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Contact
DMJ, Box 201, Sir Charles Tupper Medical Building, Dalhousie University
Halifax, Nova Scotia, B3H 4R2
dmj@dal.ca
www.dal.ca/dmj

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Editor's Message

COVID-19: A look back, one year into the 2020 pandemic

Dan Vidovic

It has now been approximately one year since the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was identified as the causative agent of coronavirus disease 2019 (COVID-19). In the past year, scientists and healthcare workers have repeatedly needed to shift their practices as an endless supply of research continued to reshape their understanding. This past year has shown us the importance of global collaboration and unity. In the next few paragraphs, I'll briefly touch on some of the major points of the COVID-19 pandemic and provide brief updates on some of the initial evidence

It is believed that patient zero can be traced back to a 55-year old man from Hubei, China who contracted COVID-19 in Nov 17, 2019, over a month before cases appeared in nearby Wuhan at the end of December 2019[1]. More recent evidence, however, shows this may not be the case. Serological blood testing of Italian patients enrolled in a lung cancer screening trial for SARS-CoV-2 antibodies revealed that up to 14% of trial participants had either IgG or IgM antibodies against the virus as early as September 2019, over two months before the hypothesized patient zero contracted the virus in Wuhan[2]. Given that an antibody immune response takes weeks to develop, it is possible the virus was present as early as the summer of 2019; this new information could reshape the history of the pandemic.

While initially thought to have had its zoonotic origins in a wet market in Wuhan, tissue samples of market animals reveal an absence of virus[3], making it unclear exactly where or when the virus made the jump from animals to humans. Pre-existing coronaviruses nearly identical to SARS-CoV-2, which are able to infect human cells in vitro, have been circulating in bats for years[4,5]. Furthermore, novel coronaviruses similar to SARS-CoV-2 have been found in pangolins as well[6,7]. Currently, it is thought that bats serve as the initial source of a myriad of coronaviruses, including high-risk strains capable of possibly infecting humans and those which are spread to pangolins. Pangolins are therefore likely the reservoir host, which mediate virus mutation and zoonotic transmission to humans. Indeed, pangolins were sold at wet markets throughout Chinese cities, including at the Wuhan market thought to be the initial origin of SARS-CoV-2. Again, with the potential of a new timeline for the virus' inception, it may be possible that the Wuhan wet market simply mediated a superspreader event, rather than being the initial birthplace of SARS-CoV-2. Only further time and epidemiological study will reveal the exact origins of SARS-CoV-2.

Early on in the pandemic, in the absence of any substantial evidence, hydroxychloroquine (often in combination with the antibiotic azithromycin) was claimed to be an effective treatment for COVID-19[8,9]; a claim that was prematurely and grossly overstated by both media and politicians alike. We now know that this combination treatment is mostly useless, and in fact causes marked QTc prolongation and liver toxicity compared to placebo-controls[10]. Remdesivir, an antiviral drug originally developed and unsuccessfully used by Gilead Sciences in 2009 to treat hepatitis C, RSV, Ebolavirus, and Marburg virus, was also in the spotlight early in the pandemic, as it had previously demonstrated anti-viral effects against SARS-CoV-2 in vitro[11]. Ongoing uncertainty in the evidence collected by numerous trials (some of which showed benefit, and others which did not) over the last 9 months have ultimately lead the World Health Organization (WHO) to recommend against the use of remdesivir for COVID-19[12]. To date, the only WHO-recommended treatment for severe to critical disease is systemic corticosteroids such as dexamethasone[12]. Since the late acute respiratory distress syndrome-like manifestations of COVID-19 are mostly due to cytokine storm rather than viral replication[13], these evidence-based recommendations seem appropriate.

In the last year, it has become abundantly clear that there is little prospect in identifying "magic bullet" medical treatments to significantly improve COVID-19 patient outcomes. For that reason, many biopharmaceutical companies immediately began assembling vaccine platforms to assess for the possibility of a vaccine against COVID-19. Moderna, the first company to produce a vaccine candidate, began platform assembly in January 2020, just over a month after China had announced the emergence of the novel respiratory virus. This fast turn-around-time is in part due to the simplicity of their platform. The vaccine is a messenger RNA (mRNA), a simple molecule that provides instructions to the host's cells to create SARS-CoV-2 spike protein. The spike protein is then recognized as antigen to the immune system, which produces a potent immune response. The most recent results of Moderna's phase III trials, just released in mid-November, reveal a very promising 94.5% efficacy with no serious adverse

events in trial participants[14] (these results have not been peer-reviewed by a journal, but are pending review and approval by the FDA and other regulators). A very similar platform also using an mRNA encoding a modified spike protein developed by BioNTech (and manufactured by Pfizer) had preliminary phase III findings revealing a 95% efficacy[15]. Both of these vaccines are the first mRNA-based platforms to be trialed in the world; the long-term efficacy and safety of these platforms has yet to be determined. However, their ability to be rapidly mobilized and adapted to different pathogens (requiring just an mRNA sequence of a potential antigen) may change the course of vaccinology indefinitely. The Pfizer and Moderna vaccines are both currently expected to be granted emergency use approval in multiple countries in coming days or weeks. Over 50 other vaccine candidates are still undergoing phase I-III trials[16].

The speed at which this pandemic has propelled global scientific unity and advancement has likely never been seen in the history of humankind. As of writing this editorial, there have been over 76,000 publications indexed on MEDLINE under the search term "COVID". This is significantly more research published this year on COVID than HIV, hepatitis C, influenza, and Ebola combined. The collective efforts of hundreds of thousands of scientists, healthcare workers, and members of the public has been paramount in putting up a fight against this pathogen. Immense sacrifices have been made, and many loved ones lost. In a sense, this pandemic has matured us as a human race. For the past year, many of us have lived a new normal: unable to socialize, see loved ones, missing important life milestones, losing jobs, and mourning for life to go back to the way it was. Many have realized what we take for granted in everyday life, and how difficult it can be to cope in the absence of our normal routine. It has been a long, isolated, and difficult year, but we're now just beginning to see the light at the end of the tunnel. Barring any major challenges with vaccine uptake, we should see a slow return to normal over the next year. And hopefully, in one to two years' time, this journey we've all unwillingly taken will just be part of our collective history.

Dan Vidovic
Editor-in-Chief

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Personal Experience

Lessons from long-term care

Hayden P. Nix, BSc MASc[1,2], Ellen Parker, BSc PhD[1,3]

1. Both authors contributed equally.
2. Medical Student – Western University
3. Medical Student – Dalhousie University

We saw the call for help in the news. There was a COVID-19 outbreak in a long-term care (LTC) home. As the outbreak flared, half of the staff stayed home. The LTC home needed assistance with the daily care of residents, and we were living right around the corner. A few weeks prior, we had finished our exams at the end of the first (EP) and second year (HPN) of medical school. For years, we had been telling ourselves that we wanted to become physicians to help others. This was our chance.

We contacted the LTC home and were hired as patient care attendants. Alongside others who responded to the call, we moved into a nearby hotel to protect our families and began work. Because of our lack of experience in caring for residents, we were assigned to a section of the LTC home with only one COVID-19 case. Our orientation session turned into a 12-hour night shift. It was the first night shift of our careers.

By the time we started work, the outbreak had been ongoing for a week and the LTC home was locked down. In the other section of the building, nearly all of the residents were infected and several had already died.

Visitors were not permitted to enter the LTC home, and residents were required to stay in their rooms. Cleaning staff clad in hazardous materials suits sanitized every room three times a day. Meals were no longer taken in the dining room, and opportunities for exercise were strictly limited. Even mail delivery was disrupted.

Two residents were separated from their spouses, who had been sent to hospital and recovered, but were not permitted to return to the LTC home. The condition of a few residents had declined such that they required a higher level of care than available, but transfer to another facility was barred. Many residents had trouble managing email; some had hearing impairments that made video calls or using the telephone difficult. They were afraid and alone at a time when human connection is vital.

Despite these hardships, the humanity and resilience of the residents shone through. As we built relationships with them, they welcomed us and taught us how to help them and their neighbours. They shared stories about their lives. Tales of building warships, long-haul truck driving, living in West Germany during the Cold War, underground cigarette cartels, and impromptu trips to Las Vegas continued to surprise and delight us. Humour came in all varieties (sometimes wholesome, other times lewd). And each evening, a collective joy spread through the home as the tune signaling Final Jeopardy echoed through the halls.

Our experience working in the LTC home was transformative. At first, the gap between online learning and hands-on resident care was overwhelming. Knowing the mechanism of action of atypical anti-psychotics is not helpful when a resident is hallucinating and wandering without his walker at 3 a.m. The pre-clerkship curriculum does not cover how frightening thunderstorms are for some, or how to help a resident worried about her grandson get back to sleep.

But, guided by the residents and staff, each day the gap lessened and it was ultimately bridged. We learned the residents' habits and preferences. We became acquainted with the names of their stuffed animals, so that we could bid them a proper "good night" too. We were instructed in transferring residents safely. For those who needed it, we assisted with bathing and toileting. Caring for someone who is vulnerable is an act of intimacy. The opportunity to help these people in such personal ways was, for us, a privilege.

We were inspired by our colleagues who also answered the call for help. Some were local, others travelled from another province to help. We were united by the common goal to provide care for those in need.

The nurses and other experienced employees in the LTC home led from the front, demonstrating courage and compassion through every resident interaction. And they were mentors to us, patiently teaching us the subtleties of resident care. These lessons will stay with us throughout our careers.

As the outbreak in the LTC home ended and our time drew to a close, it was difficult to say "goodbye" to residents and staff alike. After negative tests and a

precautionary isolation period, we emerged from the hotel to find many public health restrictions lifted. Bars and restaurants were open, restrictions on gatherings had eased, and people were eager to return to something resembling normalcy. With time, we too have felt the pull to return to normal life.

But now a second wave of COVID-19 is upon us. Residents and staff in LTC homes are yet again becoming infected. As we reflect on the costs of easing restrictions, our thoughts are of all affected residents–with their stories, humour and humanity–and the privations they will have to endure.

Original Research

Decision thresholds and minimal important difference estimates for evidence-based practice and policy

Part 2: Threshold concepts in biostatistics and epidemiology

Beth McDougall, MSc, PhD Candidate[1], Mike Reid, MMM, MSc, PhD Candidate[1]
Souvik Mitra, MD, MSc, PhD Candidate[1, 2, 3], Bradley Johnston, PhD[1]

1. Department of Community Health and Epidemiology, Dalhousie University, Halifax, Nova Scotia, Canada
2. Department of Pediatrics, Dalhousie University, Halifax, Nova Scotia, Canada
3. IWK Health Centre - Halifax, Nova Scotia, Canada

Abstract

Understanding core concepts in epidemiology and biostatistics is crucial for evidence-based clinical practice and policy. In this second installment of our two-part series on threshold concepts, we transition from understanding the ubiquitous p-value to tools and measures for decision making among clinicians-in-training, highlighting the growing importance of utilizing explicit and evidence-based approaches to make appropriate and efficient decisions. We review two related decision-making concepts: (1) Minimal Important Difference (MID) estimates and (2) Decision Thresholds, focusing specifically on patient-reported outcome measures (PROMs). These terms and many other related expressions are used regularly, and often interchangeably, but what are they? Why are they valuable? And how can they be used to support evidence-based decision-making in clinical contexts and develop strong clinical practice guidelines? We conclude our brief review on the utility of these measures with a spotlight on a local example of how the theory underlying MID estimates and decision thresholds is currently being embedded in electronic platforms in primary care contexts targeting depression in Nova Scotia.

Introduction

Understanding and applying threshold concepts such as minimal important difference (MID) estimates and decision thresholds is crucial for evidence-based clinical practice and policy. In the first installment of this two-part series on core biostatistical and epidemiological concepts[1], we learned about the ubiquitous but often misunderstood p value[2] and how it simply serves as a starting point when appraising research to better inform clinical decision making. In this second installment, we move beyond statistical significance, and address two related decision-making concepts: (1) MID estimates and (2) decision thresholds, focusing specifically on patient-reported outcome measures (PROMs). These terms and many other related expressions are used regularly, and often interchangeably[3], but what are they? Why are they valuable? And how can they be used to support clinical decisions? Clinicians and researchers acknowledge the critical role of disease symptoms, as well as the function (e.g. mental, physical) and perceptions of general well-being for evidence-based decision-making. Typically measured by direct patient inquiry, these outcomes, previously referred to as 'health-related quality of life' (HRQL), are now most commonly referred to as PROMs, and measure patient perception of health and well-being, such as pain or depression severity. PROMs provide patients' perspectives on treatment benefits and harms and are often the outcomes of most importance to patients[4]. While there is significant research on the reliability and validity of established PROMs[5], less is known regarding how to interpret changes or differences in scores, and what indicates a potentially clinically meaningful difference, which can also serve as a decision threshold.

MID Estimates

The MID can generally be described as the *smallest difference* in an outcome of interest perceived to be important and that would lead a patient or clinician to consider a change in treatment or management[6]. The MID is exclusively used in the context of outcomes that are being examined on a *continuous scale*. For example, the patient-rated Beck Depression Inventory (BDI)[7] measures depression severity on a continuous scale from 0 to 63. What minimal change in score would a patient (ideally) or clinician deem important to suggest a potential change in treatment or management?

As outlined by King et al.[3], there is no universal MID that can be used for all PROMs across all populations.

