, AI chatbots could potentially recommend medical procedures or solutions to a patient that have more side effects than necessary, and may not be able to adapt when a patient provides unusual responses.[21]

Risk to patients is managed in three ways by Wysa: practical means (apologizing when there's a misunderstanding, allowing patients to direct the conversation), ethical means (taking no personal data, natural language processing [NLP] to recognize potential ideation on suicide or self-harm), and legal means (allowing for patients to remove data, security measures on the application) (Ramakant Vempati: personal communication, 2018 Jun 4). Woebot also has safety net procedures, including unskippable informed consent, and NLP to recognize suicidal ideation and to provide resources (Dr. Athena Robinson: personal communication, 2018 Jun 10). No information was identified on the impact of these measures on risks associated with the use of the technology.

Issues to Consider

Potential issues that may arise with Internet-based AI technologies are those of access to the Internet and computer illiteracy,[22] and the lack of ability for the AI to learn from individual patients.[23] There are also potential ethical issues associated with the use of this technology related to storage, and access to and confidentiality of personal data.[22] Data protection and privacy laws may vary by jurisdiction. This issue is especially present when the chatbot is used through third-party websites, such as Facebook.

Related Developments

ECAs have been used to deliver mindfulness and lifestyle recommendations such as healthier eating and reduction of stress.[24] ECAs have also been used to create game-based simulations for primary health care providers to help screen patients for mental health issues.[25]

Outside of mental health applications, chatbots can also be used to address loneliness and act as a "friend" to chat to, with no therapy function.[26] Chatbots are also being developed as a resource for individuals looking to answer simple health questions that do not require a physician's visit.[27]

Looking Ahead

One of the pitfalls of text-based chatbot technology is the lack of recognition of non-verbal emotion by AI technologies.[28] There is interest in future research to address these non-verbal nuances in order to maintain believability and smoothness in the conversation, and to build trustworthiness with the patient.[29] Currently, there is research being done with a platform, SimSensei (or "Ellie," a continuation of SimCoach), that combines real-time audio and visual cues from the patient, and has facial expression and body language recognition for diagnostic purposes.[5,28]

There are reported gaps in the literature regarding whether chatbots are an appropriate intervention for treating mental health conditions or whether they should primarily be a screening tool.[30] It has been noted that there is a lack of evidence regarding the implementation of the technology, and that more research is required with larger samples, proper control groups, and clinical populations.[31]

Author: Charlotte Wells

See references on page 21.

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Image reproduced with permission from Brainomix

Using Artificial Intelligence for Stroke in the Emergency Setting

e-ASPECTS is an AI-enhanced decision support tool that measures the extent of ischemic damage in patients with suspected stroke.[1] It is not intended to replace the expert assessment of an image but rather to assist physicians in treatment decisions by providing an unbiased and standardized approach to image interpretation.[2]

How It Works

e-ASPECTS (Brainomix Limited) uses machine learning — a form of AI — to facilitate the automated extraction and classification of imaging features taken with non-contrast computed tomography (CT) in the emergency setting. The machine learning algorithm uses the CT imaging data to quantify the volume of ischemia (inadequate blood supply) and apply the Alberta Stroke Program Early CT Score (ASPECTS).[3]

ASPECTS is a quantitative, 10-point, validated scoring tool that measures the extent of early ischemic changes — changes in blood flow to the brain — and provides an accurate prediction of functional outcomes after thrombolytic treatment — the breakdown of blood clots formed in blood vessels.[4] It is used with non-contrast CT as part of the assessment to determine patient eligibility for mechanical thrombectomy.[5,6] ASPECTS was developed to help interpret CT images taken within the first hours of the onset of suspected stroke. The interpretation of CT images is generally challenging,[7] requires considerable expertise, and can be subject to inter-rater variability.[8] While ASPECTS scores can also be affected by differences in the reader's experience and clinical background,[6] overall it is regarded as a useful tool for the standardized evaluation of the extent of ischemic damage.[5]

e-ASPECTS was developed to further standardize these variables and interpret data objectively.[9] The e-ASPECTS application generates a heat map to aid clinicians in interpreting its output. This heat map provides information on the mechanism of arriving at the final score (Olivier Joly, Brainomix, Oxford, UK: personal communication, 2018 Aug 16). e-ASPECTS results can be accessed via picture archiving and communication systems (PACS), through a Web browser user interface, or sent via email to a smartphone.[10]

