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Table of Contents

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Letter from the Editors

The Fruits of Our Labour: The MJM Marks its 26-year Milestone in the Midst of an Ongoing Pandemic

The Journal has begun its 26th year in operation, while the world over, COVID-19 has drastically changed everyday life. Many of us in health sciences research, nursing, medicine and related fields have seen the destruction caused by this virus up close and the challenges it has posed to both healthcare delivery and scientific research.

Hosanna Galea's piece which decorates the cover motivated the theme of our 19th volume, the fruits of our labour. This volume is dedicated to the innumerable healthcare and allied professionals whose tireless fight against the pandemic, commitment to public good, and daily demonstration of resilience and compassion continue to inspire us.

We at the McGill Journal of Medicine have tasked ourselves with continuing to push the journal forward, despite the circumstances of this past year. We remain committed to providing free and open access publishing services to health sciences researchers at McGill and abroad. Of course, we continue to offer our services to academic health science conferences looking to make their proceedings available online. We consider this an especially important time to continue to support the dissemination of research and medical content to the public and we continue to look for innovative ways to pursue that aim on behalf of our authors and our readers.

We are also excited to announce the promotion of several of our members to the executive team for 2021-2022. Stefanie Perrier, currently one of our senior editors, will take over for Etienne Leveille as Co-Editor-In-Chief. Our IT managers Divleen Malhi and Brandon Arulanandam have been promoted to co-managing editors, replacing Jack Lam. With the promotion of these individuals, Etienne and Jack will remain a part of the board as Consulting Editors and remain part of the MJM executive team, as they move on to Yale's Internal Medicine Physician Scientist Training Program and McGill Neurosurgery residency programs, respectively.

On that auspicious note, we thank the editorial staff and our contributors for their productivity and dedication to the Journal over this infamously challenging year, and we look forward to a brighter and healthier future for all.

We hope you enjoy this latest volume,

Mack Michell Robinson, MSc.
Co-Editor-in-Chief, McGill Journal of Medicine
MD/PhD Candidate, 2025

Etienne Leveille, MDCM
Co-Editor-in-Chief, McGill Journal of Medicine

Jack Lam, MSc., MDCM
Managing Editor, McGill Journal of Medicine

Foreword

Dear MJM Editors and Colleagues,

Congratulations on the most recent issue of the MJM! Amid the original research articles, systematic and narrative reviews, brief reports, "approach" articles to diagnosis and management, conference proceedings, and more, the content is high-quality topical, impactful, and exciting.

Running the journal, producing such exceptional content, no doubt continues to be a nearly full-time endeavor-a calling that continues to come with sacrifices of time spent on primary academic and clinical responsibilities as well as personal life. Yet, it brings unique and invaluable opportunities to build the foundation for a successful career in academic medicine. Whether authoring or reviewing and critiquing manuscripts, the experience enables one to "hone" these skills at an early stage of career, and fuels a passion for scientific discovery, innovation, and dissemination.

I will never forget the invited visit that the MJM leadership team made to the editorial offices of NEJM (during a time in which we were grateful to have Phil Gold as our faculty advisor and I was privileged to serve as MJM's 2nd editor in chief), after having submitted recent issues of the MJM for a potential "book review" in the NEJM. When our hosts at NEJM showed us the amount of "red ink" they used when editing accepted manuscripts, we were amazed and inspired to realize that things were not all that different–with regard to editing efforts, at least–between MJM and the "big leagues". The review of the MJM that the NEJM editors wrote and published in that esteemed journal was the icing on the cake; we knew then that the MJM legacy would endure. What we probably didn't realize, was how greatly it would be carried forward, and enhanced.

The entire staff, contributors, and faculty advisors -past and present–should feel proud of all that you have achieved.

Sincerely,

Neil Goldenberg, MD, PhD
Professor of Pediatrics Medicine, Johns Hopkins University School of Medicine
Associate Dean for Research at Johns Hopkins All Children's Hospital
Director, Johns Hopkins All Children's Institute for Clinical and Translational Research

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ORIGINAL RESEARCH
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Community-based Exercise Program for Solid Organ Transplant Recipients: Views of Exercise Professionals and Patients

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ABSTRACT

Background: Community Based Exercise (CBE) programs have been shown to successfully increase exercise capacity and physical activity (PA) levels in different populations, however none exist for solid organ transplant (SOT) recipients.

Objective: To identify important factors when developing and implementing a CBE program for SOT recipients.

Methods: We conducted a qualitative study using semi-structured interviews with seven SOT recipients and six exercise professionals (EPs). The data were analyzed using thematic analysis.

Results: Six themes were identified: 1) motivators to exercise: social benefits, improved quality of life and return to normal activities, and improved health; 2) perceived barriers to exercise: financial vulnerability post-transplantation, fear of injury, lack of exercise recommendations, and medication side effect; 3) level of supervision: recipients wanted guidance without overprotective supervision, while EPs were torn between extensive monitoring and promoting independence; 4) required education and foundational knowledge in EPs; 5) the importance of CBE programs for the SOT population: guidance and support to SOT recipients, with societal benefits; and 6) tailored program structure: group setting with individualized exercise prescription.

Conclusions: Recommendations may be used to develop an effective CBE program for SOT recipients, and thus improve PA levels among this population.

KEYWORDS
exercise, physical activity, community, transplant

1 | INTRODUCTION

Solid Organ Transplant (SOT) is a life-saving procedure performed on individuals with organ failure. Despite substantial improvements in quality of life following the procedure, SOT recipients continue to have long-term limitations in exercise capacity (1) and low levels of physical activity (PA) may partly explain this. PA is defined as any bodily movement produced by the contraction of skeletal muscles that results in an increase in caloric requirements over resting energy expenditure. (2) A Canadian web-based questionnaire of 113 SOT recipients revealed that a large proportion of participants never engaged in light (60%), moderate (55%) or strenuous (43%) recreational activities. (3) A study of women following heart transplantation demonstrated extremely low levels of PA with 55% of participants in the study reporting being inactive and only 15% engaged in moderate to high levels of PA. (4) Reduced PA and exercise capacity may increase SOT recipients' risk for developing secondary complications such as osteoporosis, diabetes, dyslipidemia, hypertension, and cardiovascular disease. (5, 6) These health complications may decrease transplant recipients' quality of life, while cardiovascular disease has been identified as the main cause of non-transplant-related death in this population. (7)

Exercise is defined as a type of PA that is planned, structured, and repetitive bodily movement done to improve and/or maintain one or more components of physical fitness. (2) Exercise training that includes aerobic and resistance exercises has been shown to improve exercise capacity, muscle strength, body composition, functional performance, mental health, and quality of life in the SOT population. (5, 8) In addition, exercise training has been shown to be effective in reducing risk factors for cardiovascular and metabolic disease in many chronic disease populations including SOT recipients. (9) To date, most published studies of exercise programs in SOT recipients were offered in an outpatient hospital setting. (5, 8) In Canada, most rehabilitation programs are also offered in a hospital setting, and a large disparity exists in regards to the provision of rehabilitation and exercise training services among organ types. (10) The majority of the programs are offered to heart and lung transplant candidates and recipients. (10) The most beneficial physical rehabilitation model would include pre- and post-transplant rehabilitation programs for all organ types; however, this type of program, if held in a hospital setting, has direct cost for the centre as it needs to hire qualified personnel and purchase equipment.

Community-based exercise (CBE) programs can be defined as a group of individuals with similar health conditions who perform exercise that is led by a physiotherapist or a fitness instructor. The goal of CBE is to promote exercise in a community setting by providing social support, supervision and guidance with exercise, (11) all of which have been identified as important facilitators to PA in the SOT population. (3) CBE programs have been successfully implemented and evaluated in individuals with stroke, cancer survivors, Alzheimer's disease, and older adults, while being safe, feasible, and effective in improving cognitive and physical function in these populations. (12)

To our knowledge, no specific CBE program exists for the SOT population. SOT recipients may face unique challenges related to higher risk of infections, side effects of immunosuppressive medications, (13) post-surgical complications, organ rejection, and fear of injury and losing the new organ. (14) Therefore, there is a need to understand the factors to be considered before developing a feasible, accessible, safe, and effective CBE program for SOT recipients.

The purpose of the present study was to identify important factors for the development and implementation of a CBE for stable SOT recipients in Canada, from the perspectives of key stakeholders such as SOT recipients and exercise professionals (EPs).

2 | METHODS

2.1 | Study design

We conducted a qualitative study using semi-structured interviews with SOT recipients and EPs with and without experience working with people with chronic diseases. Descriptive phenomenology, a method that in-

vestigates the "pure" description and interpretation of people's experiences, (15) was used to understand the subjective reality of SOT recipients and EPs within their individual context. This study was approved by the ethics committee of McGill University (reference number A03-E11-18A), and all participants provided written informed consent. The reporting of this study follows the Consolidated Criteria for Reporting Qualitative Research. (16)

2.2 | Study Participants

2.2.1 | Individuals with SOT

We recruited English speaking SOT recipients through The Canadian Network for Rehabilitation and Exercise for Solid Organ Transplant Optimal Recovery (CAN-RESTORE) mailing list and social media accounts (Facebook and Twitter) (a network about exercise and rehabilitation in transplantation; www.canrestore.ca). Purposive sampling was used to gain a variety of views, and participants were recruited from urban centers and their surrounding areas, which have major transplant centers. We aimed to recruit individuals with different organ transplants types (kidney, liver, heart, lung, etc.), stages of recovery (1-2 years, 2-5 years, 5+ years post-transplant), and gender. Only liver and heart recipients were found, and one participant from a rural area was included to get the perspective of a rural resident. Participants were excluded if less than one year had elapsed since their most recent transplantation. Twelve SOT recipients were contacted, five refused and seven completed the study.

2.2.2 | EPs

English speaking EPs were also recruited through the CAN-RESTORE mailing list, Facebook, and Twitter accounts. A minimum of two years of work experience was required from fitness and community centers in in the Montreal and Toronto area. EPs with and without experience with chronic disease or coordinating CBE programs for chronic conditions were included to provide a more heterogeneous sample and richer data. Ten EPs were contacted, three refused, and six completed the study.

2.3 | Data Collection

2.3.1 | Demographics

Age, gender, organ type, number of transplants received, date of last transplant, level of PA, and if current or previous participation in a CBE program were noted for all patient participants. The International PA Questionnaire Short Form (IPAQ-SF) assessed the level of PA. The 7-item questionnaire is a valid and reliable instrument for measuring PA in individuals 15-69 years old. (17) Demographic data collected for EPs included age, gender, years of work experience, work setting, and population.

2.3.2 | Semi-Structured Interviews

Two investigators conducted in-depth, semi-structured interviews by telephone using a semi-structured interview guide. The interview guide was pilot tested with the first SOT recipient and EPs, and feedback was given on the clarity and type of questions. The pilot test interviews were included in data collection. Interviews were conducted from April to June 2018 and lasted 20-45 minutes. The interview guide for the SOT participants contained eleven open-ended questions with additional probes relating to organ transplant experience, motivators and barriers to exercise, benefits and desired structure of a CBE program, and additional services that should be offered (Appendix). The interview guide for EPs included five open ended questions with additional probes and consisted of questions about their professional background and training, barriers in training and implementing programs for chronic disease, knowledge of and information they felt would be necessary to work with SOT recipients, and factors to consider in the development and implementation of a CBE for SOT (Appendix). All interviews were audio-recorded, transcribed verbatim, and reviewed by the interviewers to ensure accuracy. Recruitment was completed once it

was deemed data saturation was reached. (18)

2.4 | Data Analysis

Interviews from SOT recipients and EPs were coded and analyzed using Thematic Analysis as described by Braun and Clark, (19) following a six-step procedure: 1) two researchers (EL, SF) developed preliminary codes; 2) transcripts were coded line-by-line without the use of software and initial codes were generated collaboratively; 3) codes were analyzed and then grouped into broader candidate themes; all themes were derived following the analysis of the data; 4) all extracted codes were reviewed and refined under each candidate theme to ensure a coherent pattern and fit of the thematic map to the data set. The entire data set was re-read and analyzed for missing or additional codes. 5) themes were named and defined; 6) final analysis of the data was completed and reported.

3 | RESULTS

Thirteen participants took part in this study, including 3 (23%) heart transplant recipients, 4 (31%) liver transplant recipients, and 6 (46%) EPs (Tables 1–2). Of the seven SOT participants, only one individual was attending a weekly post-transplant exercise program (hospital-based). Six themes are described below.

3.1 | Motivators to exercise

3.1.1 | *Social benefits*

The most recurrent motivator to exercise was a group setting. All seven SOT recipients were enthusiastic about the psychosocial aspect of exercising with other transplant recipients. One participant exposed the sense of accountability that builds within a group that exercises together, and faces similar challenges:

"You got to talk to other people on how they were doing, […], you're making a commitment to not just yourself, but to others as well." SOT6

3.1.2 | *Improved quality of life and return to normal activities*

The SOT recipients agreed that exercise experiences increase their perceived health-related quality of life and encourage a return to leisurely and meaningful activities.

"One of the things I wanted to do this year was to try and get conditioned back to be able to play a whole game [of hockey]." SOT4

3.1.3 | *Improved health*

Aware of the health risks that stem from deconditioning, three of the seven SOT recipients expressed health and weight loss as a motivation to exercise.

"I'm overweight. […] I need to start taking care of my body and start exercising more." SOT3

3.2 | Perceived barriers to exercise

3.2.1 | *General population barriers*

SOT recipients reported barriers to exercising (time constraints, cost, weather, physical accessibility, lack of motivation and fear of injury) identical to those commonly found within the general population. Furthermore, participants reinforced that these barriers are magnified by the process of receiving a new organ, and that transplant can lead to financial vulnerability.

"The cost of the program is a big thing, […] we're not only managing a new transplant, but most of the people are managing maybe no job, or changes of jobs." SOT5 Indeed, the financial commitment of a gym membership is an expense that some could not have afforded immediately post-transplantation:

"As a recipient, until you get back on your feet financially, it's a struggle. I don't think I could afford it." SOT4

3.2.2 | SOT recipient-specific barriers

3.2.2.1 | *Fear*

It was a recurring theme that, post-transplant, SOT recipients were unsure how to exercise safely, due at least

in part to having lived so long with a failing organ. SOT2 shared the additional initial fear of compromising the viability of her transplant:

"People don't know how much you can push yourself. You're always scared, your new heart is so precious, and you don't want to ruin this one." SOT2

3.2.2.2 | *Lack of physician's support*

SOT recipients expressed concerns about the lack of guidance about PA and precautions post-transplantation. SOT7 stated that he had to initiate the conversation with his physician or exercise would not have been mentioned. EP1 also expressed the consequences of a lack of exercise recommendations:

"When their doctor tells them something they'll listen, and if their doctor doesn't really talk about exercise [...], [patients] don't exercise." EP1

3.2.2.3 | *Medication side effects*

Participants reported a variety of medication side effects, and most recipients felt affected by medication. One recipient described how the side effects disrupted their quality of life:

"My biggest issue was prednisone and its side effects. It's painful and [. . .] I wouldn't be able to walk for a couple days due to muscle soreness." SOT5

All EPs agreed that medication side effects represent a major barrier to exercise intervention delivery.

"The [SOT] population is so heavily medicated, it's crazy. Anti-rejection medication interferes with their health, medical stability, and day-to-day physical state." EP1

3.2.2.4 | *Risks of infection*

Among SOT recipients, the management of infection risk was not a universal barrier. One claimed EPs should be aware of immune system fragility and incorporate preventive measures for spread of contagious illness in their exercise program. However, others did not consider the gym environment as an additional threat:

"I don't see the higher risk of getting an infection in a gym than going to the grocery store or getting in a subway. [...] Just wash your hands and be careful." SOT5

3.3 | Level of supervision and medical clearance

Among EPs and SOT recipients, the suggested amount of supervision varied. Three SOT recipients expressed that while they require guidance to exercise, trainers should not be overprotective, but simply attentive. Two SOT recipients expressed that despite having some unique differences when it comes to their ability to exercise, they wanted to be treated like normal people.

"Transplant recipients are not Martians or extraterrestrials." SOT5

"I think we can do pretty much anything, as long as the trainer doesn't overdo it." SOT3

On the other hand, SOT2, who spent 10 years in heart failure before receiving her transplant, reinforced the need of closely supervised programs as she was worried about her safety when she began exercising:

"often people with [a history of] heart failure get nervous to do too much, because for so long you couldn't."

EPs report a spectrum of supervision preference. For example, EP2 reinforced the need to initially assess all participants in order to provide the right amount of supervision and ensure safety. However, EP5, who runs a community-based program in partnership with a local hospital, thought each transplant recipient should be responsible for managing their condition once medically cleared:

"[Medical staff] are reluctant to allow individuals to be responsible for themselves. [But] rehabilitation teaches SOT recipients to know their level of exertion, how to pay attention to their body, and to be smart by making the decision not to come when they don't feel well." EP5

3.4 | Required education and foundational knowledge for EPs

3.4.1 | *Medication and side effects*

Most EPs expressed the importance of knowing their clientele's medical background as well as their medications. The SOT recipients agreed that EPs need to be knowledgeable about the possible effects of their med-

ications, and transplant process.

"Trainers should know how the body works once it's been transplanted, how the immune system works and what the immunosuppressive medications do." SOT6

3.4.2 | *General SOT knowledge*

SOT2 acknowledged that SOT recipients are underserved and that most EPs, including her kinesiologist, do not have the knowledge to treat them. She also highlighted the need for professional initiative and the effectiveness of learning through experience:

"When my kinesiologist started, he didn't have that specialized knowledge. [...] Over the years he actually increased his knowledge, not just on the physical impact of receiving a heart transplant, but also psychologically." SOT2

SOT4 not only preferred that his EPs have transplant-specific knowledge, but also stressed the need to be understood in his journey as a SOT recipient:

"I could go with anybody, but I would really feel comfortable if they have background knowledge and experience." SOT4

EPs were eager to learn about the nature of SOTs, and any specific exercise considerations. EP5 acknowledged the need for population-specific training. She also proposed helping to develop CBE programs through hospital partnerships:

"Fitness instructors who have undertaken general fitness training, they'll go to the hospital and observe therapeutic sessions of the program there. There they will get the population-specific training from the hospital, and they'll provide us with contraindications." EP5

Finally, EPs 1, 2, 3 and 4 expressed the need for evidence-based practices for exercise for SOT recipients.

3.5 | The importance of a CBE program: guidance and support to SOT recipients, with societal benefits

All SOT recipients showed interest and willingness to participate in a CBE program. However, there is a lack of services and exercise guidance, especially for certain types of organ transplants:

"I see other transplant recipients like heart. Once they get out of the hospital, they have to follow a program. [...] I think it should be like that for all the transplant recipients." SOT3

CBE programs would also give SOT recipients peer support and an opportunity to acquire new knowledge about their condition.

"I've learned more about my side effects by training for and playing at the transplant games or from other transplant recipients, than any clinicians or pharmacists." SOT5

SOT5 stated that CBE programs should provide SOT recipients with adequate tools to manage their condition. He also exposed the societal benefits:

"The government would save a lot of money by sending someone to rehabilitation, knowing that they are sparing all the complications." SOT5

3.6 | Tailored program structure with goal setting and progression monitoring

3.6.1 | *Individualized exercise prescription*

Both SOT recipients and EPs made specific suggestions about how a CBE program for transplant recipients could be optimized (Table 3).

4 | DISCUSSION

To our knowledge, this is the first study to investigate essential factors for the development and implementation of a CBE program for the stable SOT population.

All participants reported that the CBE program should be conducted in a group setting with other SOT recipients, to provide social support such as sharing and learning from others, accountability, and a sense of normality and inclusion. Previous studies have found social support to be a large influential facilitator to being physically active in this population. (3) It was also found that group programs lead to greater exercise compliance (20) and intrinsic motivation to exercise (21) in healthy indi-

SOT	Age	Gender	Organ	Years post-transplant	IPAQ (hours spent in moderate-vigorous activities/week)	Desire to be physically active
1	25	Female	Liver	4	<1	yes
2	43	Female	Heart	10	> 4	yes
3	56	Male	Liver	7	1-2	yes
4	57	Male	Heart	3	>4	yes
5	50	Male	Heart	18	<1	yes
6	40	Female	Liver	21	<1	yes
7	40	Male	Liver	1	>4	yes

IPAQ: International Physical Activity Questionnaire
CBE: Community Based Exercise
PA: Physical Activity

TABLE 1 SOT recipient characteristics (n=7)

Participant	Gender	Profession	Years of experience	Location of Employment
1	Female	Program manager/exercise leader	25	Community Center
2	Female	Certified exercise physiologist	12	University affiliated Center
3	Male	Kinesiologist	10	Private trainer
4	Female	Certified exercise physiologist	11	University affiliated Center
5	Female	Fitness Center Supervisor	29	Community Center
6	Female	Community development coordinator of therapeutics	13	Community Center

TABLE 2 Characteristics of exercise professionals (n=6)

viduals. Most of the recipients participating in the study expressed a desire for a group to be composed solely of SOT recipients. EPs, who are more focused on feasibility, were generally more willing than SOT recipients to have mixed groups if fitness levels were matched. Although it is easier to integrate SOT recipients into already existing exercise classes, it would be more beneficial for this population to create a SOT only group. This reflects the findings of Estabrooks and Carron, who have shown that group cohesion, perception of similarity, and closeness within the group can predict short- and long-term adherence in older adult exercisers. (22)

SOT recipients and EPs also voiced different important features about the program. For recipients, having a program that offered some exercise prescription flexibility (e.g. group walks in the park) was key for participants to meet their individual goals. While EPs agreed, some were more focused on the program being in a context where recipients' vital signs can easily be monitored for safety. This might reflect the EPs' lack of experience of working with SOT recipients and therefore they feel hesitant not to monitor them.

The fact that EPs felt that a 12-week program would be an ideal duration for CBE programs, whereas SOT recipients would prefer a year-round program indicates that EPs are focused on short-term improvements in physical fitness and SOT recipients are focused on long-term physical fitness maintenance through regular PA. This highlights the importance of the development of PA programing rather than only short-term exercise-based programs for SOT recipients.

Previous studies reported that the cost of fitness centers and side effects post-transplant were major barriers to exercise for SOT recipients. (14, 23) Our participants also discussed these barriers, although recipients stressed the financial burden post-transplant and the importance of the program's location. Therefore, when implementing a successful CBE program, one needs to con-

	SOT Recipients	Exercise Professionals (EP)
Individual vs group sessions	Recipients wanted a balance between individual and group exercise time.	Some exercise professionals proposed starting with individual sessions to set goals, and then be assigned to an appropriate group.
Specific program features	The program should include transplant-specific adaptations and exercise prescription flexibility, to ensure everyone meets their goals.	Some exercise professionals felt it was necessary to monitor vital signs closely, while others felt it was okay to rely on the patients' symptoms and judgement.
Group Composition	Mixed opinions: exercise with other patient population groups vs exercise with SOT recipients only. The majority preferred recipient only groups.	No specific recommendation. Creating mixed population, or SOT recipient specific groups based on physical fitness were mentioned.
Group Size	Preferred 10 - 20 participants in the group, to ensure adequate feedback and guidance.	Mixed opinions on ratio size (exercise professionals: SOT recipients). 2:16 for independent participants, and as much as 1:2 for chronically ill patient groups.
Accessibility	The program should be accessible in terms of cost and location. Target prices for a year-round membership differed, ranging from having the first year free, to a small cost.	No specific recommendation.
Environment	Should be located somewhere in the neighborhood.	Same as SOT recipients.
Duration	1-2 hours, 2-3 x/week, year-round to allow dropping in and out based on fluctuating health status.	12-week program would be an ideal timeframe, due to resource limitations and clinically meaningful health outcome changes.
Type	Recipients were open to the type of exercise, liking a mix of cardio and strength training, with the possibility to make their choice in the form of exercise (for ex: bike vs treadmill, etc). Group walks in a park were also of interest, although only a viable option during the warmer months, and not sufficient on its own due to weather constraints.	There was no consensus. Some felt outdoor group walks were an option, due to the great social benefits. Others didn't like the fact that vitals could not be monitored and measured as easily as in a gym setting.

TABLE 3 SOT and exercise professionals' perspectives about factors in developing a CBE program

sider its cost and accessibility, so that recipients can participate despite financial hardship secondary to change in employment status and increased medical expenses.

Many recipients reported being fearful of exercising, concerned that they will injure themselves or jeopardize their new organ. Zelle et al. (14) also identified fear of movement as a barrier to exercise in kidney transplant recipients. This is partly why EPs stressed the importance of having physicians play a collaborative role. Provided there are no contra-indications, SOT recipients are reassured and can feel safer when exercising. Physician recommendations have been identified as an important facilitator to PA in SOT populations (3); therefore, increased physician advocacy on the benefits of life-long exercise are imperative. Once a physician endorses a CBE program for example, recipients could meet with an EPs for education and guidance to assuage their fears even more.

Another major concern of EPs was the lack of established evidence-based exercise guidelines. SOT recipients expressed that EPs should have a basic understanding of transplant procedures, common medication and side-effects, the recovery process, the psychological impact, and physiological response to exercise. Thus, educational resources and training should be developed for EPs so they better understand the SOT population and its unique concerns when it comes to safe exercise.

SOT recipients also expressed a desire for nutritional support to assist with weight management and for nutritional and lifestyle counselling. However, because recipients usually have access to a dietician at the hospital, it is perhaps not a priority in a CBE program. However, this expressed desire may indicate an increased need for nutrition referrals outside of a CBE program.

Community-based programs would optimally partner with hospitals and rehabilitation centers in order to obtain medical clearance, collaborate with medical professionals, and to streamline the rehabilitative process. Adjunct services such as physiotherapy, psychology, social support, and nutrition were felt by our participants to be an asset to a newly developed CBE program. Offering these services would help recipients recover, and in turn, increase their adherence to exercise by increasing their confidence in their new life and preventing or managing injury. For financial reasons, strategic partnerships with medical facilities, transplant foundations, and municipal recreation organizations could be fostered to help improve sustainability for, affordability of, and access to the program for SOT recipients.

There are several limitations inherent to this study. Most participants live in urban areas and may not reflect the opinions and behavior of individuals in rural regions. Furthermore, no participating EPs had direct work experience with the SOT population; however to our knowledge, there is no CBE program specific to SOT recipients in Canada. The SOT recipients only included liver and heart transplant recipients, and therefore may not be generalized to other organ groups. Lastly, due to our recruitment strategy (CAN-RESTORE mailing list and social media accounts), the study has an overrepresentation of SOT recipients engaged in PA as indicated by the IPAQ scores and therefore the findings may not be generalizable to those recipients who are not physically active.

5 | CONCLUSIONS

This study gathered the opinions of key stakeholders that would be involved in a CBE program for stable SOT recipients and sets the stage for the development of a feasible and relevant program for this population. Future research should aim to look at the development, implementation, and evaluation of a CBE for SOT recipients.

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Appendix: Interview Guide

5.1 | SOT Recipient

Can you start by telling me about your transplant experience and what type of organ transplant you received?

- When was your transplant?
- Did you experience any complications?

How would you describe your current level of physical activity?

- What type of activities or exercise do you currently do and how often?
- Were you physically active before your transplant? If so, what type of exercise did you do and how often?

What motivates you to exercise? What are your goals?

- What type of exercise or activities do you like best?

What barriers do you face when it comes to doing exercise?

- Are any of these barriers related to your organ transplant?

Do you think a community exercise program would be beneficial for solid organ transplant recipients? Why? Why not?
Note: A community exercise program is an activity involving exercise, that is offered to a specific population (in this case SOT recipients) and led by a trained fitness instructor.
What would encourage you to participate in a community-based exercise program?
What would discourage you from participating in a community-based exercise program?
Do you prefer group training or one-on-one training (with a trainer)?
How do you think a community-based exercise program for transplant recipients should look like?

- What should be considered when it comes to the types of classes offered, length (30min , location, expertise of the instructors, group size, membership cost, accessibility, etc.?
- Would you prefer to exercise outdoors in a park (e.g. walking group, yoga in a park, etc)?
- What do you think an exercise trainer needs to know about transplant to help you with your exercise program (for instance, do they need to know about medications (immunosuppressants), risk of infections, etc)?

Are there any additional services you think should be offered in a community-based exercise program besides exercise (nutritional support, psychological support, etc.)?
Is there a location in your community that you would go to exercise (with other transplant recipients)?