However, an effect size (a quantitative estimate of the magnitude of change) based on distribution-based methods between 0.2 and 0.5 standard deviation (SD) units has been offered by Cohen as a rule of thumb[8], while Norman et al.[9] has suggested that the universal MID is half the SD of the baseline score. In addition to these suggestions, since criticized[10], multiple methods to estimate MIDs have been developed[3,11]. Of the many methods that exist, recent research generally advocates for the anchor-based approach, methods that typically involve working with actual patients to arrive at the best estimate of change that matters to patients[4]. This approach incorporates patient values by comparing the relationship between the target PROM and an anchor relevant to patients, such as global ratings of change in symptom severity[4]. Applied to the context of evidence-based decision-making for practice or policy, the choice of MID should be supported by a primary study that establishes an estimate of the MID using anchor-based methods, or a systematic review of such studies[12]. For the BDI, in particular, new research using anchor based methods has suggested that the MID can range anywhere from 17.5 to a 32% reduction in scores from baseline, with this percentage change being highly dependent on the baseline severity of depression[13].

Unfortunately, using MIDs for clinical decision-making, and using established MIDs to develop practice guideline recommendations is often challenging as there is currently no definitive resource that describes all established PROM-specific MIDs[4]. There is, however, research detailing a framework for appraising the quality of anchor-based MID estimates underway, and the application of the framework to over 300 PROMs is under-review[14]. Until this definitive resource is published, those who wish to search for MIDs are left to conduct their own search of the literature and to interpret the estimates based on their own judgement. Moreover, we are unaware of similar work for distribution-based MID methods. Despite these challenges, the best MID estimates should be sought for PROMs as they provide a clear indicator of the minimal change that patients consider important for a change in treatment or management[13]. Further, MIDs are important estimates for sample size calculations in clinical trials and for making clinical guideline recommendations to evaluate interventions evaluated for PROMs.

Decision Thresholds

When we think of a decision threshold in the context of clinical practice decisions, we are considering the boundary to sway a decision and related action in one way versus another[3,6]. For an outcome that has been dichotomized, a threshold, or cut-off value is used to assign a person to one of the two categories. Clinically, a decision made using a binary decision threshold can strongly impact the approach to treatment. For example, a patient who no longer meets the threshold for clinical depression may be viewed as responding favorably to a recent treatment, such as an antidepressant, and may be monitored less frequently by the treating clinician. Within clinical research, not meeting the threshold for clinical depression may exclude a potential participant from a randomized clinical trial of alternative management strategies for depression. What decision threshold estimate should be used to determine if a patient is likely to be clinically depressed or not?

For health-related status such as depression symptoms measured on a continuous instrument, there are various methods for arriving at a decision threshold. Ideally, if the instrument in question is a PROM, the threshold used should be the best estimate of the MID derived using anchor-based methods4. If the instrument is not patient-reported (e.g. Hamilton Rating Scale for Depression, Montgomery Asberg Depression Rating Scale), the threshold is likely to be determined by clinical consensus or through the use of distribution-based MID methods such as half the baseline standard deviation (SD)[9], a method with universality but that may be oversimplistic[15]. Regardless, clinicians should be aware of the minimum and maximum scores of the instrument, whether a higher score is considered desirable or undesirable, and, when available, the best estimate of the decision threshold or MID. For instance, the Montgomery Asberg Depression Rating Scale[16] contains 10 items, each scored 0-6, with a total possible score between 0 and 60. Mild depression is associated with a score of 12 to 23. Therefore, a threshold score of 12 is often used for diagnosis or a change in clinical management. However, the distribution-based MID estimate suggests a minimum change of 3 in the overall score for determining treatment decisions[16-18].

The decision threshold estimate will differ depending on the measure being used, including the validity and reliability of the measure and the severity and heterogeneity of the condition itself[19]. Decision thresholds on established rating scales for depression with sound measurement properties not only vary by measure, but can also vary by patient characteristics such as age, sex, and clinical profile[20,21].

In the context of clinical decision-making, decision thresholds are attractive as they provide a simple tool to allow the translation of a continuous score on a measure to a 'yes' or 'no' decision. However, with multiple methods of generating decision thresholds being published, the threshold could vary greatly[22,23]. Typically, the optimal decision threshold for a continuous measure such as depression severity is

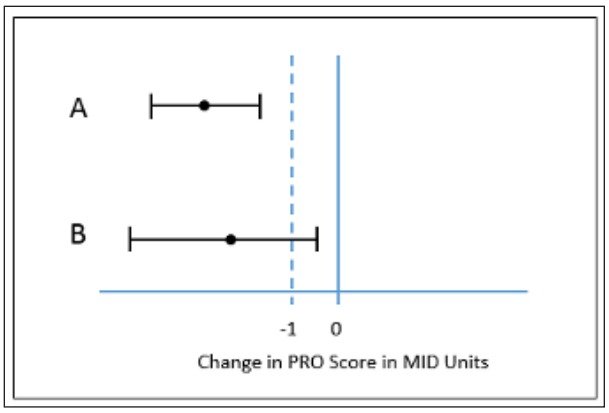

Figure 1. Two hypothetical interventions in which a lower PRO score is deemed better. Intervention A demonstrates a treatment effect that is to the left of the decision threshold (the associated MID), and represents a significantly large and precise treatment effect. Intervention B includes the MID decision threshold, and the quality of evidence for this comparison would be rated down for imprecision (wide confidence interval).

derived from the best estimate of the MID[24].

The value of MID in primary mental health care

There has been a notable increase in cases of depression over the past ten years[25,26], with the highest rates of mood and anxiety disorders being found in Canadians between the age of 15 to 24[27]. Most patients who seek treatment for depression are treated in primary care contexts through a trial and error process of identifying the appropriate antidepressant medication or behavioral or psychological support(s). Primary care clinicians are faced with the challenge of making evidence-based clinical decisions collaboratively with their patients typically in very short consultations. Approaches to simplify decision making, such as using established MIDs can support this challenging task.

For example, in the primary health care context in Nova Scotia, the Maritimes Depression Registry is being piloted among primary care providers and patients with depression[28]. The freely available web-based application houses a battery of standardized measurement tools and allows clinicians and patients to regularly complete PROMs, such as depressive severity using the BDI. Instruments are automatically scored, and established MIDs and decision thresholds, where available, are highlighted for clinicians when considering clinical treatment decisions. Standard clinical practice guidelines are also embedded in the tool and individualized recommendations can be made tailored to patients' self-identified personal goals for recovery.

Capitalizing on the notion of measurement-based person-centered care, the tool is a local demonstration of the potential value that can be added by incorporating the best estimates of MIDs for routine clinical care for patients with depression. Challenging clinical decisions, such as starting or discontinuing antidepressants, are facilitated by visual cues of MIDs and decision thresholds on established measures, where available.

Ultimately, if it exists for a given PROM, decision makers should find the best estimate of the MID and consider where the MID lies in relation to the best estimate of effect and the corresponding 95% confidence interval (CI). If the effect estimate surpasses the MID, a treatment or management decision is well-supported (Figure 1). Figure 1 offers a visual representation of this using two hypothetical interventions. Intervention A demonstrates a treatment effect that is to the left of the decision threshold (the associated MID) and represents a significantly large and precise treatment effect. Intervention B includes the MID decision threshold, and the quality of evidence for this comparison would be rated down for imprecision.

Conclusion

We have reviewed important concepts, namely decision thresholds and MIDs, and have highlighted a local example of how the theory underlying these concepts is currently being embedded in electronic platforms in primary care contexts targeting depression in Nova Scotia. Decision thresholds and MIDs – particularly anchor-based MIDs for PROMs – are important concepts and can provide valuable information for decision makers.

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Review Article

Application of the Canadian Cardiovascular Society's heart failure guidelines in a heart function clinic

Brynn Victoria Margaret Aucoin, BSc[1], Robert S. Stevenson, MD CCFP FRCPC[2, 3]

1. Doctor of Medicine Candidarte 2021, Dalhousie University
2. Associate Professor, Dalhousie University
3. Cardiologist, Horizon Health-NB Heart Centre

Abstract

Keywords: Heart Failure, Guideline Adherence, Evidence Based-Practice
Purpose: Heart failure is a significant diagnosis that poses serious mortality and morbidity risks. Many studies have assessed the efficacy of evidence-based guidelines in improving patient outcomes in the management of heart failure; however, there is limited data on how these guidelines are applied in clinical practice.
Methods: A retrospective, cross-sectional approach was used to examine a physician's adherence to the Canadian Cardiovascular Society's (CCS) most recent practice guidelines on managing heart failure. Data was collected from electronic hospital health records and patient charts of patients enrolled in a heart function clinic. Qualitative and quantitative analyses were done to compare current clinical practices related to investigations, treatment, and follow-up to the guidelines.
Results: A total of 37 patients met inclusion criteria for this study (n=37). The majority of patients were males, 81%, with an average age of 71 years, 10 medications with 5.5 comorbidities. Recommendations regarding wait times, frequency of follow-up, and blood work were met 97%, 78%, and 64% of participants, respectively with most patients being reassessed more frequently than the guideline recommendation. Medical therapy recommendations were met in over 70% of participants. All participants had EF assessments as frequently or more frequently than guideline requirements.
Conclusion: Overall, the Heart Function Clinic practices assessed in this study align well with the current guidelines recommended by the CCS. Although this study is by no means comprehensive, it provides an initial glimpse into how practice guidelines may be applied in clinical practice and identifies areas where further work needs to be done.

Introduction

Heart disease is the second leading cause of death in Canada and poses significant costs to our healthcare system[1] through a high number of hospitalizations, high readmission rates, and outpatient visits[2]. Patients with heart failure (HF) have high rates of morbidity and mortality and its prevalence has been increasing in recent years. The incidence of HF is expected to continue to rise in the coming years[2] as well. Due to the increasing burden being placed on the healthcare system, and the burden this condition places on individuals and their families, it is essential that the care these patients receive is optimal, to improve patient outcomes and decrease stress on healthcare systems.

Evidence-based practice guidelines are created by the Canadian Cardiovascular Society (CCS) and are regularly updated and disseminated to reflect current knowledge which can help to provide the best possible care to patients and to improve outcomes. Adherence to heart failure guidelines in Austria, specifically regarding medical therapies, has been shown to decrease long-term mortality[3]. Evidence-based guidelines are the standard of care against which physicians are held when treating patients with HF and can improve patient outcomes and decrease cardiac events[4].

It has been shown that despite evidence supporting the efficacy of guidelines, many physicians do not meet recommended targets around HF management[5]. Multiple studies conducted in the US have consistently found low rates of physician adherence to evidence-based practice guidelines in the treatment of HF with rates ranging from 33% to 63%[6,7]. One study, by Atwater et al.[8], examined the rates of guideline adherence and suggested that they may be underestimated due to the lack of accountability for therapeutic contraindications. Another study, based on the European Society of Cardiology HF guidelines, found better adherence rates when contraindications to recommended therapies were taken into account[9].

In Canada, there is limited data on how evidence-based guidelines for the treatment of HF

are applied in clinical practice. By exploring the current practices regarding guideline adherence in the management of HF, it may be possible to improve the use of these evidence-based practice guidelines in the future..

Methods

This study is a retrospective, cross-sectional analysis conducted to examine one physician's adherence to national practice guidelines conducted at the Saint John Regional Hospital. Staff of the Heart Function Clinic screened potential participants to the inclusion criteria. Inclusion criteria were patients of the Principal Investigator who were ≥18 years old, diagnosed with congestive heart failure, being followed through the outpatient Heart Function Clinic at the Saint John Regional Hospital, and who consented to participate. Patients were classified into three groups based on their most recent left ventricular ejection fraction (EF) assessment, in accordance with the CCS guidelines, as either heart failure with preserved ejection fraction (HFpEF) with an EF ≥50%, heart failure with mid-range ejection fraction (HFmEF) with an EF 41%-49%, or heart failure with reduced ejection fraction (HFrEF) with an EF ≤40%.

Data were extracted from electronic hospital health records and charts from the Heart Function Clinic including patient demographics, current therapy, and past medical history. Qualitative and quantitative analyses were done to compare current practices against ten recommendations made in the Canadian Cardiovascular Society's most recent guidelines on the management of heart failure: *2017 Comprehensive Update of the Canadian Cardiovascular Society Guidelines for the Management of Heart Failure* and *The Canadian Cardiovascular Society Heart Failure Companion: Bridging Guidelines to Your Practice*[10,11]. The *Comprehensive update* is based on current medical literature, best evidence, and clinical consensus from a panel of experts. The *Companion* article is based on expert consensus. The ten recommendations were selected based on feasibility and access to appropriate data. The ten CCS recommendations analyzed include recommendations surrounding the timing of care and investigations as well as recommended medical therapy (Table 1).

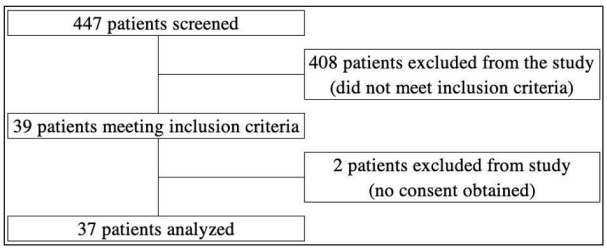

Figure 1. Study population flow.