The software is intended to assist clinical experts in decision-making by providing a second opinion and confirming expert assessment. In addition to reviewing the AI assessment, a physician is required to assess each CT image to rule out hemorrhage and other pathologies.[2]

It has been shown that the integration of e-ASPECTS into mobile stroke units can help with triage decisions related to selecting the appropriate hospital to send stroke patients to, such as those with a comprehensive stroke unit or a primary stroke unit.[3] e-ASPECTS may also play a role in aiding decision-making for patient selection conducted via telemedicine and in selecting patients for transfer to stroke centres that perform mechanical thrombectomy.[11]

Who Might Benefit?

Approximately 62,000 Canadians experience a stroke each year, and approximately 13,000 die after having a stroke.[12] It is estimated that 405,000 Canadians are living with the effects of stroke[12] and this number is expected to increase to between 654,000 and 726,000 over the next 20 years.[13]

People over the age of 70 are the most likely to experience a stroke.[14] However, according to a 2014 report, over the preceding decade, the number of strokes in people in their 50s and 60s increased by 24% and 13%, respectively.[14] As well, stroke rates in younger people (between the ages of 24 and 64) are expected to double by 2030.[14] Early treatment with thrombolytic drugs reduces the mortality and the morbidity of stroke, and more patients who receive early treatment are discharged home, rather than to a rehabilitation centre.[15,16]

Availability in Canada

e-ASPECTS is not currently approved in Canada. It was granted the Conformité Européenne (CE) certification as a Class IIa medical device in 2015 by the European Union and is used in Europe and Brazil.[17]

Beyond Europe and Brazil, e-ASPECTS is installed for research purposes in Canada (Olivier Joly: personal communication, 2018 Jul 2).

> "Since… e-ASPECTS is anticipated to speed up the diagnosis of acute ischemic stroke — allowing earlier thrombolytic treatment — it may change how quickly stroke is diagnosed and managed."

What Does It Cost?

Brainomix sells e-ASPECTS as an annual licence subscription that allows the hospitals to process the scans of all stroke patients who are admitted (Olivier Joly: personal communication, 2018 Jul 2).

The cost of the device is not known and may vary depending on the setting in which it is used. In facilities with rapid network connections that do not require the installation of hardware, one installation can be accessed by several hospitals. In hospitals with less modern technological infrastructure, remote installation may not be feasible and the cost of the device may subsequently be higher.[17]

Current Practice

The 2015 Canadian Stroke Best Practice Recommendations note that brain imaging with non-contrast CT should be completed without delay for any patient with suspected stroke. To determine the eligibility for endovascular therapy, it is suggested that the initial brain CT should be assessed using ASPECTS to identify patients with a score of six points or higher. Patients may be eligible for endovascular therapy within six to 12 hours of onset of symptoms and should ideally begin treatment within 60 minutes of CT imaging.[18]

The American Heart Association guidelines also recognizes ASPECTS as a key tool for the management of acute stroke and suggests mechanical thrombectomy for patients with a baseline ASPECTS score of 6 or more.[6]

Published Studies

Four clinical utility studies on e-ASPECTS have been published, including one randomized controlled trial,[1] one prospective cohort study,[11] and two retrospective cohort studies.[2,19] Three of the studies compare e-ASPECTS with either expert-derived clinical scores using ASPECTS[2,19] or expert opinion alone[11] to predict functional outcomes. Two of these studies examine the correlation of e-ASPECTS scores with clinical outcomes after thrombectomy[11] or thrombolysis.[1]As well, a feasibility study was published that examines the clinical integration and utility of e-ASPECTS into a mobile stroke unit[3] (an ambulance equipped with portable imaging equipment).