5.2 | Exercise Professionals

What is your professional background and training?

- How long have you been working in the field of exercise training?
- How does your job relate to implementing exercise prescription or programming in the community?
- What chronic disease populations do you work with?
- Can you describe the program you run (number of participants, how often it is given, types of exercises, type of supervision)?

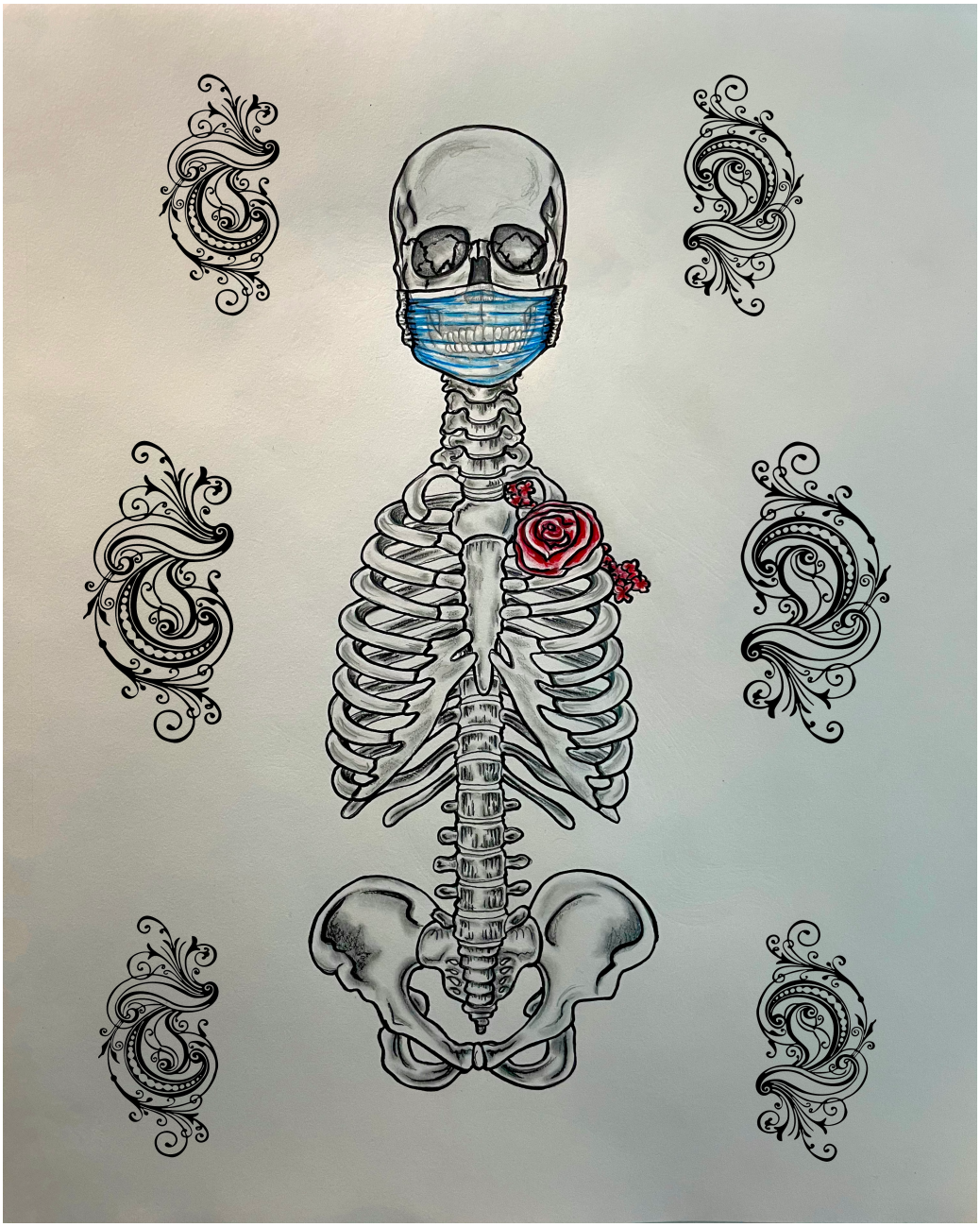
What barriers or challenges do you face when implementing exercise to people with chronic diseases?
What barriers do you think people with chronic diseases face when it comes to exercising or adhering to an exercise program?
Have you ever worked with solid organ transplant recipients before?

- Would you feel comfortable working with solid organ transplant recipients?
- What type of information do you feel you would need, in order to be confident working with this population?
- What challenges do you foresee with regards to implementing an exercise program for this population?
- Would you feel comfortable working with a recently transplanted recipient?

If your center decided to create a community exercise program for solid organ transplant recipients, how would it look like?

- Would individual or group sessions be recommended?
- Would the center be able to offer this population a reduced rate?
- Would activities outdoor (walking program, Yoga at the Park) be an option? What would be the advantages and disadvantages of such programs?

SYSTEMATIC REVIEW



Artist: Caroline Najjar

SYSTEMATIC REVIEW
McGill Journal of Medicine

Incidence of Concussions and Injuries Among Quidditch Players

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ABSTRACT

Purpose: To evaluate the rates of concussion and injury in quidditch, a high-contact sport growing in worldwide participation. **Methods**: A systematic review of the MEDLINE database was performed according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRIMSA) guidelines for all studies reporting on concussion and/or injury rates in quidditch epidemiology. **Results**: Five studies were identified that had been published in the last 15 years on the concussion and injury rates among quidditch players worldwide. Each of these five studies included a concussion analysis and two included overall epidemiological rates. **Conclusions**: Injury rates seen in the two studies were found to be lower than those seen in other high-contact sports. There is a need to further study concussion symptoms among this understudied population.

KEYWORDS
Quidditch, Injury, Concussion, Epidemiology, Systematic Review

1 | BACKGROUND

Established in 2005, quidditch is a fast-paced, high-contact sport which has seen explosive growth over the past decade, with thousands of players in over 39 countries now engaging in the sport (1). Despite this immense popularity, quidditch is behind other high-contact sports cohorts in terms of international attention to safety and concussion risk.

Unlike most high-contact sports, the game is played in a gender-inclusive format (2). The unique nature of this game requires clinicians to develop a compounded knowledge of treatment compared to other sports, which are usually separated into men's and women's

divisions. Like rugby, the game is traditionally played in a 7-on-7 format with players wearing little protective equipment. In the US version of gameplay, each player serves a specific position (e.g. Chaser, Beater, Keeper) and can experience collisions during play (3). All players are currently mandated to wear a mouthguard during gameplay, and quidditch matches have a league-sanctioned medical staff for injury management (1). Despite the injury-risk attention, the literature on this sport is scarce. The purpose of this article is to outline the current epidemiological literature of quidditch sport injuries and propose future innovations for injury surveillance.

2 | METHODOLOGY

In May 2020, a systematic review of literature was performed on MEDLINE, Google Scholar, and the Cochrane Database of Systematic Reviews for quidditch injury epidemiological studies. The search was performed using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and checklist (4). Contingent valuation studies within quidditch sports medicine were identified using search terminologies that combined the following epidemiological terms: *quidditch injuries*, *quidditch concussions*, *return-to-play quidditch*, *quidditch incidences*. Variations of the terms were also used when deemed necessary by the reviewers (e.g. “injury” vs. “injuries”).

The initial search yielded 698 articles. Duplicates were removed, and each article was reviewed for the following inclusion criteria: English language, pertained to quidditch related injuries, and full-text (Figure 1). To further ensure that all appropriate studies were identified, the reference list of each identified study was also reviewed, and no further articles met the inclusion criteria. The studies included in qualitative synthesis yielded five articles (Table 1).

3 | RESULTS

3.1 | Overview of Study Characteristics

Following review, two articles were identified as prospective injury epidemiological studies based on their inclusion of injury epidemiology, which was composed of various injury types (i.e. fractures, sprains) (5, 6). Two other studies were identified as primarily concussion studies for their inclusion of injury epidemiology which only recorded concussions (7, 8). One article fit the review’s inclusion criteria, but focused on radiological epidemiology study through evaluation of six radiology cases and was non-peer reviewed (9). While there were no inclusion criteria for the publication date, all studies were from the past three years. Beidler et al. and Brezinski et al. included other sports in addition to quidditch. Quidditch injury data were isolated from articles with multiple sports injury data sets during the review.

3.2 | Injury Data

Pennington et al. (5) reported 315 injuries to 180 athletes (n=348 total respondents), with an overall incidence of 4.06 injuries per 1000 hours. Brezinski et al. (6) reported 16.2 per 1000 athlete-exposures (n=25 quidditch respondents). In general, an athlete exposure is “one athlete participating in one practice or competition during which the athlete was exposed to the possibility of athletic injury” (13). Pennington et al. noted in their study that players were to report average hours played per week instead of exposures as the nature of a quidditch match makes it difficult to measure the exact time of a game being completed. Unlike other sports, matches in quidditch do not abide by a certain time period, and quidditch matches end after the snitch is caught, thus creating variability in the actual time played. Pennington et al. also noted that players of higher skill were likely to report higher injury rates, using the identifying variable of “skill” in their survey questionnaire. However, it should be noted that survey questionnaires were not available for analysis for all of the

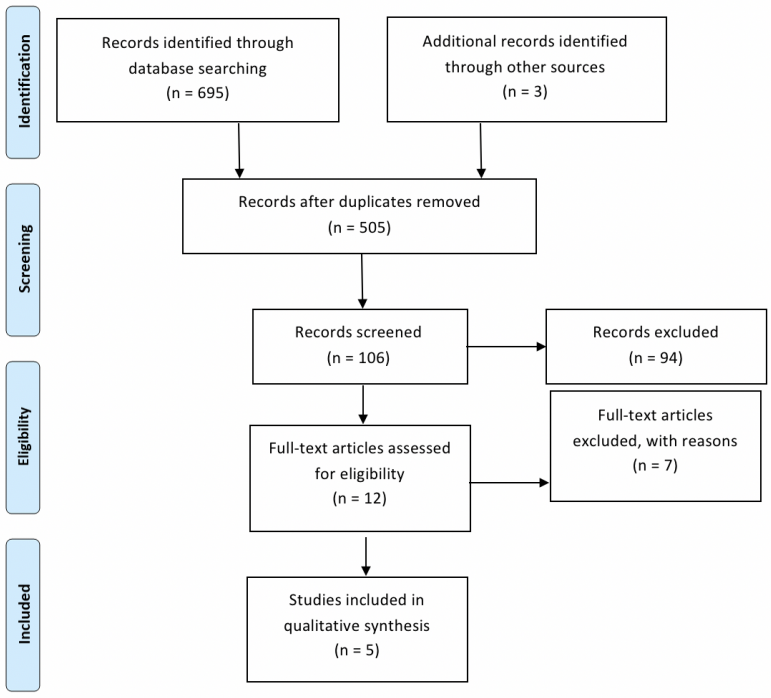

FIGURE 1 Flowchart of the study selection process. Initial search criteria produced 695 articles of which ultimately 5 studies were included.

AUTHOR	JOURNAL	YEAR	(n=)	Additional sports included in study	Injury Rate	Concussic analysis	Body Region of most incidence
Pennington et al.	*International Journal of Sports Physical Therapy*	2017	348	NO	4.06 injuries per 1000 hours	YES	Head & Extremities
Tsakok et al.	*European Society of Musculoskeletal Radiology*	2017	12	NO	-	*	Upper Limb
Beidler et al.	*Journal of Athletic Training*	2018	10	YES	-	YES	**
Tran et al.	*Journal of the Neurological Sciences*	2019	157	NO	-	YES	**
Brezinski et al.	*Athletic Training and Sports Health Care*	2020	25	YES	16.2 per 1000 athlete-exposures	YES	***

* Study was a radiological examination and indicated "neck" injuries which reviewers may consider potential for concussions though not explicitly stated

** Studies were focused primarily on concussion epidemiology.

*** Unavailable.

TABLE 1 Overview of study characteristics including injury rate, concussion analysis, and body region of most incidence.

studies included in this review. This study noted that head injuries (n=86) and lower (n=97) and upper extremity (n=85) injuries had the highest prevalence, whereas pelvic injuries had the lowest (n=2) prevalence. It is also noteworthy that the studies used the traditional variables for sex (male and female).

3.3 | Concussion Data

The study by Beidler et al. (8) was not focused on documenting player injuries, but rather used a survey questionnaire to observe knowledge of sports-related concussion signs and symptoms. Within this study, there were six quidditch players, which presents a limitation as this cannot be considered a significant representation of the quidditch community as a whole. Tran et al. (7) noted that of the players with head injuries, only 39% sought medical treatment. Tsakok et al. (9) evaluated radiological examinations of quidditch player injuries, but the epidemiology was not defined by injury type as seen in the Pennington et al. (5) and Brezinski et al. (6) studies. However, the radiology determined that 25% of its quidditch player injuries were considered neck injuries. This is important when considering that concussion knowledge data in the Beidler et al. (8) study showed that only 27.6% of the sports athletes were aware that neck pain is a sign of a concussion. Pennington et al. (5) also stated that the overall rate of concussions in males was 0.651/1000 hours and in females was 1.163/1000 hours (0.877/1000 hours overall). The reviewers were not able to identify such quidditch-isolated values in the Brezinski et al. (6) study.

4 | DISCUSSION

The game of quidditch is both mentally and physically demanding of its players. The overall epidemiological literature of quidditch injuries is minute and often combined within other variables to add significance to their study. Moreover, it is imperative to conduct future studies specific to the sport of quidditch. The most prominent study the reviewers noted was the Pennington et al. article for including the largest population of quidditch players, with a methodology corresponding to injury surveillance literature similar to rugby and lacrosse studies. The injury rates seen in the two studies were found to be lower than those seen in rugby (46.8/1000 player hours) or American football competitions (36.94/1000 athlete exposures) (3, 10). However, the aforementioned variability among “player hours” and “athlete exposures” makes it difficult to draw conclusions towards comparing the safety across sports. On the other hand, the results of this study can also suggest that quidditch is a safer sport, which can help to serve as an example for concussion and injury protocols found in other leagues. However, the data presented by Pennington et al. cannot encompass quidditch play internationally due to the variation of gameplay among the different quidditch leagues.

Concussion data between studies were too limited to allow for significant conclusions to be drawn on concussion epidemiology in quidditch. Beidler et al. (8) established the need to further educate quidditch players on concussion symptoms. Additionally, there is significant literature showing head cap protection does not decrease injury rates among football and lacrosse players, however, it is not possible to apply such a conclusion on quidditch players without direct investigation (11, 12). It is also possible that the nature of the sport could imply lower concussion rates compared to others due to the unique tackling method in quidditch, as tackling is conducted while holding onto a stick, or “broom”, in the game. This may have a significant effect in preventing head collisions. Moreover, this warrants future investigation for a large scale concussion study among quidditch players.

In conclusion, this study addresses the current state of the literature on an emerging novelty sport. While initial studies on the safety of quidditch are encouraging, it is difficult to draw precise conclusions due to the smaller sample size of players compared to studies on other sports. Moreover, the variability among rules of play, gender inclusivity, and variation of multiple leagues suggests a need for the development of future collaborative concussion and injury epidemiological studies to

provide further literature and recommendations to the quidditch community.

5 | ACKNOWLEDGEMENTS

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SYSTEMATIC REVIEW
McGill Journal of Medicine

Quality of the reporting of exercise interventions in solid organ transplant recipients: a systematic review

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ABSTRACT

Background: Exercise training programs must be described in detail to facilitate replication and implementation. This study aimed to evaluate the quality of exercise training program descriptions in randomized controlled trials (RCTs) involving solid organ transplant (SOT) recipients.

Methods: We evaluated 21 RCTs reporting on exercise interventions in SOT recipients that were included in a recent systematic review/meta-analysis conducted by the research team. This previous review investigated the effects of exercise training (versus no training) in adult SOT recipients. Several databases (MEDLINE, EMBASE, CINAHL, and Cochrane Central Register of Controlled Trials) were searched from inception to May 2019. Three reviewers independently rated the exercise programs for SOT using the Consensus on Exercise Reporting Template (CERT).

Results: Mean score of the CERT was 6/19. None of the RCTs described all items of the CERT. Items of crucial importance, such as adherence, whether the exercise was done individually or in a group, whether there were home program or non-exercise components, and the type and number of adverse events, were either not mentioned or not described in detail.

Conclusion: RCTs in exercise in SOT recipients did not satisfactorily report their exercise protocols, which can lead to difficulties in replication by researchers and implementation by clinicians.

KEYWORDS

Solid organ transplant, Exercise interventions, Systematic review

1 | INTRODUCTION

Solid organ transplantation (SOT) provides a second chance of life for people with end-stage diseases of the kidney, heart, pancreas, liver, and lung, improving the quality of life of patients. (1-3) Although some recipients can return to work, enjoy recreational activities, and participate in sports after a transplant, (2, 4-6) many patients present diminished exercise capacity and low levels of physical activity. (7-10) Regular exercise training may improve fitness in these patients, however, the majority do not reach activity and exercise capacity levels observed in healthy individuals. (2, 10, 11) As a result of reduced physical activity levels after transplantation, SOT recipients are at increased risk for cardiovascular complications, diabetes, and mortality. (12, 13)

There are numerous studies that have examined the role of exercise training post-SOT. (14, 15) Our team recently conducted a systematic review and meta-analysis on the effects of exercise (aerobic exercise, resistance exercise, or a combination of both) in SOT recipients (15) and showed that exercise training post-transplant improves exercise capacity, muscle strength, and quality of life in SOT recipients. While there have been recent scientific advances in SOT rehabilitation and convincing evidence for the benefits of exercise post-transplant, (14,15) the exercise programs included in published articles are generally poorly described (14) with incomplete information on volume, intensity, and progression of exercise. The lack of information on these important variables causes difficulty in interpreting and replicating SOT exercise programs. Since exercise prescription parameters have a direct influence on the training outcomes, it is imperative that they are well-defined and clearly reported to allow for interpretation, design of future research trials, implementation into clinical practice, and ultimately, the development of guidelines. (16, 17) A systematic evaluation of reporting quality of exercise interventions in SOT recipients has not been conducted.

Although guidelines such as the Template for Intervention Description and Replication (TIDieR) (17) and Consolidated Standards of Reporting Trials (CONSORT) (16) exist to assist authors to report their interventions with details, these guidelines are not well-tailored for exercise interventions. Specifically, these checklists do not require precise and complete information about the type of exercise intervention, dosage, intensity, frequency, and presence of a supervisor during exercise, all of which are required to fully interpret and replicate these interventions. (16, 17) Recently, a more specific guideline – the Consensus on Exercise Reporting Template (CERT) – has been developed to provide direction on specific items that are necessary to report replicable exercise programs. (18) These items should be reported in all studies of any exercise type, identifying that supplementary information may be required for individual studies, depending on the exercise program under study. (18)

In this systematic review, we used the CERT checklist to evaluate the quality of the exercise training program descriptions in randomized controlled trials (RCTs) involving SOT recipients. (18) By systematically evaluating the quality of intervention reporting, suggestions can be made to improve future trials and the translation of interventions into practice.

2 | METHODS

We followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines (19) and used the CERT (18) to evaluate the quality of the descriptions of the exercise training programs included in the studies.

2.1 | Search strategy

The articles included in this review were identified in a previous systematic review on the effects of exercise in SOT recipients that was conducted by our group. (20) The search strategy was designed to identify RCTs on exercise in SOT recipients (heart, lung, kidney, liver and pancreas). An example of the search strategy is shown in Appendix 1. The following databases were used: MEDLINE, EMBASE, CINAHL and Cochrane Central Register of Controlled Trials. ClinicalTrials.gov was

used to identify clinical trials that were under way or recently completed. All clinical literature was searched from database inception to May 1, 2019. The following keywords were used: physical activity, exercise, physical fitness, transplant, transplantation, transplanted, organ, heart, lung, liver, kidney, pancreas. Articles in English, French, Portuguese and Spanish were considered based on the investigators' comprehension. The reference lists of all primary studies included and pertinent reviews were checked for additional references. Two researchers independently screened all titles and abstracts identified by the literature searches using Covidence software. The same pair of reviewers applied the inclusion/exclusion criteria on the full text of the potentially eligible studies. Disagreements were resolved by consensus between the reviewers.

2.2 | Study selection

To be eligible for the original review,(20) published studies had to: 1) be RCTs examining the effects of exercise training programs in SOT recipients, 2) study adults (> 18 years) who are recipients of heart, lung, kidney, pancreas or liver transplant, 3) involve an inpatient, outpatient or home-based program that included exercise training (aerobic, resistance training, or a combination of both) at any time post-transplant, and 4) compare an exercise training program with a control group (no exercise). Studies were excluded if they were editorials, letters to the editor, or abstracts without published peer-reviewed manuscripts. For the current systematic review, we screened 29 articles that were included in the original review. (20)

2.3 | Consensus on Exercise Reporting Template

The Consensus on Exercise Reporting Template (CERT) is a 16-item tool and is internationally endorsed. (18,21) It was developed using the Enhancing the QUAlity and Transparency Of health Research (EQUATOR) Network methodological framework and elaborates and expands on the previously developed TIDieR checklist. (17) Forty-nine international multidisciplinary exercise experts participated in a modified Delphi strategy to develop the template. With three rounds of online communications, 41 initial items were distilled to the final 16 items necessary to fully describe an exercise program. The template includes "7 sections or domains: what (materials); who (provider); how (delivery); where (location); when; how much (dosage); tailoring (what, how); and how well (compliance/planned and actual)." (18) Each CERT item is rated as 0 (not described or description unclear) or 1 (yes, well-described). The maximum score of the CERT is 19. As of this writing, the CERT explanation and elaboration statement has been cited 228 times.

2.4 | Data extraction strategy

One investigator (UR) independently extracted and entered data regarding study characteristics into a standardized data extraction form. Two investigators (TS and FP) double-checked the data to ensure consistent reporting. Three investigators (UR, TS and FP) independently applied the CERT to all of the included articles, extracted information on the description of the exercise training program and entered data into a standardized form. The independent application of the CERT checklist was done in triplicate (each article was assessed by 3 investigators). One investigator (UR) then compared the responses and disagreements were resolved by consensus with the consultation of a fourth investigator (TJF). The template was pilot tested on one article to ensure that all evaluators were interpreting the CERT in the same way.

3 | RESULTS

3.1 | Studies screened

In the original review, (20) 1490 articles were identified after duplicates were removed. Fifty-nine full text .pdfs were assessed for eligibility and 29 articles met the inclusion criteria. In the current study, we have included 21 articles of the 29 that had been included in the original systematic review. (20) Eight articles were excluded

because they were second publications of original studies and therefore used the same intervention. We chose to evaluate the first published article from each of these series. The complete PRISMA diagram for the two studies is shown in Figure 1 and the characteristics of the 21 included articles are shown in Table 1.

3.2 | Quality of exercise intervention reporting

The average CERT score of the 21 included studies was 6 points out of 19. Table 2 outlines the scores of each study. The scores ranged from 1 to 14. Table 3 reports on the frequency of CERT items being delineated in the included studies. Items 1 (Type of exercise equipment; n=15 (71%)) and 13 (Detailed description of the exercise intervention – for example: number of exercise repetitions/set/sessions, session duration and program duration; n=18 (86%)) were the most commonly described items. Conversely, Item 8 (Detailed description of each exercise to enable replication [e.g., photographs, illustrations, video, etc.]) and 16a (Description of how adherence or fidelity to the exercise intervention is assessed) were the least described (Table 3).

4 | DISCUSSION

The main finding of our systematic review is that RCTs on exercise interventions in SOT recipients (published before the publication of CERT) are not well described. No study described all items on the CERT. Important aspects of the exercise program were not reported, such as examples of the actual exercise, progression of the exercise, or how the starting point for intensity was chosen. Because there are currently no specific guidelines on exercise intervention in SOT, clinicians and researchers are obligated to rely on individually published RCTs and systematic reviews in this field. The lack of specific information about the exercise interventions in these trials may impede the appropriate implementation of these interventions into clinical practice or research.

The authors of TIDieR, an extension of the CONSORT Statement, have made general recommendations for the reporting of complex interventions in clinical trials. (17) The final 16-item CERT (18) is based on the TIDieR domains and headings (17) but contains items that are specifically related to the description of an exercise protocol to help with the actual implementation.

The most well-described item related to the characteristics of the exercise protocol was Item 13: "Detailed description of the exercise intervention (e.g., number of exercise repetitions/set/sessions, session duration and program duration)". However, illustrations (or detailed written descriptions) of actual exercises to enable replication were rarely seen in the reviewed RCTs. Scientific journals have limited the number of figures allowed for publication and therefore providing illustrations of all exercises included in the study may not be feasible unless the journal offers space in an online supplement. It was also rarely mentioned in the RCTs if exercises were done individually or in a group. The descriptions of these items are important to allow clinicians and researchers to replicate the exercise program as peer support can influence outcomes. (18) Items that describe whether the exercises were generic or tailored, and how they were tailored to the individual, were included in less than half of the reviewed studies. Exercise programs can be a standardized set of exercises or they may be tailored to the individual for various reasons such as comorbidities, musculoskeletal problems, etc. A guide of decision rules for the tailoring and implementation of time points should be provided to enable researchers to administer the program. (18)

Several other important areas that may help clinicians and researchers decide to adopt a particular exercise protocol have also been poorly described. Motivation strategies and adherence were mentioned in only 16% and 28% of the articles, respectively. Information about motivation strategies can greatly help clinicians and researchers determine which strategies can be used to ensure adherence and completion rates. Furthermore, adverse events were reported in only 12% of the articles. With safety being a basic factor affecting adherence and success of exercise interventions, detailed reporting of these events is required to decide whether an

exercise program should be undertaken. (18) In addition, whether the intervention was delivered as planned was not described in most articles. Sometimes, an intervention needs adjustments and is not delivered as planned. The level to which this occurred must be reported, as it provides an explanation for the effect or lack of effect of an intervention and can be used to inform future studies. (18)

The CERT has been used in other patient populations, such as those who are mechanically ventilated in the intensive care unit (ICU), (22) have fibromyalgia, (23) hypertension, (24, 25) knee osteoarthritis (26) or osteoporosis, (27), and athletes with groin injury. (28) Similar to our findings, all of these studies (22-28) concluded that exercise interventions are not well described, though most of the studies evaluated were published prior to the publication of the CERT guidelines. One systematic review (25) limited the studies evaluated to those post 2016, but these authors also found inadequate reporting for exercise interventions in pulmonary hypertension patients. Since exercise and advice to stay active is recommended for the management of many chronic conditions, (29-32) detailed descriptions of these exercise interventions are essential.

Our study has some strengths and limitations. Our review included a rigorous methodology (with an experienced librarian) and expertise of the research team in knowledge synthesis and exercise prescription in transplant patients. An important limitation is that the CERT explanation and elaboration statement was published in 2016 (18) while all studies identified in our systematic review were published during or before 2016. While we could have used the CONSORT or TIDieR checklists in our review, these guidelines are not tailored for exercise interventions. In addition, even though the CERT was not available before 2016, the evaluation of the exercise intervention reporting is still relevant. Now that the CERT has been developed, it is hoped that more authors will become acquainted with the tool and that this will lead to the improvement in the quality of reporting of exercise interventions.

5 | CONCLUSION

Despite the important role of exercise training in the management of SOT recipients, RCTs of exercise in SOT recipients did not satisfactorily report their exercise protocols. It is recommended that researchers reporting on future clinical trials describe their exercise protocols for SOT recipients in more detail to enable replication in research and facilitate implementation of these interventions in clinical practice.

6 | AUTHORS' CONTRIBUTIONS

UR, SM and TJF contributed to the design of the study. UR, TMS ad FES applied the CERT and extracted data about the exercise programs. UR extracted other relevant data, created the tables and wrote the manuscript. All authors read the manuscript, interpreted the data and provided critical feedback.