The timing of visits and interventions recommended by CCS is based on level of acuity. Wait times are defined as the length of time between the referral and the patient's first visit in clinic. The CCS guidelines on wait times are stratified into a 4-tiered system. Urgency

Table 1. Canadian Cardiovascular Society recommendations on the management of heart failure. Recommendations taken from the *2017 Comprehensive Update on the Management of Heart Failure*[10] and the *Heart Failure Companion: Bridging Guidelines to your Practice*[11].

Routine referrals should be seen within 12 weeks, ideally within 6.
Stable HF patients should be seen in clinic every 3-4 months.
Bloodwork, including serum electrolytes, creatinine, and BUN, should be routinely measured every 1-3 months in stable patients.
Stable HF patients should have their LVEF reassessed every 2-3 years.
We suggest candesartan be considered to reduce HF hospitalizations in patients with HFpEF (Weak Recommendation; Moderate-Quality Evidence).
We recommend loop diuretics be used to control symptoms of congestion and peripheral edema (Strong Recommendation; Moderate-Quality Evidence).
We recommend systolic/diastolic hypertension be controlled according to current Canadian Hypertension Education Program hypertension guidelines (2017) to prevent and treat HFpEF (Strong Recommendation; High-Quality Evidence).
We recommend that most patients with HFrEF be treated with triple therapy including an ACEi (or an ARB in those who are ACEi-intolerant), a b-blocker and an MRA unless specific contraindications exist (Strong Recommendation; Moderate- Quality Evidence).
We recommend against the use of nonsteroidal anti-inflammatory drugs as well as cyclooxygenase-2 (COX-2) inhibitors in patients with HFrEF (Strong Recommendation; High-Quality Evidence).
We recommend against the routine use of calcium channel blockers (CCBs) in patients with HFrEF (Strong Recommendation; Moderate-Quality Evidence).

HF = heart failure; LVEF = left ventricular ejection fraction; BUN = blood urea nitrogen; HFrEF = heart failure reduced ejection fraction; ACEi = angiotensin converting enzyme inhibitor; ARB = angiotensin II receptor blocker; MRA = mineralocorticoid receptor antagonist; HFpEF = heart failure preserved ejection fraction.

Table 2. Study population characteristics.

	n=37
Age, mean (range)	71 (47-95)
Years since admission to the heart function clinic, mean (range)	2.6 (0.07-7.5)
Medications, mean (range)	10 (3-20)
Male	30 (81)
Ejection Fraction	
>50%	10 (27)
40-50%	13 (35)
<40%	14 (38)
NYHA functional classification	
1	0 (0)
2	25 (68)
2-3	9 (24)
3	3 (8)
4	0 (0)
Comorbidities	
Diabetes	18 (49)
Hypertension	24 (65)
Obesity	11 (30)
Dyslipidemia	13 (35)
Atrial fibrillation	12 (32)
Coronary artery disease	8 (22)
COPD	11 (30)
Chronic kidney disease	10 (27)

Values are reported as number (%) unless otherwise specified. NYHA = New York Heart Association; COPD = chronic obstructive pulmonary disease.

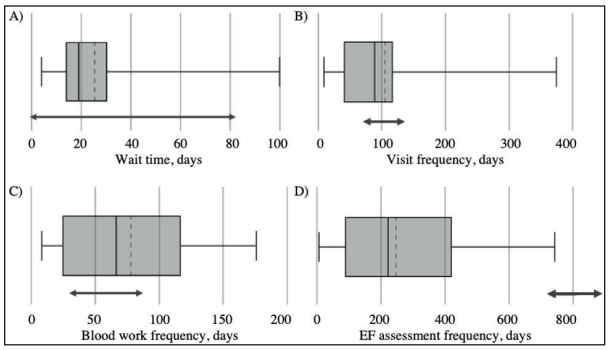

Figure 2. Comparison to Canadian Cardiovascular Society guidelines for the timing of events in heart failure management to current physician practice. Dotted lines indicate the group mean for each data set. Double-headed arrows indicate the Canadian Cardiovascular Society's recommendations on timing of the event. A) Individual data on wait time. Time from referral to clinic to the patient's first visit. B) Individual mean frequency of visits to the heart function clinic. C) Individual mean frequency of bloodwork. D) Individual mean frequency between ejection fraction (EF) assessments.

of referral is determined by NYHA classification, compensated vs decompensated HF, response to therapy, and recent HF exacerbations requiring an emergency department visit or hospitalization. Based on this classification system, it is recommended patients be seen within 24 hours if it is an emergent referral, within 2-weeks for urgent referrals, within 4-weeks for semi-urgent referrals, and within 6-weeks for routine referrals. The recommended frequency for follow-up visits is based on high, intermediate, or low risk individuals as evidenced in symptomatology, NYHA class, recent HF decompensations, titration of medical therapies, and comorbidities. High risk individuals are recommended to be seen every 1-4 weeks, with low risk individuals followed every 6-12 months.

Investigations such as bloodwork and EF assessment are recommended every 1-3 months and 2-3 years, respectively in stable HF patients. Routine bloodwork typically includes electrolytes, serum creatinine, and BUN. More frequent monitoring of bloodwork and EF is advised by the CCS for patients during acute illnesses, significant clinical changes or to monitor response to therapies.

This study was approved by the Horizon Health Network research ethics board file #2018-2612.

Results

Through the screening process, 447 patients were screened against the inclusion criteria. Of the 447 screened, 39 met inclusion criteria. The main reason for failing to meet inclusion criteria were patients not followed by the principal investigator. Informed consent was obtained from 37 participants (Figure 1). The study population had a median and mean age of 71 years with 81% of participants being male (Table 2). The average length of time from admission to the Heart Function Clinic was 2.6 years. Patients were on an average of 10 medications (Table 2), which are reported by medication class (Table 3).

Timing of events

The referral system in the clinic studied uses a 3-tiered system with urgent, semi-urgent, and routine referrals. Wait times in this clinic ranged from 4 days to 14.2 weeks, with an average wait time of 25 days (Figure 2a). The majority of patients, 66%, were seen within 4 weeks, with 30% being seen within 2 weeks, and 89% of referrals seen within 6 weeks. The frequency of follow-up visits ranged from 9 to 374 days with an average frequency of 105 days (Figure 2b).

The frequency of bloodwork in the study population ranged from 9 to 176 days, with an average frequency of 77 days for all participants (Figure 2c). Thirteen participants (35%) had an average frequency of bloodwork greater

Table 3. Medical therapy in heart failure patients. Patients are classified according to ejection fraction. Medical therapies are classified according to drug class.

Medication class	HFrEF, n=14	HFmEF, n=13	HFpEF, n=10
ARB	0 (0)	2 (15)	1 (10)
ACEi	3 (21)	2 (15)	6 (60)
ARNi	6 (43)	5 (38)	0 (0)
Documented contraindication to ARB/ACEi/ARNi	5 (36)	2 (15)	1 (10)
Beta Blocker	1 (7.1)	12 (92)	9 (90)
Documented contraindication to beta blockers	0 (0)	1 (7.7)	0 (0)
MRA	6 (43)	2 (5)	1 (10)
Documented contraindication to MRA	6 (43)	2 (5)	1 (10)
Diuretics	13 (93)	12 (92)	10 (100)
Nitrate	1 (7.1)	1 (7.7)	0 (0)
Digoxin	1 (7.1)	2 (15)	4 (40)
CCB	0 (0)	4 (31)	4 (40)
ASA	7 (50)	4 (31)	5 (50)
Statin	10 (71)	9 (69)	6 (60)

Values are reported as number (%). HF = heart failure; EF = ejection fraction; r = reduced, EF≤40%; m = mid-range, EF 41-49%; p = preserved, EF ≥50% ; ARB = angiotensin receptor blocker; ACEi = angiotensin converting enzyme inhibitor; ARNI = angiotensin receptor-neprilysin inhibitor; MRA = mineralocoritcoid receptor agonist; CCB = calcium channel blocker; ASA = acetylsalicylic acid.

than 90 days.

Frequency of echocardiography, as extrapolated from ejection fraction (EF) measurements, ranged from 7 days to 743 days. This was assessed using any EF evaluation completed since their admission to the heart function clinic. The average time between assessments was 274 days (Figure 2d).

The CCS recommendations regarding wait times, frequency of follow-up, and bloodwork were met for 97%, 78%, and 64% of patients, respectively with many patients being assessed more frequently than the recommended intervals.

Medical management of HFpEF

None of the participants were on candesartan at the time of this study including patients with HFpEF. A contraindication to the use of candesartan in the form of an alternative angiotensin II receptor blocker (ARB), or angiotensin converting enzyme inhibitor (ACEi), currently in use or an intolerance to candesartan was documented for 80% of patients with HFpEF (Table 4). Two patients with HFmEF were treated with candesartan. Overall, 89% of participants were prescribed an ACEi, ARB, or had documented reason for not being on one of these therapies.

All patients in this study with HFpEF were on a loop diuretic and 95% of participants overall were prescribed loop diuretics (Table 4).

Of the 10 participants with HFpEF, 8 had a documented history of hypertension. At their most recent clinic visits, 7 of those had BP readings ≤140/90mm Hg and one had BP ≤120mmHg systolic.

Medical management of HFrEF

Of the 14 patients with HFrEF, 43% were on triple therapy and an additional 29% had a documented contraindication to triple therapy such as intolerance to one of the classes of medication.

No participants were on a CCB at the time of this study and no patients were documented to be taking NSAIDs except for ASA. There were 14 patients (37% overall) taking ASA, including 35% of patients with HFrEF.

Discussion

The timing of events, as per CCS recommendations are reasonably well met. The majority of patients are seen within a timeframe appropriate to their referral urgency, and have appropriate frequency of follow-up with a few exceptions. Possible reasons for longer wait

times could be due to patient preference, coordinating visits with other appointments or tests, the availability of transportation options, or weather.

Ejection fraction assessment is done more frequently than the recommendations, but this may be due to certain patient factors. Seven patients only had one EF assessment and therefore could not be included in the analysis for frequency of assessment. Over 90% of patients had a prior emergency room visit or HF hospitalization which initiated their referral to clinic or occurred since their admission to clinic. EF may be reassessed more frequently to assess for changes that may occur such as in a heart failure decompensation or in order to monitor response to therapy. This suggests that this patient population is not made up of stable HF patients as would be expected of EF evaluations every 2-3 years. Due to the nature of HF patients and decompensations, it would be surprising to find any patients who would be considered stable for the duration of that time unless they were early on in their illness trajectory.

The majority of patients had routine bloodwork completed within the 1 to 3-month recommendation for stable HF patients. Some patients had more frequent bloodwork due to higher risk individuals' characteristics, medication titration, or comorbidities. One individual with the most frequent bloodwork assessment at every 9 days, had a recent admission during which bloodwork was drawn on a daily basis, leading to an overestimation of the true frequency of bloodwork for that individual. This could be true for other individuals as well in bloodwork frequency and frequency of EF assessment. Comorbidities, heart failure decompensations and medication titration could also play a role in the frequency of these investigations.

Medical management of patients with HFpEF saw no patients prescribed candesartan despite the recommendation that it may lower rates of hospitalization. It is possible that prescriber preference favours other medications in the ARB class or an ACEi. The recommendation for the use of candesartan is a weak recommendation according to the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) standards which could also contribute to providers choice for alternative agents. Provider preference shows ACEis were more popular overall in this patient population, with most patients with HFpEF being on an ACEi instead of an ARB. Loop diuretic use was seen across all patients in this study and given its importance in symptom management is most likely well tolerated with few therapeutic contraindications.

Hypertension Canada recommends a target BP of ≤140mmHg for all patients with hypertension and no other risk factors. However, intensive BP control to a pressure of ≤120mm Hg systolic is recommended for patients with risk factors, such as heart failure, other cardiovascular diseases and renal insufficiency. According to this lower targeted BP, only one of the 8 patients with HFrEF and hypertension had a blood pressure that was being adequately controlled.

Rates of NSAID avoidance may be overestimated as some NSAIDs, such as ibuprofen and naproxen, are available over the counter and require patient education to ensure they are properly avoided. The same would not be true for CCB use, as these medications require a prescription which lends more support that this finding is accurate.

Triple therapy was prescribed, or therapeutic contraindications were documented for 72% patients with HFrEF. This demonstrates the possibility of 28% of patients with HFrEF in this study population being undertreated. However, with retrospective data from electronic health records and patient files from the Heart Function Clinic alone, therapeutic contraindications and patient preference may not have been clearly documented. This could lead to underestimations of prescribing practices in guideline adherence as contraindications may be underreported. The rate of adherence to guidelines regarding triple therapy prescribing found by Atwater et al[8] was similar to the current study, at 43% prior to accounting for therapeutic contraindications and rising to 72% when they were taken into account.

The choice of therapy in HF management is based in part on EF at the time of initiation; however, EF can improve with treatment or worsen with progression of disease. Based on this, it is difficult to determine whether members of the three groups classified as HFrEF, HFmEF, and HFpEF in this study started with a higher or lower EF and how this may have impacted changes in therapy over time.

Limitations

Limitations to this study include a small, predominantly male study population. The choice of inclusion criteria, in particular to only include patients of the principal investigator at this time, was to ensure consent, data collection and data analysis could be completed in a timely and accurate manner with the resources available. Due to the small size, subgroup analysis would not have been possible with any significance. Suggested factors that may contribute to physician non-adherence to guidelines, as demonstrated by Calvin et al. were age, comorbidities, NYHA class, and minority status[7]. These factors were not independently assessed in this study due to the sample size but could be contributing factors in areas where adherence was reduced. Frankenstein et al[13] found that a patient's

sex could impact optimal dosing of medications with female patients receiving suboptimal medical therapy more often than males. Other studies have assessed the role of suboptimal dosing of medical therapies as an important predictor in improving outcomes for HF patients[5]. Dosing of medications was not assessed in this study but could be an area for further assessment.