Issues to Consider

A concern for any AI application used in health care is that the data informing algorithms is applicable to the population that the AI tool will be used in. This underscores the importance of using AI to augment, rather than replace, a physician's perspective. No information was found on how e-ASPECTS' predictions are made or on the demographic used to train the algorithm.

It is suggested that, to be consistent with evidence-based practices, issues concerning transparency should be addressed prior to the integration of machine learning tools into clinical practice. Transparency regarding how predictions are made is lacking because the technical logic and mechanisms can be difficult to understand. This is known

as the black-box paradox.[20] Consideration should be given to the appropriate use of AI in reading and interpreting medical images. This may include establishing standards for AI interoperability, testing algorithms, and addressing regulatory, legal, and ethical issues.[21]

According to the manufacturer, the e-ASPECTS program was developed and tested using a largely Caucasian, adult population. While ethnic differences in brain anatomy and CT-based ischemic changes are reported to be minor,[22] the generalizability of the e-ASPECTS platform to other ethnic groups could be further validated (Olivier Joly: personal communication, 2018 Jul 2).

e-ASPECTS can only be used in facilities that have access to CT. Canada has approximately 561 CT units[23] but 89% of rural hospitals do not have access,[24] indicating potential inequity in access to stroke care in urban and rural settings.

Related Developments

In addition to e-ASPECTS, Brainomix has developed a platform called e-CTA[25] to analyze CT angiography of stroke patients and has partnered with Olea Medical to introduce the e-STROKE SUITE[26] in Europe and Brazil. The e-STROKE SUITE utilizes information from other acute imaging modalities for stroke, including perfusion imaging. (Olivier Joly: personal communication, 2018 Jul 2).

Numerous AI-enhanced support systems have been developed to detect the presence of stroke from brain images. In 2018, the FDA approved a similar decision support software, developed by Viz.ai, that incorporates AI and analyzes CT images of the brain.[27] The software sends a text notification to a patient's specialist to alert them if a suspected large vessel blockage has been identified.[27] There are a number of other AI-enhanced tools for stroke that use machine learning to automate segmentation to measure the volume of ischemic damage in brain CT to predict the outcome of stroke.[28,29]

Looking Ahead

Since "time is brain"[30] and e-ASPECTS is anticipated to speed up the diagnosis of acute ischemic stroke — allowing earlier thrombolytic treatment — it may change how quickly stroke is diagnosed and managed. This software may be particularly useful to medical staff with limited experience in stroke imaging, such as family physicians and paramedics.[20]

The window of time in which it is optimal to treat stroke patients with mechanical thrombectomy has recently expanded from six hours up to 24 hours in select patients.[31] e-ASPECTS may play a role in helping to quickly identify patients for mechanical thrombectomy within the expanded time frame.

Author: Andra Morrison

See references on page 22.

BrainFx tablet-based assessment; Image reproduced with permission from BrainFx

Detection of Cognitive Impairment and Dementia With Artificial Intelligence

Current diagnostic criteria for dementia have limited predictive ability for individuals.[1,2] It is proposed that artificial intelligence (AI) technologies may improve screening for cognitive impairment and dementia.[3,4] Machine-learning algorithms are being used to detect patterns of cognitive impairment by quantitatively analyzing medical data including imaging; demographic and genetic data; and speech, language, and cognitive neuropsychological test results.[3,5,6]

How It Works

BrainFx is an assessment tool that measures neurofunctional performance in individuals with mild to moderate brain dysfunction, and uses AI technology to support early detection and identification of risk factors for cognitive impairment and dementia.[12]

Dementia is a broad clinical term that includes vascular dementia, Parkinson disease dementia, and, most commonly, Alzheimer disease.[7,8] Patients with dementia have damaged nerve cells in the brain, which impair memory, speech and language, and cognitive functions, and can eventually affect daily activities, physical mobility, and safety.[9,10] Early detection during the pre-dementia stage known as mild cognitive impairment supports the timely and effective use of treatments to slow dementia progression.[6,11]