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7 | TABLES & FIGURES

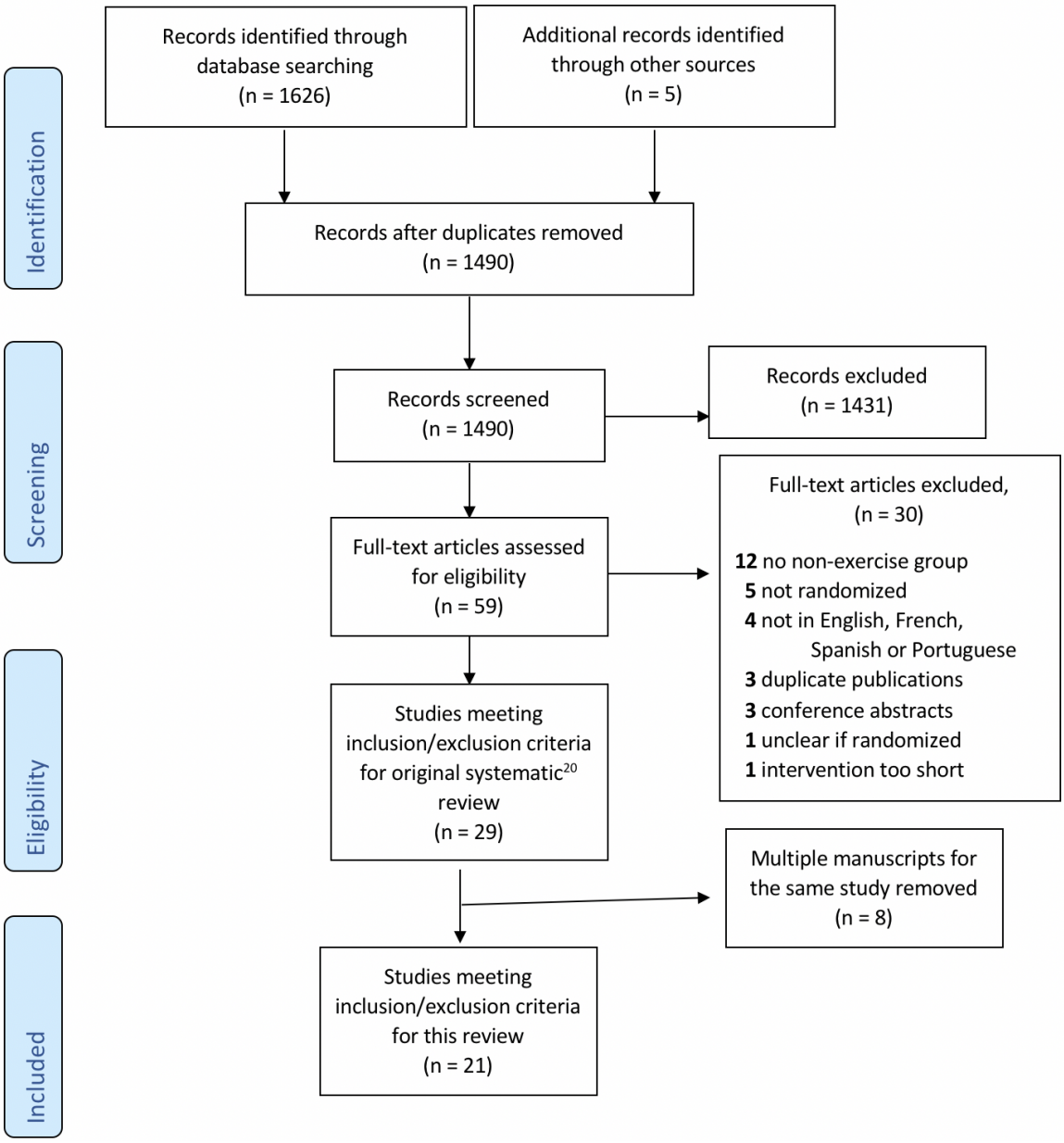


FIGURE 1 PRISMA Flow Diagram

Author & year	Country	Organ type	Type of exercise	Training load	Program duration
Basha et al. (2015)	Egypt	Liver	Aerobic & resisted exercise	Three sets of 8–12 repetitions performed at 85% of initial 1-RM, intensity of less than 50% of HR max.	12 weeks
Bernadi et al. (2007)	Italy	Heart	Aerobic	Exercise at 50 rpm for 30 min, 5 days a week at 60–70% of their peak oxygen consumption.	6 months
Braith et al. (2008)	USA	Heart	Aerobic	Exercised 3 days per week. 35–40 minutes of exercise as tolerated.	12 weeks
Eatemadololama et al. (2017)	Iran	Kidney	Resistance training	Exercise training 2 days per week. Single set of 10–15 repetitions. Resistance increased by 5–10 % next sessions.	12 weeks
Greenwood et al. (2015)	UK	Kidney	Aerobic or resistance training	Started with 1–2 sets and 10 repetitions (based on 80% one repetition maximum and on tolerance) increasing to 3 sets and 8–10 repetitions.	12 weeks
Haykowsky et al. (2009)	Canada	Heart	Aerobic and strength training	For 8 weeks, treadmill and cycle exercises were performed at a heart rate equal to 60–80% VO_2 peak for 30–45 min. In the final 4 weeks, continuous aerobic training was performed 3 days/week (45 min/session at a heart rate equal to 80% VO_2 peak) and interval training was performed 2 days/week.	12 weeks
Hermann et al. (2011)	Denmark	Heart	High intensity aerobic exercise	After warming up, a 42-min high intensity exercise program followed, with interval blocks of 4 min/2 min/30 s according to 80%, 85% and 90% of VO_2 peak and recovery periods of 1/2 min. Finally, 10 min of staircase running up according to 80% of peak VO_2 and recovery walking down according to 50% peak VO_2.	2 months
Juskowa et al. (2006)	Poland	Kidney	Physical exercise	30 min per session.	4 or 5 weeks post transplantation
Karelis et al. (2016)	Canada	Kidney	Resistance training	45–60 min in-hospital RT program. The intensity of the exercise training sessions was approximately 80% of the 1-RM.	16 weeks
Kouidi et al. (2013)	Greece	Kidney	Aerobic and strengthening	30–40 min aerobic exercise programme followed by 10–30 min of strengthening exercises. The target intensity was scheduled to be close to the anaerobic or ventilatory threshold (50–75% VO_2 peak or 65–85% HR max).	6 months
Langer at al. (2012)	Belgium	Lung	Resistance training	Session lasted for about 90 min. Patients performed 3 times 8 repetitions using leg press equipment, with the initial load set at 70% of the 1-RM.	3 months
Leasure et al. (1995)	USA	Kidney	Aerobic	Completion times for the exercise sessions progressed from 30 to 60 minutes: 5-min warm-up and a cool-down, an aerobic portion, and a strengthening portion.	12 weeks

TABLE 1 (Continued on next page)

Mitchell et al. (2003)	USA	Lung	Resistance training	One set of variable resistance lumbar extensions through a 72-degree ROM with a weight load that allowed 15–20 repetitions to volitional muscle fatigue.	6 months
Moya-Najera et al. (2017)	Spain	Liver	Aerobic and resistance training	During the first 3 months, patients had to perform 3 sets of 25 repetitions at a velocity of 2 seconds for each concentric and eccentric contraction. During the second 3-month period, patients had to perform 3 sets of 15 repetitions at a velocity of 2 seconds for each concentric and eccentric contraction.	24 weeks
Nytroen et al. (2012)	Norway	Heart	HIIT	The HIIT-sessions consisted of 10 min warm-up, followed by four 4-min exercise bouts at 85–95% of maximum heart rate (HR max), interposed by 3 min active recovery. periods (Figure 2) corresponding to ~11–13 on the Borg, 6–20 rated perceived exertion (RPE) scale.	24 weeks
Painter et al. (2002)	USA	Kidney	Cardiovascular exercise (walking or cycling)	Frequency of at least 4 times per week; duration that worked up to at least 30 min per session; and an intensity that was initially 60–65% of maximal heart rate, which was gradually (approximately every 2 weeks) increased to 75–80% of maximal heart rate.	1 year
Pascoalino et al. (2015)	Brazil	Heart	Exercise training	Thrice-weekly exercise training program. Supervised sessions consisted of 5 min of warm-up, 40 min of endurance exercise at an intensity of 80% of the respiratory compensation point and 5 min of cool-down.	12 weeks
Pooranfar et al. (2014)	Iran	Kidney	Aerobic and resistive exercises	Three 60–90-min sessions per week. Aerobic exercise on fixed bicycle or treadmill with 40%–70% maximum heart rate intensity and resistive exercise with 45%–65% of maximum frequency.	10 weeks
Riess et al. (2014)	Canada	Kidney	Endurance and strength training	Endurance (3 days/week) and strength training (2 days/week). Endurance training was performed on a cycle ergometer and treadmill at 60%–80% VO_2 peak for 30–60 min/session. Lower extremity strength training was performed at 50% 1-RM for 2 sets of 10–15 repetitions. The intensity increased by 5%–10% when 2 sets of 15 repetitions were performed.	12 weeks
Shakoor et al. (2016)	Iran	Kidney	Aerobic and anaerobic	Three sessions per week for 60-90 min. Each session included a 15-min warm-up, 20 min of aerobic exercise, 20 min of resistance exercise, and a 10-min cool-down including running with a slow pace followed by stretching and light exercises.	10 weeks
Tzvetanov et al. (2014)	USA	Kidney	Resistance training	Individual physical training using low-impact, low-repetition, resistance-based weight training with two 1-hour sessions each week.	1 year

1-RM: one-repetition maximum, HR: heart rate, VO_2 peak: highest value of VO_2 attained on a particular exercise test, RT: resistance training, ROM: range of motion, HIIT: high-intensity interval training, RPE: rating of perceived exertion

TABLE 1 Characteristics of the included studies

Study	1	2	3	4	5	6	7a	7b	8	9	10	11	12	13	14a	14b	15	16a	16b	Score
Basha et al. (2015)	☺	☺	☹	☹	☺	☹	☺	☺	☺	☺	☹	☹	☹	☺	☹	☹	☺	☹	☹	9/19
Bernadi et al. (2007)	☺	☹	☹	☹	☺	☹	☹	☺	☹	☺	☹	☹	☺	☺	☹	☹	☹	☹	☹	6/19
Braith et al. (2008)	☺	☹	☹	☹	☹	☹	☹	☹	☹	☹	☹	☹	☺	☺	☹	☺	☹	☹	☹	4/19
Eatemadololama et al. (2017)	☹	☺	☹	☺	☹	☹	☹	☺	☹	☹	☹	☹	☹	☺	☹	☹	☹	☹	☹	4/19
Greenwood et al. (2015)	☺	☺	☹	☺	☺	☺	☺	☺	☹	☹	☺	☺	☺	☺	☺	☺	☹	☹	☺	14/19
Haykowsky et al. (2009)	☹	☹	☹	☹	☹	☹	☹	☺	☹	☹	☹	☺	☹	☺	☹	☹	☹	☹	☺	4/19
Hermann et al. (2011)	☺	☹	☹	☹	☹	☹	☹	☹	☹	☹	☹	☺	☺	☺	☺	☹	☺	☹	☹	6/19
Juskowa et al. (2006)	☹	☺	☹	☹	☹	☹	☹	☹	☹	☹	☹	☹	☹	☹	☹	☹	☹	☹	☹	1/19
Karelis et al. (2016)	☺	☺	☹	☺	☺	☹	☺	☹	☹	☺	☹	☹	☺	☺	☺	☹	☺	☺	☺	12/19
Kouidi et al. (2013)	☹	☹	☹	☺	☹	☹	☺	☹	☹	☹	☹	☹	☺	☺	☺	☺	☺	☹	☹	7/19
Langer at al. (2012)	☺	☹	☹	☹	☹	☹	☺	☺	☹	☹	☺	☹	☹	☺	☺	☺	☺	☹	☹	8/19
Leasure et al. (1995)	☺	☹	☹	☹	☹	☺	☹	☹	☹	☹	☹	☹	☺	☹	☺	☹	☹	☹	☹	4/19
Mitchell et al. (2003)	☺	☺	☹	☹	☹	☹	☺	☹	☺	☹	☹	☹	☹	☺	☹	☹	☹	☹	☹	5/19
Moya-Najera et al. (2017)	☺	☺	☹	☺	☺	☹	☺	☺	☹	☹	☹	☹	☺	☺	☺	☹	☹	☹	☹	9/19
Nytroen et al. (2012)	☺	☺	☺	☺	☹	☹	☹	☹	☹	☹	☹	☹	☹	☺	☺	☺	☹	☹	☹	7/19
Painter et al. (2002)	☹	☹	☺	☹	☺	☺	☹	☺	☹	☹	☹	☹	☺	☺	☺	☺	☺	☺	☹	10/19
Pascoalino et al. (2015)	☺	☹	☹	☹	☹	☹	☹	☹	☹	☺	☹	☹	☹	☺	☹	☹	☹	☹	☹	3/19
Pooranfar et al. (2014)	☺	☹	☹	☹	☹	☹	☹	☹	☹	☹	☺	☹	☹	☺	☺	☺	☹	☹	☹	5/19
Riess et al. (2014)	☺	☺	☹	☹	☹	☹	☺	☺	☹	☹	☹	☹	☹	☺	☺	☺	☹	☹	☹	7/19
Shakoor et al. (2016)	☺	☹	☹	☹	☹	☹	☹	☹	☹	☹	☹	☹	☹	☺	☹	☺	☹	☹	☹	3/19
Tzvetanov et al. (2014)	☹	☹	☺	☺	☹	☹	☹	☹	☹	☹	☺	☹	☺	☹	☺	☹	☹	☹	☹	5/19
Average score																				**6.0**

Yes: ☺, No: ☹

TABLE 2 Consensus on exercise reporting template items of articles examining the effects of exercise training programs in SOT recipients

#	Question	n (%)
1	Type of exercise equipment	15 (71)
2	Qualifications	9 (43)
3	Individually/in a group	3 (14)
4	Supervised/unsupervised	14 (67)
5	Adherence to exercise	6 (29)
6	Motivation strategies	3 (14)
7a	Decision rules for exercise progression	8 (38)
7b	Description of exercise progression	9 (43)
8	Description of each exercise to enable replication	2 (10)
9	Home program component	4 (19)
10	Non-exercise components	4 (19)
11	Type and number of adverse events	3 (14)
12	Setting in which the exercises are performed	10 (48)
13	Detailed description of the exercise intervention	18 (86)
14a	Generic/tailored	12 (57)
14b	Detailed description of how exercises are tailored	9 (43)
15	Decision rule for determining the starting level	6 (29)
16a	Description of how adherence is measured	2 (10)
16b	Intervention delivered as planned	3 (14)

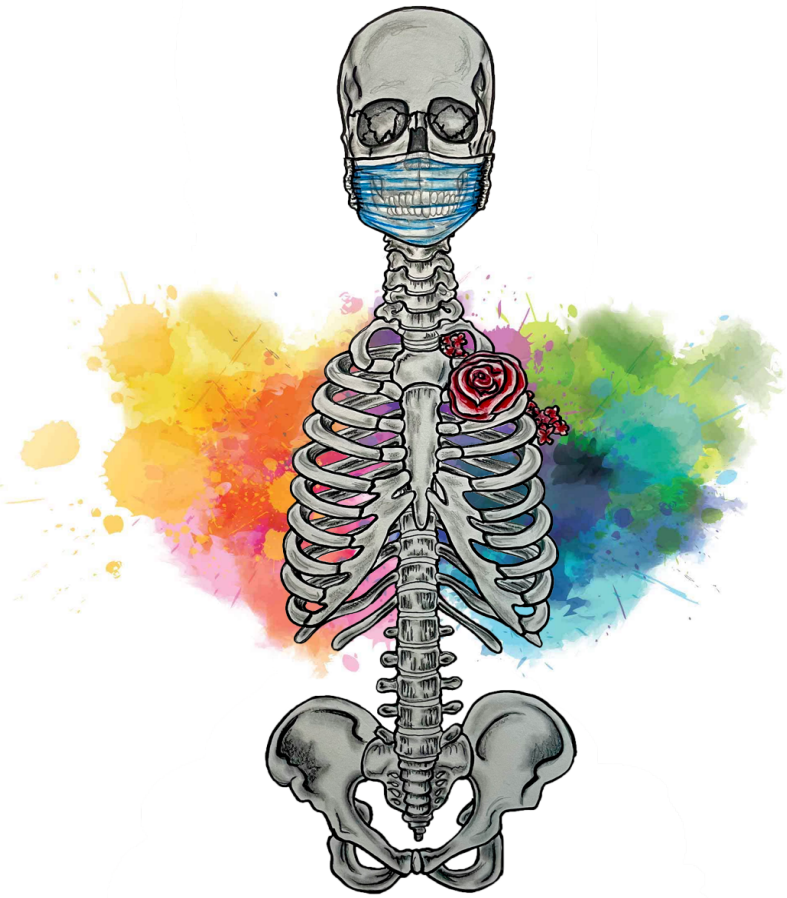
TABLE 3 Percentage of articles that describe items of Consensus on Exercise Reporting Template

8 | APPENDIX 1

8.1 | Ovid Medline (All) Search Strategy

1. Physical activity.ti,ab,kf.
2. exercise.ti,ab,kf.
3. exp Exercise/ or exp Exercise Therapy/
4. Physical Fitness/
5. physical fitness.ti,ab,kf.
6. exp Organ Transplantation/
7. ((organ or heart or kidney or pancreas or liver or lung) adj (transplant or transplantation or transplanted or transplants)).ti,ab,kf.
8. 6 or 7
9. 1 or 2 or 3 or 4 or 5
10. 8 and 9
11. randomized controlled trial.pt.
12. controlled clinical trial.pt.
13. randomi?ed.ab.
14. placebo.ab.
15. drug therapy.fs.
16. randomly.ab.
17. trial.ab.
18. groups.ab.
19. or/11-18
20. exp animals/ not humans.sh.
21. 19 not 20
22. 8 and 21 and 9

NARRATIVE REVIEW



Artist: Caroline Najjar

NARRATIVE REVIEW
McGill Journal of Medicine

Mechanisms of Action by Antimicrobial Agents: A Review

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ABSTRACT

Microorganisms and their associated conditions comprise some of the world's leading causes of death and have the potential to cause a significant effect on human activities during pandemic states. Despite such significance in the healthcare field, attention and funding directed towards microbiological research lags behind those given to cancer and cardiovascular disease. In the current SARS-CoV-2 pandemic, the need of healthcare providers to remain knowledgeable on antimicrobial therapy for their patients is greater than ever before. The scope of this review is to provide clinicians a semi-comprehensive, up-to-date understanding of the mechanisms of action among antimicrobial agents as well as key distinctions in clinical manifestations of pathogens.

KEYWORDS

Antimicrobial Activity, Mechanism of Action, Antiviral, Antifungal, Antibiotic

1 | INTRODUCTION

The explosive growth in the use of antimicrobial therapy has provided a degree of control on microbial-related diseases in humans. However, microbial resistance to antibiotics also developed over time, resulting in an arms-race for developing newer agents against these more resistant strains. As a result, practicing clinicians have an obligation to remain informed on modern antimicrobial agents and to understand their core mechanisms of action. Bacteria and fungi differ in cellular composition, but the levels at which these microbes can be altered are similar: protein synthesis, nucleic acid synthesis, cell wall, and cell membrane. Viruses, on the other hand, are different structurally as they do not contain a cell membrane or cell wall. (1) The aim of this review is to provide a categorical overview of antimicrobial agent mechanisms and brief clinical manifestations.

2 | METHODS

An electronic database search was performed on MEDLINE (PubMed) using the following criteria: ("antimicrobial agents" [All Fields]) OR ("penicillin" [All Fields] OR ("sulfonamide" [All Fields]) OR ("protein synthesis

antibacterial "[All Fields]) OR ("antifungal" [All Fields]) OR ("antiviral"[All Fields]) AND “access”[All Fields] AND “outcomes”[All Fields]). The results were narrowed down to 810 publications after filtering for free, full-text, and 88 publications were selected by the reviewers (SPS and AQ) for analysis. Afterwards, the reviewers excluded 18 duplicate publications, resulting in 70 publications for the final analysis. Additionally, two medical textbooks were used to yield relevant clinical information for medical students. (1, 63)

3 | ANTIBACTERIAL AGENTS

3.1 | Agents Acting Through Cell Wall Synthesis

While the organic synthesis and structure of the cell wall is different between bacteria and fungi, its presence helps limit changes in the internal osmotic pressure of both microbes. (1,2) Since the cell wall is not present in mammalian cells, this structure is a key antimicrobial target that minimizes impact on normal host tissue. (1)

3.1.1 | Beta-Lactam Containing Antimicrobials

Penicillin is a group of antimicrobials that resembles a structural analogue of D-alanyl-D-alanine in most cases. (2) This analogue competes for the D-alanyl-D-alanine transpeptidase, also known as the penicillin-binding protein, which joins layers of peptidoglycan on the cell wall. By inactivating peptidoglycan synthesis, penicillin creates higher internal osmotic pressure that leads to cell lysis. (2) Additionally, penicillin is a ß-lactam drug because it contains an eponymous ß-lactam ring essential for its function. When the ß-lactam ring is destroyed, penicillin loses its analogous quality and no longer competes for transpeptidase. (4) Additionally, patients who are allergic to penicillin may resort to using alternative ß-lactam drugs such as cephalosporins and carbapenems. (3) This group of molecules are structurally different from penicillin but are functionally similar and have a broad-range spectrum of bacterial coverage. (1-7) Bacterial resistance to ß-lactam-containing agents develops during endogenous production of penicillinases/ß-lactamases by bacterial strains. To protect the ß-lactam ring from degradation by these penicillinases, a large molecular side chain structure may be added. (2) This addition led to the creation of penicillinase-resistant penicillin (e.g. dicloxacillin, nafcillin, oxacillin). They have a smaller spectrum of activity, with targeted efficacy against *Staphylococcus aureus*. (1) Monobactams (e.g. aztreonam) comprise another ß-lactam drug class that affect transpeptidation and are primarily used against aerobic Gram negative bacteria due to their molecular structure. (2-6)

3.1.2 | Vancomycin

While ß-lactam drugs specifically target the transpeptidase, preceding enzymatic steps in peptidoglycan synthesis can also serve as antibacterial targets. For example, vancomycin binds directly to D-alanyl-D-alanine transpeptidase to inhibit cross-linking. (63) Vancomycin thus prevents peptidoglycan synthesis without being susceptible to ß-lactamases. (1) Vancomycin is clinically used against methicillin-resistant Staphylococcus aureus (MRSA). Noteworthy side effects of vancomycin include nephrotoxicity, ototoxicity, and thrombophlebitis (similar effects are also found with aminoglycosides). (1) This review search yielded a case study of a patient who presented with “red man syndrome” due to vancomycin’s ability to directly bind to mast cells causing them to release histamine, promoting vasodilation. (69)

3.1.3 | Bacitracin and Cycloserine

Bacitracin is an antibacterial agent that inhibits transport of peptidoglycan subunits from the cytoplasm to the cell wall by inactivating its phospholipid carrier. (7) In contrast, cycloserine inhibits synthesis of D-alanyl-D-alanine inside the cell. (7) Comparatively, the literature on cycloserine was scarce compared to other agents in this review, which could also imply that cycloserine is used less often in clinical settings than other agents.

3.2 | Agents Acting Through Microbial Protein Synthesis

3.2.1 | Aminoglycosides

Aminoglycosides are a broad-spectrum bactericidal class of antibiotics that can be semi-synthetic or naturally derived from Gram positive actinomycetes. (13) They exert their antibacterial effects by inhibiting the prokaryotic ribosomal initiation complex, which results in misreading of messenger RNA (mRNA). (1) Oxygen-dependent active electron transport is required for aminoglycoside uptake into cells, explaining their lack of activity against anaerobic bacteria. (13) Streptomycin is an aminoglycoside that irreversibly binds to the A-site 30S ribosomal subunit of the initiation complex in bacteria. (1,15) Furthermore, streptomycin can be nephrotoxic as well as ototoxic due to degeneration of sensory cells in the basal cochlea. (15,16) While streptomycin is no longer used as widely in Canada or the United States anymore, it holds historical importance because it was the first aminoglycosides discovered for clinical use, specifically against tuberculosis, bubonic plague, and brucellosis. (1) Other aminoglycosides include gentamicin (used against various Gram-negative rods such as *Pseudomonas aeruginosa*), amikacin (used against gentamicin-resistant organisms), and neomycin (used against various enteric gram negative rods). (13) Aminoglycosides usually are not given orally as they are poorly absorbed in the GI tract. (1,13) However, oral neomycin is given in preoperative bowel preparation. (1)

3.2.2 | Tetracyclines

Tetracyclines are bacteriostatic antibiotics that, like aminoglycosides, inhibit microbial protein synthesis by binding to the 30S ribosomal subunit. (63) However, rather than binding irreversibly to the A-site 30S ribosomal subunit of the bacterial initiation complex, tetracyclines reversibly inhibit the binding of transfer RNA (tRNA) to the acceptor site, hindering polypeptide growth. Tetracyclines also chelate calcium and iron, and hence should not be taken simultaneously with supplement forms of calcium and iron to avoid micronutrient deficiencies. In addition, tetracycline is contraindicated in infants and in pregnancy due to tooth discoloration through calcium-chelation. (17) A newer class of antibiotics called tigecyclines are structurally similar to tetracyclines and also bind to the 30s ribosomal subunit. (1) Clinically, tigecycline are used to treat complicated intra-abdominal infections and skin/soft tissue infections, with notably activity against MRSA. (59)

3.2.3 | Chloramphenicol

Chloramphenicol is a broad-spectrum antibiotic that blocks peptidyltransferase at the 50S ribosome subunit to prevent protein synthesis. This class of antimicrobials is bacteriostatic against many bacteria responsible for ocular infections. The literature notes bactericidal activity against the meningitis-causing microbes *Haemophilus influenzae*, *Neisseria meningitidis*, and *Streptococcus pneumoniae*. (63) Chloramphenicol toxicity comes in two forms: 1) a predictable, reversible, dose-dependent bone marrow suppression that can start soon after administration; 2) an unpredictable, rare, and disastrous irreversible agranulocytosis, which generally occurs during prolonged therapy.18 Metabolically, chloramphenicol is detoxified through UDP-glucuronyl transferase.1,18 Toxic chloramphenicol serum concentration may result in gray-colored skin and cyanosis in infants, which has been documented as infantile “gray-baby” syndrome. (71)

3.2.4 | Macrolides and Clindamycin

Macrolides interact through the 50S ribosome subunit of bacteria via blocking translocation of tRNA. (63) Azithromycin is a macrolide used to treat respiratory tract infections and *Chlamydia*-induced genital tract infections. (18) Clarithromycin has a similar spectrum and treats *Helicobacter* infections such as peptic ulcer disease. Side-effects include arrhythmia from QT-prolongation and cholestatic hepatitis. (63) Both clarithromycin and erythromycin were shown in a study to inhibit cytochrome P-450. (19)

Clindamycin also inhibits translocation of tRNA on

the 50S ribosome subunit of bacteria. (1,63) It is used to treat anaerobic infections above the diaphragm such as aspiration pneumonia and lung abscesses. (1,19) A major adverse effect of clindamycin is the overgrowth of a drug-resistant strain of *Clostridium difficile* in the gastrointestinal tract, which can produce an exotoxin leading to pseudomembranous colitis. (19)

3.2.5 | Oxazolidinones

Oxazolidinones inhibit the formation of the initiation complex on the 50s ribosomal subunit. These agents are particularly useful against MRSA, vancomycin-resistant *Enterococci*, and penicillin-resistant *Streptococcus pneumoniae*. (21,63) Adverse effects include serotonin syndrome and tyramine-induced hypertensive crisis, since some oxazolidinones such as linezolid are monoamine oxidase inhibitors. (21)

3.3 | Agents Acting Through Nucleic Acid Synthesis

3.3.1 | Sulfonamides and Trimethoprim

Sulfonamides competitively inhibit p-aminobenzoic acid (PABA), an early precursor of tetrahydrofolic acid, which is required for nucleic acid synthesis of all nitrogenous bases except cytosine. (22) By inhibiting PABA, sulfonamides render the dihydropteroate synthase inactive. (1,22,63) Clinically, sulfonamides are used to treat urinary tract infections caused by *Escherichia coli* as well as middle ear infections caused by *Streptococcus pneumoniae* and *Haemophilus influenzae*. (22) Moreover, it is critical to understand that while nucleic acids are present in both prokaryotes and eukaryotes, mammalian cells do not have PABA-containing precursor enzymes and instead rely on exogenous folic acid to meet their metabolic requirements for nucleic acid synthesis (23), which in theory can limit sulfonamides targeting of mammalian cells. Sulfonamides are commonly used in combination with trimethoprim. (23) Trimethoprim similarly inhibits the production of tetrahydrofolic acid, but its mechanism involves the inhibition of a later enzyme in the pathway, dihydrofolate reductase. (1,63) Thus, sulfonamide and trimethoprim act synergistically. However, as trimethoprim inhibits folic acid synthesis, bone marrow suppression may result, leading to potential megaloblastic anemia. (22)