Additional limitations include sample population characteristics. There was a wide range in the time from admission to clinic, ranging from less than 1 month to greater than 7 years. When patients initially enter the clinic, they may initially be seen frequently and have many investigations completed, especially with adjustments to medications. Over time, if they remain stable, these visits and investigations may become less frequent which could explain some of the wide time ranges in the results. The comorbidities of this patient population may also play a role in their frequency of visits, investigations, and medications. Again, due to the small sample size, these possible confounding factors could not be analyzed independently.

Broadening the inclusion criteria to include all patients in the heart failure clinic could lead to a better understanding of more generalized HF management practices and may allow for subgroup analysis which was not possible with this study.

Conclusion

There are more than 195 recommendations made by the CCS in the *2017 Comprehensive Update* and *Companion* guidelines regarding the current best practices in the management of heart failure. Of the ten CCS recommendations assessed in this study, most recommendations are being partially met with four recommendations regarding medical management being strictly adhered to. Further work is necessary to determine if these trends are more broadly seen in the management of heart failure across Canada and how specific patient or physician characteristics may play into the adherence to these guidelines.

Acknowledgements

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Humanities

Mould juice: A brief history of penicillin

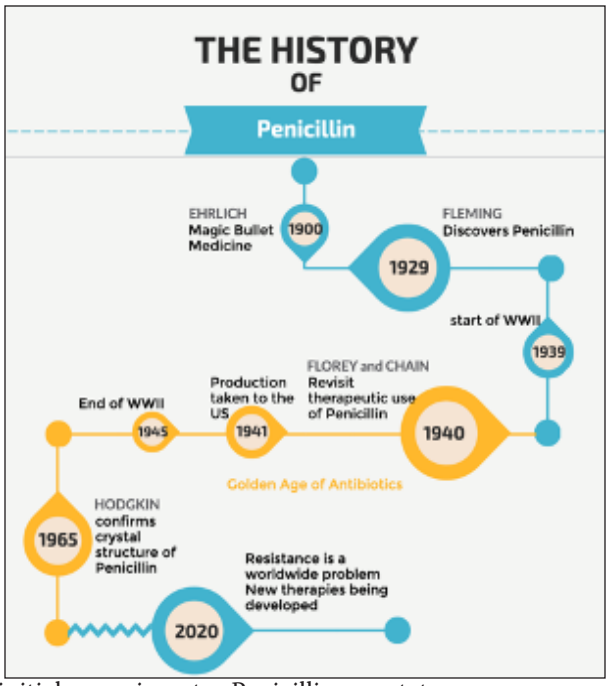
Bridgette Chan

In 1900, Paul Ehrlich developed the concept of magic bullet medicine[1]. He theorized that, because different cells could be targeted with different stains, cells could also be targeted with medicines – much like a bullet targets a victim. This simple theory led to the development of antibiotics that are able to kill bacterial cells, but not human cells. Ehrlich dedicated his life to discovering these so-called magic bullet cures and in 1909, he discovered the antibiotic Salvarsan, an arsenic-containing compound that was the first known cure for syphilis. Ehrlich used the term chemotherapy, defined as "treatment of diseases by chemical substances", to describe his drug[2]. As discussed later, the term antibiotics did not take on its current meaning until the mid-20th century. Ehrlich's discovery was proof of principle and paved the way for a century of "magic bullet" discoveries.

Unlike Ehrlich's tireless work to discover Salvarsan, the discovery of penicillin came after a vacation. To briefly retell the famous story, Alexander Fleming returned from a vacation in Scotland to discover that one of his Staphylococcus petri dishes had been contaminated with mould and that the mould lysed the Staphylococcus (Figure 1)[3]. In 1929, he published his findings that the "mould broth infiltrate" of Penicillium notatum had bactericidal and bacteriolytic properties[3]. In this paper, he first used the term penicillin to describe the active substance since he considered "mould broth infiltrate" too cumbersome a term.

Although the quest for antibacterial agents had been set in motion years earlier by Ehrlich, Fleming and his team were unable to generate sufficient quantities of Penicillium notatum to test the substance and research halted. Fleming predicted that growth inhibition by penicillin may be a helpful characteristic in the classification of bacteria, like urease and catalase, and he and his research team moved on to other topics[3].

About a decade later, Howard Florey and Ernst Chain, who investigated how bacteria and mould naturally kill each other, found Fleming's paper and replicated the experiments. Soon Florey ran into the same problem as Fleming: Penicillium notatum was difficult to grow. The mould had to be mass produced because up to 2/3rds of the product could be lost during purification and extraction[4,5]. Norman Heatley, a biochemist at Oxford, was the first in a long line of chemists to address this challenge. Production was eventually outsourced to the US, but for Florey's



initial experiments, Penicillium notatum was grown in broth in open containers. Heatley repurposed every container available at the Radcliffe infirmary, including bottles and bedpans, to grow penicillin[6].

Animal testing was conducted by Florey and involved infecting mice with Group A streptococcus and giving half of the mice penicillin[7,8]. At this point, WWII had begun and scientists knew the impact a compound like penicillin would have on the war. Within a couple of months, they began testing on humans. The first toxicity study was in a woman with terminal cancer who volunteered as a subject[9]. She developed severe tremors and fever, which the scientists realized were due to the impurities in their compound. The first patient to be treated with penicillin was a policeman who had a facial infection after being scratched with a rose thorn[9,5]. Unfortunately, he died 5 days after initiating therapy because the "penicillin supply was exhausted"[5,10]. This may seem inconceivable given the current large-scale production of antibiotics, but to achieve the recommended dose for streptococcal pneumonia, Florey and Heatley would have had to produce thousands of litres of broth daily[5,11]. The scientists observed a noticeable improvement in the policeman after receiving penicillin5, so they continued to give their product to patients. They often collected the patients' urine; roughly 60% of penicillin is excreted

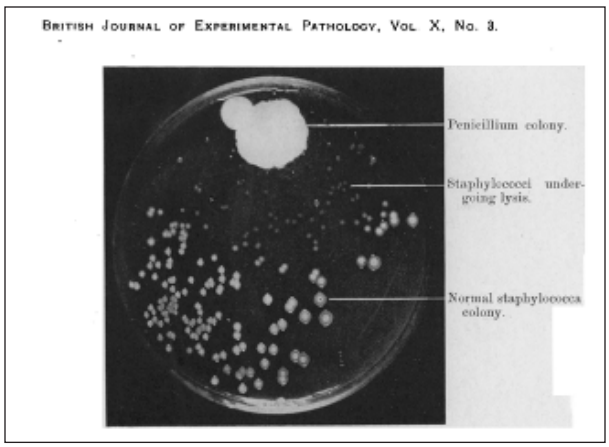


Figure 1. A photo of penicillin-lysed Staphylococci colonies from Alexander Fleming's original paper "On the Antibacterial Action of Cultures of a Penicillium, with Special Reference to their Use in the Isolation of B. influenzæ" (1929).

in the urine unchanged and they could recover about 30% of their initial dose through re-extraction[5,12].

Florey and Chain recognized that, with the war, Britain would be unable to produce enough penicillin to supply the troops. In 1941, they took their discovery to the US where the Northern Regional Research Laboratory (NRRL) in Illinois improved the fungus strain and production technique. The NRRL scientists successfully induced mutations in a high-yield strain isolated from a piece of cantaloupe[4]. They also increased yield by substituting lactose instead of sucrose, adding a corn-steeped liquor, and adding penicillin precursors to the broth. Once the NRRL had a viable Penicillium strain and technique, they offered the patent to American pharmaceutical companies, one of which was Pfizer. Pfizer agreed to make the compound and later developed the deep-tank fermentation method, the critical production technique that allowed the supply of the antibiotic to meet wartime demand[4]. In 1944, Pfizer opened a large-scale penicillin manufacturing plant in the Bronx. At this point, the value of penicillin was undeniable, and companies and workers were constantly reminded of the importance of the compound (Figure 2). Eventually, production reached adequate levels and George Stone, a Pfizer employee, wrote an internal report stating that in 1943 they could produce in one day what they did in the entire year of 1942[4].

Following the discovery of penicillin, we entered the Golden Age of Antibiotics. Within a short span of time, numerous other compounds with antibacterial properties were discovered including streptomycin, bacitracin, nitrofurans, chloramphenicol and the first cephalosporin. Between 1940 and 1960, about 20 antibiotics were discovered. In fact, 50% of antibiotics we still use today were discovered during this time. This is also when the term chemotherapy was exchanged for the more precise term: antibiotic. Antibiotic, which comes from the Greek word for "against life", was first used in 1860 but took on its current meaning in 1941 when it was used by the soil microbiologist Selman Waksman[13]. In addition to giving antibiotic its modern meaning, Waksman also discovered streptomycin (the first aminoglycoside). Four years later, the first cephalosporin was isolated from Cephalosporin acremonium. Giuseppe Brotzu, an Italian pharmacologist and politician, wondered how the people of Cagliari did not get typhoid fever while swimming in water contaminated with Salmonella. Upon culturing the water, Brotzu, like Fleming, discovered a fungus with antibacterial properties.

Throughout this Golden Age, numerous scientists received Nobel prizes for their work related to antibiotics. Waksman was awarded the Nobel Prize in Physiology and Medicine in 1952. Years earlier, in 1945, Fleming, Florey, and Chain received the Nobel prize for the discovery of penicillin. During Fleming's acceptance speech, he cautioned listeners about the dangers of resistance in the famous quote:

> *It is not difficult to make microbes resistant to penicillin in the laboratory by exposing them to concentrations not sufficient to kill them, and the same thing has occasionally happened in the body. The time may come when penicillin can be bought by anyone in the shops. Then there is the danger that the ignorant man may easily underdose himself and by exposing his microbes to non-lethal quantities of the drug make them resistant[14].*

It was unlikely at this time, however, that Fleming grasped the full consequences resistance would have. In part, this was because syphilis – one of the main diseases treated with penicillin – did not develop resistance to penicillin despite repeated treatments. This proved to be the exception rather than the rule.

After the war, Australia was the first country to make penicillin available to civilians and it soon became a panacea worldwide. As resistance developed, penicillin drug development struggled to keep up. Dorothy Mary Crowfoot Hodgkin, the inventor of x-ray crystallography, confirmed the structure of penicillin in 1945. In 1964, she too was awarded the Nobel Prize in Chemistry for her achievements. Other developments included the invention of the first major penicillin derivative, ampicillin. Ampicillin was developed as a broader spectrum alternative. Following ampicillin, the ß lactam resistant penicillins (eg. methicillin) were created. Despite multiple iterations and improvements, the inappropriate and widespread use of antibiotics has led to worldwide resistance and a large resistome – a collection of antibiotic-resistant genes in bacteria. In

addition to inappropriate use in humans, an estimated 82% of antibiotic use in Canada and the US is in livestock, which likely contributes to the inappropriate overuse of antibiotics[15, 16]. Encouragingly, the dangerous use of antibiotics in animals in Western countries is decreasing, and in 2006, the European Union banned the use of antibiotics for growth promotion in animals. However, the worldwide use of antibiotics is increasing overall and one estimate expects antimicrobial use to rise by 67% by 2030, largely due to rising consumption in growing and developing countries[17].

Currently, penicillin is indicated as monotherapy for ß hemolytic streptococcus infections and syphilis, and it can be used in combination to treat a wider variety of infections. Penicillium species can also be found on mouldy fruit and cheeses such as Brie and Roquefort. While penicillin is not obsolete, antibiotics no longer have the curative power they used to. In 2018, 26% of infections were resistant to first-line antimicrobials[18]. The invention and development of penicillin has resulted in numerous Nobel prizes which is indicative of the significance of its advent, but the Golden Age of Antibiotics is behind us and we need to adapt. This includes promoting drug research of novel solutions such as bacteriophage therapy, nanoparticles, and antimicrobial polymers, and while these new magic bullets are being invented, physicians – who prescribe 65% of outpatient antibiotics – must continue to be stewards[19].

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Humanities

Will it ever grow back?

The psychosocial impacts of alopecia

Aryan Riahi, Bsc.

Abstract

Alopecia is a common clinical complaint in the offices of family physicians and dermatologists. Here, we discuss common subtypes of alopecia, including androgenic alopecia and alopecia areata. Unfortunately, few resources have been invested in researching the effectiveness of psychological treatment for alopecia Pharmacological treatments alone are not enough. Medications can be a frustrating experience for both patients and their physicians due to their limited effectiveness. A case is made for health professionals taking an all-encompassing approach with patients is critical for skin conditions including alopecia.

Introduction

Alopecia (hair loss) is a common clinical complaint. Two common subtypes of non-scarring alopecia are androgenic alopecia and alopecia areata. While the former is due to the effects of a genetically determined excessive response to androgens[1], the latter is the product of an autoimmune phenomenon[2]. Chronic skin conditions can cause patients a great deal of distress in part due to fear of judgment from others. In this commentary, we will be discussing the role of psychosocial factors in the quality of life of patients with alopecia.