BrainFx SCREEN and 360 Assessment Tools

BrainFx (BrainFx, Pickering, Ontario) assesses complex cognitive skills and other neurofunctions using predictive analytics through interactive, tablet-based activities administered by trained clinicians.[12] BrainFx does not provide a diagnosis or treatment recommendations — the information produced must be assessed by qualified clinicians.[12]

Individuals fill out a self-report prior to completing the BrainFx Assessments.[12] The initial BrainFx SCREEN tool is a 10-minute screening assessment of seven cognitive skills and the BrainFx 360 Assessment tool is a 90- to 120-minute assessment that measures 30 cognitive skills including functional impacts.[12]

BrainFx uses a machine-learning algorithm to compare an individual patient's performance data to anonymized patient-consented data from the BrainFx Living Brain Bank, and clinical neuroscience and demographic data to detect early cognitive impairment and dementia, and improve assessments and comparative data[12-14] (Tracy Milner, BrainFx, Pickering, ON: personal communication, 2018 Jul 13). The BrainFx SCREEN and 360 assessment performance results are produced as a report and integrated with a patient's medical history and quality of life information to produce a secondary report.[12,15] The patient's health care team receives the reports, including the self-report, for use as a supplementary tool in the diagnostic and treatment-planning process.[12,14,15]

Using BrainFx to Support Proactive Disease Detection

A separate proactive detection tool is under development by BrainFx in partnership with Saint Elizabeth Healthcare, ThoughtWire Corp, (Wilfred) Laurier University, four family health teams in the Waterloo Wellington Local Health Integration Network, and the Southlake Regional Health Centre.[13,14,16] It is intended as a brain health assessment and risk management tool for the early detection of cognitive impairment and dementia.[13,14,16] BrainFx Assessments are being used to screen 10,000 patients to detect cognitive decline.[16,17] This data will be combined with Canadian Institute for Health Information data to train machine-learning algorithms to identify early risk factors.[16,17] The intention is for health care professionals to use the early identification algorithm under study to proactively scan electronic medical records to identify at-risk individuals for assessment.[13,14,18,19]

Who Might Benefit?

In Canada, more than 564,000 individuals live with dementia, and this is expected to increase to 937,000 by 2031.[20] An estimated 30% of patients with dementia in Canada may never receive diagnostic assessment, and the identification approaches used may fail to detect 10% of the patients who are assessed.[21]

Risk factors for dementia include age, family history, unhealthy diet, alcohol, smoking, high blood pressure and cholesterol, diabetes, physical inactivity,

> "Early detection during the pre-dementia stage known as mild cognitive impairment supports the timely and effective use of treatments to slow dementia progression."

severe brain injury, depression, and socioeconomic factors.[21-24]

Availability in Canada

BrainFx Assessments received a Class I Medical Device Establishment License from Health Canada in 2013[12,25] (Tracy Milner: personal communication, 2018 Jun 28). The assessments are used by more than 700 clinicians and approximately 120 health care organizations throughout Canada (Tracy Milner: personal communication, 2018 Jun 28). No information was found on regulatory approval of the BrainFx AI integrated application of the Living Brain Bank or for its use in proactive disease detection.

What Does It Cost?

The Canadian cost of BrainFx SCREEN and 360 Assessments is about $125 per month per individual health care provider, for use with an unlimited number of patients (Tracy Milner: personal communication, 2018 Jun 28). Discounted pricing is available for provider groups, including hospitals and clinics, and for individual assessments (Tracy Milner: personal communication, 2018 Jun 28). No information on the cost of the BrainFX AI integrated application using Living Brain Bank data or its use in proactive disease detection was obtained. As well, no studies on cost implications or considerations related to BrainFx technology were identified.