3.3.2 | Fluoroquinolones

Unlike sulfonamides and trimethoprim, which are independent bacteriostatic agents, fluoroquinolones are bactericidal drugs that inhibit DNA gyrase and DNA topioisomerase in bacteria. (26) Fluoroquinolones (e.g. ciprofloxacin, levofloxacin, etc.) can be used to treat urinary tract infections and lower respiratory tract infections caused by Gram negative rods. (1) Side effects of fluoroquinolones include tendonitis and/or tendon rupture in elderly patients. (63) Fluoroquinolones have been contraindicated in children and pregnant women due to potential interference with bone growth, but this has only been reported in animal models. (26-27)

3.3.3 | Rifamycin

Rifamycins selectively bind to the ß subunit of bacterial RNA polymerase, rendering it inactive for mRNA synthesis. (1) Rifampin is specifically useful in the treatment and prophylaxis of *Mycobacterium tuberculosis*-caused tuberculosis and meningitis, respectively. (31,63) It also aids in the treatment of leprosy by attenuating antimicrobial resistance to dapsone. (31) Patients on rifampin may have harmless reddish orange urine (1) due to the drug's color being distilled by body fluids. Rifampin may also result in hepatotoxicity as it induces cytochrome P-450 enzymes; thus it is not recommended for HIV patients. (1) Rifabutin is a rifampin derivative that can be used by HIV patients as it induces cytochrome P-450 enzymes to a lesser degree than rifampin. (30,31)

3.4 | Agents That Alter Cell Membranes

3.4.1 | Polymyxin and Daptomycin

Polymyxins such as Polymyxin E proteins disrupt the charge of phospholipids in the bacterial cell membrane. (32) They are useful against many Gram-negative rods and carbapenemase-producing *Enterobacteriaceae*. (63) Daptomycin similarly disrupts the cell membranes of gram positive cocci and MRSA through depolarization, but is not effective in the lung due to pulmonary surfactant interfering with its mechanism of action. (32)

4 | ANTIFUNGAL AGENTS

The fungal cell wall is composed of a solubilized chitin-ß-(1,3)- glucan linked by a ß-(1,6)-glucan to mannoproteins on the outer surface of the fungal cell wall. (10) ß-glucan is synthesized by a multi-subunit enzyme, 1,3-ß-glucan synthase. (11) Previous literature on this enzyme shows that its inhibition results in physiological cell cycle arrest and hence has become a key target in antifungal therapy through the echinocandin lipopeptide class of antifungal therapy. (10-11)

4.1 | Agents that Alter the Cell Wall

Caspofungin is a part of the echinocandins, a lipopeptide drug class that non-competitively inhibits 1,3-ß-glucan synthase. It is mainly used against systemic yeast infections, such as disseminated candidiasis and invasive aspergillosis. (11) However, caspofungin has been shown to be ineffective against *Cryptococcus* or Mucor-induced infections at normal doses. (12) Additionally, another lipopeptide drug, micafungin, has been used for prophylaxis in patients undergoing hematopoietic stem cell transplantation. (70) Anidulafungin is another semisynthetic echinocandin used against invasive esophageal candidiasis in clinical use. (12) *Cryptococcus* is not susceptible to any of the three semisynthetic echinocandins, but the mechanism of this resistance is not well understood. (1, 11)

4.2 | Agents that Alter the Cell Membrane

Amphotericin B is an antifungal that alters the cell membrane by binding to ergosterol - a compound exclusive to fungi. (1) This results in the formation of ion channels in the fungal cell membrane leading to depolarization of the cell membrane and subsequent cell death. (33) Additionally, amphotericin B is associated with nephrotoxicity and arrythmia, which causes its use by clinicians to be reserved for salvage therapy. Nystatin is a topical antifungal agent that functions similarly to amphotericin and is used for topical *Candida* infections. (1) Azoles are another class of antifungal cell membrane agents. They work by directly inhibiting ergosterol synthesis. (34) Terbinafine inhibits a squalene epoxidase in ergosterol synthesis and is used in finger and nail fungal infections. (33,63)

4.3 | Agents that Alter the Nucleotide and Protein Synthesis

The scope of fungal nucleic acid inhibitors is smaller. The primary antifungal agent is flucytosine, a nucleoside analogue that can inhibits a thymidine precursor enzyme, resulting in inactive DNA synthesis. (28,29) Griseofulvin and pentamidine are antifungal agents that alter microtubules and DNA synthesis, respectively. (63) Pentamidine is used for treatment and prophylaxis against *Pneumocystis jiroveci*. (35) Griseofulvin, like terbinafine, is useful in fungal infections of the nailbed. (35,36)

5 | ANTIVIRAL AGENTS

Unlike bacteria and fungi, viruses are acellular structures containing their own set of DNA or RNA and a limited variety of proteins necessary for nucleic acid replication and structural attachment/maintenance. (1,63)

5.1 | Herpesvirus

The primary herpesviruses of this review are Herpes Simplex Virus type 1 & 2 (HSV-1 & HSV-2), cy-

tomegalovirus (CMV), Epstein-Barr virus (EBV), and Varicella-Zoster virus (VZV). (58) While HSV-1 is commonly associated with oral cold sores, HSV-2 is usually associated with genital blisters or sores generally below the waist. (42) Patients acutely infected with VZV initially present with febrile symptoms and can develop varicella, while post-latency VZV re-activation commonly causes a dermatomal rash known as shingles. VZV is also associated with vesicular rashes, neuritis, and encephalitis. (1,42) Regarding CMV infection, congenital manifestations such as intracranial calcifications, hydrocephalus, and retinitis are present both with and without symptoms. (42,63) Symptoms in patients infected with CMV include mononucleosis (more common post-neonatally), rash, and malaise. (1) EBV and CMV infections are similar in that both infected children and adults present with mononucleosis-related glandular fever. (1,58)

Inhibitors of the herpesviruses can be separated into nucleoside inhibitors and non-nucleoside inhibitors. Acyclovir, ganciclovir, and trifluridine are nucleoside inhibitor analogues that vary in function. Acyclovir is a nucleoside analogue that is preferentially activated by a virus-encoded thymidine kinase primarily found in HSV. (1) Upon phosphorylation of acyclovir, a cellular by-product, acyclovir triphosphate, inhibits the viral DNA polymerase and subsequent nucleic acid synthesis. Clinically, acyclovir is used in the treatment of genital herpes and is used as a prophylactic agent in patients who are immunocompromised or elderly. (73) Despite its efficacy against active HSV, acyclovir has minimal effect on latent HSV and VZV. (58) Ganciclovir is structurally similar to acyclovir, but is preferentially activated by a CMV-encoded phosphokinase to inhibit viral nucleic acid synthesis. (58,63) Cidofovir is another nucleoside analogue that is approved to treat CMV-induced retinitis. (63) In contrast, the non-nucleoside inhibitor of HSV is foscarnet, a pyrophosphate analogue that directly binds to DNA polymerase during pyrophosphate cleavage. This agent is clinically useful against acyclovir-resistant active HSV and CMV infections. (37,38)

5.2 | Hepatitis B and C

There are multiple types of hepatitis viruses (A, B, C, D, E), but this review will focus on Hepatitis B and C (HBV & HCV) as they are more likely to cause chronic infection and can also progress into hepatocellular carcinoma (1,52-53); however, it is imperative to know that malaise, jaundice and transaminitis are common manifestations in acute viral hepatitis of any cause. The primary agents acting against chronic HBV infections inhibit viral DNA polymerase, but each of these primary drugs are structurally different analogues, such as entecavir (guanosine analog), adefovir (adenosine monophosphate analogue), and telbivudine (thymidine analogue). The prominent HCV antiviral agents can be separated into RNA polymerase inhibitors (dasabuvir, sofosbuvir & simeprevir), nonstructural protein 5a (NS5A) inhibitors (ledipasvir, ombitasvir), and nonstructural protein 5B (NS5B) inhibitors. Their mechanisms of action are beyond the scope of this review. (42-44) Recombinant alpha interferon can also be used against hepatitis B and C infections, but this treatment has fallen out of favor in the past decade due to an unfavorable side-effect profile. (72)

5.3 | Influenza B and C

All case studies derived for this review noted the specific strains of Influenza A and B during seasonal epidemics of the flu. Oseltamivir is an oral antiviral medication used to prevent influenza A and B outbreaks. (39,54) Once activated, this pro-drug selectively binds to neuraminidase, an enzyme found on the outer surface of all influenza viruses, to prevent viral release. (1) Other analogues include zanamivir and peramivir. (1,39,54) Baloxavir is a selective inhibitor of influenza cap-dependent endonuclease, and has been shown in clinical trials to reduce viral load more efficiently than oseltamivir. (74). It is currently clinically approved for its medical use in Influenza A infections in the United States. (54)

5.4 | Human Immunodeficiency Virus

Human Immunodeficiency Virus (HIV) is characterized by a unique diploid set of viral RNA. The virus infects and destroys CD4+ T helper cells, thereby weakening the immune system. (1,63) Patients often initially present with a febrile illness resembling mononucleosis, marking the acute phase of the viral infection. (1) The virus then enters the latency phase where it seeds and replicates within latent HIV reservoirs in the body.(1,63) This period can take months to years while the patient is asymptomatic. (1) Eventually, CD4+ serum count decreases causing moderate immunocompromise followed by the Acquired Immunodeficiency Syndrome (AIDS) phase of the infection, characterized by severe opportunistic infections. (5,57)

To delay this decline in immune function, multiple agents against HIV are given in combination. (57) The first two major classes of HIV drugs are nucleoside reverse transcriptase inhibitors (NRTIs) and non-nucleoside reverse transcriptase inhibitors (NNRTIs). (57) NRTIs include Abacavir, Didanosine, Emtricitabine, Lamivudine, Stavudine, Tenofovir, and Zidovudine. (63) While each NTRI vary slightly in structure, they all competitively. bind to the HIV reverse transcriptase active site to inhibit viral DNA synthesis, causing chain termination. (1) NNRTIs include Delavirdine, Efavirenz, Etravirine, Nevirapine, and Rilpivirine, all of which inhibit viral DNA synthesis through allosteric inhibition of reverse transcriptase activity. (1,57) Other classes of HIV drugs include protease inhibitors (i.e. lopinavir, ritonavir) and integrase inhibitors (i.e. raltegravir, dolutegravir), which work on their namesake enzymes involved in the systemic growth of the virus. (1)

6 | DISCUSSION

The core target mechanisms of antimicrobial structure and macromolecule synthesis that were discussed remain classic starting points for the study of novel therapeutic techniques. This review analyzed over 70 academic pieces of literature to provide the most current understanding for healthcare professionals. While most of the antimicrobial agents discussed are likely to be seen in clinical practice, this review does not encompass all agents approved for treatment, nor does it provide new data on the efficacy of these agents. This review suggests that future systematic reviews are needed to provide directions for research on antimicrobial agent mechanisms. Additionally, the timing of this paper coinciding with the ongoing worldwide COVID19 pandemic serves a key role in providing a semi-comprehensive, up-to-date understanding of the mechanisms of action of antimicrobial agents in times where many entities are exploring variations and manipulations of these agent mechanisms. (63, 66) For example, recent literature suggests that members of the aforementioned fluoroquinolone family of nucleic acid synthesis inhibitors can be used as a form of therapy against COVID-19. The basic mechanisms of action are therefore more pertinent than ever before and open an avenue for discussion of the uses of combination and crossover therapies by these agents.

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NARRATIVE REVIEW
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Childhood Obesity Interventions by Setting

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ABSTRACT

Background: To combat the global health crisis of obesity, many interventions have been implemented, including in children and adolescents. This age range is uniquely important because health behavior continues into adulthood, resulting in lifelong health risks or benefits. This narrative review aims to provide a cross section of the scientific literature regarding obesity interventions by setting, including school-based, daycare-based, home-based, healthcare-based, and digital-based, as well as to highlight gaps in research. **Methods**: Articles written in English addressing childhood and adolescent obesity interventions were sought online using PubMed and Google Scholar searches. Although some articles were from a global perspective, the majority focused on children in the United States. This search included reviews, individual studies, and other related papers. **Results**: School-based interventions are accessible to many, but there is limited evidence of long-term benefits. Home-based interventions were the only setting to have compelling evidence of long-term benefits, although there are several barriers to participation. Healthcare-based interventions are often successful when specific strategies and unique advantages of healthcare settings are utilized. Digital interventions have limited success now, but show potential for cost-effective scaling up as technology improves. **Conclusion**: The clearest gap in research is the lack of long-term studies, especially of school-based and healthcare-based interventions. Thus, it is imperative that investments are made into studies that include follow-up components continuing at least 1-2 years after the intervention. Additionally, home-based interventions have been more successful during early childhood while school-based interventions tend to be more successful during adolescence.

KEYWORDS

Obesity, childhood, obesity interventions, cancer prevention, adolescence

1 | INTRODUCTION

Obesity is a growing public health crisis in North America and around the world. Childhood obesity prevalence, in particular, is alarmingly high, with 18.5% of children between the ages of two and 19 (13.7 million people) in the United States being classified as obese by the Centers for Disease Control and Prevention (CDC) in 2015-2016. (1) Since obesity is linked to hypertension, stroke, type 2 diabetes, coronary heart disease, and many other negative health outcomes, it is important to implement interventions to decrease obesity prevalence, starting in childhood. These negative health outcomes create massive costs for healthcare systems, so decreasing obesity rates would save much needed resources in addition to many lives. (2)

The CDC defines childhood overweight as having a body mass index (BMI) between the 85th and 95th percentile, and obesity over the 95th percentile for the same age and sex. Other methods of determining childhood obesity are also used, such as fat percentage of body weight, waist circumference, and skin fold thickness.

Childhood obesity interventions are generally implemented in one or more of these five settings: school, daycare, home and family (home and family will be used interchangeably throughout this paper), healthcare, and digital technology. The primary strategies of childhood obesity interventions are usually increasing physical activity (PA) and/or improving diet (e.g. decreasing caloric intake or replacing consumption of unhealthy foods with fruits and vegetables). While public policy interventions (e.g. soda taxes) also exist, this is not considered a setting for intervention for the purposes of this paper.

Schools are the most common setting for childhood obesity interventions, and have consequently been the subject of the most research. Thus, many different methods have been tried, some successful and some unsuccessful. Daycares have also been the setting for many interventions during early childhood. However, due to the COVID-19 pandemic, many classes and activities have been moved online and children spend much more time at home. (3) It is therefore more essential than ever to also understand childhood obesity interventions in the three other settings: the home, healthcare, and digital settings. This is illustrated in Figure 1.

As a major factor contributing to eating and activity behaviors of children, it is more important than ever for home and family life to be settings for treating and preventing childhood obesity. Interventions included in this category are programs that are carried out primarily at home. In this case, the parents are usually the ones who implement the program for their children. While many other settings often include parent involvement aspects, only interventions where the program is based almost entirely within the home will be included in this category.

The healthcare setting includes any interventions where the program is carried out through the healthcare system; a physician, nurse practitioner, physician assistant (PA), physical therapist, nurse, dietician, and/or other healthcare professional is the one who implements the program. Additionally, these interventions usually involve regular trips to the intervention site (usually a doctor's office or clinic) for monitoring adherence and outcomes, exercise training sessions, and/or diet and PA information sessions. While parents are often involved in healthcare-based interventions, if the primary implementer of the program is a healthcare professional or the program occurs primarily in a healthcare facility, it is categorized in the healthcare-based category. For example, if an intervention occurs primarily at a doctor's office, but includes help from the parents in implementing the program, then it is still considered healthcare-based.

The digital-based category is very broad. It encompasses any interventions where the primary mode of delivery is through technology, usually computers, cell phones, applications, and/or tablets. Like parents, technology is often a component of interventions based in other settings. However, only interventions where technology is the main (and often only) mode of delivery are included. While interventions based in the other settings sometimes include components to reduce screen time, digital-based interventions aim to use technology as a tool to reduce childhood obesity.

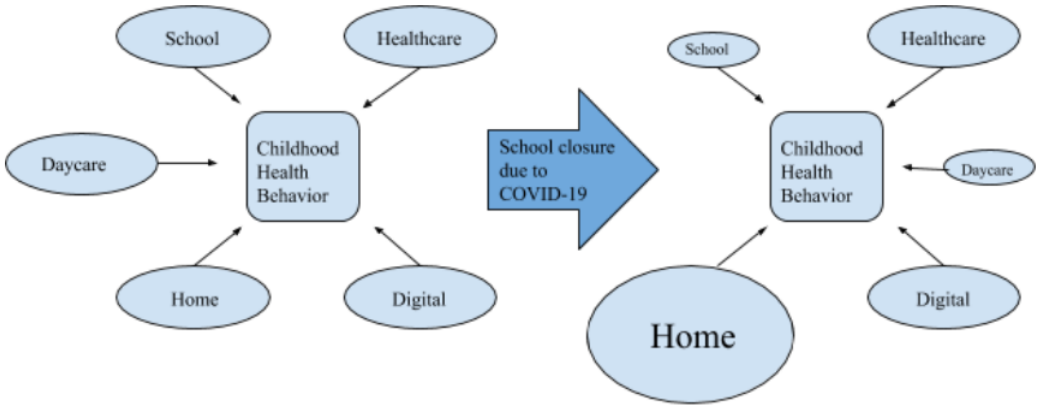

FIGURE 1 Due to COVID-19, classes have been moved online and many daycares have been closed, meaning that children are spending more time at home with their families. Consequently, Home and family-based obesity interventions must play a larger role in combating the obesity epidemic.

2 | METHODS

In this paper, interventions can target both overweight and obese children, and measurements other than BMI will also be considered. These interventions can be preventive or they can aim to decrease the weight in already obese or overweight children. Finally, "childhood" will be defined as anyone between the ages of zero and eighteen. Early childhood (from infancy to age 6), middle childhood (ages 7 to 11), and adolescence (ages 12 to 18) are the main subgroups for childhood in this paper. These age ranges correspond to the usual age at which children start first grade (age 7) and middle school (age 12). Using these criteria, Pubmed and Google Scholar were used to find studies, scientific reviews, and other relevant articles. Searches included the following phrases: "Childhood obesity interventions", "School-based childhood obesity interventions", "Daycare-based childhood obesity interventions", "Home-based childhood obesity interventions", "Family-based childhood obesity interventions", "Healthcare-based childhood obesity interventions", "Digital-based childhood obesity interventions", and "Technology-based childhood obesity interventions". Additionally, all these searches were repeated with "adolescent" substituted for "childhood." Over 150 papers were screened for relevance using their titles (or their abstracts in some cases, if the title was ambiguous). In total, 33 citations were used in this review. Only papers written in English were considered.

3 | DISCUSSION

3.1 | School-based Interventions

Many studies have found school-based interventions to be successful in the short-term. In a literature review of 20 interventions, primarily targeting early childhood, all interventions led to an improvement in at least one of their identified primary outcomes (e.g. BMI, incidence of overweight/obesity, PA, nutrition knowledge), although in some cases the improvements were very modest. (4) Key features identified by the authors as useful for improving results include incorporation of environmental factors and parent involvement. Environmental factors, which were more likely to be studied by international and more recent interventions, are factors that can hinder or enhance access to PA and/or healthy food. Parents have significant influence over their children's health behaviors and can be involved in a school-based obesity intervention through phone calls, meetings, or instructions to reinforce the information given at

school. The authors also noted that each of the 20 interventions used different approaches to achieve success, suggesting that a "one-size-fits-all" approach is not necessary to produce positive results and that school-based interventions should utilize culturally specific strategies. (4)

The necessity of tailoring school-based interventions is evident in studies targeting the middle and, to a lesser extent, adolescent childhood age ranges as well. For example, an intervention to increase PA in low-income, urban middle schools used a curriculum provided by SPARK (Sports, Play, and Active Recreation for Kids) but did not result in an increase in moderate-to-vigorous physical activity (MVPA) which was the goal of the intervention. (5) The SPARK curriculum has been used in thousands of schools in the US and it is possible that the program was unsuccessful in this case because it was not modified sufficiently to meet the specific needs of low-income, urban schools. This need for modifications is supported by a previous SPARK intervention program which had no structured curriculum and resulted in increased MVPA. (6) In this intervention, Physical Education (PE) teachers were assisted in improving existing programs, instead of being given a specific program to follow. (6) Although this intervention may have been more successful because it was implemented at different schools (not low-income and urban), it could be that greater program flexibility played a part in the latter intervention's success.

Fewer studies specifically targeted high school students (adolescents). This lack of studies focusing specifically on adolescents is a problem because it is known that the shift from middle childhood to adolescence (and middle school to high school) is linked to a significant decrease in sports participation and PA more generally, as well as an increase in BMI. (7) One study of the "New Moves" intervention program targeting adolescent girls (8) included an all-girls physical education class (n = 356, 46% overweight or obese), supplemented with nutrition and self-empowerment components, individual sessions using motivational interviewing, lunch meetings, and parent outreach. Although no differences in weight status between the control (PE class did not use "New Moves" curriculum) and intervention (PE class did use "New Moves" curriculum) groups were found, the program did result in improved sedentary activity rates, eating patterns, unhealthy weight control behaviors, and body/self-image. It is imperative that more interventions be developed that specifically target adolescents, especially interventions that are based in high-schools.

Some studies have explored interventions that target all three stages of childhood. One such intervention, which gave funding to schools in order to increase PA opportunities before, during, and after school, was implemented in 13 Colorado school districts. It successfully increased average daily PA from 48 minutes in the first year to 90 minutes by the end of the third year ($p < .05$), with schools reporting higher rates of free/reduced lunch students having less PA ($p = .04$). Those involved in the intervention cited professional development and administrative support as reasons for its success. (9) Here, the exceptional support and training for the teachers who were implementing the program demonstrate the necessity of tailoring interventions to the needs of the school or school district. In this case, the intervention emphasized training and development which were desired by the schools.

According to a review of school-based obesity interventions for children and adolescents in the US and UK, (10) most of the examined interventions were based on a behavioral theory, usually social cognitive theory. This theory posits that parts of one's acquisition of knowledge comes directly from observing and interacting with others. (11) It makes sense that social cognitive theory would be the basis for school-based interventions because schools are a very social setting. However, this theory may not be as useful in other settings that do not involve as much interpersonal interaction, especially with peers of the same age range. This paper (10) concluded that school-based interventions should target both PA and nutrition behaviors, and that TV watching was the most modifiable behavior.

A clear limitation of school-based interventions is that even when positive results are found, improvements lasting more than a year after the program are rarely observed because of a lack of long term stud-

ies. A 2008 review found that although many interventions have significant short-term improvements, very few have evidence of long-term effects. (12) The authors cite economic and environmental reasons as preventing long-term interventions and studies. Despite the high cost, research of this nature is necessary to determine the long-term effects of school-based childhood obesity interventions. Another important limiting factor is the difference in obesity rates among low socioeconomic status (SES) and high SES children. When designing interventions, researchers should consider the SES of the participants in order to better tailor the program to their specific needs.

3.2 | Daycare-based

Before children are old enough to start school, many of them spend much of their time at daycares (in 2012, 58% of children in the US ages 4 and 5 attended daycare). (13) This makes daycares a feasible setting for childhood obesity interventions that target early childhood. However, like high school-based interventions, few daycare-based interventions have been implemented. (14)

The Nutrition and Physical Activity Self-Assessment for Child Care (NAP SACC) developed a daycare-based intervention that involved dieticians with PA experience giving workshops, advice, and support regarding diet and PA to the daycare center staff, as well as educational information to the parents of the children. (14) In a study that aimed to determine the efficacy of this intervention, 26 daycare centers, with 209 total children, were split evenly into intervention and control groups (13 centers in each group). The intervention group increased total daily PA by 11.4 minutes ($p < .05$), whereas the control group increased total daily PA by 2.5 minutes ($p < .05$) after six months. (15) PA was tracked using accelerometers.

Prevention is also very important in the very early months of childhood. In a study examining an obesity prevention program in children under 2 years old ($n = 191$), 3 intervention daycare centers (126 children) were compared with 3 control daycare centers (65 children). (16) The intervention involved encouraging increased consumption of water, milk, fruits and vegetables, while increasing daily physical activity and decreasing daily consumption of sweets and savoury snacks and daily screen-time behavior. This was communicated through an informational poster and tailored feedback for parents about their child's PA and diet. However, over the course of a yearlong intervention, consumption of soft drinks and sweets increased while consumption of fruits and vegetables decreased. These findings highlight the importance of encouraging healthy behavior at a very early age. Although both the control and intervention groups experienced an increase in negative health behaviors, the intervention group had a significantly lower BMI. (16)

From these articles, (13-16) it is apparent that daycares are a necessary setting to promote healthy behavior during early childhood. Long-term studies should be conducted to test if these healthy behaviors carry on into the later stages of childhood and adulthood.

3.3 | Home and Family-based

As millions of children spend more time at home due to the current COVID-19 pandemic, it is essential to closely evaluate the efficacy and methods of home-based interventions. Decreases in PA during the quarantines and lockdowns could lead to permanently entrenched behavior in children. (17) While it is well-known that parents influence the behavior of their children, it is important to establish the efficacy and duration of interventions implemented by parents to instill healthy behavior.

A 2011 meta-analysis of family-based childhood obesity interventions targeting all three stages of childhood found that the family is an effective setting for interventions. Family-based interventions produced significant weight loss in both the short-term and long-term. (18) Interestingly, the meta-analysis also suggested that the opposite sex parent plays a uniquely large role in influencing and sustaining a child's weight loss. In contrast, a 2014 review of family-based interventions in the UK (also of all three childhood age ranges) deter-

mined that although short-term decreases in adiposity were evident, there was insufficient evidence to support long-term benefits. (19) This article did not rule out the possibility that family-based interventions can produce long term effects, but rather the authors did not find sufficient evidence of it in the UK. Thus, the 2011 article (18) is not contradicted by the 2014 one (19). The 2011 paper was likely able to find evidence of long term benefits because it was more comprehensive (a full meta-analysis of 20 studies was completed), whereas the 2014 article (19) only examined 10 studies, all of which were in the UK, and did not include a meta-analysis. Ultimately, home and family-based interventions can be effective for all three age ranges. In contrast to the very limited evidence of long-term benefits of school-based interventions, the literature regarding home-based provides some compelling evidence that home-based interventions have produced long-term results.

It is also important to determine what aspects of home and family activity are linked to decreased obesity. A very useful 2005 study focusing on preschoolers (early childhood) analyzed a nationally representative sample of 8,550 children to find associations between certain household routines and obesity prevalence. (20) The results were substantial: preschool-aged children who regularly ate dinner as a family, obtained adequate sleep, and had limited screen time had an approximately 40% lower prevalence of obesity compared to children who were exposed to none of these routines. Additionally, when analyzed individually, eating dinner as a family, obtaining adequate sleep, and having limited screen time were each linked to decreased prevalence of obesity by 4.4%, 3.9%, and 3.9% respectively ($p < .005$ for each). A limitation of this study is that it is only correlational and did not involve an intervention, so a causal relationship cannot be established from these results. Although more recent data would be useful, it is apparent that these three home-based routines (regular family dinner, adequate sleep, and limited screen time) are connected to childhood obesity. Interventions targeting these routines are warranted, and interventions trying to find a causal relationship should target all three routines for maximal effect.

One family-based intervention that targeted middle childhood attempted to decrease BMI in overweight and obese children (aged 9-12) by training and educating the parents and child about strategies to reduce screen time. (21) This study found no significant difference in BMI or screen time between the control and intervention groups, whereas the previous 2005 study found that children who had limited screen time were 4% less likely to be obese than those who did not. Several conclusions can be drawn from the difference in findings regarding the impact of reduced screen time between the previous study (20) and this one (21). Firstly, it could simply be that screen time and BMI have only a correlated relationship, not a causal one, since the 2005 study (20) was not an intervention. Another possibility is that a stated limit on screen time is more effective than educating parents and children about how to reduce screen time. In other words, being educated about strategies to reduce screen time may not have a significant effect on actual screen time. Finally, it is possible that household routines and habits are less impactful during middle childhood than in early childhood. The latter is supported by a systematic review comparing school-based and family-based interventions. (22) While both settings were found to have positive results, family-based interventions were found to be more effective for children under the age of 12, and school-based interventions were more effective for children between the ages of 12 and 17. Since the children in the Maddison study (21) were between the ages of 9 and 12, it could be during this range (middle childhood) that the decrease in home-based efficacy begins to take effect.