The Role of Stress

Long term exposure to stressful stimuli and ineffective coping skills can exacerbate skin conditions. Many skin conditions such as alopecia, urticaria, and delayed wound healing carry a psychosomatic component[3]. Emotional trauma from the feeling of abandonment is a risk factor for alopecia areata4. The literature shows that individuals diagnosed with alopecia areata commonly experience a severe antecedent mental stressor such as the death of a loved one prior to receiving their diagnosis[4]. The average number of stressful events that patients with alopecia face is also higher compared to healthy controls[4].

Stress can be debilitating for patients. Those suffering from alopecia areata experience a lower quality of life because of their condition compared to healthy controls[5]. This has a negative impact on the social functioning, general health, and emotions of affected individuals[5]. Patients with alopecia areata experience more negative emotions including anger, fear, and low self-esteem compared to healthy controls[6]. Negative emotions are a predictor of many chronic conditions including cancer, diabetes, hypertension, and psoriasis. With so many conditions being associated with stress, it should be imperative for healthcare providers to work with patients to develop coping skills.

The Role of Family History

Heredity is a major contributing factor to alopecia. A study on androgenic alopecia found that men with fathers who experienced hair loss faced a 2.5 times greater likelihood of reporting hair loss than those whose fathers did not experience hair loss[7]. Other studies have confirmed the association between the patient's hair loss and positive family history for first-degree relatives[8]. Approximately 80% of androgenic alopecia is accounted for by family history[1]. Similarly, 20% of patients with alopecia areata have a positive family history[9].

The experience of growing up in a household where balding is commonplace is one that is all too familiar for patients suffering from alopecia. Male androgenic alopecia has an autosomal dominant heredity and affects 30-50% of men by the age of 50[1]. Most males from my maternal and paternal family tree began losing their hair in their teens and twenties. Awaiting a similar fate as them is a source of anxiety for me. The distress that many patients face once the process of hair loss begins is understandable and requires empathy from healthcare professionals.

Mental Disorders: From Depression to Suicide

Chronic and severe alopecia can result in debilitating mental disorders due to alienation from society. Alopecia is not the only skin condition associated with psychological disorders. Psoriasis, atopic dermatitis, and acne all have prominent psychosocial aspects. In addition to stress, some major psychiatric disorders include major depressive disorder, anxiety disorders

including obsessive compulsive disorder (OCD) and social anxiety disorders as well as somatoform disorders including body dysmorphic disorder (American Psychiatric Association, 1994).

Psychological distress may lead to psychiatric disorders. Depression and general anxiety disorder are the most common mental disorders experienced by patients with alopecia, occurring in 39% of patients[6]. Depression has a higher prevalence in patients less than 20 years of age[6]. This emphasizes the importance of building a network of psychosocial support for patients before their condition affects their mental health. Patients with anxious, dependent, and obsessive-compulsive personality disorders are particularly at risk of comorbid alopecia. Since personality disorders can occur at an early age, healthcare providers must be willing to support patients from a young age through shared decision making and referrals to mental health professionals.

Ensuring optimal mental health is a critical component of patient care. Healthcare providers are taught throughout their years of education to screen for depression when a patient presents with a debilitating chronic illness. However, the definition of "debilitating" is subject to debate. But what is clear is that chronic dermatologic conditions such as alopecia have a strong burden of disease. The social stigma and yearning to be normal can take a toll on the mental health of patients. This is why more attention must be drawn towards complementing pharmacologic treatments with psychotherapy.

Few resources have been invested towards researching the effectiveness of psychological treatment for alopecia[10]. Since medical treatments are viewed as largely ineffective, learning to live with alopecia through psychotherapy may benefit patients more than hoping for a possible cure. More research is required to determine how effective psychological treatment modalities are for patients coping with the psychological sequelae of alopecia.

Are Pharmacologic Treatments Strong Enough?

Pharmacological treatments for subtypes of alopecia such as androgenic alopecia or alopecia areata can be a frustrating experience for both patients and their physicians due to their limited effectiveness, undesirable side effects, long timeframe for treatment, and slow growth[11]. For example, for androgenic alopecia, topical minoxidil and oral finasteride only partially reverse hair loss[1]. Minoxidil only achieves cosmetically acceptable results in a subset of patients[12]. Research in stem cell therapy to create new hair follicles is being explored[11]. As for alopecia areata, no treatment offers permanent remission at the moment[13]. Novel therapies have demonstrated promising results of JAK inhibitors such as Ruxolitinib[11]. However, the lack of knowledge on the long-term efficacy and side effects of JAK inhibitors paired with their high costs limits their use in everyday practice[14]. High costs in particular are a concern for Canada's healthcare system, as expensive pharmaceuticals are out of reach for patients who rely on the public healthcare system. Thus, emphasizing the importance of a holistic and psychosocial approach would be of particular interest in such a system.

Pharmacotherapy is oftentimes insufficient in providing patients with alopecia relief. As health professionals, the psychological aspects of alopecia must be advocated for as an important tool for managing or preventing deteriorating mental health. Recognizing the distress and societal stigma that chronic skin conditions carry can help healthcare providers provide the best care for their patients.

A Holistic Approach

Currently, there are no widespread programs in Canada aimed at addressing the mental health of patients with hair loss. Cognitive behavioral, group, and interpersonal therapies may potentially be of benefit to patients with alopecia and other skin conditions. A 2019 systemic review found that cognitive behavioral therapy is an effective treatment option for moderate-to-severe psoriasis[15].

Moreover, programs are needed to deliver greater holistic care to patients. Other skin conditions are receiving more attention on this front. Patients with atopic dermatitis and their family members can participate in educational programs that cater to the unique needs of each patient[16]. These multidisciplinary clinics include dermatologists, psychologists, and nurse practitioners. These centers have been implemented and have received positive feedback across North America, Europe, and Asia. As far as we know, Canadian programs aimed at delivering such services for alopecia are limited.

In addition, national campaigns that aim to decrease stigmatization of alopecia by society may have a positive effect on patients. Compared to older groups, younger patients suffering from androgenic alopecia cope better than older patients in part due to less stigmatization by fashion and media compared to older groups[8]. This is in part because today's metro-sexual youth culture adopts unique hairstyles[8]. An older study on youth by Wells in 1995[17] noted marked decreases in levels of self-esteem and a greater sense of unattractiveness in the younger generation of that era. This suggests an increased tolerance by society of hair loss over time. More awareness programs for hair loss may catalyze these positive changes.

Conclusion

Taking an all-encompassing approach with patients is critical for skin conditions including alopecia. Healthcare providers must be aware of the psychological consequences of hair loss. Not all patients completely respond to pharmacologic therapy. Providing treatment to such patients may do more harm than good.

Considering the limited response to pharmacological treatment that both androgenic alopecia and alopecia areata have shown thus far, it is time to consider other treatment modalities. We advocate for a more psychosocial model of care that considers the social, emotional, and physical wellbeing of patients with alopecia. Well-rounded care starts with mental and physical wellbeing.

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Original Research

Medical students' perceptions of nutrition in medical education and future practice

Peri Fenwick[1], Alyson Colborne[1], Olga Theou[1, 2], and Leah E Cahill[1, 3, 4]

1. Department of Medicine, Dalhousie University, Halifax, NS
2. Physiotherapy, Dalhousie University, Halifax, NS
3. Department of Nutrition, Harvard T. H. Chan School of Public Health, Boston, MA, USA
4. Department of Community Health and Epidemiology, Dalhousie University, Halifax, NS

Abstract

Keywords: medical education, nutrition, medical students, physicians, undergraduate, lifestyle medicine
Background: Physicians are relied upon as knowledgeable sources of nutrition information; however, many report low nutrition knowledge.
Objective: The present study assessed first and second-year medical students' perceptions of nutrition education within the medical curriculum, in terms of their attitudes, learned body of knowledge, and satisfaction.
Methods: An online questionnaire was administered to Dalhousie University medical students completing their first or second year (N=125). Mann-Whitney U tests compared the responses of first-year to second-year students, as well as those with and without previous nutrition education.
Results: 97.6% of respondents agreed that nutritional counselling can positively influence patient outcomes, with 91.2% agreeing that physicians play a key role in nutritional counselling. Compared to second-year students, first-year students had greater self-perceived knowledge of basic nutrition concepts ($p<0.001$) and nutrition in the treatment of disease ($p=0.005$), as did students with previous nutrition education compared to those without ($p=0.019$ and 0.018 respectively). Satisfaction was <30% agreement, with first-year students more satisfied with their nutrition education than second-year students ($p<0.05$).
Conclusion: First and second-year medical students regard nutrition as an important component of medical practice that can positively impact patient outcomes. However, low satisfaction with their nutrition education suggests that additional nutrition curriculum would better prepare them for future practice.

Introduction

The importance of nutrition in achieving and maintaining good health is well recognized. A report by the World Health Organization describes a global shift in dietary habits toward an increased intake of processed, low-quality foods, contributing to the development of chronic, non-communicable diseases[1]. A recent study reported that diet is the top risk factor associated with death and the second highest risk factor associated with disability in Canada[2]. As such, diet is an important modifiable lifestyle behaviour for the health care system as well as those who provide primary care, to target.

Family physicians are relied upon as knowledgeable sources of nutrition information[3]. However, evidence suggests that they do not provide this type of counselling to patients, due to reasons such as perceived lack of knowledge and access to resources[4–6]. This may be attributed to a lack of nutrition education during medical school[7] and in residency training[8–10]. Results from a pivotal survey of primary care physicians demonstrated that 67% of respondents reported a lack of training in nutrition counselling[5]. Previous surveys of Canadian medical students' perceptions of nutrition education reported high perceived importance of nutrition in medical practice alongside low satisfaction with nutrition education[11,12]. In the current Dalhousie Medical School curriculum, the primary nutrition-centered lectures are delivered in the middle of first-year of medical school during the gastroenterology unit. There is occasional integration of nutrition content dispersed throughout other units, when relevant; however, first-year is the primary source of formal, dedicated nutrition education in the medical school curriculum. Yet, no studies to date have examined first year medical students' perceptions of their nutrition education to further elucidate its current state and potential avenues for improvement.

The primary purpose of this study was to determine first and second-year medical students' perceptions of nutrition education at Dalhousie medical school,

in terms of their attitudes toward its use in general medical practice, their learned body of knowledge, and their satisfaction with how the medical school curriculum links nutrition content with its application to medical practice. Secondary goals of the current study were to determine if there are any differences in these domains according to year of study and previous nutrition educational experiences.

Methods

Subjects

Participants were first and second-year Dalhousie University medical students at the Halifax and New Brunswick campuses. The survey was administered after completion of their respective year of studies. First and second-year comprise the pre-clerkship period, when the majority of didactic teaching is provided identically to all students (same instructor, content, and delivery) prior to students entering the clinical environment where learning is less uniform. First and second-year medical students were chosen for the present study to assess medical students' perspectives on nutrition directly after lecture-based nutrition education is provided, in order to minimize the potential confounding influence of the variation of nutrition education students may receive in clinical clerkship. Upon completion of their respective years of medical school (spring-time), first and second year Dalhousie medical students were invited to participate through emails distributed by the Undergraduate Medical Education office and Dalhousie Medical Student Society, as well as through social media. This study was approved by the Dalhousie University Research Ethics Board (file # 2018-4468). All participants provided informed consent prior to participating in this study.

Survey

Because there was no existing standardized questionnaire to collect the data we required, the Nutrition and Physical Activity Education Questionnaire (NPAEQ, see Additional File 1) was developed for the present study to capture (1) attitudes towards nutrition in medical practice, (2) self-assessed knowledge of nutrition-related topics, (3) satisfaction with nutrition content within the medical curriculum, and (4) demographic information, including of year of study and previous nutrition education. These four domains were chosen after reviewing preexisting literature[10,13–17] which assessed and evaluated curricular aspects of undergraduate medical education in order to create the optimal survey for our specific research objective. A novel survey was created by the authors of the current study in order to examine our objectives that did not fit within the parameters of pre-existing surveys. For example, prior Canadian research on similar topics, such as that of Gramlich et al., used a broader survey. They examined medical students' perceptions of nutrition education Canada-wide, compared to our study which focused on a single institution. Gramlich et al. assessed areas such as students' preferred learning format, number of hours dedicated to nutrition education, and which topics within nutrition education were being included in the various programs[11]. This is valuable data that provided a helpful basis for our study. Our survey was unique such that it focused specifically on students' subjective perceptions, rather than an objective evaluation of the curriculum, which was not the objective of the current study. Another reason why a novel survey was created was to maximize the response rate among busy medical students by formulating a concise yet comprehensive data collection tool that would be easy to complete.

We conducted a literature review on Google Scholar using the following terms: 'Nutrition Education,' 'Undergraduate Medical Education,' 'Undergraduate,' 'Nutrition,' 'Education,' and 'First-Year Medical School,' as well as combinations of these aforementioned terms. In the process of creating a novel survey, we critically considered each of the questions we included based on feedback from experts, thus ensuring a rigorous methodological approach and foundation for our research question. Questions were based on the 5-point Likert scale method of measuring beliefs, attitudes and opinion[18]. The NPAEQ contained similar questions pertaining to physical activity education, which were not included in the present study. The NPAEQ underwent a face-content validation and professional validation by graduate students and researchers in the fields of nutrition and physical activity which followed the recommended methods[19–21] of assessing six survey domains: visual appropriateness, language appropriateness, relevance, clarity, representativeness and ease of online survey tool. This face-content validation was an anonymous process carried out using the same survey tool as the questionnaire sent to participants in order to also validate the survey tool itself. A Likert scale was used for the validation process to simulate the final survey and additional open-ended comments were gathered to generate both standardized and novel forms of feedback. The questionnaire was distributed using the online survey tool Opinio (version 7.11)[22]. The survey was open online between May 10th to June 18th, 2018.