Current Practice

Dementia is typically detected by clinicians through manual neuropsychological assessments, the patient's medical history, and observations by family and health care workers.[11,26] An extensive series of cognitive screening tools including the Montreal Cognitive Assessment and the Mini-Mental State Examination are often used for assessment.[9] Imaging methods including magnetic resonance imaging (MRI) and positron emission tomography (PET) are also used to measure and detect early changes in brain features.[11] Currently, post-mortem analysis of brain tissue is considered to be the only method for obtaining a definite diagnosis because accurate diagnosis during a patient's life is challenging, as the underlying pathologies of different neurodegenerative diseases can result in overlapping clinical symptoms.[11,27]

Summary of Evidence

Few studies have used machine-learning algorithms with behavioural, functional, and cognitive data to detect dementia.[4] The BrainFx website lists several completed studies but no published study results in individuals with dementia were identified.[19]

Safety

Dementia testing can potentially impact patient care because of test inaccuracies and variations in the interpretation of results by clinicians, leading to imprecise detection.[28,29] No information was found on the number of incorrect test results with the BrainFx Assessments.

Issues to Consider

Data Collection

AI technologies for dementia and cognitive impairment detection can be introduced into standard medical protocols, and data can be retrieved quickly and easily to

complement other diagnostic tools used by clinicians.[30] Additionally, clinicians do not need to know AI algorithm-programming details to use the technology.[2]

However, a large and diverse data set is needed to train machine-learning algorithms.[31] Multi-centre health care data that is currently available may not be usable due to unclear labelling for diagnoses, inadequate disease specifications, and differences in data collection protocols, which prevents the merging of multiple data sets.[31] Multi-modal data creation can also be challenging if necessary data types are missing because of clinical trial costs, high dropout rates, imaging equipment availability, or a lack of patient consent.[3,6]

There is also uncertainty regarding how algorithms trained for specific tasks perform their analysis, and what the values in the algorithms represent.[32] This "black box" problem makes understanding the mechanism by which an AI system arrived at decisions difficult.[32] Legal concerns that have been raised include medical malpractice concerns for clinicians who do not use AI systems to support diagnosis.[33,34]

Cost Considerations

Canadian out-of-pocket and public health system costs for the care of individuals with dementia in 2016 were estimated at $10.4 billion; this is expected to increase to $16.6 billion by 2031.[20,30] In the UK, the cost for each dementia diagnosis is an estimated $6,000 at minimum, not including indirect costs to patients.[33,35] Earlier detection of dementia could reduce costs by enabling earlier intervention.[20] One UK, industry-sponsored, cost-utility study reported that higher up-front and treatment-related costs were offset by downstream savings in patient care — related to more timely treatment, resulting in less severe disease and time spent in institutions — for patients with suspected mild cognitive impairment.[35]

Related Developments

Automated analysis of speech samples can be used as a tool for the early detection of dementia.[30] WinterLight Labs (Toronto, Ontario) has created a tablet-based assessment system, which can characterize and quantify language and speech patterns to detect and monitor dementia and other cognitive disorders.[36,37]

Several AI-based approaches incorporating imaging data to support the early detection and monitoring of Alzheimer disease progression are in development. Avalon Ai (London, UK) has developed software that uses machine learning to detect signs of brain degeneration and dementia disease progression based on MRI scans.[37-39] In the Netherlands, researchers are combining machine-learning algorithms with an MRI technique called arterial spin labelling imaging.[40] The program recognizes patterns on perfusion maps — images showing the amount of blood delivered to various brain areas — to distinguish patients with varying cognitive impairments, and to predict the stage of Alzheimer disease in newly diagnosed individuals.[40] Scientists at McGill University have developed an algorithm capable of recognizing signs of dementia two years prior to onset using one PET scan of the brain of individuals at-risk for Alzheimer disease.[41]

Aequa Sciences (London, UK) is using machine learning and artificial neural networks to predict Alzheimer disease onset based on genetic data from healthy individuals and those with the disease.[38]

Looking Ahead

Research using machine-learning algorithms for the prognosis and detection of dementia is progressing quickly. There is interest in incorporating additional model inputs such as socioeconomic and lifestyle factors, behavioural data, and consideration of patient comorbidities in the algorithm assessment models, and in using deep-learning algorithms for the early detection of dementia.[4,6,42]

Author: Humaira Nakhuda

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CADTH

Focus On: Artificial Intelligence in Population and Public Health

In January 2018, CBC News reported that the Public Health Agency of Canada had partnered with an Ottawa-based market research firm to use artificial intelligence (AI) to analyze Canadians' public Facebook posts to predict increases in suicide risk. This was in an effort to improve prevention and intervention.[1] Since then, other media outlets have reported on how AI could use new and existing sources of data to open the door to novel approaches to population and public health.[2-4]

Photo: iStock/spainter_vfx

Why Population and Public Health?