While it is unclear why this difference in effectiveness exists, one study (23) found several ways that parent- and adolescent-reported barriers to intervention participation can be overcome. The most common barriers to participation reported by the adolescents included research demands (questionnaires, wearing accelerometers), program components (too much work, sessions were boring), and practical barriers (transportation, school work). On the other hand, the most common parent-reported barriers included program compo-

nents (too many behavior changes, adolescent disapproval of being monitored), treatment motivation (lack of adolescent effort), parent-adolescent conflicts, and practical barriers. The authors state that parents and adolescents may find it easier to participate in interventions if "research and out?of?session program demands are minimized, efforts are made to enhance adolescent motivation, and treatment is offered in a convenient location and scheduled around school holidays and other family demands."(23, p1) Additionally, the results suggest that pre-emptively addressing adolescent unhappiness, family stressors, and parent-adolescent conflict could improve retention. These insights can be used to try to make family-based obesity interventions as successful during adolescence as they are earlier in childhood.

In summary, home-based obesity interventions can be effective on all childhood age ranges, although effectiveness decreases as children grow older (there is evidence (22) that there is an opposite trend in school-based interventions, however). Additionally, there is more evidence of long-term efficacy for home-based interventions than in school-based interventions. As children spend more time at home and less time at school due to the Covid-19 pandemic, home-based childhood obesity interventions, including preventive, have the opportunity to create lasting change.

3.4 | Healthcare-based

A 2015 review of primary-care based pediatric obesity interventions for children ages 0-18 compared 31 studies and identified eight interventions that had significant positive results. (24) The interventions were carried out by a physician, nurse practitioner, physician assistant, nurse, dietician/health coach, and/or a psychologist. All eight successful interventions had two things in common. First, they had parent-targeted components, although for the successful adolescent interventions parents had a more limited role. Second, they targeted multiple weight-related behaviors, and tended to use multiple modes of delivery. For example, one intervention (25) included "1) computer-guided behavior change plan and behavioral assessment for the adolescent; 2) in-person physician visit to discuss the adolescent's physical activity, nutrition, and sedentary behaviors and their behavior change plan; 3) adolescent and parent session with study PI [principal investigator] to learn food self-monitoring; 4) adolescent phone coaching sessions with a study counselor; and 5) informational materials for the adolescent and parent." (24, p6) Other common, but not universal, components of the successful interventions were daily caloric goals/plans, daily PA goals/plans, and regular weighing.

Additionally, the authors cited several advantages to healthcare-based interventions over other settings. (24) First, they can build on the pre-existing relationships between physician, child, and family. Second, parents and children regularly go to the doctor's office together. Third, families generally trust the medical knowledge of healthcare professionals. However, the authors also cited some disadvantages associated with healthcare-based interventions. Time is often a constraint for families who do not want to drive to the doctor's office regularly. Additionally, some medical professionals believe parents are not always concerned with the weight of their child. (24)

The efficacy of healthcare-based interventions is also supported by a study of 100 overweight or obese children aged 5 to 14 who underwent an intervention with their family. (26) 13% of the children in the intervention group (n=100) became normal weight, compared to 4% of the obese or overweight children in the control group (n=943). (26) No dropouts were noted. This intervention involved many different health professionals; a physician, dietician, physical activity coach, and psychotherapist all had key roles in the intervention. Furthermore, this study is especially useful because it included follow-up research to determine the long-term effects of the intervention, which is rarely incorporated into childhood obesity intervention studies. In this case, the intervention group sustained improved weight compared to the control group for over 14 months when follow-up research ended. Although more studies are needed to confirm this long-term success, this study suggests that healthcare-based interventions can lead

to enduring improvements.

Healthcare-based childhood obesity interventions have shown some positive results when they incorporate several key components, such as parent involvement, multiple modes of delivery, and multiple health professions. While some research has demonstrated long-term improvements, more studies with long term follow-up components are necessary to verify this.

3.5 | Digital-based

Because technology is improving so rapidly, it is important to identify how the digital setting can be harnessed to effectively develop childhood obesity interventions. Interestingly, nearly all research regarding digital-based interventions focuses on adolescents. Perhaps this is because reducing screen time is a major focus of childhood health interventions and digital obesity interventions may conflict with these goals, or because adolescents are very adept at using technology. Thus, not every technology platform had studies for each age group.

One study that did address early childhood utilized multiple digital-based methods for intervention. (27) The goal was to prevent childhood obesity in their first two years, and consisted of "scientifically substantiated content, tools, and telephone-based professional support delivered in an anticipatory and sequential manner via the internet, email, and text messages, focusing on educational modules addressing the modifiable factors associated with childhood obesity." (27, p1) This paper only outlined the design of the intervention, incorporating best practices, but did not address whether or not it resulted in decreased childhood obesity. However, the paper did conclude that a multi-component digital intervention is a cost-effective method that fits into the lifestyle of new mothers and has the potential to be scaled up to make real and sustainable change. These conclusions were based on the fact that the intervention design met criteria for intervention best practices, as well as followed theoretical and behavioral frameworks.

Virtual reality (VR) has also been used to increase childhood PA. One study examining "exergaming" (the use of VR and other digital video games to increase PA) during middle childhood, yielded several important insights. (28) Existing exergames such as "Wii Sports" and "Dance Dance Revolution" produced PA equivalent to a brisk walk and were therefore better than the sedentary behavior associated with traditional video games. However, according to several studies cited in the article, PA produced by exergaming is not vigorous enough to replace participation in sports, implying that exergames could be used to complement-rather than replace-sports participation. It is also expected that with continued development of VR technology, the intensity of exergames will be able to increase.

A major method for delivering digital obesity interventions to adolescents is texting, the preferred mode of communication for teenagers. (29) An intervention involving texts with goal prompts (e.g. texts to set step goal for the week) and Self Determination Theory-informed messages resulted in modest increases in steps per day and PA. (30) Such texts promoted the satisfaction of the three basic psychological needs-autonomy (having choices), competency (having skills and knowledge), and relatedness (having connections with oneself and others)-that are outlined by the theory. Not only did participating adolescents record increases in steps and PA (using pedometers), but they also reported positive reactions to the intervention. Another intervention for children (not just adolescents) involving texting used text-based healthcare chatbots (THCB) to have conversations about health behavior with the participants. (31) While only preliminary results have been published and no data regarding obesity reduction has been released, the preliminary findings suggest that the chatbots are effective in having multiple interactions with the participants and the program seems to be scalable for greater use.

Smartphone applications are also being explored as a potential mode of delivery for obesity interventions. A study of the efficacy of a nutrition education app for adolescents found that 76% of the participants preferred getting the information from the smartphone app rather than brochures. (32) This preference for digital-based delivery of information can be applied to the other settings as well, since they often include an edu-

cational component. Switching from brochures to apps could improve transmission of information, particularly with adolescents, but simply improving knowledge is not enough to guarantee behavioral change.

Considering that digital-based interventions are new and rapidly changing, it is important to keep in mind several important strategies when creating these kinds of interventions. A paper published in 2018 outlines three key practices for use in technology-based childhood obesity interventions. (33) These user-centered strategies are: co-designing with adolescents and children, personalization (developing individualized programs), and just-in-time adaptation (often using data from wearable devices).

Taken as a whole, texting, smartphone applications, exergaming and VR, and multi-component interventions show potential to cost-effectively improve childhood obesity on a large scale. However, most research regarding digital-based obesity interventions has focused on adolescents and more attention should be given to early and middle childhood. Additionally, more research should be done to explore the extent of the benefits of technology-based interventions (i.e. Does improved transmission of knowledge via digital devices lead to increased behavioral changes? How long do benefits last?).

4 | CONCLUSIONS

As obesity continues to be a health crisis in North America and the world, it is imperative that effective childhood interventions be implemented. The overarching goal of childhood obesity interventions is to prevent the long-term negative health consequences of obesity from carrying into the adulthood of yet another generation. Unfortunately, the COVID-19 pandemic has distorted the daily lives of children and parents across the planet, changing how and where our time is spent. Thus, it is essential to understand the different settings for childhood obesity interventions and what strategies work best in each setting.

Several important conclusions can be drawn from the current literature regarding school-based interventions. Overall, school-based interventions do show signs of effectively producing short-term improvements in obesity, but more studies are needed to determine if there are long-term benefits. Additionally, when implementing obesity interventions at schools, a "one-size-fits-all" approach may not be as effective as tailoring each intervention to the specific needs of each school or school district. Additionally, because participation in structured physical activities, particularly organized sports, among children decreases from middle school to high school, and because school-based interventions appear to become relatively more effective than home-based interventions as age increases, more studies should be done that focus directly on high school interventions.

Daycares, which can be a setting for intervention during early childhood, have been the site of multiple successful programs. The NAP SACC intervention was particularly effective at increasing MVPA. Additionally, it is important for daycare-based interventions to pay close attention to diet during early childhood, which becomes significantly unhealthier over a child's first 2 years. Interventions during early childhood can build a firm foundation of healthy behavior that can hopefully carry on into middle childhood, adolescence, and adulthood.

With the closure of many schools and daycares during the pandemic, childcare is taking place more frequently within homes. Families, therefore, will likely influence their children's health behavior even more than is already known. Studies of home-based interventions have found significant short-term, and in some cases long-term, decreases in obesity. Additionally, several household family routines have been linked to decreased prevalence of childhood obesity (eating dinner as a family, limited screen time, and adequate sleep), and interventions should explore implementing all three of these. Another key finding has been the relationship between the impact of setting on the efficacy of an intervention and the child's age: according to some evidence, home-based interventions are more impactful with younger children (0-12) while school-based interventions are more impactful with older children (12-18). Overall, family-based interventions currently seem to

be the most effective because of the potential for long-term benefits. However, the other settings have advantages as well.

Healthcare has also been assessed as a setting for childhood obesity intervention because families make regular visits and because they usually trust the information given by physicians and other healthcare professionals. Successful healthcare-based interventions tend to involve multiple modes of delivery (meetings with physicians, computer assessments, phone calls with dieticians) and parent involvement. Instances of long-term impacts have been found, but more studies are necessary to confirm this.

Finally, digital-based interventions, utilizing various types of technologies, have shown potential to be effective during childhood, with adolescents almost always being the focus of studies. Texting and smartphone applications have been effectively used with adolescents to increase MVPA and improve nutrition knowledge, respectively. Other strategies and technologies that may improve efficacy are personalization, co-designing interventions with children and adolescents, just-in-time adaptation (usually with wearable devices such as accelerometers or pedometers), and exergames (improvements in exergaming, especially with VR, can increase intensity). Digital-based interventions are especially exciting because of their potential for cost-effective scaling up as technology improves.

Overall, the single most important conclusion that can be drawn from the literature is the need for research into the long-term effects of these interventions. This means studies that continue for years in order to determine which interventions lead to lasting benefits. While the cost of such research is extremely high, the benefits of combating the obesity pandemic outweigh these costs.

4.1 | Future Research Questions

The most notable research gap is the lack of sufficient follow-up components of studies to determine if the effects of interventions continue in the years following the intervention. These are especially needed for school-based and healthcare-based interventions. Several other questions for future research include: What are the effects of school-based obesity interventions that directly target high school students? How can family-based interventions be improved and adjusted in response to the increase in time spent at home during the pandemic? Can digital-based interventions be effective during early and middle childhood? How can digital-based interventions be cost-effectively scaled up to make significant global change? How can the SES obesity gap be effectively addressed by childhood obesity interventions?

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NARRATIVE REVIEW
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From Syphilis to Autism, How the Anti-Vaccination Movement of Today is an Echo of the Past

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ABSTRACT

Introduction: The anti-vaccination movement has led to decreased vaccination rates and increased vulnerability to vaccine-preventable diseases in the general population. In order to better understand the anti-vaccination movement of today, the anti-vaccination movement that emerged in the 19th century is examined and measured against the one observed in the 20th century. **Discussion**: Though the population of the 19th and 20th centuries differ in many regards and our knowledge of vaccine and immune mechanisms are far greater; the anti-vaccination movement seen today stands on the same pillars as that of the 1800s with the sentiment of fear at its core. Though the façade of these pillars has been altered to suit the world today, both movements exploited the influence of prominent public figures, maintained false associations with dire vaccine consequences and emphasized these through the use of visual media, repetition and personal narratives. The persistence of the anti-vaccination movement lies largely in the use of personal stories which are more impactful and memorable then the statistical characteristics of scientific study. **Conclusion**: The pro-vaccination movement must respond to the tactics used by the anti-vaccination movement and create accessible, understandable and equally impactful communication strategies in order to prevent the spread of misinformation and counter the efforts of the current anti-vaccination movement. **Relevance**: Vaccine hesitancy was listed amongst the top 10 global health threats in 2019 by the World Health Organization. In order to shift the negative rhetoric surrounding vaccines, the anti-vaccination movement of today and its historic roots need to be understood.

KEYWORDS

Anti-vaccination, Dr. Edward Jenner, Vaccine Hesitancy, Global Health

Vaccinations, like many other medical interventions, rely heavily on public opinion for their success. Regardless of the positive or consistent results demonstrated through precise scientific study, if the public does not believe in the efficacy or safety of these interventions then they will fail. Hence, an understanding of public opinion and controversy is key to increasing compliance and acceptance of the intervention in question. From the start, vaccination was rife with controversy within the medical field which spilled out into the lay discourse and set the groundwork for the anti-vaccination movement (1). Despite advances in knowledge related to vaccine mechanism of action, vaccine targets, and immune system responses the anti-vaccination movement persists. Regardless of increased health literacy and increased education in the general population, individuals remain susceptible to the influence of misinformation and fear spread by the anti-vaccination movement. The ability of this movement to influence public practice is evident in the falling rates of vaccine compliance which has left people susceptible to vaccine-preventable diseases and led to outbreaks of diseases like measles in several western countries (2). The consequences of this movement have contributed to the World Health Organization (WHO) listing vaccine hesitancy among the top 10 public health threats in January 2019 (3). It is therefore imperative that health care professionals have an understanding of the movement and its strategies in order to address the issue, if and when, it should arise in the clinical context. In this paper we will take a glimpse at the past in an effort to understand the present and shed light on just how the anti-vaccination movement has persisted all these years. The consequences of the movement in present-day society will then be discussed, as well as, some of the current efforts being made to mitigate the consequences of the anti-vaccination discourse at the level of individuals and the larger community.

1 | THE BIRTH OF ANTI-VACCINATION IN THE 19TH CENTURY

In 1801, Dr. Edward Jenner published *On the Origin of Vaccine Inoculation* in which he described his observations that individuals previously exposed to cowpox did not develop smallpox when exposed to the disease (4). He went on to hypothesize that inoculation with cowpox would lead to sustained immunity against smallpox and supported this with descriptions of his experimentation and success (4). One key characteristic of Jenner's new technique was that those inoculated were not contagious, and therefore posed no threat to those around them (1). Another important aspect of the vaccine was its scalability. Given that the vaccine material could be cultured, dried, transported, and re-animated for later use it was possible to reach a large population of people in vast areas (1) The propagation of the vaccine was later made even easier when it became possible to culture the lymph of previously vaccinated individuals and extract the necessary vaccine material (1) Thus, Dr. Edward Jenner had just demonstrated a safe method, without the risk of contagion that could help stop the spread of smallpox, the disease responsible for 10-20% of burials in urban British cities in the 18th century (5). Yet, rather than being met with praise Jenner was faced with strong opposition from peers and the public alike.

At the time of Jenner's discovery, the accepted practice for smallpox prevention was variolation (1). Variolation involved infecting individuals with matter from the pustules of individuals infected with smallpox (6). Though this technique showed some promise, it was responsible for the death of approximately 2% of variolated patients and held the drawback that those inoculated became highly contagious themselves; thus, posing a significant risk to others (1). This technique, though hazardous, was supported by influential British physicians such as Dr. Moseley and Dr. Rowley, who largely gleaned their livelihood from its administration (1). The advent of vaccination was perceived as a threat to the variolation business and thus became the target of scorn and misinformation on the part of Dr. Mosley,

Dr. Rowley and others in the medical field. These physicians successfully led the campaign to skew the vaccine discourse from a medical success story to one wrought with deceit; instilling fear and doubt in the public and associating vaccines with public taboos like bestiality and venereal disease (1). This was achieved through the use of caricatures and images in booklets that were distributed to the public as early as 1802 (1). One such caricature, titled *The Cow-Pock* (see Figure 1), depicts a scene in which Dr. Jenner administers his vaccine to a woman while surrounded by a mass of individuals in various degrees of distress as they grow horns, birth a bull-like creature, or have cow-shaped growths sprout from their body. Though far from being proof that Jenner's vaccine led to such consequences, these caricatures were enough to associate vaccination with bestiality and influence public opinion on the morality of vaccines (1). These caricatures were closely followed by drawings, published by Dr. Mosley and based on the findings of Dr. Rowley, depicting individuals who developed animal-like features following the inoculation with the smallpox vaccine (see Figure 2) (1). These drawings were an important step in solidifying the growing fear regarding the consequences of vaccines. By publishing verisimilar drawings of animal-like people, the anti-vaccination movement bluntly implied that what happened to the subjects of these drawings could, and would, happen to any regular person who received the new smallpox vaccine.

FIGURE 1 "The Cow-Pock" by James Gillray, 1802 (Wellcome Library, London). Patients developing horns or cow-shaped growths following administration of smallpox vaccine.

FIGURE 2 Drawing of Ann Davis, 1806 (Wellcome Library, London). Depiction of patient who developed horns after being vaccinated against smallpox.

In addition to its association with bestiality, the smallpox vaccine soon came to be associated with syphilis through the careful suggestions of prominent physicians like Dr. Moseley (1). The lack of knowledge regarding the mode of transmission of syphilis and the mechanism of action of vaccines, compounded with the authority these figures held, allowed for these unfounded suggestions to be considered fact (8). Hence, smallpox vaccines became linked to syphilis and the anti-vaccination movement had one more argument against vaccines.

The clergy soon joined these physicians in the ranks

of the early anti-vaccination movement. The Catholic Church opposed vaccination on the basis that it involved injecting people with animal matter which threatened the sanctity of the human body (6). In addition, the Church maintained the belief that it was God's decision whether the suffering of the devoted was to be ended or not. Hence, interfering with God's choice through interventions like vaccination, was disrespectful to Him (6).

The battle between the pro and anti-vaccination movements of 19th century England came to a head in 1853 when the first law making vaccination compulsory in the first three months of life came into effect (7). Vaccination became a political issue and led to the foundation of official anti-vaccination groups, such as the Leicester Anti-Vaccination League, in 1869 (7). Following escalating protests and public opposition to vaccine laws, the British government launched the Royal Commission on Vaccination which concluded in 1897. One of the myths the Commission targeted was the fear that the smallpox vaccine could infect individuals with syphilis. Although the Commission found that there was no evidence that the smallpox vaccine had caused individuals to become infected with syphilis, this public fear, along with the other myths that had been propagated since the birth of Dr. Jenner's vaccine, persisted (1).

Between the voices of influential physicians, the warnings of the Church, the propagation of frightening images of metamorphosis and the association with syphilis, Dr. Jenner and his vaccine faced great challenges in gaining public trust and the anti-vaccination movement continued to grow.

2 | THE ANTI-VACCINATION MOVEMENT OF THE 21ST CENTURY

Since the 19th century, the pillars upon which the anti-vaccination movement was supported have largely been eliminated; physicians, and prominent health organizations like the WHO support vaccination, the Catholic Church holds that followers have a moral responsibility to vaccinate, and the mechanism of action of vaccines with their subsequent immune responses are better understood such that concerns over metamorphosis and syphilis have been eliminated (9,10). In addition, smallpox was officially eradicated in December 1979 following a global vaccination campaign led by the WHO, thus demonstrating the efficacy of the vaccine and the potential of the technique (11). Despite these advances in knowledge and the proven success of vaccination, the anti-vaccination movement remains present, influential, and widespread in the 21st century.

The success of the anti-vaccination movement in getting their ideas to the public, for getting their ideas heard, repeated, and easily accessible is largely attributed to the interplay between two factors: decreasing trust in institutional medicine and increasing digital connectedness in the Western world (12). Over the past 50 years, studies have found a significant decline in the confidence of the public towards the medical system (13). During this same period, there has been a surge in the amount of health information accessible to the patient population. Additionally, societal values have shifted the patient-physician relationship from a paternalistic relationship to a model of shared decision making in which patients expect to be given a voice in their medical care (12). The combination of these changes has led the patient population to seek medical information outside of the traditional medical system, often using the Internet as their first and main source. Hence, similarly to how patients in the 19th century distrusted Dr. Jenner because of the presence of contradictory information from seemingly reliable sources, many patients of the 21st century have come to distrust physicians due to an excess of health information that is contradictory, ever-changing and without distinction between accurate or misleading.

The anti-vaccination movement has taken advantage of this new platform to propagate their message instilling doubt and fear regarding vaccination in a growing faction of our population. A closer examination of the rhetoric used today shows a degree of continuity between the anti-vaccinators of the 19th and 21st centuries. In other words, the anti-vaccination movement we know today stands on the same pillars as that of that

19th century but has simply altered the façade of these pillars to suit the media of the time. Hence, fear mongering remains at the forefront of the movement, but instilling fear and doubt in individuals about vaccines is now achieved with modernized tactics and reflects the fears of our society.

Prominent physicians have been replaced with important public figures in the ranks of celebrities including Jenny McCarthy, Robert De Niro, and political leaders including President Donald Trump (2).

Fear of the development of syphilis and animalistic metamorphosis have been replaced with fears of the development of autism, immune disorders, allergies and sudden infant death syndrome (SIDS) (14). The association, in particular, between the measles, mumps, and rubella (MMR) vaccine and autism is one of the most frequent concerns cited by parents when deciding whether or not to vaccinate their children (15). MMR, as a causative agent of autism, became popularized in the 1990s following the publication of Dr. Wakefield and colleagues' article in the *Lancet*, which claimed to have evidence of an association between the MMR vaccine and "chronic enterocolitis and developmental regression" (16). Though the methodology of the study was questioned, its results disproven, and the paper retracted, the association remains at the forefront of the vaccination debate (17). The MMR vaccine-autism association is reminiscent of the smallpox vaccine-syphilis association of the 19th century by its consequences on the population despite a lack of supportive evidence. In both cases, the words of a physician coupled with repetition through visual media and by prominent figures have had a strong impact on the general population.

Caricatures published in booklets and handed out on street corners have been digitalized and bolstered by memes and pictures propagated by social media platforms such as YouTube, Instagram, Facebook, and Tumblr. A study on the presence of anti-vaccination content on YouTube in 2019 found that 32% of videos about vaccination were against the practice and that these videos had more views and higher ratings then content supporting vaccination (2). Quick searches on other social media platforms yielded caricatures which perpetuated beliefs that vaccines cause autism or SIDS (see Figures 3 and 4). In addition to these platforms, anti-

FIGURE 3 Billboard sponsored by Anti-Vaccination movement and posted on Twitter.

FIGURE 4 Caricature found on Instagram and posted on anti-vaccination page. Suggests that vaccines are controlled by Big Pharma and makes associations between vaccines and autism, seizures, bribery and money.

vaccination groups have been able to reach a broader audience through carefully constructed websites that emphasize the risks of vaccines and claim a lack of evidence for vaccine safety and efficacy. One of the most effective tools used by anti-vaccination websites today is the use of personal stories as proof of the danger of vaccines (17). Take, for example, *Vaccine Choice Canada*:

a prominent anti-vaccination group that has accounts on all social media platforms and an independent website (https://vaccinechoicecanada.com). Though their name suggests a degree of neutrality, the website is predominantly filled with warnings to parents about vaccine risks, and suggestions that parents should not trust the medical establishments or body of research supporting vaccines, which have often been sponsored by pro-vaccine groups like public health departments and vaccine manufacturers (18). In addition to this, there is an emphasis on the sharing of personal stories and an invitation for parents to share their own stories of the adverse effects experienced by their children following routine vaccinations (19). There is an evident absence of pro-vaccination personal stories on these pages. Just like the verisimilar drawings of animalistic metamorphosis had an impact on the people of the 19th century, these personal stories have an impact on parents of today who see their children in the stories of other parents and fear that the same adverse effects that others claim to have witnessed will happen to them and their families. Hence, the decades of scientific study supporting vaccine safety, efficacy, and their benefits are no match for the personal stories that pull at our heart strings.

In sum, vaccines of today face similar challenges to their predecessors; the science of vaccines is measured against the word of prominent and trusted public figures, vaccine efficacy is called into question by unfounded associations with grave consequences, and their opponents' exploitation of fear and emotions is more impactful than the technical communication of empirical scientific research.

The culmination of these strategies has led to growing fear and concern amongst parents who have started to question the vaccine recommendations made by the health departments of their countries. One of the challenges in addressing the anti-vaccination movement lies in the diversity of beliefs held amongst its members. In an attempt to represent this spectrum of beliefs, the WHO coined the term *vaccine hesitancy* and defined it as "a delay in acceptance or refusal of vaccines despite availability of vaccination services" (12). The growing number of vaccine hesitant parents, particularly regarding the MMR vaccine, is evident in the growing number of measles cases worldwide and the reversal of the disease status in the United States, a country where measles was considered eradicated in 2000 (20).

3 | FACING ANTI-VACCINATION RHETORIC

Falling vaccination rates and increasing vaccine hesitancy amongst parents are growing public health concerns that must be addressed at the systemic and individual level. Many studies have tried to understand the anti-vaccination movement in an effort to formulate recommendations to counter the negative rhetoric that has plagued vaccines for centuries. From these studies, it seems that the anti-vaccination movement has a cultural advantage and that health professionals are starting from a position of weakness. While anti-vaccinators need only instill an ounce of doubt in the minds of the public to make them question vaccine safety, the pro-vaccination movement is held to a different standard and must prove, beyond a doubt, that vaccines are safe, effective and necessary. Even if science were able to deliver a study meeting all of these demands, the hard reality is that the numbers, careful analysis and statistical characteristics of meticulous scientific study will not change minds without an effective communication strategy that can directly address doubt and risk in plainly understandable language or imagery. In this regard the medical and scientific fields have not been successful for decades. In the case of vaccines, sensational rhetoric and imagery remains a primary cause of vaccine hesitancy. Effective strategies to combat sensationalism and its effects remain elusive. Though the chances of the pro-vaccination movement may sound bleak, there are efforts being made to leverage the strength of science and the power of governments to mitigate the misinformation and limit the fear produced by the anti-vaccination movement. A recent survey-based retrospective study examining the rise and fall of vaccine confidence in 149 countries between 2015-2019 shows just how much political, religious and environmental fac-

tors play a role in public confidence in vaccination (21). As the study points out, there is a great need to further examine the interplay between these factors and medical decisions made by individuals (21). When narrowing down a diagnosis and determining an appropriate treatment strategy, physicians are taught to view patients through the lens of the social context in which they exist, but it is becoming increasingly obvious that this social context has a strong impact on whether or not patients seek and trust medical care. Hence, individual physicians and larger public health authorities must continually monitor societal opinions and norms in order to ease the effects these have on vaccine uptake. Vaccines aim to prevent the complications of disease before they can even manifest. The pro-vaccination movement must emulate the very therapy it wishes to promote and take a pro-active preventative approach in addressing vaccine hesitancy.

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BRIEF REPORT

Artist: Athena Ko

BRIEF REPORT

McGill Journal of Medicine

Assessing the appropriateness of colorectal cancer screening in very elderly women: A cross-sectional analysis

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ABSTRACT

The Canadian Task Force on Preventive Health Care recommends against screening for colorectal cancer after age 75. This recommendation is based in part on lag time to mortality benefit and a reduced life expectancy in the very elderly. To explore the extent to which screening for colorectal cancer is appropriately ordered in primary care, we performed a cross-sectional study in women aged 80-84 at an academic family medicine clinic in Montreal. Appropriateness was assessed using a validated life expectancy calculator, with a 10-year life expectancy of >50% serving as the threshold for appropriateness. Among women 80-84 years of age under the care of a physician in 2016 (N=144), 95 fecal immunochemical tests were ordered from 2016-2019. Of these, 41 were screening tests, and 16/41 (39%; 95% CI 24% to 54%) were deemed to be inappropriate. This finding suggests a need to improve screening decisions for elderly women followed in primary care.