Statistical analysis

Results were analyzed using SPSS software version

Table 1. Participant demographics.

Participant Characteristics	N (%)
Gender	
Male	41 (32.8)
Female	82 (66.4)
Prefer to self-describe	1 (0.8)
Previous Nutrition Experience	
No	91 (72.8)
Yes*	34 (27.2)
Degree in nutrition	2 (1.6)
Nutrition research	3 (2.4)
Nutrition education (e.g., post-seondary courses, workshops)	24 (19.2)
Clinical nutrition experience	14 (11.2)
Other	10 (8.0)
Year of Medical Studies	
1st	76 (60.8)
2nd	34 (27.2)

* Respondents could select more than one type of previous nutrition education.

19.0. Descriptive statistics were used to summarize survey responses and participant characteristics. Percentage agreement was analyzed according to the 5-point Likert scale[18], with a score of 4 (agree) or 5 (strongly agree) indicating agreement, a score of 3 indicating a neutral response, and a score of 1 (strongly disagree) or 2 (disagree) indicating disagreement. A Mann-Whitney U test was used to compare the percent agreement between the first-year students and second-year students, as well as those with and without nutrition education. The significance level was set at $p<0.05$.

Results

Respondent characteristics

Of 220 first and second-year students, 125 students completed the survey (response rate of 57%) (Table 1), with a higher proportion of responses from first-year students (60.8%). Overall, 66% of respondents were female and 27% reported previous nutrition experience.

Students' attitudes toward nutrition in medical practice

In the first section of the survey, students were asked about their level of agreement with four statements relating to their attitudes toward nutrition in medical practice. As shown in Figure 1, the percentage of students who agreed with statements about the importance of nutrition counselling and the role of physicians in the provision of such counselling ranged from 44 to 97.6%. Respondents reported higher levels of agreement with statements that focused on the importance of nutrition for health outcomes and the role of physicians in improving such outcomes, compared to the statements addressing nutrition assessment and counselling.

Perceived knowledge of nutrition-related information

Self-perceived knowledge of basic nutrition concepts was the highest (90.4% agreement), while the lowest percentage agreement was seen in the pathophysiology of specific diseases (56.8% agreement) (Figure 2). First-year students and students with previous nutrition education had significantly greater levels of self-perceived knowledge of basic nutrition concepts (1st year: 97.4% agreement vs. 2nd year: 79.6%, $p<0.001$; previous nutrition education: 100% agreement vs. no previous education 86.8%, $p=0.019$) and nutrition in the treatment of disease (1st year: 84.2% agreement vs. 2nd year: 63.3%, $p=0.005$; previous education: 85.3% agreement vs. no previous education: 72.5%, $p=0.018$). Students with previous nutrition education reported greater knowledge of how and where to access credible nutrition information compared to students without previous education (82.4% vs. 64.8% agreement, respectively; $p=0.027$).

Satisfaction with nutrition education

First-year students reported significantly higher agreement with all satisfaction-related questions, compared to second-year respondents (Figure 3). Previous nutrition education was associated with higher satisfaction with the amount of time dedicated to nutrition in the medical school curriculum (29.4% agreement among students with previous education vs. 18.7% among those without; $p=0.051$, data not shown), but was not associated with satisfaction with nutrition integration in the curriculum ($p=0.272$), or preparedness for future medical practice ($p=0.461$).

Discussion

In this survey study of first and second-year medical students, we found that respondents not only perceived nutrition counselling as an important component of health, but also viewed physicians as important players in providing nutrition counselling. Students at the end of their first year reported significantly higher knowledge of basic nutrition concepts and the role

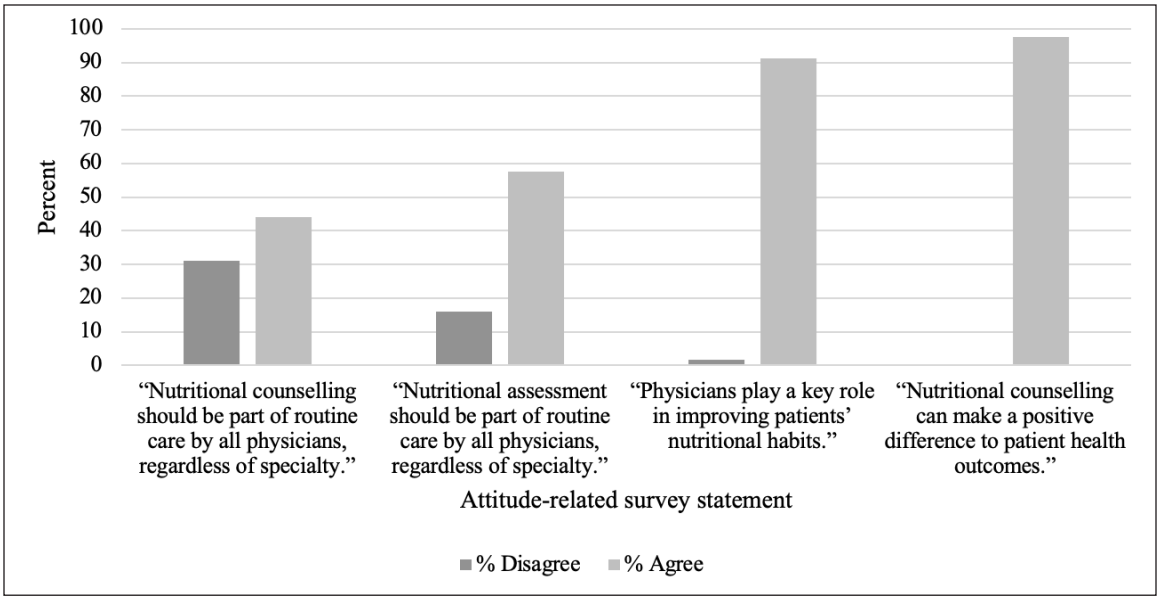

Figure 1. First and second-year students' attitudes toward nutrition in medical education and practice. There were no significant differences in % agreement for attitude-related statements between first and second-year students or between those with or without previous nutrition education ($p>0.05$ for all statements). Percentage agreement was analyzed using a Mann-Whitney U test according to the 5-point Likert scale, with a score of 4 (agree) or 5 (strongly agree) indicating agreement and 1 (strongly disagree) or 2 (disagree) indicating disagreement.

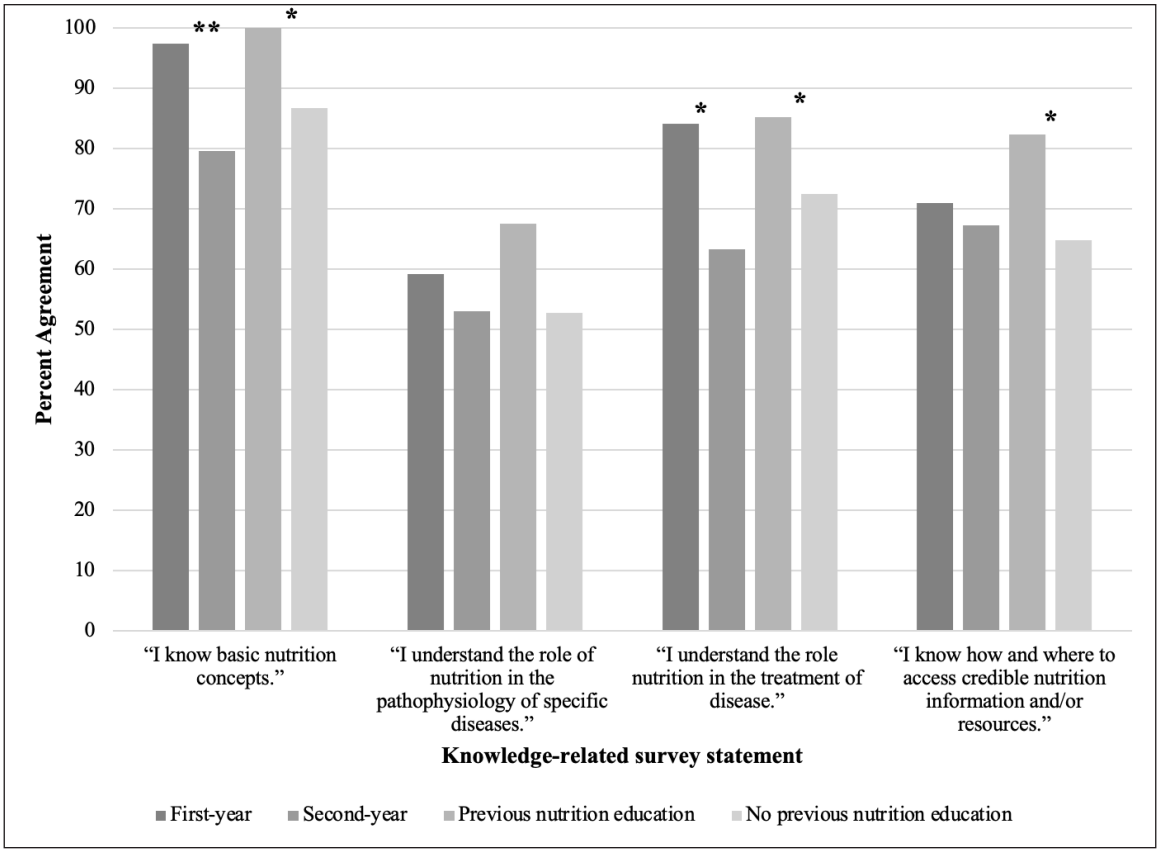

Figure 2. Self-perceived knowledge of nutrition-related subjects according to year of study and previous education. There were significant differences in % agreement between first-year and second-year students, and between students with previous nutrition education and those without previous nutrition education (*$p<0.05$, **$p<0.001$). Percentage agreement was analyzed using a Mann-Whitney U test according to the 5-point Likert scale, with a score of 4 (agree) or 5 (strongly agree) indicating agreement.

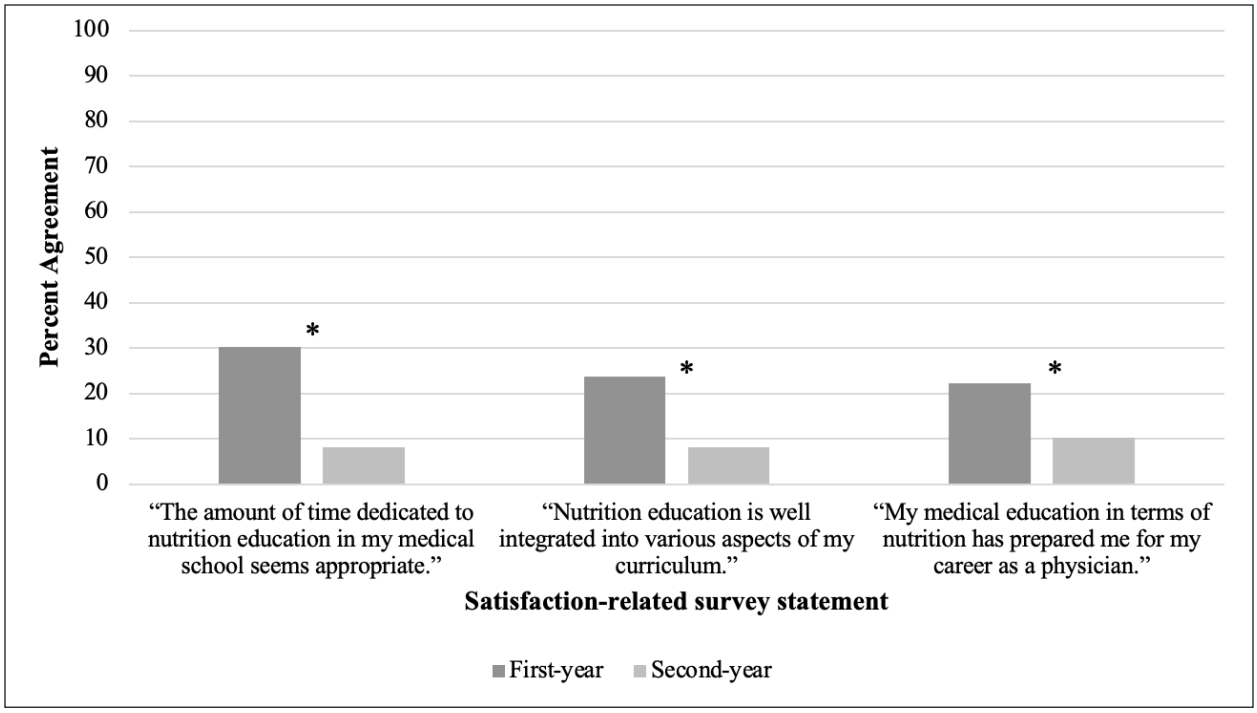

Figure 3. Satisfaction with nutrition education (% agreement) among first-year medical students compared to second-year medical students. There were significant differences in % agreement between first-year and second-year students (*p<0.05) for all satisfaction-related questions. Percentage agreement was analyzed using a Mann-Whitney U test according to the 5-point Likert scale, with a score of 4 (agree) or 5 (strongly agree) indicating agreement.

of nutrition in the treatment of disease, compared to students finishing second-year. Furthermore, students with previous nutrition experience had higher agreement with most knowledge-related questions compared to students without previous nutrition education. Students' overall satisfaction with the nutrition education they receive in medical school is low. Interestingly, first-year respondents reported higher agreement with all satisfaction-related questions compared to second-year students.