AI systems rely on large amounts of data to learn and function.[5,6] For that reason, health care specialties — such as population and public health (particularly disease surveillance and disease forecasting), which already use consistent and reliable sources of data — are areas of active research in the AI community. Existing data collection systems often rely on clinician reporting, or data that can be weeks or months old, which may impair the ability to identify outbreaks, for example.[7,8] The ability of AI systems to consider additional and potentially more timely or complex sources of data such as electronic medical records (EMRs) and information from social media sites is of interest to address current limitations, and may help improve the ability to predict future disease from past data.[2,3] A 2018 workshop jointly hosted by the Canadian Institutes of Health Research's Institute of Population and Public Health and CIFAR identified potential opportunities for incorporating AI into public health practices such as supporting and promoting healthy behaviour and modelling policy decisions to understand their impact on public health.[9]

Types of AI Used

The variety of challenges encountered in population and public health lend themselves to a range of AI solutions. Scenarios where determining or predicting the presence or absence of an outcome is required (such as whether a virus can be transmitted from animals to humans) can be evaluated by support vector machine (SVM) programs.[6,10-13] More complex problems, such as predicting disease outbreaks from multiple unlinked data sources with unclear relationships, may be better suited to using artificial neural networks,[6,8,14-18] or deep learning.[5]

Natural language processing (NLP) and text mining — AI approaches that analyze the content of text-based data sources for patterns and relationships — are used by researchers to explore problems where data are unstructured or vary by source, as in EMRs and social media posts.[7,19-22]

Areas of Active Research

Population and public health researchers have explored using AI for a number of clinical areas including infectious diseases,[5-8,10,11,15,17,18,21-27] food-borne illnesses,[13,14,16] the opioid crisis,[19,20] and transmission of viruses and bacteria from animals to humans.[12,17]

Applications identified within the clinical areas include using AI for disease forecasting and modelling,[11,15,22,23,25] and using data from emerging sources such as social media posts[8,10,19-21] or geographical information systems[10,14,28,29] to improve existing surveillance and forecasting techniques.

Infectious Diseases

Influenza is a common respiratory illness affecting thousands of Canadians each year.[30] Research into how AI could change the approach to influenza management includes:

- using clinical notes in EMRs from four US health systems to develop, train, and test the ability of two NLP tools to detect influenza cases across organizations[7]
- improving the monitoring of influenza outbreaks by combining location data and an SVM approach to better distinguish social media posts that describe a case of influenza from those that do not[10]
- testing the ability of three artificial neural networks to predict regional influenza-like illness from social media posts compared to CDC-Centers for Disease Control and prevention reports over a 55-week period in the US[8]
- using an artificial neural network to determine what avian influenza viruses could infect humans.[17]

Dengue fever is a mosquito-borne illness that affects tens of millions of people each year.[31] The role of AI in predicting and monitoring dengue has been investigated.[11,15,22,24] AI research has included: the prediction of cases of dengue in Thailand[24] and China[11] by combining population data, climate data, dengue case data, and (in the Thai study) mosquito infection data and performing SVM analysis; a comparison of four dengue outbreak prediction models, including one artificial neural network model, in Brazil;[15] and the creation of a text mining tool to monitor media reports for dengue cases in India.[22]