KEYWORDS
Overscreening, Colorectal Cancer, Low-Value Care, Quality Improvement, Choosing Wisely

1 | INTRODUCTION

Screening is used to identify unrecognized disease in asymptomatic, seemingly healthy patients. In making decisions about cancer screening in clinical practice, determining the probability of benefit and harm is difficult. Hence, many physicians follow recommendations from clinical practice guidelines, such as those from the Canadian Task Force on Preventive Health Care (CTFPHC). When screening falls outside the recommendations of such guidelines and occurs in the absence of high-quality evidence, physicians run the risk of over-

screening their patients. Overscreening refers to the use of a screening test at ages younger or older than the range recommended by national guidelines, or at a greater frequency than recommended. This can be harmful to patients and increases costs to the health care system. Awareness of overscreening is increasing, due in part to organizations such as Choosing Wisely Canada, which operates as the national voice for avoiding unnecessary medical tests.

Colorectal cancer is a leading cause of mortality, but despite a rising incidence of colon cancer with increasing age, the CTFPHC recommends against screening for it after the age of 75. (1) This weak recommendation is based on reduced life expectancy (LE) in the very elderly, the long time lag needed for any mortality benefit from screening, and the harms associated with invasive follow-up diagnostic tests and treatments. (2) On balance, when screening offers a greater probability of harm than benefit, it should not be offered. Evidence suggests a LE of less than 10 years represents a reasonable threshold for suspending screening for colorectal cancer. (3) Specialty groups such as the Canadian Association of General Surgeons endorse this 10-year LE threshold. (4) In this study, we sought to assess the extent of fecal immunochemical test (FIT) overscreening for colorectal cancer in women aged 80-84 in primary care.

2 | METHODS

We performed a cross-sectional analysis of data obtained from the electronic medical records of an academic family medicine center in Montreal. Ethics approval was granted by the Research Ethics Committee of the CIUSSS West-Central Montreal.

We identified all women aged 80-84 who were followed at the center by a family physician. Since men and women have different average LEs at any given age, males were excluded to keep the number of chart reviews to a manageable number. Furthermore, to our knowledge, there is no evidence of a sex or gender bias in screening for colorectal cancer. The age range of 80-84 was chosen because at 80 years of age, Canadian women have a median LE of 10.1 years. Thus, 80 represents the age at which screening decisions based on a 10-year LE are challenging given roughly equal probabilities of a LE less or greater than 10 years.

We filtered our total patient list by selecting women referred for a FIT from January 2016 to December 2019. FIT is the screening test presently used in Quebec for colorectal cancer screening in average risk populations.

Each patient record was independently examined by two reviewers (ZF, JW). First, all women whose FIT was ordered by a resident physician were excluded to avoid a possible bias related to test ordering decisions made by trainees. Second, we excluded cases where FIT was ordered for diagnostic purposes, such as patients with gastrointestinal symptoms or anemia. The senior author reviewed cases where the reason for ordering the test was unclear.

We assessed patient LE at the time of ordering the FIT using an online calculator to determine the appropriateness of screening of each patient in our cohort. (5) This calculator was based on the Charlson Comorbidity Index, a validated method of predicting the probability of 10-year mortality. (6) All comorbidities weighted in this calculator were considered, and a LE prediction for each patient was recorded. We considered FITs to have been inappropriately ordered for patients whose 10-year LEs were less than 50%. A 95% confidence interval (CI) was calculated using the normal approximation method.

3 | RESULTS

A total of 144 women aged 80-84 were registered at the clinic in 2016. Between 2016-2019, 95 FITs were ordered among 80 women. Eleven women received two tests over this period, and two women received three. Of the 95 FITs, 22 were excluded because they were ordered by a resident physician. An additional 32 FITs were excluded because they were ordered for diagnostic purposes. Forty-one FITs were ordered as screening tests by attending physicians for 41 different women

(Figure 1).

Of these 41 cases, 10-year LE estimates for individual patients ranged from 2% to 53%. Sixteen of these 41 tests were ordered in patients with a 10-year LE of less than 50%. The percentage of inappropriate FIT testing was therefore 39% (95% CI 24% to 54%). It is worthwhile to note that no women received more than one inappropriate test.

4 | DISCUSSION

We found that, according to current best practice, approximately 40% of FIT screening tests ordered for women between the ages of 80-84 were inappropriate. Taking the lower bound of the 95% CI as a conservative estimate, one quarter of screening FITs confer more harm than benefit. Because this study was based in a single center, the findings may not generalize elsewhere. However, our findings reinforce the notion that there is room to reduce unnecessary care in Canada. (7)

Overscreening cannot be ignored given the burden it places on our publicly funded health system, and on individuals. With regard to the former, when scaled to an entire province, overscreening represents a waste of limited healthcare resources. In Alberta, 1.7% of seniors over the age of 75 received an inappropriate colorectal cancer screening test at least once in a 3-year period (2012-2015). (8) At a cost of $669 per person, these 4,035 tests amounted to a cost of $269,415. As Quebec has twice the population of Alberta, significant cost savings may be possible if colorectal cancer overscreening is reduced. With respect to patients, overscreening is not merely a waste of their time. The most serious harm from overscreening is the avoidable anxiety and unnecessary invasive follow-up that arises when a screening test produces a false positive result.

Reducing overscreening will likely require a multifaceted approach, as many factors influence physician decision-making. Further education on how screening guidelines are constructed, and on the underlying logic of using LE in screening decisions, may represent an important start. Schoenborn et al. found that even if physicians appreciate the problem of overscreening, some are

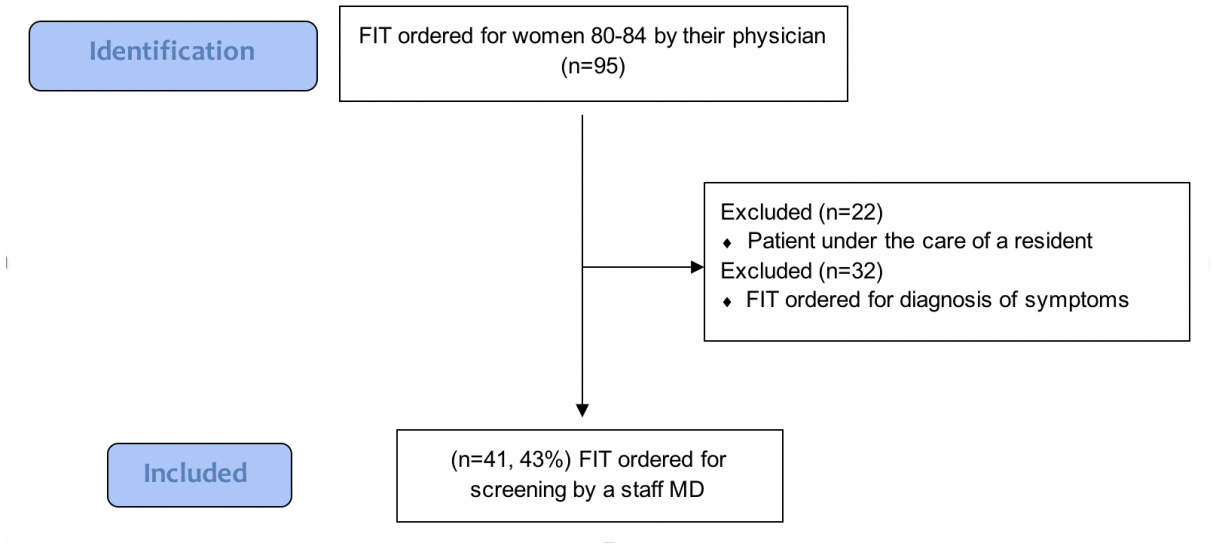

FIGURE 1 Identification of appropriate screening FIT. 95 FITs were requested for 80 women with an average age of 83 years. 41 of these were screening tests. Of these 41 FITs, 16 (39%; 95% CI 24% to 54%) were deemed to be inappropriate requests.

Retrieved from: Citation: Eldridge SM, Chan CL, Campbell MJ, Bond CM, Hopewell S, Thabane L, et al. CONSORT 2010 statement: extension to randomised pilot and feasibility trials. BMJ. 2016;355.

skeptical of applying population-level guidelines to individual patients, which appears to be due to a misunderstanding of the epidemiological basis for these recommendations. (9) Confronting the action bias that afflicts both patients and their physicians will also be of critical importance. (10)

In conclusion, we see a need to improve colorectal cancer screening decisions for women aged 80-84 in primary care in Quebec.

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COMMENTARY

Artist: Caroline Najjar

COMMENTARY
McGill Journal of Medicine

The Commodification of Humanism: Methods, Marketing, and Morals of a Postmodern Shift in the Philosophy of Medicine

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ABSTRACT

Consideration of the history of medicine reveals a postmodern shift in the philosophy of medicine, one that arguably strays from its humanist foundations. Though often attributed to Sir William Osler's contributions, the modernization of medicine extends beyond his influence, as well as beyond his time. Peaking in the mid-1900s, the paradigm shift in the philosophy of medicine continues to compel a certain dichotomy between humanism and medicine today. Despite being historically intertwined, medicine distances itself from humanism amidst the institutionalization, depersonalization, and monetization of the medical field. Notably, the commodification of medicine entails three central themes: methods, marketing, and morals.

KEYWORDS
Commodification of medicine, Humanism in medicine, Sir William Osler

1 | INTRODUCTION

Bearing witness to the results of progress in the medical field during the 20th century and into the 21st century, the practice of medicine is arguably at its peak. The contributions of Sir William Osler towards modernizing the medical curriculum through the implementation of bedside clinical teaching at the turn of the 20th century, followed by the predominant emphasis on humanism in medical philosophy thereafter, permanently altered the course of medicine. (1) Osler advanced the scientific basis of medicine whilst recognizing that an interaction between both science and humanism was imperative, (2) and that maintaining a dichotomy between the two was neither feasible nor beneficial. Yet, Osler understood that humanism could easily be lost amidst scientific progress, and his teachings tend to emphasize this. Indeed, his adamance towards prioritizing the patient

in medical practice might now be viewed as an overt awareness, and perhaps a warning, concerning the future of medicine.

Despite the apparent success of medicine, the changes that Osler initiated were developed beyond his intentions. What began as a culmination of patient-centered teaching and treatment soon evolved into a sometimes depersonalized approach reliant on a hierarchical systemization within hospitals. Among other factors, this brought about an unforeseen deviation from Osler's widely-adopted humanist narrative in which he insisted that "it is much more important to know what sort of a patient has a disease than what sort of a disease a patient has". (3)

While Osler was seen as a pioneer of innovation in his time, he is now perceived by medical students as the embodiment of an ideal physician - one that demonstrates profound medical knowledge and maintains a humanist attitude. (2) Yet, this idealization acknowledges that the embodiment of both science and humanism is not presently a reality. An understanding of the medical field today requires a consideration of both the history and philosophy of medicine in the 20th century.

The postmodern era, defined primarily by the 1960s, (4) saw the emergence of new technologies, a redefinition of the norms in medical practice, a distancing from Hippocratic traditions, and ultimately, the commodification of medicine. Indeed, an exploration of the medical field following the scientific and technological revolution of the mid-1900s reveals a shift in the philosophy of medicine - one that strays from the very humanism upon which medicine was founded. With the rise of evidence-based medicine amidst new technologies, the specialization and institutionalization of doctors, and a shift in the values of medicine towards depersonalization and monetization, the commodification of medicine entails three central themes: methods, marketing, and morals.

2 | METHODS

The scientific and technological revolution of the 20th century gave rise to an explosion of scientific knowledge, an increase in communications technology, and a series of innovations that would jumpstart progress in the realms of physics, chemistry, and biology. Following the Second World War specifically, the sudden flux of scientific technologies and discoveries permitted nations to adopt a sentiment of modernization, (5) and most importantly, improvement. Characterized by a decreased prevalence of bacterial diseases thanks to the development of antibiotics, as well as the elimination of polio and smallpox as a result of effective vaccines, the medical field was among those revolutionized. (5) Laboratory technologies permitted medical advances beyond the hospital's walls, while the introduction of computerized tomography, magnetic resonance imaging, and radiation therapy improved treatment and diagnosis within the hospital. Yet, along with this development of new technologies came a certain dependence on these innovations as the only means of furthering medicine. For instance, between 1997 and 2006 in Washington State alone, 377,048 patients underwent 4.9 million diagnostic tests with the uses of computed tomography and magnetic resonance imaging doubling and tripling, respectively. (6) In part due to the modern widespread availability of advanced technologies, the use of technology in hospital settings is now unprecedented. Yet, while the use of technologies has increased, there has not been an associated change in the frequency of illness - which could suggest an overuse of diagnostic medical imaging. (6) The use of diagnostic technology "defensively" - as a means of eliminating anxiety in the face of ambiguity - has implicitly created an obligation to utilize technology, sometimes regardless of actual need. (7) Indeed, this trend has not only contributed to a rapid growth in medical costs, but also an increase in radiation exposure - one that has been suspected to contribute to cancer. (7) Ultimately, neither the increased costs nor the increased radiation exposure prioritizes the patient's wellbeing.

Albeit providing the option of reliable diagnostic testing, technological advancements are often overused and have arguably eroded communication within hospitals. Despite being enforced as ways to reduce human error and facilitate documentation, electronic health records

(EHRs) and health information exchanges (HIEs) have been associated with a weakening of physician's abilities to make informed clinical decisions. (8) Similarly, new technologies have been linked to a decreased willingness to learn and retain bases of medical knowledge because they are readily accessible online. This phenomenon is reflected in the 12% decrease found in the overall pass rate of the Maintenance of Certification (MOC) internal medicine board exam from 2009 to 2013. (8) Most importantly, studies have found that the standardized use of EHRs and HIEs by healthcare professionals can impede doctor-patient communication. (9) While there have undoubtedly been doctors who perform excessive documentation on paper charts, the implementation of EHRs and HIEs have normalized an emphasis on record taking, with many doctors admitting to the use of "cut-and-paste boilerplate text" in patient charts. (10) Pressured to fill endless boxes with patient information, physicians may inadvertently adopt a nearly robotic interrogation of patients, rather than an empathetic conversation. With physicians' eyes glued to the screen, patients may feel a lack of human connection and care. The addition of a screen between the doctor and the patient has not only added a literal barrier, but also a symbolic gap in communication and understanding.

Beyond the devolution of individual interactions between physicians and patients following the postmodern era, the systemic treatment of patients has also experienced a paradigm shift - one from clinical judgement to evidence-based medicine (EBM). (11) Formally introduced to medical literature in 1992 by Gordon Guyatt at McMaster University, (12) EBM was presented as a method which "de-emphasizes intuition, unsystematic clinical experience, and pathophysiologic rationale as sufficient grounds for clinical decision making and stresses the examination of evidence from clinical research". (11) With only two published articles referring to EBM in 1992, (13) and over 20,000 in 2015, (14) EBM soon became one of the milestones that shaped the medical field. (15) Despite attempts to redefine current EBM as a combination of both research evidence and clinical experience, it is the initial "de-emphasiz[ing] intuition" which conflicts physicians today, regardless of agreed-upon definitions. Opponents of EBM argue that its approach to scientific knowledge prioritizes internal validity, which consequently promotes the explanatory randomized controlled trial (RCT) as a means of standardizing medical treatment. (14) While evidence from RCTs has proven effective for single disease conditions, it largely fails to address multimorbidity and social determinants of health. (14) Indeed, with the focus of clinical trials on entire populations rather than individuals, (5) the threat of EBM lies in its imposition of uniform instructions instead of care designed for the needs, context, and predisposed risks of each patient. (16)

3 | MARKETING

Concomitant with the rise of EBM resulting from a new emphasis on science in medicine, and science as medicine, there came about a new image of physicians—that of the specialized technologist. (17) Amidst an environment of advanced technology and evidence-based approaches, the subjective patient was often bypassed for undisputable images from medical instruments - disregarding unnecessary costs that might be avoided through patient interaction. Meanwhile, the financial approach to medicine, that of commodification, is arguably the basis of an ever-growing depersonalization culture. For example, in the United States approximately 25% of total healthcare spending is deemed wasted on factors including over-treatment. (18) Moreover, while nearly 18% of the gross domestic product goes towards health care in the United States, (18) 28 million Americans remain uninsured. (19) As such, there exist immense disparities in access to - and quality of - healthcare.

Following the mobilization of social programs during World War II, employer-financed private health insurance was adopted. (17) Whereas most other developed countries opted for a social insurance model based on sharing the cost of sickness, (17) the United States fared with a business model. By the 1970s, most politicians were in full support of privatization and deregulation,

(20) a decision that would distinguish the state of the American healthcare system going into the 21st century. The expansion of healthcare from the private sector into the public sphere was introduced as neoliberalism. (21) With a restructured healthcare system emphasizing free market capitalism, individuals were granted the choice of care rather than equitable access to care. (21) However, this choice could be perceived as more of a burden for those without the knowledge or the funds to distinguish "good" healthcare from "bad" healthcare. (21) Market theory in itself constitutes that the consumer is aware of their needs and holds bargaining power over different prices. (17) While transferable to industrialization where there exists a legitimate choice to consume or not, market theory does not hold up in the context of medicine where patients do not choose to be ill and often are not familiar with their diagnostic options. (17) Business ethics in medicine condone unequal care based on the ability, or lack thereof, to afford treatment. (22) With an inflation of 176% in the average cost of emergency room entry (excluding treatment) from 2008 to 2017 in the United States, there is little evidence of an improvement in the quality of care provided to support this increase. (21)

While the privatization of medical care in the United States is an overtly tangible example of the commodification of medicine, there exist subtler, yet nonetheless prevalent, presentations in hospitals worldwide. When one thinks of physicians today, the range of different specialties comes to mind, as they are so ingrained in medical culture that we do not stop to question it. However, the over-specialization of physicians is integral to the commodification of medicine, as it greatly contributed to the standardization of care and thus a distancing from patient-oriented care. Initiated due to a combination of increasing medical knowledge as well as economic incentives, specialization was normalized, and the family physician that patients trusted was lost. (23) The limitation of one's practice to a single area, along with rising patient distrust, essentially facilitated the transition into standardized care. Amidst an increasing understanding of the responsibility held by physicians, and the accountability brought about by misdiagnoses, came the rise of defensive medicine - an overuse and reliance on tests, procedures, and prescriptions to treat patients. (24) The progression into standardization led to continuity of care becoming scarce and paved the way for managed care organizations. Instead of treatment by a single physician, corporations were perceived as the "doctor" who would provide someone to deliver the commodity of medicine. (22) Indeed, the institutionalization of corporate medicine decreased personalized patient-physician relationships and eliminated any remnants of the idolized "top-hatted nineteenth-century physician." (23) Nowadays, the hierarchical systemization of healthcare professionals implicitly emulates an assembly-line approach to medicine. (25) Ultimately, these changes make it difficult to insist that humanism and altruism are at the forefront of 21st century medicine.

4 | MORALS

Dating back to 2600 BC, (26) medicine as a concept, profession, and virtue has undergone a lengthy evolution. This is particularly true with respect to the patient-physician relationship, the philosophy of medicine, and the presence of humanism - or lack thereof. Notably, the formal founding of modern medicine has been credited to Hippocrates, due largely to the prevalence of his Hippocratic Principles and Oath outlining the pillars of physician responsibility. (27) Referred to as "the techne of iatrike", the earliest formal account of medicine concerned itself with the health of the body and held intricate relations with ritual and philosophy, which centered around the soul. (28) Inaugurated as a "techne"—an art, (28) the ancient Greek practice of "iatrike" held connotations (in both science and art) distinct from later definitions of medicine. Though, within this art of healing, there exists speculation that Hippocrates aimed to establish medicine as a scientific domain, thereby denying ties to philosophy. (29) Medicine, being nested in philosophy, was initially based on the pretext that "doctors" held curative powers as wizards and clergy. (25) Concomitantly, the origins of philosophy have also

been said to be rooted in the methodology and worldview of medicine. (25) To this day, medicine and philosophy remain intrinsically linked, whether that be implicitly or explicitly. Upon further inspection of Hippocrates' supposed desire to dichotomize medicine and philosophy, (29) it is evident that by virtue of distancing from philosophy in medicine, a philosophy of medicine emerged. Integral to the early philosophy of medicine, the notion of humanism guided the responsibilities of the physician. Only formally coined by physician Scribonius Largus in the first century AD, *humanitas* was intended as the philosophical foundation for the role of the physician, and the love of mankind. (30) The centrality of humanism within the philosophy of medicine gave rise to the depiction of physicians as "benign, benevolent, all-knowing authoritarian" figures. (30) Amidst a public lack of medical knowledge, however, patient rights were absent from Hippocratic ethics, (31) which dealt solely with the concepts of benefit and duty in a physician-centered model of the patient-physician relationship. (32)

Progressing well into the Middle Ages, Christian religion heavily influenced the Western concept of medicine, (33) thereby allocating a moral authority - based on Hippocratic values - to physicians. Up until the mid-17th century, patient passivity imposed by the authority of physicians was left relatively undisputed. Moral authority was only formally replaced by legal authority in 1690 with the publication of John Locke's *Two Treatises on Civil Government*, which proposed a theory of human rights and subsequently altered the patient-physician relationship. (33) Translated to the context of medicine, Locke's philosophy presented the formerly physician-centered model as a contract for service between two autonomous individuals. (30) Entering the Oslerian era of the early 20th century, this model persisted, withstanding criticism associated with the progressive loss of the benevolent physician. Representing an embodiment of the humanist qualities ingrained in the philosophy of medicine, Osler advocated for the maintenance of a patient-centered model in medical practice. (1) Efforts included a modernization of the medical curriculum to include bedside teachings, as well as a strong opposition to the dichotomization of science and humanism. (2) Despite the amplification of Osler's contributions towards maintaining a humanist philosophy of medicine, his then-revolutionizing perspective in the medical field dissipated during the very next revolution.

The scientific and technological revolution of the mid-20th century enabled a paradigm shift in the philosophy and practice of medicine. Hippocratic traditions, which had prevailed until the 1960s, were suddenly under question. (33) This was in part due to rising mass demonstrations and social upheavals in the United States, (33) as well as the swift global prevalence of new technologies. Indeed, public dismay emerged from a predominant distrust towards institutions - including that of medicine. While previous societies had been immobilized in a spectator's role on the subject of national decision-making, (33) a radicalization in societal participation permitted widespread advocacy for the traditional patient who had assumed a passive role in medical practice. (32) Newly informed on the basics of medicine and their fundamental rights, patients adopted the role of consumers in a field focused on promoting "customer satisfaction". (34) The commercialization and institutionalization of medicine, facilitated by a rise in technologies and standardization in practices, permitted a paradigm shift in the philosophy of medicine: the commodification of the patient-physician relationship as a business model. With medical knowledge as proprietary ownership, (30) the business model is based on the understanding that medical practices are analogous to a transaction between a customer (patient) and a provider (physician). (32) Indeed, this model can be categorized as patient-centered as it challenges the physician's unilateral authority and permits the patient to 'shop' for a physician who satisfies their needs. (32) However, within a model comprising savvy providers and wary consumers, there exists a foundation built on distrust. (32) Certainly, the presence of distrust in medicine is seemingly counterintuitive, yet it is more so exemplified within a model where medicine exists as a commodity analogous to quotidian purchases. Along with said commodification, the postmodern era gave rise to the ques-

tion of depersonalization in the patient-physician relationship. The increase in medical perspectives regarding the patient not as a person in need, but rather as a case, an ailing organ, or a part in an assembly line, (25) have heralded the loss of humanism. Effectively, a philosophy based on commodification and depersonalization cannot claim reasonable ties to humanism.

5 | CONCLUSION

Despite undoubted progress in the medical field, there continues to exist immense discrepancies in the access to - and quality of - medicine worldwide. Further, contextual differences invariably remain in what "good" medicine is perceived to be. In acknowledging that these factors may neither have been considered nor relevant in Osler's time, it is not appropriate to adopt a former approach that has become incompatible with the complex reality of 21st century medicine. However, given the lasting idealization of Osler in the minds of ambitious medical students and accomplished physicians, the desire to revolutionize the medical field is not uncommon. Certainly, the last century has brought about exponential and continuous progress in medical technologies, yet it has nonetheless predominantly overlooked progress in the medical perspective. Consequently, the philosophy of medicine has strayed from its humanist foundations. Indeed, a complete understanding of modern criticism requires an exploration of the history of medicine - primarily ensuing the scientific and technological revolution of the mid-20th century. Consideration of the methods, marketing, and morals of the medical field, through both individual physicians and healthcare systems, reveals a paradigm shift in the philosophy of medicine - one which institutionalizes and normalizes practices lacking a humanist approach, and sequentially risks neglecting patients. Amidst prevailing antihumanist trends revealed in present politics and prejudices, a mandate to uphold humanism in medicine ultimately extends beyond hospital walls. (35) Healthcare professionals are not only challenged with restoring humanism in the medical field itself, but concomitantly serving as models to confront a gradually dehumanizing society.

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COMMENTARY
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Deconstructing Canada's efforts to integrate artificial intelligence in medicine and medical education

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ABSTRACT

Artificial intelligence (AI) has gained momentum in the last decade in various professional domains, but its usage remains scarce in the field of medicine. Available AI-enhanced devices are not integrated in a consistent fashion throughout Canadian health facilities, and current medical practitioners and students are not well prepared for AI's impact on their careers. Undergraduate medical students lack fundamental knowledge of AI in medicine, from its impact on patient care and its potential as an adjunct decision-making tool, to the general fundamentals of how AI-enhanced devices work. Currently, postgraduates don't have access to AI-enhanced devices; this could potentially limit their understanding of how these devices might affect their future clinical practice. Canadian medical universities can play a critical role in familiarizing students with these new devices. Incorporating new topics into the already heavily charged medical curricula may be challenging, but students could make use of extracurricular activities to learn the concept of AI and strengthen interdisciplinary collaboration. Educational institutions would also need to propose policies for the safe and ethical use of devices in classrooms or internships. However, they might require guidance to draft new policies targeting AI in medical education. Canadian medical associations could take the lead to draft AI policies in healthcare to guide the equal and safe implementation of AI-enhanced devices across the Canadian medical community. Our paper will explore the work that has been done related to AI-specific policies in healthcare, focusing on Canada, and provide key points that could be used to organize future policies.

KEYWORDS

Medical education, Artificial intelligence, Canadian education, Policy analysis

1 | INTRODUCTION

Artificial intelligence (AI) in healthcare refers to a spectrum of technologies that consist of an algorithm receiving data as input, processing it, and giving an output to assist in diagnosis, treatment, patient monitoring, and trainee education. Although AI is gaining popularity across diverse fields such as finance and aviation, it has not yet been widely adopted within healthcare systems internationally. Currently, the most popular implemented role AI holds in medicine is providing evidence-based personalized treatment regimens for patients by processing local and widely available data libraries (e.g. Gemini by GNS Healthcare, or DynaMed-Micromedex by IBM). The impact of fully integrating AI-enhanced devices into clinical routine, from triage and early diagnosis to comparative drug effectiveness and office operations, is hence unknown. AI-related discoveries are mostly kept within the research and development community, leaving healthcare professionals inadequately informed about new AI developments. (1) This could impede medical professionals from using AI with ease as increasingly more complex tools are introduced to the market. Thus, there is a rising need to educate healthcare professionals about these devices. Currently, undergraduate and postgraduate medical education do not provide students with the foundations to comprehend the challenges of emerging AI technologies. Therefore, it is important to incorporate AI-related courses in medical education.

In order to properly integrate AI-enhanced devices into the healthcare system and educational institutions, medical associations and universities need to devise AI-specific policies. Policies would help introduce the devices to a greater audience of trainees and achieve equity in their access and safe use (e.g., protecting patient data) in medical practice and in educational settings. In Canada, legislation to adopt AI into the healthcare system does not currently exist. However, in recent years, there has been an initial governmental collaborative effort to develop new policies on AI in medicine and medical education. Whether there has been significant progress on their redaction has yet to be documented. In what follows, we discuss the position of the Canadian government and medical associations on the topic of AI in medicine, medical schools' efforts to integrate AI in coursework and medical research labs, AI policies related to medical education internationally, and finally, suggestions for Canadian policymakers. If there is sufficient guidance from Canadian medical associations, universities could build on it to put forward their own norms on implementing AI in medical education and healthcare facilities.