Comparison to previous findings

In line with previous research, the present study observed that first- and second-year medical students believe nutrition is an important topic in medicine while feeling low satisfaction with their nutrition education. Previous research in the U.S. demonstrated that insufficient time spent on nutrition education[23], as well as other barriers, including lack of time and compensation, are contributing factors to physicians' reporting a lack of preparedness to help their patients adopt healthier eating habits[4,5]. Canadian research has demonstrated similar results[11]. Among the 933 medical students from all years of study who completed their survey, Gramlich et al. demonstrated that knowledge of basic nutrition concepts was higher than perceived preparedness to provide nutrition counselling.

The current study has similarities in its objective and approach to a study by Hanninen and Rashid[12], as their findings were published shortly after our research endeavours began. In their study of second, third, and fourth-year Dalhousie University medical students, upwards of 95% of students agreed on the importance of nutrition in disease prevention and treatment, as well as the role of physicians as role models for positive nutrition behaviours; however, satisfaction with their nutrition education was low, with 30.3% of respondents dissatisfied or strongly dissatisfied with the nutrition curriculum and 78.6% in agreement that more nutrition education should be provided. Their report of relatively higher satisfaction with the nutrition curriculum compared to our satisfaction results suggests there may be an increase in satisfaction that occurs in the upper years of medical school. However, their study did not find any differences in mean satisfaction level when comparing second, third and fourth-year students. As such, further research is needed to delineate whether there is indeed a difference in satisfaction based on year of study.

Although there is now an element of repetition in the body of literature on nutrition education in Canadian medical schools, this does not detract from the significance of the current research. Rather, the complementary findings highlight the discrepancy

between students' agreeable attitudes yet low levels of satisfaction with their nutrition education. Furthermore, the study published by Hanninen and Rashid excluded first-year students, as their survey was distributed early on in the academic year before these students could provide insight into the nutrition curriculum. Our study adds a unique perspective such that it was distributed at the end of the academic year, allowing us to include the first-year students immediately after they received the majority of their didactic nutrition education. Including this group of students revealed that the nutrition curriculum delivered in first-year led to increased self-perceived knowledge among this group, which reflects positively on the medical school's first-year nutrition education.

Potential explanations for findings

In today's society where there are varying opinions about which diet is optimal for health[24], students may not know how to appraise this information while simultaneously participating in a demanding medical curriculum. A need for increasing multidisciplinary care may also contribute to current issues surrounding the integration of nutrition into patient care[25]. Cambridge University identified a collaborative approach among doctors, dietitians, nutritionists and nurses as a key factor in the success of their nutrition education initiative[26].

Our finding of differences in knowledge and satisfaction based on year of study may be a result of the structure of the Dalhousie University medical school curriculum. At Dalhousie, the majority of structured nutrition education is delivered during students' first-year, which may have influenced our survey as a result of the proximity between when the first-year students learned the nutrition content of the curriculum and the time of survey distribution. Alternatively, perhaps the higher perception of nutrition knowledge in first-year versus second-year students is an expression of Albert Einstein's adage 'the more I learn, the more I realize how much I don't know.' Previous research found that students earlier on have more positive perceptions of nutrition counselling by physicians[11,27,28]. This may be related to a cognitive bias known as the Dunning-Kreuger effect, in which those who are less skilled in a given area often rate their knowledge as greater than those who are more experienced in the same discipline[29–31].

Our study found that self-perceived knowledge of basic nutrition concepts was the highest, while the lowest percentage agreement was seen in the pathophysiology of specific diseases. This suggests that a potential strength of the current Dalhousie curriculum may be teaching on basic nutrition concepts, such as types of macronutrients and micronutrients. However, the translation of this information into understanding the impact on specific disease processes may be lacking. For example, students may be familiar with concepts related to macronutrient balance (i.e. needing a combination of carbohydrates, fat, and protein to maintain a healthy diet) but may not feel as comfortable explaining how saturated fat can contribute to the development of atherosclerosis and heart disease. This highlights a possible area for targeted improvements in the current nutrition curriculum.

Strengths and limitations

This study is based on self-report and does not include objective measurements of nutrition knowledge; however, previous research has reported that perceived quality of nutrition training in medical school is positively correlated with proficiency scores, providing evidence that self-perceived knowledge may serve as a reliable proxy for clinical proficiency[32]. The findings of the current research were strengthened by a response rate of 57%, which is higher than similar previous studies[11,12,33]. Our study cohort was limited to a single institution in order to assess the current state of nutrition education at Dalhousie medical school specifically, which at the time of our literature review, had not yet been explored. Although this limits the generalizability of our findings, this research serves as a pilot-style project and a foundation for future research that may extend to other institutions.

Implications and future directions

The current study indicates that the first two years of medical school could be an appropriate time to incorporate additional nutrition education to increase physician competency in nutrition counseling. The NPAEQ may be used in future research to explore similar questions among different cohorts, such as family medicine residents who are at the front-line of primary care, an area where nutrition counselling can be used as a form of preventative medicine to reduce the prevalence of lifestyle-associated diseases. This study serves as a springboard for future nutrition education research at Dalhousie, such as comparing pre-clerkship, post-clerkship, and beyond. Moreover, future research may assess which specific areas of nutrition students would like more instruction around, as our study showed that students had relatively low self-perceived knowledge of the role of nutrition in the pathophysiology of disease processes. Research is currently being conducted by other members of our team on recent Dalhousie Medical School graduates' perceptions of nutrition, based on the methodology

and results of the current study. Further avenues for future research may extend to examining and comparing nutrition education at other institutions across Canada, with the ultimate goal of increasing nutrition competency among physicians to better the health of our population.

This research adds to the growing body of evidence supporting improved nutrition in medical education[10,11,34]. A number of American medical schools have implemented culinary medicine electives, in which students receive cooking instruction and review principles of dietary counselling[35,36]. The University of Toronto recently began teaching undergraduate medical students how to prepare affordable, healthy food, and ways to help support patients to do the same[37]. Future research could evaluate education changes like these on the improvement of physician comfort and competence in providing dietary advice to patients.

Conclusion

This cross-sectional survey of first and second-year medical students found that attitudes towards nutrition in medical practice were positive; however, perceived knowledge of nutrition information and satisfaction with nutritional education were low. These findings contribute to our understanding of the status of nutrition education in the undergraduate curriculum of Canadian medical schools.

Declarations

Ethics approval and consent to participate: This study was approved by the Dalhousie University Research Ethics Board. All participants provided informed consent prior to participating in this study.

Consent for publication: Not applicable.

Availability of data and materials: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests: The authors have no conflicts of interest to disclose.

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Authors' contributions: PF and LC conceived the study idea and design in discussions with OT and AC. PF performed the statistical analyses and drafted the manuscript under the supervision of OT and LC. All authors contributed to additional drafts of the manuscript and approved the submitted version, and each author satisfies the authorship criteria of the International Committee of Medical Journal Editors. All authors agree to be accountable for all aspects of the work.

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Original Research

Pixelated vision:

Validation of the complaint with no objective findings

Emily A. L. Sheppard BSc MScPT[1], Kevin E. Gordon MD MS[2]

1. Dalhousie University Medical School
2. Division of Pediatric Neurology, Department of Pediatrics, Dalhousie University, Halifax, Nova Scotia

Abstract

Background: We encountered a young female presenting with a complaint of "pixelated vision". A brief literature search at the time of consultation showed no peer reviewed publications. Our objective was to use an infodemiologic approach to investigate the possible occurrence of an unidentified visual phenomenon.
Methods: An Internet search with the metabrowser search engine Dogpile (www.dogpile.com) was conducted on April 24, 2018, using free text words "pixelated" and "vision." The first 100 results were scanned for forum posts and cross-referenced to minimize duplication.
Results: Of the first 100 results, 15 unique posts were identified. The majority of posts were made by the affected individual (n=14, 93%). Sex was female (n=5, 33%), male (n=2, 13%) or unknown (n=8, 53%). Onset was identified as new (n=10, 67%) or chronic (n=5, 33%).
Conclusion: The availability and content of these forum postings suggest that pixelated vision is an uncommon, non-pathological visual phenomenon not yet documented in conventional medical literature.

Background

Complaints of visual phenomena are a common reason to consult pediatric neurologists. These can be divided into negative symptoms, for example: visual field loss, and positive visual phenomenon including scotoma and the creation of false visual images caused by the brain's perception of the incoming visual stimuli[1].

We encountered a young female presenting to a pediatric neurology clinic with a complaint of "pixelated vision." She described her vision as having normal acuity and color but had an overlay of finely pixelated dots, similar to what one would experience while looking at an older analog television. Symptoms were binocular, persistent, included the entire visual field and had been present for several years. A previous ophthalmological examination was normal with intact visual fields and normal acuity testing. No abnormalities were identified on neurological examination and brain imaging was not pursued.

A brief review of the literature at the time of her consultation showed no peer reviewed publications within the conventional medical literature describing such a phenomenon described as "pixelated vision". Self-reported posts reporting this description were however, readily encountered on the Internet. We decided to explore this possible phenomenon using nontraditional data sources. Eysenbach et al. described a Web-based method known as "infodemiology" which they defined as "the science of distribution and determinants of information in an electronic medium, specifically the Internet, or in a population, with the ultimate aim to inform public health and public policy[2]." Our objective was to use a supply side, information prevalence infodemiologic approach to investigate the possible occurrence of pixelated vision as a yet unidentified visual phenomenon within the conventional medical literature.

Methods

We conducted an internet search with the metabrowser search engine Dogpile (www.dogpile.com) that retrieves results from several search engines including Google, Yahoo!, Live, and Ask[3]. The search was conducted on April 24, 2018, using the free text words "pixelated" and "vision." The first 100 results were scanned specifically for forum posts discussing symptoms of pixelated visual phenomenon. After the first 100 results, subsequent results were found to be primarily irrelevant or duplicates. Username, reported age, and sex were recorded for each post if available. These details were then cross-referenced to minimize the potential for duplicate inclusions.

Results

Of the first 100 results, 15 unique posts were identified describing "pixelated visual" phenomenon (for specific posts, see Table 1). Posts were made by the

Table 1. Unique forum posts that describe pixelated visual phenomenon.

Age (y)/Sex	Synopsis
Unknown/Unknown	"For over 20 years I have suffered from what I call "Pixelated" vison. I see a swimming pattern of minute dots or "pixels" super imposed on everything. The lower the light level, the more prominent the pixels appear. It makes driving at night extremely difficult".
56/Male	"This past year however I have had on three or four occasions the disturbing occurrence of pixelated vision. It seems to affect the lower outer edge of my sight spectrum. Both eyes are affected. It does not seem to be a problem with my eyes per se; that is, if I cover the left eye, the identical problem pixelated pattern is in the opened right eye and vice versa when the right eye is covered and the left eye opened the same pixelated pattern is there".
Unknown/Female	"It is something that works like white noise. I don't notice it, but its there. It simply just fills the air. Tiny pinpricks of light, all of which seem multicolored, but do not alter my perception of color. As previously mentioned, it's like the pixels of a tv screen. This condition has not altered my vision in any way, nor does it hurt me, or annoy me. It's just the way it is for me. I want to know what it is that I have, and if its common or not"
Unknown/Male	"However, the specific visual phenomenon that concerns me most is the wavy or "pixelated" appearance of straight lines. It is worse on the computer, but apparent on any high contrast straight line on paper, highway signs, etc. These are not huge waves or distortions that would indicate AMD or other obvious retinal issues, but more like "noise"
Unknown/Female	"Has anybody else experienced pixelated vision? This started a few weeks ago with me. It is not constant but I've started to notice that when I blink and then open my eyes my vision is darkness with white and greenish dots like pixels. This lasts a split second and my vision returns to normal but was just wondering if this is another MS thing or something else".
25/Unknown	"It looks like the pixels on a tv screen, or like static. Especially noticeable in the dark, or against a solid-colored background. It's definitely not dust. It's too concentrated and too small. It isn't "floaters," which are larger, and fleeting. It appears to be only in the air, and not resting on objects"
Unknown/Unknown	"Since the beginning of September I have been having like fuzzy vision. The best way I found to describe it is if you go to Photoshop and use the Noise filter, that's what I see...its like a fuzzy screen over my vision...its not a major problem, but it gets annoying. I still see in the same clarity and my prescription is fine I still see everything, its just this like fuzzy screen over my vision".
Unknown/Female	"Hi, I have come upon a recent phenomena call 'visual snow', but I prefer to call it pixelated vision, because it resembles the reverse images of pixels on a computer. Lately, I have been seeing it, and I was wondering how many people also have been experiencing this problem".
13/Unknown	"Ok. So last night (and still a little bit this morning) I had blobs which made everything in real life pixelated and blurry - they were making it impossible to see anything. I had a really bad headache while this was happening"
Unknown/Female	"My vision is very densely pixelated. like thousands of tiny dots swarming around everywhere in my field of vision and they are still their when I close my eyes. my eyes can't even adjust to the dark because the dots are white and swarming and flashing around everywhere".
Unknown/Unknown	"Why is my vision pixelated, like on a tv? Is this an eye condition or am I going crazy?"
Unknown/Unknown	"Why is my vision pixelated, like on a tv? What does it mean when my vision is fine but it s fuzzy"
61/Female	"The patient has a 30+ year history of Type 1 diabetes, has had cataract surgery in both eyes and never had laser or vitreo-retinal surgery for treatment of her diabetic retinopathy. Essentially, she has been doing very well. I see her at least twice a year to insure there is no diabetic macular edema and no sign of proliferative diabetic retinopathy. She has been complaining of a "pixelated" change to the vision of the left eye".