The severity of the 2014-2015 Ebola outbreak in West Africa led researchers to explore how AI could help improve our understanding of the virus.[6,21,23] Research includes efforts to develop a model to predict the prognosis for people infected with Ebola using a publicly available clinical data set and artificial neural network and SVM approaches.[6] Researchers also explored public perception and concern in response to an Ebola case in Dallas using the text

mining of social media posts.[21] Preparing for future Ebola outbreaks is important, but it is challenging to predict epidemic situations, particularly in regions with no prior outbreaks. To address this challenge, one study used machine learning to predict the spread of, and response to, a simulated Ebola outbreak in Beijing.[23]

Zika virus has also drawn the attention of AI researchers.[25,26] One initiative studied an approach that combined climate data (such as annual rainfall), environmental conditions (such as relative humidity), and socioeconomic factors (such as travel time to the nearest city), with global data on Zika virus infection to map the risk of virus transmission using three machine-learning models.[25] To investigate a new way of screening for Zika virus infection, another study used a machine-learning approach to analyze mass spectrometry data from blood samples to identify biomarkers and patterns that can be used to predict whether a patient is infected with Zika virus.[26]

Other uses of AI in infectious diseases include using a machine-learning approach to determine how clinical and magnetic resonance imaging-related signs of hand-foot-and-mouth disease interact to help predict the risk of developing severe disease,[27] developing intelligent building systems (for example, hot water systems) that could help prevent legionnaires' disease, [18] and combining mobile technology with deep learning analysis of chest X-rays to support the timely diagnosis of tuberculosis in remote and resource-poor communities.[5]

Food-Borne Illnesses

Food-borne illnesses caused by bacteria, viruses, and parasites cause an estimated 4 million Canadians to become sick each year, resulting in more than 11,000 hospitalizations and more than 200 deaths.[32] Detecting and preventing outbreaks of food-borne illnesses such as salmonella, *E. coli*, norovirus, and *Listeria*, using AI, have been studied.[13,14,16] Researchers have used an artificial neural network to explore relationships between salmonella and *E. coli* infection data, and socioeconomic data, from five US states;[14] predicted oyster-associated norovirus outbreaks along the US Gulf Coast by combining historical outbreak data and environmental predictors of outbreaks such as ocean temperatures, rainfall, and offshore winds, and analyzing with an artificial neural network;[16] and explored how SVM compares to expert opinion when determining the persistence of *L. monocytogenes* in a deli environment.[13]

Opioid Crisis

In 2017, there were more than 3,900 apparent opioid-related deaths in Canada.[33] AI may help public health officials combat this crisis: researchers have explored text-mining social media posts to supplement formal surveys of non-medical use of prescription drugs to improve the understanding of their use[20] and to help public health officials evaluate the public's perception and reaction to the opioid crisis.[19]

> "While not unique to population and public health applications of AI, the quality, quantity, availability, and interoperability of data needed for AI systems to perform accurately should be considered"

Animal to Human Disease Transmission

Understanding which viruses and bacteria have the potential to move from animal hosts to human hosts is important for disease surveillance and preparing for outbreaks. By combining genomic information about viruses such as influenza,[17] and bacteria such as *E. coli O157*,[12] with historical outbreak data, researchers have investigated the ability of artificial neural networks and SVMs to distinguish between variants that have the potential to jump between species and those that do not.

Other Uses

In an effort to redefine existing climate regions and understand how climate affects the hospitalization of elderly people, researchers in the US used machine-learning approaches to analyze combined data from satellite images, meteorological data, spatial data, and Medicare subscriber data.[28] At the University of Waterloo, a proof-of-concept study used AI to detect blue-green algae levels in drinking water.[34]

Issues to Consider

While not unique to population and public health applications of AI, the quality, quantity, availability, and interoperability, of data needed for AI systems to perform accurately should be considered.[5,6] Creating generalizable machine-learning models requires data from as many patients in as many settings as possible.[6] Missing data in existing data sets complicate the ability to create predictive models.[6] Some diseases, like tuberculosis, may lack large, publicly available data sets.[5] Developing such a database could require many steps and resources or be challenging because of the complex presentation of the disease.[5]

Data sets from emerging sources, such as EMRs, are often created to be tailored to a specific setting, making it challenging to compare unstructured information across organizations.[7] NLP programs may also be challenged by regional or organizational variations in terminology.[7]