2 | HOW ARE THE CANADIAN GOVERNMENT AND MEDICAL ASSOCIATIONS ADDRESSING AI POLICIES IN HEALTHCARE?

Canada was the first country to adopt a strategy on AI in the 2017 Budget to initiate its appraisal. (2) Led by the Canadian Institute for Advanced Research (CIFAR), the Pan-Canadian AI Strategy's objective was to bring together academic and industrial talent for potential innovation. To ensure that the use of AI would be governed by clear values and laws, the National Research Council was quick to release an advisory statement and a white paper draft on the responsible and ethical use of AI in 2017. (3,4) While it addresses critical issues such as ethics, privacy, and bias, it does not go in-depth for applications in healthcare. It is the AI4Health Task Force under CIFAR that undertook the responsibility to underline urgent actions the government should take with respect to the deployment of AI in healthcare. Their report from July 2020 lists recommendations under four broad key messages: 1) Establish the infrastructure to securely access datasets, 2) Support the growth and the procurement of AI in the healthcare system, 3) Advance digital health by coupling it to policies, investments and partnerships of private enterprises and public institutions, and 4) Encourage federal and provincial healthcare partners to commit to a joint effort to ensure policy development. (5)

Canada's medical and subspecialty associations are also aware of the need to discuss the future of AI. In

2013, the Canada Health Infoway wrote a summary on the high volume of available unstructured health data and stated that health ministries should address data policies on privacy, security, intellectual property, and liability. (6) AI-enhanced devices use algorithms trained using these types of datasets that should be prepared such that the data does not permit patient identification, but contains enough information to improve the algorithm's results. Since health data is part of the development process of AI-enhanced devices, these issues require their own sets of policies. Additionally, in 2014, the Canadian Medical Protective Association followed with a call for physicians to become familiar with the concept and utility of "big data". (7) AI is one of the analytical devices that can process, contextualize, and visualize big data to recognize patterns. Therefore, it would be critical to write policies on collecting high quality data in a standardized way, while being aware of patient privacy concerns.

The Canadian Medical Association (CMA), especially during the COVID-19 pandemic, has been concentrating its efforts on virtual care and electronic medical records, since 63% of Canadians stated that they would like to be able to virtually access their family doctor according to a February 2020 task force report. (8) The report did not mention the relevance of AI within the telemedicine sphere. The last time the CMA acknowledged AI directly was during their 2018 Health Summit. (9) However, they reiterated in the 2020 report the potential of big health data in precision medicine, and that AI will improve diagnostic accuracy when using a high volume of datasets. Likewise, the Royal College of Physicians and Surgeons of Canada's (RCPSC) AI task force published a report in February 2020, in which they defined the place AI holds in medicine and gauged the impact it will have on healthcare and affected staff. (1) The report complemented the summit primer the CMA used to explore the potential of virtual care, big health data, and technological developments. (10) The RCPSC acknowledged that current health professionals are overlooking AI development due to the lack of AI-related content in the medical curriculum. The report found that about half of the surveyed fellows answered that they had limited familiarity with AI. Only 3.9% of the surveyed fellows rated themselves as experts in the field. Additionally, the Canadian Association of Radiologists released a white paper on their stance on AI in 2018, which listed recommendations for preparing radiologists for the impact of AI regarding its implementation, governance, clinical implication, and education. (11) Overall, the governing bodies of the medical community (CMA and RCPSC) have engaged with the topic of AI in medicine. Therefore, they are well placed to initiate a collaboration among themselves to combine their respective insights and suggest future directions for AI in medical education to prepare current and future physicians.

3 | THE PRESENT STATE OF AI IN MEDICAL SCHOOLS AND UNIVERSITIES

3.1 | What are the actions set in motion by Canadian universities to prepare medical professionals for the impact of AI in healthcare?

Based on the Canadian Association of Radiologists report, there is a need to offer an unbiased AI education to current and future physicians. The RCPSC report confirms this need, as 85% of surveyed residents affirmed not receiving adequate knowledge regarding the future usage of AI in their practice. Students from University of Toronto's medical school have taken the initiative to focus on this gap as part of the Ontario Medical Students Association (OMSA). In 2019, the OMSA drafted a position paper with recommendations to prepare students for the impact of AI. (12) It sums up learning objectives to gain AI competencies, comprehend the ethical implications and bias of algorithms, and expand interprofessional collaborations with other fields (e.g., computer science). The revised version of the paper has been included as one of the resolutions adopted at the 2020 Annual Grand Meeting of the Canadian Federation of Medical Students. (13) From their appendix table, only the faculties of medicine from the University of Toronto and

the University of British Columbia have lectures dedicated to AI, with the latter mentioning it in a few radiology lectures. Other curricular offerings include AI in health research groups or education centres, which are available at Dalhousie University, McGill University, Western University, the University of Saskatchewan, and the University of Alberta. Medical school programs could also use existing courses on AI in medicine as templates to build their own courses. There could be difficulty in modifying the already established core curricula, so the course could be offered as an elective. For example, the course on AI in Medicine offered by the McGill University Faculty of Medicine and Health Sciences Department of Experimental Surgery could serve as a course template for other programs and universities. (14) There is an urgency to integrate AI into medical education to help future professionals gain familiarity with AI and its potential applications in the healthcare system. The OMSA's paper has shown that 50% of the 14 interviewed medical schools had no extra-curricular interest groups dedicated to AI. (13) Therefore, having consistency in available workshops and seminars throughout all the Canadian medical schools would at least increase the awareness of AI among students, which could be a good starting point before more robust additions to the curricula.

Some Canadian universities' stances on AI in healthcare can be inferred from their latest academic strategic plans. The University of Toronto, for example, has marked AI as one of its priorities in their "Groundbreaking Imagination" domain of focus. In 2020, they established a Centre for AI Research and Education in Medicine as a common hub for multidisciplinary collaborations. (15) The University of Alberta, through their Precision Health Initiative, has made recommendations for AI seminars, capstone projects, and training opportunities in the Faculty of Medicine and Dentistry. They have also established an Education and Engagement Task Force to develop educational strategies to involve their trainees. (16) Such efforts could provide students with the necessary conceptual knowledge to understand the place AI can hold in various medical subspecialties. This includes a brief history on AI, the research and development progress of AI in different cases, the ethical issues behind optimizing AI, the need for improvement, and how the accuracy of such devices can affect clinical outcomes. After the initial undergraduate education, residents could have the chance to familiarize themselves with using AI-enhanced devices as a part of their decision-making process, through both simulated practical scenarios and during their clinical rotations. In the near future, several Canadian medical universities could be using AI in their simulation centers, although currently, it is only found among their research and development groups. For example, although still in the research phase, a project in the University of Alberta's Surgical Simulation Research Lab demonstrates the feasibility of obtaining data from residents during an augmented reality surgical procedure to feed into a learning algorithm to detect the moment of performance difficulty. (17)

These two instances – the implementation of AI conceptual knowledge and literacy in undergraduate medical education and the use of AI-enhanced devices in postgraduate programs – illustrate the need to develop educational AI policies in faculties, simulation labs, and educational research centers. While universities might find it hard to truly gauge the effect of AI in medicine, they can always turn to existing research institutes for direction. The Vector Institute, the Montreal Institute for Learning Algorithms (MILA), and the Alberta Machine Intelligence Institute (Amii), to name a few, are AI hubs that could help institutions navigate the multiple facets of AI and act as a link to CIFAR, which has already begun a nationwide AI policy labs initiative. (18) By evaluating the full effect of AI in medicine, universities can create policies to incorporate relevant conceptual and practical AI knowledge into medical school and residency curricula, respectively, focusing on the safe and ethical use of AI-enhanced devices with the provided data.

3.2 | How are AI policies in medical education integrated internationally?

The American Medical Association (AMA) has taken the

North American lead by passing its first AI policy in 2018 titled "Augmented Intelligence in Health Care". (19) It broadly sets the agenda, ensuring that AI initiatives be smoothly integrated and thoughtfully designed, minimizing disruption of patient-physician interaction. Additionally, in 2019, the AMA's Council of Medical Education adopted 10 additional policies to ensure AI-specific advances were supported by medical education. (20) Their goal is to study the most effective ways to include AI in licensing standards, modify the curricula to include specialty-specific educational modules, ascertain the quality of AI instruction in medical education, and judge the disparities in institutional access to AI.

Internationally, there seems to be no other mention of adopting AI policies in medical education since curriculum modifications to align humans and machines in practice have only recently been sought in editorials and published reviews. (21–23) The Academy of Royal Medical Colleges in the United Kingdom acknowledges that clinicians' education will require changes in order for them to be involved in the development of new technologies as the main users. (24) As the graduate medical curricula advocates for student-personalized education, AI could also provide custom training by evaluating previous training sessions. (25) However, such changes would require collaboration between medical schools and medical associations to ensure an appropriate reform to the curricula.

4 | HOW SHOULD CANADIAN STAKEHOLDERS MOVE FORWARD?

On the national, provincial, and local levels, every stakeholder will need to collaborate closely to ensure the follow-through of recommendations and adoption of broad AI in practice and educational policies. The AI4Health Task Force could act as the main body and serve as a connection in the network of research institutes and universities, relaying and summarizing the latest information on the development of AI and its availability throughout the provinces. They already have the AI Futures Policy Labs, which paves the way for discussion among policymakers from the public, private, academic, and not-for-profit sectors across Canada. (18) Medical associations could collect comments from clinicians who have had contact and experience with AI-enhanced devices. This feedback could be forwarded to medical schools, resulting in relevant learning objectives and assessments. This also includes potentially modifying the CanMEDS framework of the RCPSC to include AI competencies in defined roles, such as digital literacy for scholars or transparent implementation of technologies as a leader. (26) Canadian universities, using feedback and newly-acquired knowledge from university-associated research institutes, should review their curricula to encompass an overview of medical usage of AI, societal issues, clinical impact, and training with AI-enhanced simulation devices. The CMA and RCPSC could jointly draft tentative educational policies that universities could adapt to their needs. Based on the above-mentioned reports and the AMA's policies, the following key points could be used to organize future broad educational policies into different sections:

A policy to fill the knowledge gap. Current practitioners and trainees should receive training modules to complement their clinical practice. Care should be taken to ensure that the material presented in the workshops or modules covers the basics of AI algorithms, available accessible AI-enhanced devices, and the relevant usage instructions of each device.

A policy to practice data protection. Secure Canadian data banks should be created and have clear policies and procedures for collecting patients' informed consent. Data privacy and confidentiality should be a top priority. A policy in this case would ensure that the right information is shared with health professionals, with additional details pertinent to subspecialties, such as radiology, pathology, and surgery. Such a policy would also digitally secure patients' personal information.

A policy to guarantee the competence of medical students. Universities should offer extracurricular activities to promote collaboration between medical students, residents, healthcare providers, data scientists,

and engineers to develop new devices and gain new perspectives. Students in medicine do not have to learn the mathematical development behind an algorithm, but they should learn how to describe their users' needs and the clinical applications of AI-enhanced devices developed by other researchers. Students should also learn about the relevance of AI and its evolution in each medical specialty. Additional courses, such as predictive imaging analysis for radiologists or robot-assisted surgery in surgical education, would also be advantageous for students, as would the use of simulation labs to carry out simulations and research involving AI. This policy would aim to provide undergraduate students with access to the conceptual knowledge of AI and interdisciplinary team collaborations, in addition to ensuring that postgraduate students have hands-on experience receiving input from AI-enhanced devices during their residency.

5 | CONCLUSION

Although AI policies are still in their infancy, there is a strong foundation for future iterations among the reports of the Canadian health task forces and medical associations. They provide a baseline of recommendations that could serve to develop further policies on data management, digital literacy, and ethical issues brought by AI in medicine. The next step would be to appoint policymakers from Canadian medical associations, specifically the CMA and RCPSC, to introduce a clear first set of policies on the integration of AI in the healthcare system, and subsequently broad ones for AI in medical education. Canadian universities can draw on frameworks and guidelines from medical associations to guide their own policies and curricula. While some universities might not yet have access to AI-enhanced devices, they could include a course to introduce key concepts to undergraduate medical students that could include common use cases and ethical issues of AI in medicine. Policies would ensure that knowledge on AI is being taught to students ahead of the era of AI in medicine. Such a course design was successfully piloted at the University of Toronto in 2018 and included in the core curriculum in the 2019-2020 and 2020-2021 school years. (27) Postgraduate medical education could then integrate clinical usage of AI with real-life examples, in collaboration with university research centers and AI institutes. Doing so would support medical students in building competency to effectively use AI in their daily practices as future physicians.

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Addressing COVID-19 vaccine hesitancy - healthcare workers and trainees must be equipped for discussions about vaccines

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ABSTRACT

The coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has challenged our world throughout the past year. As we end 2020 conversing with loved ones, the topic of COVID-19 vaccination is inevitable. Throughout the next year, our gradual return to a more familiar society will be influenced by vaccine compliance. It is therefore paramount that healthcare professionals and trainees are equipped with current knowledge to address the questions and concerns of our loved ones. The Holidays should be viewed as an opportunity to address misconceptions and questions. This brief review outlines some arguments for why a COVID-19 vaccine is necessary and clarifies some features of the current top vaccine candidates. By addressing the questions and concerns of our loved ones before they need to decide whether or not they will receive a COVID-19 vaccine, we lay the groundwork for them to make informed choices.

KEYWORDS
COVID-19, vaccination

1 | REFLECTION

As we reflect on the Holiday season, the world is still grappling with what was a year dominated by personal, professional, economic, and health challenges. We have seen how coronavirus disease 2019 (COVID-19) has flipped our society on its head, and we have experienced the tolls of lockdowns to prevent the spread of SARS-CoV-2. We ended the previous year with hopes that a return to normalcy in our society is approaching, prompted by news that vaccine development efforts were charging forward with success. However, this previous year had also been marked by significant political unrest, immense personal and economic sacrifices, and

decreased trust in the very systems that are working to resolve the pandemic. Indeed, vaccine hesitancy is a significant hurdle that must be overcome - it is vaccinations, and not vaccines themselves, that offer us a return to normalcy. As we finished the year having conversations with our loved ones, many of us healthcare trainees and professionals might have unknowingly stepped into a boxing ring where misinformation from social media and inflammatory reporting has ruled victorious throughout the past months. Although it is clear that misinformation on this topic is widespread, some of our family members might also have reservations about the COVID-19 vaccines that stem from uncertainty around how the vaccines work or difficulties in understanding their safety profiles. It is therefore paramount that we, as representatives of the healthcare field, be prepared to address the questions and concerns that will inevitably arise in our future interactions with the people in our personal lives. We should view our conversations with friends and family as an opportunity to lay the groundwork on the role that vaccinations will play in resolving the pandemic. This summary aims to provide health trainees and professionals with current information on COVID-19 and vaccination. This is not an exhaustive review, but rather a small collection of information that will arm healthcare trainees and professionals with knowledge and resources to engage with questions on this topic that might arise from our loved ones.

2 | WHY VACCINES ARE NECESSARY

To understand why a vaccine is our best shot at resolving the COVID-19 pandemic, we need to make note of some disease characteristics. SARS-CoV-2 is an incredibly infectious virus with the capacity to spread uncontrollably in our population. The reproductive number (R_0) – the number of individuals one infected person is likely to infect – is estimated based on how long someone with the virus is contagious, the probability of an infected person passing the virus on to someone they are in contact with, and the frequency of contact with others in society (1,2). The R_0 for SARS-CoV-2 is estimated to be between 2.0 and 3.0 (3), higher than seasonal influenza which is typically around 1.3 (4). To help understand the significance of this difference, if we were to compare a typical influenza with an R_0 of 1.3, and the more conservative estimate of the R_0 for SARS-CoV-2 at 2.0, after ten cycles of infection we would estimate that influenza would affect approximately 56 people and SARS-CoV-2 would affect 2,047 people. A part of why SARS-CoV-2 can spread so uncontrollably in our society is that individuals without any noticeable symptoms or signs of disease can spread the virus (5–7). The incubation period – the time separating exposure to SARS-CoV-2 and the onset of symptoms – ranges from 1-14 days (8) with a median of 4-5 days (9,10). Indeed, many individuals are infectious days before noticing illness (11), making the control of outbreaks logistically complex. The R_0 can be decreased by limiting our contact with others in society (e.g. lockdowns, social distancing, masks) and we prevent the growth of infections only when this number falls below 1.0 (12). COVID-19 has claimed the lives of over 16,000 Canadians since the first death nine months ago (13). Although influenza mortality can be challenging to accurately determine, the mortality of COVID-19 is much higher than the estimated 3,500 Canadians who die from seasonal influenza each year (14). Notably, these deaths occurred while implementing strict containment practices. Between March and June, Canada had an excess of 7,000 deaths aligning well with the first wave of the COVID-19 pandemic (15). To resolve the COVID-19 pandemic, it is clear that our society must achieve a significant degree of immunity.

Early on in the pandemic, social media posts suggesting the use of 'COVID parties' became widespread, advocating that individuals intentionally expose themselves to SARS-CoV-2 so as to 'get their infection out of the way.' There are many reasons why vaccine-mediated immunity is preferable to infection-acquired immunity. Firstly, our healthcare system cannot manage such a rapid influx of patients sick with COVID pneumonia – though our containment efforts help to reduce the number of cases and hospitalizations, COVID-19 has still

managed to place immense stress on our healthcare system. At the time of this article, nearly 700,000 Canadians have tested positive for COVID-19 (16), comprising about 1.8% of Canada's population. The minimum number of immune people needed to protect the whole population from transmission (i.e. 'herd immunity') can be estimated using the R_0 value by the formula 1-(1/R_0) (17). Since the estimated R_0 of SARS-CoV-2 ranges from 2.0-3.0, we can predict that between 50-67% of Canadians (at least 19 million people) would have to contract COVID-19 to reach this objective, and this is likely to be an underestimate. With the current case mortality rate estimated at 2-4%, this would equate to 380,000-760,000 COVID-19 deaths in Canada to reach natural herd immunity. This is assuming that reinfection does not occur, and that immunity following natural infection is long-lasting, which are not valid assumptions given that re-infection has been described in a growing population of patients (18,19). This is also not considering the non-COVID-19 mortality that would result from a lack of resources in a healthcare system overrun with COVID-19 patients. Thus, the massive number of deaths that would result from a pursuit to obtain natural immunity is an unacceptable and preventable cost. Secondly, COVID-19 is a novel disease, and there are many potential long-term health consequences to infection. Indeed, there is an increasing awareness that 'long COVID' will be a significant sequela to the pandemic, and includes a myriad of complications such as prolonged fatigue (20), cognitive impairment (21–23), cardiomyopathy (24,25), lung scarring and fibrosis (26,27), and many other serious consequences of the inflammatory and immunogenic insults of COVID-19 (28,29). These long-term manifestations of COVID-19 infection may very well impact our health system for decades to come, so obtaining targeted immunity without these long-term consequences is ideal. Thirdly, many might have heard speculation that previous infection with seasonal coronaviruses (which cause about 30% of common colds) may confer immunity to SARS-CoV-2. However, a retrospective clinical investigation found that the serum from individuals with previous seasonal coronavirus infection had protection against seasonal but not pandemic strains, suggesting that this immunity is not generalizable (30). Moreover, immunity to seasonal coronaviruses typically lasts approximately 12 months, and reinfection with the same strain of virus beyond this timeline does occur (31). We do not yet know exactly how long COVID-19 immunity lasts, either by vaccination or by infection, but one recent report suggests that immunity following infection lasts for at least six months (32). A recent update on the Moderna mRNA-1273 vaccine demonstrated elevated antibody titers at 119 days following initial inoculation (33). Finally, some have argued that vaccines are not necessary since SARS-CoV-2 will continue to mutate as the pandemic continues, attenuating or becoming less pathogenic over time. Though it is true that this phenomenon is observed for other RNA viruses, such as influenza, the per base mutation rate of SARS coronaviruses is less than that of influenza due to proofreading enzymes and complex mismatch repair machinery that correct errors in replication of the viral genome (34–36). Some experts estimate that effective attenuation of SARS-CoV-2 would take years to develop, with each year infecting millions more. These statements are not intended to intimidate the reader or their family members, but rather to dispel misconceptions about COVID-19 epidemiology and immunology, and to reaffirm why vaccination is being pursued. By creating vaccines, we are effectively able to achieve herd immunity to COVID-19, minimize the number of deaths, hospitalization, and long-term disability, while sustaining immunity safely through the use of boosters if necessary.

3 | VACCINE CANDIDATES: MECHANISMS AND SAFETY

Now that we have discussed some reasons why vaccinations will be so important in resolving the pandemic, we will review some information about the current vaccine candidates. This commentary is not meant to be an exhaustive review of the vaccine candidates themselves – a useful website for staying up to date with the status of all 60 current vaccine candidates is COVID19 Vaccine

Tracker (https://covid19.trackvaccines.org/). The Pfizer and Moderna vaccines deliver a small messenger RNA (mRNA) molecule to our cells which lets them produce a small fraction or a modified version of the viral spike protein without ever having virus in the body. This allows the immune system to naturally react and produce antibodies against these proteins so that if the virus does ever enter the body the immune system can attack and clear it before infection can happen. The Oxford vaccine uses an adenovirus that does not cause disease in humans to deliver some of the SARS-CoV-2 genetic material to the body, so that the body can produce a small fraction of the viral protein and build immunity through almost the same mechanism as the mRNA vaccines. Although all of these vaccines work by introducing a small amount of viral genetic material into the body, this material is not stable and is degraded a short time after vaccination and does not enter the nucleus of cells or change the host's DNA (37). The benefit of these technologies is that a person is never exposed to the unmodified or disease-causing parts of the virus. In the opinion of the authors, they are the most technologically advanced and controlled vaccines ever made. Early phase III trial data from these vaccine candidates have shown at least 90% efficacy in preventing infection, and one showed 100% efficacy in preventing severe COVID-19 (38,39). Better efficacy estimates will be determined as more data becomes available, but this data is very encouraging since there was a chance that none of the candidates would show efficacy. Importantly, this does not mean that the pandemic is over, and we must remain vigilant to reduce the spread of COVID-19 throughout the next year.

With any new treatment or intervention, safety is a top priority. These will be the first vaccines to use this type of technology in humans, and care must be taken to develop them and test their safety and effectiveness. As physician-scientists in training, we have watched in awe at how rapidly the scientific community has learned about SARS-CoV-2 and COVID-19. However, when taking the perspectives of those outside of science, we can appreciate why many may observe this incredible velocity with skepticism. Indeed, many will question whether vaccine development was rushed, and if safety was sacrificed due to urgency. To understand why this is not the case, we need to briefly discuss the process of vaccine development. Vaccines are developed and distributed in numerous stages, including pre-clinical scientific investigation, animal studies, human trials with increasing numbers of participants (phases I-III), approval, manufacturing, distribution, and monitoring. Although this development course typically takes approximately 10-15 years before the monitoring stage, there are factors that have contributed to increasing the efficiency of this process for COVID-19. Firstly, research and development into pandemic coronaviruses had already begun prior to the existence of SARS-CoV-2. This is because the related coronaviruses, SARS-CoV and Middle Eastern respiratory syndrome (MERS) coronavirus already had ongoing vaccine development efforts. Indeed, the technology that had been developed to vaccinate against MERS allowed for the efficient focused scientific investigation of vaccines against SARS-CoV-2 (40). Recruitment of volunteers for human trials can take a long time, but due to the global influence of COVID-19 many were eager to volunteer, willing to aid in the testing of vaccines. Due to the urgent need for a vaccine, research programs were able to overlap different phases of human trials, beginning phase II trials at the time that phase I trials were being completed, for example. Manufacturing is labour-intensive and costs billions of dollars, and thus it typically only begins once phase III trials have been completed and approval has been granted. The need for a vaccine to be available to the public once it has been definitely demonstrated to be both safe and effective meant that manufacturing could begin early for promising candidates. This was done with the complete acceptance that millions of doses will be disposed of if the candidate is not definitely demonstrated to be both safe and effective. All of these factors have greatly increased the efficiency of vaccine development, without sacrificing any assessment of safety. Vaccines are only approved if they meet incredibly high standards of safety.

With over 20,000 participants involved in the individual clinical trials for any of the approved vaccines, corners are not being cut. It is worth pointing out that due to the large number of participants in these trials, by

the time that a vaccine is made available to the public, thousands of volunteers have taken it and those in earlier trial phases have now been monitored for months. The clinical trials also boast diverse patient populations (38,41), so the utility of the vaccines for different populations is well-determined. It is also of paramount importance to point out that while there may be side effects of drugs that are used for diseases, many of which have been overlooked historically, vaccines are arguably the safest, and most effective medicines in human history. These vaccines are no exception and rely on the same natural action of the human body to build an immune response against this virus. They just use a different delivery system – they allow our immune systems to react to an incomplete part of the virus in a controlled way, avoiding the serious complications that uncontrolled infection can have on multiple organ systems.

This controlled activation of our immune systems by vaccination may be associated with side effects such as headache, fever, body aches, pain at the injection site, and very rarely, allergic reactions (38,42). To help illustrate how rare severe allergic reactions are, consider the example of anaphylaxis following COVID-19 vaccination, which has an incidence of 11.1 cases per million doses (43). If a healthcare worker vaccinated one person every minute of every day throughout an eight-hour shift, they would expect to see one case of vaccine-induced anaphylaxis after six months of work. This case would be rapidly identified and treated effectively. If you were to alternatively expose people to COVID-19 at the same rate, you would expect between 10-20 deaths due to COVID-19 every day throughout a six-month period. The benefits of vaccination far outweigh the low risk of serious allergic reactions to vaccines, despite their media presence. These side effects are possible in other vaccinations which are given to millions of people safely each year (e.g. measles, polio, influenza). Side effects from vaccination are a product of the vaccine activating our immune systems and the vast majority resolve within a few days. Importantly, the side effects advertised as possibly occurring due to a vaccine can also occur from infection itself, and the incidence of some (e.g. Guillain-Barre Syndrome) is an order of magnitude more likely to occur from infection than vaccination (44).

The hope with this new technology is that it will allow for a more targeted and effective immune response and faster vaccine production. These are technologies which scientists around the world have been developing for years, being catapulted to the forefront of the medical frontier today because of dire need. This is not the first time that science has answered a call of extreme urgency with incredible leaps forward, and it will not be the last.

4 | CONCLUSION

As we reflect on the COVID-19 pandemic last year and wonder what the current year holds, it is important that health professionals and trainees remain informed about this global disease. With vaccines now being administered at a record pace, vaccine hesitancy should be addressed before hesitant individuals are asked to get in line for their shot. Our return to normalcy will not occur over night - it will occur gradually throughout a logistically complex national vaccination campaign and depend on the degree of immunity that we are able to develop and maintain in our population. This will take time and there will be delays, but these delays can be reduced significantly if we have good vaccine compliance throughout the entirety of this vaccination campaign. We have discussed some points that we believe will be useful for healthcare professionals and trainees when addressing some of the concerns of their family members.

Approaching conversations on this topic should be done with great care and should be tailored to one's audience. Though the information in this commentary may help you to construct answers to some of the questions your family members might have on this topic, providing this information will likely not be sufficient to convince someone who is vaccine-hesitant to jump to the front of the line when vaccines are made available to them. However, the tactful communication of this knowledge will allow you to address some of the concerns and perhaps misinformation on this topic that would prevent

individuals from making informed decisions regarding vaccination. Laying the groundwork now means preparing our loved ones for the decisions they will need to make throughout the next year regarding vaccination. The pandemic has placed a massive stress on many aspects of our society, and we must listen carefully to the concerns of our loved ones, empowering them to make informed choices. The pandemic will end with vaccination, and as we write this article both Pfizer's and Moderna's mRNA COVID-19 vaccines have been approved by Health Canada and are being administered to citizens. The authors will gladly line up to receive any approved COVID-19 vaccines as soon as they are made available to us. We encourage our colleagues and loved ones to place similar trust in the rigorous systems involved in vaccine development and approval in Canada.