Photo: iStock/gremlin

Incorporating new data sources (such as social media posts) may also raise questions about privacy and ethics.[35] For example, genome sequences or geospatial data could inadvertently identify individuals, and additional care and thought may be needed to explain how their data will be used.[35]

Some AI programs, such as SVMs, may be prone to overfitting of data — where the information used to make distinctions between groups is random, or not biologically relevant, making generalizability beyond a set of training data difficult.[12] Some machine-learning algorithms perform better than others for different problems, so it may be necessary to compare a number of approaches against each other to determine which one provides the best answer, given the data at hand.[25]

Additional challenges identified by participants at the joint Canadian Institutes of Health Research's Institute of Population and Public Health and CIFAR workshop included a need to build cross-disciplinary relationships between AI and public health researchers, and educating and training public health researchers and practitioners in AI skills.[9]

Looking Ahead

AI applications in population and public health are still in their early stages, with many possible applications yet to be studied and potential yet to be realized.[2,3] AI could also provide researchers with new ways of understanding how largely incompatible data, such as the social determinants of health, are connected and interrelated, broadening our understanding of how they affect the health of Canadians.[3] It could also reduce the need for human intervention by automatically monitoring our environment for potential disease outbreaks.[18] As the influence and uses of AI expands, a deeper knowledge of health informatics may prove an important skill for health professionals' understanding of increasingly data-reliant health systems.[36]

Author: Jeff Mason

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CADTH

Mini-Roundup: Recent Reports From CADTH and Other Agencies

CADTH

***Health Technology Update* newsletter**

- Issue 21, August 2018, Theme issue on rural and remote health care technologies

***Issues in Emerging Health Technologies* bulletins**

- Monoclonal Antibodies for Osteoarthritis of the Hip or Knee
- An Overview of Clinical Applications of Artificial Intelligence

Recent Reports on Artificial Intelligence Technologies From Other Agencies

Agencies Included in the Mini-Roundup below:

- Health Education England, UK
- Healthcare Improvement Scotland, Scottish Health Technologies Group (SHTG), UK
- House of Lords Select Committee on Artificial Intelligence, UK
- JASON/Agency for Healthcare Research and Quality (AHRQ), USA
- The Medical Futurist
- National Institute for Health and Care Excellence (NICE), UK
- Nesta Health Lab, UK
- Nuffield Council on Bioethics, UK
- Reform, UK
- Wellcome Trust, UK

Cancer, Imaging, and Radiology

- ColonFlag for Identifying People at Risk of Colorectal Cancer (NICE)

Home Care

- Homechoice Claria With Sharesource — an automated, overnight, peritoneal dialysis system (SHTG)

Trends, Forecasts, and Strategic Initiatives

- 5 Reasons Why Artificial Intelligence Won't Replace Physicians (The Medical Futurist)
- Could A.I. Solve the Human Resources Crisis in Healthcare? (The Medical Futurist)
- *Artificial intelligence (AI) in Healthcare and Research* (Nuffield Council on Bioethics)
- *AI in the UK: Ready, Willing and Able?* (House of Lords Select Committee on Artificial Intelligence)
- *Artificial Intelligence for Health and Health Care* (AHRQ)
- Thinking on its own: AI in the NHS (Reform)
- *Ethical, Social, and Political Challenges of Artificial Intelligence in Health* (Wellcome Trust)
- *Confronting Dr Robot: Creating a People-Powered Future for AI in Health* (Nesta Health Lab)
- The Topol Review: *Preparing the Healthcare Workforce to Deliver the Digital Future: Interim Report June 2018* (National Health Services Health Education England)

Canadian Initiatives on Artificial Intelligence

- Health Canada's Approach to Digital Health Technologies
- Canada.ai
- Launch of Special Call for Research on Artificial Intelligence, Health and Society
- Canadian Association of Radiologists White Paper on Artificial Intelligence in Radiology
- Pan-Canadian Artificial Intelligence Strategy (CIFAR)

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