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REFLECTION
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Not Knowing What to Do: A Narrative Reflection on a Medical Student's First Patient Encounter

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ABSTRACT

Medicine, though fundamentally a scientific discipline, is the art of transferring experimentally derived knowledge onto the care of patients. The clinician's role is to master precisely that process. Therefore, in addition to acquiring a strong command of the biomedical sciences, integral to the clinician's professional duty is the development of his or her identity as a healer.

This first-person narrative essay explores a clinical encounter between myself, a first-year medical student with very limited clinical experience, and an elderly man whom I found collapsed on the sidewalk. Fumbling in my clinical decision-making, I settle on simply holding the man's hand to reassure him that his ambulance is on its way. Later, after reflecting on the event and obsessing over my blunders and hesitations, I finally recognize that the simple act of holding his hand was essential to my role as a future physician and healer, rather than implying clinical inadequacy.

KEYWORDS
Narrative, Physicianship, Medical Humanities

I was walking over to my father's apartment to pick up his old iPhone; mine had decided to die its programmed death that day. For medical students, Friday evenings offer both the blessing of freedom and the curse of exhaustion from a week spent studying to circuit-failure. For this reason, I decided to walk-and not take the metro-to my father's apartment, with nothing but my thoughts supplied by the cold air, a smooth jazz album to calm the neurons, and the faces of strangers with whom I could lock eyes even if only for a transient moment, each of them a sacred snapshot of humanity amidst the masked figures of quarantine.

As medical students, we are constantly reminded by experienced clinicians that a healthy mental life should not be sacrificed for the sake of tireless, self-destructive perfectionism. This advice comes as a relief, given that popular culture tends to depict medical superiors as authoritarian drill sergeants with nothing but hard lessons to teach us by means of pain, sweat and psychological abuse. But how quickly I was, in my first few months

of medical school, already betraying their advice. Relaxation already seemed like a waste of time, especially when exams were around the corner. "And on top of that," I would always repeat to myself robotically, "I'm going to have to save lives one day. Damn it, I shouldn't excuse any moment spent wavering from that goal."

In time I learned that tireless studying and annihilating every facet of my private life was not conducive to well-being, nor to a better understanding of the material. So that's why I decided, that Friday evening, to walk over to my father's apartment instead of taking the metro. It feels almost serendipitous now, thinking back, that the first time that I would provide urgent medical care was also the first time I would decide, with much deliberation, to distance myself from the study of medicine for one short evening.

It was dark and the streetlights shone puddles of warm light like flattened blood oranges across the sidewalk. From a few meters away, all I could see was the silhouette of backward stumbling legs-drunk, seemingly-and a couple of teenagers sharing Tik Tok clips while waiting for the bus. However, when I approached the bus stop, I realized that the silhouette belonged to an elderly man who had lost function in both legs, suddenly crumbling down against the brick wall behind him and attempting to clutch an invisible buoy in the air.

To my surprise, my response was automatic. I removed the crumpled mask from my back-pocket, strung it around my ears, and directed the teenage boys standing by the curb to "Call 9-1-1 right now and tell them exactly what I say."

Recognizing the urgency in my tone, the taller, thinner teenager did not hesitate to call the ambulance, while the other came over and admitted, in a tremulous voice that was part guilt and part innocence, that he had noticed the man was having difficulty standing but had mistakenly assumed he was drunk. I reassured him that I had thought the same thing.

I leaned over and felt the elderly man's pulse in his wrist. I could hardly differentiate it from my own heart, which was beating hard and fast through the distal end of my thumb. Of course, I thought to myself, foolishly, they told you a hundred times in that CPR course: do not use your thumb.

"Is he conscious? Is he conscious?" asked the teenager whom I had instructed to call 9-1-1.

"Yes," I said, hesitating, as I felt the man's carotid artery with my index and middle finger. "Yes, yes, yes," I then repeated when I had confidently appreciated the man's pulse, and proceeded to confirm that he was, in fact, breathing.

"He's conscious," the teenager screamed over the phone. "But where are you? Why are you asking questions? Send the ambulance!"

"Just relax," I said to the boy, without heeding to my own advice, "they'll be here soon."

The old man started falling to his side. I held him in my arms and heaved his body back to a seated position. I looked into his eyes; he could barely open them, and his tongue was slipping out of the right side of his mouth.

"Do you speak English?" I asked him.

He responded by slurring something that sounded vaguely Italian.

"Français?"

This elicited a similar response, except with an accent of intense, visceral panic.

Emptiness swallowed the world. A clear, elucidating emptiness: here I was, a useless student. I had already exhausted everything I knew to do in this situation, which wasn't much at all. I was staring at a man's suffering face, the folds in his cheeks traveling the thin parameters of consciousness, with nothing to offer him. All I knew, in that moment, was that he was conscious and alive-at least for that moment-and that he was suffering a great deal. But then I felt a squeezing pain in my forearm that I will never forget-a pain that will be imprinted like a wax seal in my memory: the man's right hand, grasping me, with a force only exerted when the pull of death is tugging at you hard.

His eyes opened.

"Sir," he pleaded, clearly and audibly this time, "please help me."

"The ambulance is coming," I replied, as I moved his hand toward my own and he squeezed it with even greater compression. "They will be here soon," I stressed.

I held his hand like this for at least five minutes until the paramedics arrived. Clearing my way for them, I was grateful to surrender my position to the paramedics who, unlike me, were experts in managing such situations. They performed all sorts of tests and quickly concluded that the man had most likely suffered an acute neurological episode, which, on reconsideration, was quite obvious (of course, in retrospect, everything always seems so obvious).

A police officer interrogated the two teen boys and me and then asked us to leave with a procedural smile.

"You can go now."

The officer had seen this a thousand times before and knew the drill, just like the firemen and the paramedics. With experience and application, their theoretical lessons had long ago evolved into intuitive, visceral practice. I went into the metro station, disinfected my hands, and glanced over at the scene through the window before going off to my father's apartment building. I picked up his old iPhone from the mailbox (pandemic precautions) and turned around to head back home again.

I followed the same route in reverse, replaying the scene in my mind in endless loops, with each playthrough more detailed than the last. The details tortured me, every one of them like a sharp pin-needle pricking my brain, evoking all of the wrong decisions I might have made and, worse, all of the potential disastrous consequences of those decisions.

Upon passing the bus stop, a kind of mundanity set in. What was, roughly 30 minutes prior, a space of chaotic disturbance, alarmed by the constant flickering of ambulance and police lights and energized by the coordination of emergency care workers, had been replaced with its usual late evening scenery. Employees were waiting in line for the bus, open metro doors vacuumed the air, and a loud choir of honking dominated the intersections. All of my concerns regarding my actions, decisions, and indecisions already seemed irrelevant in the renewed atmosphere of regularity; they were things of the past, errors to be forgotten rather than scrutinized. The man whose hand I held was likely in an emergency room by now, hopefully still breathing, and surrounded by healthcare workers.

Ironically, the day I decided to distance myself from the study of medicine was the same day I was forced to practice it. I took a man's pulse, held his hand, and told him that the paramedics were arriving. Perhaps my contributions to that man's health were minimal, but the incident reinforced the notion that medical theory will never provide a complete picture of medical care-the gestalt will only come to fruition once the floating abstractions of our knowledge are forced to face a human person with a real pulse, real problems, and real fears.

It was out of desperation that I ended up holding that man's hand to reassure him, just as it was out of desperation that he pleaded for my help. One day, in a not-so-distant future, I will have learned to apply clinical medicine, and I hope never to end up holding a suffering patient's hand out of desperation again. Yet, at the same time, physicianship demands of us that we do not treat basic acts of humanism in medicine as surrendered acts of desperation, but as integral to our very profession. Unfortunately, I can already foreshadow that the relentless drive toward improving my clinical abilities might one day overhaul my drive for empathy, just as I became obsessive with every negative detail of my first patient-encounter without counterbalancing them with successes. I treated myself, that Friday evening, like a broken physiological mechanism whose satisfactory function emerges only at near-perfect operation, rather than like a person.

Nobel prize-winning physician Dr Bernard Lown, referring to "medicine's profound crisis", wrote that "doctors no longer minister to a distinctive person but concern themselves with fragmented, malfunctioning biologic parts. The distressed human being is frequently absent from that transaction". (1) I often worry that I will eventually find my professional self to be more robotic than human and in turn treat patients like alien systems. In this sense, I should not assume that empathy will always come to me naturally; we ought to think of empathy as an ongoing clinical requirement, a kind of intuition with its own set of practical applications rather than a noble, but ultimately stagnant, principle.

So, as it turns out, I owe a lot to the man whose hand

I held on the side of the road-he allowed me to put principle into practice.

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REFLECTIONS
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A Medical Student's Perspective on "Fighting for a Hand to Hold"

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ABSTRACT

Fighting for a Hand to Hold by Dr. Samir Shaheen-Hussain is a heartbreaking and compelling read depicting the history of injustices, terror and trauma inflicted upon Indigenous children by the Canadian medical system. As an emergency pediatrician at the McGill University Health Centre and associate professor at McGill University, Dr. Shaheen-Hussain weaves his clinical experiences and long-standing advocacy efforts alongside archival research to shed insight on medical colonialism. This piece is structured in two parts: a book review followed by a personal reflection. It is accompanied by a podcast interview with Dr. Shaheen-Hussain in which he discusses his social justice work, his book, and advocacy advice for students in healthcare. This book review highlights the importance of *Fighting for a Hand to Hold* as a seminal piece of literature for all healthcare professionals and trainees across Canada. In the personal reflection, the author considers their own experiences with race and racism as a person of colour, settler Canadian, and medical student. This reflection concludes by advocating for more emphasis on Indigenous health in Canadian medical education and practice.

KEYWORDS
Indigenous health, Book review, Medical colonialism, Race, Medical education

1 | *FIGHTING FOR A HAND TO HOLD*: A BOOK REVIEW

Written by physician-author Dr. Shaheen-Hussain, (1) *Fighting for a Hand to Hold: Confronting Medical Colonialism Against Indigenous Children in Canada* is a four-part book that brings together first-hand accounts from victims and witnesses, archival material and scholarly documents including peer-reviewed research and memoirs. While the book establishes a rich historical context, the

author simultaneously ensures that readers never falter in understanding the modern-day relevance of these issues. Alongside perspectives from Indigenous scholars, the author accomplishes this by highlighting the recent #aHandtoHold campaign. *Fighting for a Hand to Hold* serves to anchor the past to the present through the author's description of his own grassroots efforts that ended the decades-long practice in Quebec of prohibiting caregiver accompaniment of Indigenous children during medevac flights. (2) By drawing upon this tangible example, Dr. Shaheen-Hussain illustrates many ways in which the healthcare system has and continues to perpetuate practices harmful to Indigenous Peoples in Canada.

Fighting for a Hand to Hold reinforces the existence of systemic racism in our medical system by applying the United Nations definition of genocide as a framework to illustrate Canada's history of medical colonialism against Indigenous children. (3) The book ends on the author's meditations to remedy medical colonialism, which include land-back movements, self-determination, and Indigenous sovereignty. These processes implicate the reclamation of traditional territories, stewardship over educational, cultural, social and health services, and the right to participate in political decision making. In the book's afterword, Katsi'tsakwas Ellen Gabriel provides a sobering personal reflection on the barriers to sovereignty over health care for Indigenous Peoples, emphasizing the importance of authentic reconciliation such that efforts may coalesce reparations and restitution. These efforts must centre upon the demolition of oppressive institutions and policies and the incorporation of sincere actions that demonstrate a commitment to trust rather than empty platitudes.

Towards this goal, Dr. Shaheen-Hussain asks readers to consider voice, and the ways in which a single voice may be uplifted by many. In this sense, he curates multiple quotes from Indigenous Peoples throughout the book. When discussing the memoirs of Dr. John B. Dosseter, a leading Canadian physician who performed skin grafting experiments on Inuit teenagers in the 1970s, Dr. Shaheen-Hussain quotes Paul Quassa, former Nunavut Premier and victim of these experiments: "We are not monkeys, we are not animals, we are another human being that deserves respect." (4) Quotes like these bring into sharp focus the voices of those who are so often ignored, a topic that is further discussed in the accompanying audio interview with Dr. Shaheen-Hussain, recorded in December 2020. These voices remind us, as allies, as advocates, and as Canadians, of the importance of spotlighting and listening to the perspectives of others when telling stories that are not our own. They also remind us to reconsider our intentions. Alongside the author, we must examine our actions in the context of 'do no harm'.

Many other features of the author's honest writing style are striking. For instance, he admits to his own privileges as a settler and healthcare provider. In this vulnerability, he in turn invites us to consider the consequences of our inaction. He challenges the audience to expand our notions of healthcare-inflicted harms by discussing distressing and perhaps surprising examples of Canadian medical colonialism. On a systems level, this included unethical practices whereby nutrition deprivation experiments were conducted in residential schools, Indigenous girls were forcibly sterilized, and skin grafting experiments were performed on Inuit teenagers. On an individual level, he refers to eminent Canadian physicians and researchers, like Dr. Dossetor or Dr. Lionel Bradley Pett who led the skin grafting and nutritional experiments, respectively. The justification for these experiments had been the desire to advance scientific knowledge in the field of medicine and to improve health outcomes for future patients, as evident in documented perspectives from physicians like Dr. Dosseter: "…the goals of [Dr.Dosseter's] research team were, first, to study the human leukocyte antigen (HLA) system in the Inuit and, second, to apply this knowledge to test theories about the impacts on skin grafts at the time when the field of organ transplants – including transplant rejection – was still being actively studied." (1, p.158) However, by inflicting such pains upon young test subjects who had minimal to no understanding of English, their pursuit for knowledge directed by 'beneficence' for future patients led them to ignore two other ethical pillars of medicine: to 'do no harm' and to respect

patient autonomy. It is a powerful reminder for modern medical researchers to carefully consider the ethics and motivations of their research, including informed consent and patient autonomy.

In short, through his poignant reflections and carefully curated breadth of historical examples, Dr. Shaheen-Hussain successfully illuminates not only the complacency but the culpability of the Canadian medical system in perpetuating systemic violence against Indigenous children. He does this by relying on direct quotations from Indigenous People and offering his perspective as a medical expert. History cannot bear to repeat itself and Dr. Shaheen-Hussain engages the reader in an important dialogue on how to move forward. This book is an uncomfortable but meaningful read, especially for those interested in or belonging to the healthcare field.

Fighting for a Hand to Hold is available at your local independent bookstores, and online at Left Wing Books or McGill-Queen's University Press. The French version, *Plus aucun enfant autochtone arraché: Pour en finir avec le colonialisme médical canadien* published by Lux Éditeur, is available on their website.

2 | REFLECTION: A MEDICAL STUDENT'S PERSPECTIVE

I struggled to finish reading this book, but not for lack of interest. It was not pleasant to read about the forced transmission of smallpox in the 1860s and sterilization of Indigenous girls in the 1970s. Amid my visceral reaction of disgust, however, I realized that I had the autonomy and privilege to act on my circumstance. This was a choice that did not exist for Indigenous Peoples, who experienced violence and detrimental health outcomes at the hands of the Canadian healthcare system. Yet, despite being the subjects of centuries-long marginalization, discrimination, and genocide, Indigenous Peoples have shown extraordinary resilience by not simply surviving, but continuing to advocate for their rights to their stolen lands, self-determination and self-governance. Moreover, as Dr. Shaheen-Hussain mentions in the audio interview, these instances of violence are "not an exhaustive or comprehensive study of the issue." Indeed, these inequities continue to persist. I acknowledge that my learning will continue beyond this book.

Thus, Dr. Shaheen-Hussain's humble writing encouraged me to engage in reflective practice, which is repeatedly emphasized throughout our medical training at McGill University. Change begins with a sense of ourselves, and this book has held a mirror to my own experiences as a Chinese Canadian and as a medical student.

I admit that I possess my own biases about Canada and its perceived diversity. When I first moved to Calgary, the "cleanest city in the world" (5), I envisioned it only as the place of cowboys, AAA beef, wealth, and oil. I was unprepared for the sight of the precariously housed, hopping on and off the CTrain between the free-ride zone. It was almost comical to see how the expensive tailored suits jutted out from a grey backdrop of tattered and stained jackets – a visual reminder that even one of Canada's wealthiest cities was unable to care for its most vulnerable, many of whom were Indigenous. As a younger version of myself, my preconceived notions about others – as well as about my own capabilities – delayed any meaningful action. Meanwhile, my memories from that time in Calgary are still tinged with the shrieking taunts of "konichiwa" across the street and the leering Caucasian male at the Calgary Stampede breathing "ching-chong, ching-chong" into my face. In those callous moments, I felt the weight of intolerance. Yet, could I condemn others for their behaviours, as I condemned my own lack thereof? I wonder now which one ultimately leads to more pain: action or inaction?

As a medical student, I have become more engaged in anti-racism, with much credit to the recent attention to the Black Lives Matters movement and increased accessibility to educational resources. In my own "activism", I have acquired a better appreciation for the role of medical education systems in promoting health equity. Notably, as a volunteer for the Anti-Racist Undergraduate Medical Education Curricular Review at McGill, which was organized by several motivated peers, I helped conduct a critical evaluation of educational materials in the pre-clerkship curriculum. This activity forced me to ex-

amine a hidden curriculum, as Dr. Shaheen-Hussain mentions in his book. I assessed each statistic, epidemiological map, image, and sentence. In doing so, I flagged slides where skin conditions were only represented in light skin tones, maps that showed health outcomes but omitted the historical context of slavery and colonialism, images that desensitized us by overrepresenting suffering and emaciated black bodies, but rarely the healthy. I discovered how even the invention and scientific basis of some clinical measurement tools perpetuated discriminatory attitudes. For instance, the practice of race 'correction' in spirometry was based on racist studies performed on Black slaves and used to justify their position in society due to their perceived lower lung capacities. (6) Today, the use of these tools can potentially lead to inaccurate measurements of lung capacity, which can in turn underestimate disease burden and result in implications for fair compensation and treatment for Black patients. (7)

I now have more tools to address injustices than before. As a medical student, I recognize there are ways to advance healthcare beyond basic science research, which includes advocacy through medical education. With this knowledge, I am inspired to think more critically about how I choose to spend my spare time. Every step towards educating myself is now contributing to the greater goal of helping others as a healthcare professional. The question is no longer 'why am I uncomfortable with racism?', but 'how can I best serve marginalized and racialized populations as a future physician?' I recognize that being an effective advocate will require ongoing self-education.

I'll reiterate that this book is not an easy read by any means. It is distressing. However, it delivers a necessary shock and I believe readers should be educated about its content, especially for future (and current) physicians, and other allied health providers. It imparts knowledge on Canadian-Indigenous history that reminds us of our duty to prevent harm like the death of Joyce Echaquan, who was the subject of racial epithets and slurs moments before her passing. (8) As front-line providers, the lessons learned from the exploitation of Indigenous Peoples challenge us to practice culturally safe care. Many of our future patients will be of cultural backgrounds different from our own, and as much as 5% of the Canadian population is Indigenous. (9) Besides responding to diverse needs, practicing compassionate care leads to improved health outcomes. (10) By advocating for the needs of a specific group that was disproportionately affected, the #aHandtoHold campaign effectively ended non-accompaniment for all children in remote areas of Quebec. This makes the #aHandtoHold campaign a compelling case study that demonstrates how health policy benefits everyone, not just those who are the target of the intervention. This is the essence of equitable access to care.

Those who are moved by the traumatic stories told in *Fighting for a Hand to Hold* might be inspired to reflect more critically on how they can be contributors of culturally-safe clinical care to the benefit of not only Indigenous Peoples, but the diverse Canadian population at large. By detailing the history of the Canadian medical system's culpability in violence against Indigenous people, *Fighting for a Hand to Hold* asserts itself as an essential resource for all Canadian healthcare professionals and trainees. I hope that we can stand together in solidarity with our Indigenous patients when advocating for equitable health care, while simultaneously offering the compassionate and quality care that all Canadians deserve.

3 | ACKNOWLEDGEMENTS

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EDITORIAL

Artist: Caroline Najjar

EDITORIAL
McGill Journal of Medicine

Exploration of Social and Political Factors that Impede Migrant Healthcare Availability and Access in Canada Amidst COVID-19

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ABSTRACT

Canada is a leading nation for international migration, yet fails to adequately respond to the healthcare needs of migrant populations. In this editorial, we explore why this is so. We posit that the reactive approach of the systems and stakeholders responsible for assuring healthcare access during the COVID-19 pandemic has been detrimental to our vulnerable and marginalized populations, and by extension, all citizens. Now, amidst a second wave of COVID-19, we must act – more decisively and compassionately than ever before, with the support of rigorous research and co-designed sustainable strategies. Otherwise, we remain bystanders abetting a system that has failed to effectively address the health needs of those that enter this country seeking a better life.

KEYWORDS
Migrants, Access, Health Policy, Health System, Canada, Inequity

1 | INTRODUCTION

Canada has a global reputation for attracting and welcoming international migrants, including temporary workers, students, refugees and asylum seekers. (1) Yet, as a nation, we consistently fail the migrants crossing our borders with respect to their healthcare needs and access. (2-4) International migrants face numerous and longstanding barriers to care, magnified in complexity as a result of their diversity in origin and legal status within

Canada. (2,3) While these issues have been raised in Canadian political discourse, policy attention remains limited. (5) The COVID-19 pandemic has served to bluntly resurface many of these barriers to care among international migrants, whose particular vulnerability to COVID-19 is well-documented. (4-8) For many, cultural and language barriers, alongside overcrowded living conditions, present challenges in being able to observe public health advice and measures. (4-6) For others, poor or insecure working conditions, financial precarity, and stigma from host populations heighten vulnerability by increasing the fear associated with seeking treatment or disclosing symptoms. (4, 6)

Although some measures have been taken to facilitate access to care amidst COVID-19 for some migrant populations in Canada, such as the expansion of public health insurance in certain provinces, these measures appear temporary and have been poorly communicated. (4) The ambiguity of these initiatives and their inconsistent implementation has furthered injustices towards migrants. (7) Furthermore, while media reports and scientific literature have highlighted unacceptable disparities in healthcare access among migrant populations, discourse around why these disparities exist and why addressing them is difficult is less apparent. In this editorial, we explore three reasons for our lack of headway in advancing policies and actions to assure healthcare access to international migrant populations living in Canada, both during and beyond the COVID-19 pandemic.

2 | PRESSURE, SPOTLIGHT, AND REPERCUSSIONS

Despite the persistent demand by activists for political action to improve healthcare provision for international migrants in Canada, (2, 3) as well as the spotlight that COVID-19 has placed on the injustices towards migrant populations, (4-8) action has been slow. It is not until there are "unacceptable" or "unpopular" consequences affecting the general Canadian populous that political action seems to occur. Consider the treatment of migrant farmworkers across Canada, whose crowded housing conditions have triggered several outbreaks during the COVID-19 pandemic. (4, 5) Outbreaks among this population, who comprise 10% of all agricultural workers in Canada, occurred in the spring, sparking concerns about a possible food shortage. Only with this threat to Canadian food security did action seem to be triggered on the policy front. (5)

3 | CONFUSION AND DIFFUSION OF RESPONSIBILITIES

The complexity and labyrinthine processes of health policy and decision-making have also contributed towards delays in establishing and implementing needed reforms in healthcare access for international migrants. There appears to be a lack of clarity in terms of who holds responsibility and decision-making "power" among both the general public and policymakers themselves. This confusion regarding accountability has contributed towards a diffusion of responsibility across various levels of the health and policy landscape. Exemplifying this is the stop-gap measure whereby the federal government allocated funds to farm owners (i.e., $1,500 per worker) in order to address migrant farmworker housing issues (i.e., provide migrant workers with suitable accommodation and supplement salaries while they quarantine). (5) However, without appropriate oversight and attention to where this money was directed, farmers may have misused these funds and possibly pressured migrants to work during quarantine periods. (5) Preferable to a one-off allocation would be the implementation of provincial or federal policies to prevent the situation from happening in the first place by protecting the rights of migrant workers. For instance, two key policies in this regard include "income support and open work permits for migrants who will lose wages or jobs because of sickness, quarantine, or economic downturn" and "access to paid emergency leave as needed, with a minimum of 21 days for all workers, regardless of immigration status." (5)

4 | ECONOMIC ESSENTIALITY

Enacting federal or provincial health policy changes that address inequities in migrant healthcare becomes even more complex given that migration policy is largely motivated by economic interests. For example, migrant populations that bolster the economy in their respective provinces seem to be the ones that receive quicker support and action from the government. For instance, in Québec, regulations for international students were established relatively rapidly, given their financial importance in supporting institutions of higher education, and the overall provincial economy. (9) Additionally, those migrant populations providing essential services during the first wave of the COVID-19 pandemic were given accelerated healthcare and social support. (8) By contrast, less economically attractive migrant populations, such as undocumented or illegal migrants who may be more vulnerable to COVID-19, have yet to see measures taken on their behalf. (7) Unfortunately, this tendency to view the deservingness of action (i.e., provision of care or legal status) as a function of essentiality of international migrants to individual provinces or the national economy is not exclusive to Canada, nor confined to the current pandemic. (10)

5 | MOVING FORWARD

The social and political context in which we attempt to address the healthcare needs of those among the most vulnerable in our country is highly complex. The demand and rationale for policies that provide equitable access to migrant healthcare are strong, especially given the urgency for strengthening public health measures during the pandemic. However, unclear jurisdictional responsibilities, diffusion of responsibilities, and lack of a long-term vision impede serious policy attention. Exploring these ideas further through the systematic analysis of policy statements, journal articles, and media reports is necessary. Moreover, the co-development of actionable strategies by political and health decisions makers will be especially critical as we transition into a period of vaccine provision, the uptake of which may be resisted by migrant populations overlooked in public health efforts.

The reactive approach that we have historically pursued in addressing inequities in healthcare access has been detrimental to our vulnerable and marginalized populations, and most notably to international migrants. As advocates of universal healthcare in Canada, at a time where it is essential to safeguard the health of all people in our boarders, we must act now – more decisively and compassionately than ever before. Otherwise, we remain bystanders abetting a system that has failed to effectively address the health needs of those that come into this country seeking a better life.

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LETTER TO THE EDITOR

Artist: Jenny Xinyu Ji

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On the Measure of Intelligence During the COVID-19 Pandemic

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> *"I propose to consider the question, 'Can machines think?' This should begin with definitions of the meaning of the terms 'machine' and 'think'."*
>
> *Alan Mathison Turing, Mathematician*

Dear Editor,

There are two commonly accepted ways to conceptualize intelligence. One involves competency in certain skills, such as problem-solving. The other, more abstract – dare I say innate – view holds that *being good* at a specific task is an insufficient condition for intelligence. Historically, the medical and artificial intelligence communities have grappled for position vis-à-vis these philosophies, with each side staking its claim for the more "authentic" definition of intelligence. This dispute has endured, for the most part, unresolved since the advent of artificial intelligence and its first foray into healthcare applications in the early 21st century. What is occurring when data scientists leverage massive quantities of data to replicate complex clinical decision-making, while still failing to teach a machine to correctly *think* about disease? This simultaneously validates imitative capacity as a metric for intelligence (machines can learn from infinite correct or incorrect diagnoses, far more than any human physician can absorb throughout an entire career) and preserves the medical profession's breadth of clini-

cal expertise and logic.

The COVID-19 pandemic has been an opportunity for armistice between technologists and clinicians. In the setting of unlimited priors, a machine can master a specific sequence of actions while disguising its poor proficiency in other tasks. In the case of a novel virus, longitudinal training data from the clinical setting is extremely limited and the body of scientific evidence is growing at an unprecedented pace. Physicians with general expertise are poised to lead the fight against COVID-19 while leveraging the throughput of technology to synthesize an updated account of what is known about the disease, its treatment and manifestations. There is an onus on both physicians and data scientists, as well as the larger research community, to work together in order to improve the infrastructure for assistive clinical technologies. Medical experts can create standardized data collection protocols in the clinical setting and provide feedback to inform the iterative design of AI technologies. At the same time, computer scientists can publish reproducible code and contribute to the translation of evidence into practical insights for immediate clinical implementation.

It is my hope that collaboration during these trying times will foster long-lasting bonds between the medical and AI communities. Physicians should be equipped to participate in technical conversations and optimize data collection for use by their peers, within and beyond medicine.