Unknown/Unknown	"Relaxed start to the day...light breakfast...suddenly peripheral vision in left eye is slightly blurred...like viewing TV... where the screen is pixilated at the very edge...taken BG reading...up from 5.8...to 9"
Unknown/Unknown	"One day, I was hanging out with my friend, and he told me that he's started seeing everything in pixels. strangely, I've always seen everything in pixels or like everything had a grainy texture to it. after asking more about it, he said around a few months ago, his vision entirely went pixelated like you'd see looking at your computer screen".

affected individual the majority of the time (n=14, 93%) or a health care provider (n=1, 7%). The affected individuals' sex were female (n=5, 33%), male (n=2, 13%) or unknown (n=8, 53%). Pixelated vision was a new onset phenomenon in (n=10, 67%) and a chronic phenomenon in (n=5, 33%).

Discussion

Our infodemiologic approach identified 15 independent web-based forum postings describing pixelated vision as an unidentified visual phenomenon. Of these, one third were described as a life-long experience while the remaining two thirds were more acute in onset. The majority described pixelated vision as an isolated symptom with no other health concerns suggesting that this is unlikely pathological in nature. The availability of these forum postings suggests that pixelated vision is an uncommon, but normal visual phenomenon as yet undocumented in conventional medical literature.

Beyond this case report, limited studies have been noted in the migraine literature describing a similar phenomenon referred to as "visual snow". Schankin et al. described visual snow as a persistent disturbance in the entire visual field similar to that of an analog television. Through a retrospective chart review, those with visual snow were often found to have additional visual symptoms such as palinopsia or photophobia, comorbid migraines and normal ophthalmological examinations. They concluded that although these associations exist, the temporal overlay does not support a hypothesis of visual snow being the result of migraine type aura but rather a unique clinical syndrome requiring further characterization and research[4,5]. Furthermore "visual snow" within the pediatric literature is limited, with less than 10 peer reviewed publications at the present time. "Visual snow" and "pixelated vision" may represent similar phenomena, however, one may argue that for millennial youth who have a large exposure to screen time "pixelated vision" may be a more appropriate term. Moreover, some of our descriptions of acute "pixelated vision" could be more accurately ascribed to migraine scotoma had more information been reported (Table 1).

The strength of our study was the relative accessibility of online posts describing this phenomenon, which are not otherwise found in more traditional scientific literature. The isolation of the visual phenomenon in the majority of cases suggests a real, non-pathological process, with an unknown incidence and prevalence in the population. Conversely, our approach is limited to its qualitative design and reported co-morbidities, where objective validation of information is not possible. It is important to note that non-refereed information on the internet, though abundant at times may lead to premature conclusions. This further necessitates the need for vigorous scientific methodology in the medical community. Nevertheless, this study confirms utility for web-based infodemiology studies when conventional medical literature fails to characterize unusual and uncommon subjective medical phenomenon. This knowledge may provide a role in both identifying pixelated vision as a potential variation of normal and providing reassurance to patients seeking medical care of the validity of their symptoms and its apparent benign nature.

Conflict of Interest Statement

The authors have no competing interests to declare.

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Humanities

Promoting skin cancer awareness

Aryan Riahi, Bsc.

While the incidences of many cancers are declining in Canada, skin cancer continues to be on the rise. For instance, the incidence of melanoma rose by 2% for men and 1% for women between 1986 and 2010[1]. By 2031, it is estimated that the annual financial burden for skin cancers will reach $922 million in Canada alone[2]. In addition to the economic implications, the morbidity, mortality, and psychological distress associated with skin cancer are significant.

The increasing incidence of skin cancer is rather surprising, considering its largely preventable nature. Among different risk factors, natural and artificial sources of ultraviolet (UV) radiation are responsible for over 50% of skin cancers worldwide[3]. Protection strategies from UV exposure are warranted, such as staying in the shade, and using clothing items or sunscreen when exposure is unavoidable. Unfortunately, these behaviours are less prevalent than one would expect. Canadian surveys reveal that only 30-40% of Canadian adults apply sunscreen or seek shade[4]. Furthermore, 37% of adults experience sunburns during summer, indicating non-adherence to the sun protective strategies[4]. Sunburns indicate skin damage, and are associated with skin cancers as both are linked to excessive UV radiation[5-6].

The skin cancer epidemic in Canada persists in part from a lack of public awareness of its prevalence, seriousness and prevention techniques. Nevertheless, the preventable nature of skin cancers makes them a low-hanging fruit for public health intervention. In this commentary, we explore specific populations that are at-risk of skin cancer due to greater vulnerability to UV exposure. The need for public health campaigns and legislative policies aimed at these populations is discussed. Successful public health efforts in Australia area also mentioned, serving as a model for Canada.

Occupational Exposures

Individuals whose outdoor activity forms a large portion of their employment are at greater risk for UV radiation. These include, but are not limited to, workers in construction, landscaping, and recreational industries[7]. The levels of sun exposure experienced by these workers may be hazardous and reach the threshold for causing skin cancer. For instance, a study by Peters et al. measured sun exposure levels among Australian outdoor workers. An overwhelming proportion (90%) of workers experienced exposures that were well above the exposure limits established by the International Radiation Protection Association[8]. We speculate that this would be comparable to Canadian figures, where many individuals are employed in outdoor industries.

Despite their increased risks, outdoor workers show different levels of awareness with regards to the hazards of UV exposure. In a 2012 review, 35% of farmworkers in California reported no knowledge of skin cancer[9]. Such unawareness may, in turn, translate to reduced adherence to sun protective behaviours. Accordingly, the authors found that 50-80% of building workers and farmers in multiple countries do not readily protect their skin using long-sleeved clothing[9]. Canadian figures are similar, with only 29% of construction workers applying sunscreen[10].

Previous efforts aimed at promoting skin protection awareness among outdoors workers have yielded variable results. Among 16 studies investigating the efficacy of sun-safety educational programs, six reported long-term positive effects[9]. The most popular beneficial effect observed was on sunscreen application[9].

These efforts ought to be trumpeted, expanded and appropriately modified to improve their outcomes while better tailoring for workers in different industries. For instance, workers in landscaping industries may be more receptive to a combination of wearing hats and sunscreens. In contrast, construction workers already have extensive personal protective equipment, and may find additional clothing to be burdensome and too hot. Lifeguards would require water resistant protective equipment, owing to the nature of their employment.

Moreover, legislation does not necessarily translate into compliance. More effort must be invested towards enforcing workplace guidelines to protect outdoor workers from non-ionizing radiation. A study by Peters et al. found that workplaces that requires hats and sleeved shirts to promote safety also happened to have higher sun protection behaviour scores[7]. Workers practiced better sun protection behaviour at the workplace compared to on weekends. When mandated, workplace policies can be effective. Young people in particular report a higher ability to cope with risk.[7] This may explain why they tend to protect themselves less[7]. Expanding and enforcing effective workplace policies that targets the younger generation of workers is critical in promoting efficacious and lifelong sun protection behaviours.

Furthermore, educational efforts should be complemented by legislations that promote sun protective behaviours. To the best of our knowledge, no national policy exists for promoting sun protection among outdoor workers. Current governmental policies focus on providing water for employees and preventing heat stress[23]. These can be further adapted to also protect employees from excessive sun exposure. For example, employers can be required to provide sunscreen of adequate protection at their work site. Employees would then be mandated to apply and appropriately reapply sunscreen to ensure their skin remains protected at all times. Sunscreen can be added to the existing collection of personal protective equipment, such as helmets and closed toe boots. Such legislations require advocacy from the medical community at all levels of federal, provincial/territorial, and local governments.

Since Canada employs a significant number of outdoor workers in comparison to other sectors, the nation may have much to gain in investing towards policies and programs aimed at skin care prevention and awareness.

Indoor and Outdoor Tanning

Tanning, in both indoor and outdoor environments, poses risks of excess UV radiation. Tanned skin continues to be associated with desirability and attractiveness, encouraging many individuals to voluntarily expose themselves to natural and artificial UV exposures[11]. Among the general population, indoor tanning is five times more common in young white women compared to other demographics[12]. Moreover, Google search trends indicate that interest in tanning salons peak during March in Canada and the United States[13].

Previous legislative efforts have led to recent regulations that ban indoor tanning for minors across all Canadian provinces[14]. Moreover, governmental guidelines mandate tanning salon owners to follow an appropriate tanning schedule. For instance, 48 hours must pass between first and second tanning sessions, and client records should be maintained to keep track of total exposure[15].

These actions are not only warranted, but are necessary and thus should be expanded. Tanning salons can be mandated to openly report their average UV exposure dose, and the consequences of tanning. Similar to how cigarette packages contain warning messages, tanning salons could put up signs so that consumers are aware of the risks associated with tanning. These include not only skin cancer, but also premature skin aging, loss of skin elasticity, burns, and immune suppression[4].

To complement these legislative actions, public health programs can aim to educate the public and increase awareness around the link between tanning, UV exposure, and skin cancers. These programs ought to be year-round, with greater efforts to reflect the demographics and temporal aspects of risk. On top of campaigns dedicated to the general public, more efforts can be placed for young white women, and during the months leading up to March.

Lessons from Australia

Sun exposure is ubiquitous across the globe, and Canada can follow successful examples from other countries. For instance, public health efforts over the last 30 years in Australia demonstrate the importance of employing several different approaches in tackling the skin cancer epidemic. In addition to educational programs, tax-free sunscreens, support for tree-planting, and sun protection policies in schools were implemented to protect children and adults alike[16].

Now, 30 years later, the results of these efforts are clear[17]. The public's comfort with getting suntans has decreased, while the usage of hats and sunscreens has increased. The incidence of melanoma has considerably declined, especially for the younger generations who were exposed to these reforms at an early age[18]. These examples indicate that well-designed public health initiatives towards skin cancer are effective, and should be used as models to encourage Canada to begin implementing similar protocols. These efforts ought to be directed at not only the aforementioned at-risk populations, but also the general public.

Steps in the Right Direction

While the recent move to ban minors from accessing tanning salons was a start, adults may also benefit from legislation that limits exposure to carcinogenic non-ionizing radiation. The first steps would include awareness campaigns. Such campaigns have been successful in other nations. For example, ever since Australia banned the use of tanning for cosmetic purposes for all ages, more people have turned to alternatives including spray tan equipment. While banning indoor tanning would protect adults from exposing themselves to a carcinogen, informing adults shares a similar goal while promoting autonomy over paternalism.

An Investment Worth Considering

Indeed, skin cancer is a public health problem that is thankfully preventable. Public health strategies aimed at protecting the general public and vulnerable subpopulations will lead to a win-win situation

through reduced morbidity, mortality, and healthcare expenditures associated with skin cancers. Given the progress that has been made in reducing the burden of many other cancers, it is time that we take skin cancer in Canada more seriously.

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Humanities

Acne: Advocating for holistic support

Aryan Riahi, Bsc., David Jung

Abstract

As health practitioners, having a holistic approach to patients is critical. Patients are a complex interplay of physical, emotional, and social well-being. Limiting treatments to only some of these domains will inevitably yield suboptimal health and reduced quality of life. Thus, it is imperative that we advocate for acne-prone individuals so that they can receive the well-rounded care they deserve.

Introduction

For many people, acne is like an unwanted gift. The surprise associated with discovering new acne is similar, but more unpleasant. Acne is a fairly common phenomenon in the general population, especially among adolescents. However, despite its prevalence, it is associated with negative societal perspectives. The embarrassment and shame tied to acne could inevitably increase its burden on the bearer.

In this commentary, we explore the stigma associated with acne and its implications. Acne occurring in the general population is discussed, including adolescents and beyond. The multifaceted impacts of acne and the need for more holistic therapies will be the focus of the commentary.

A History of Stigma

The stigma associated with acne has a longstanding history that has stood the test of time. In 1951, a paper claimed that individuals affected by acne were more prone to becoming social outcasts due to societal ridicule and avoidance. Acne carried the stereotype of living an "immoral life," and acted as barriers to enjoying the basic privileges of people with clear complexions1.

More than 60 years later, the negative connotations still hold today. A 2013 study by Timms[2] divided 143 subjects into two groups. One group was shown photos of people with acne, while the other was shown clear-skinned people. Individuals affected by acne were perceived to be less mature, less attractive, and less likely to be befriended by the study participants.

In 2017, an anti-acne drug advertisement featured a famous actress tearing up as she described her experiences with bullying in school due to acne. She went on to mention how happy she became after discovering the drug and becoming clear-skinned. This advertisement was banned, as it made implications that teenagers with acne who do not use anti-acne medications are more at risk of being targeted for bullying[1].

The negative perception of acne is fairly obvious, and becoming more easily accessible with advancements in media technology. For instance, simply turning on the television could fill an evening of relaxation with a sense of insecurity and social inadequacy. These social repercussions could also translate to real-life difficulties in social interactions and even in seeking employment[3-5].

The Role of Family History

Heredity is a major contributing factor to alopecia. A study on androgenic alopecia found that men with fathers who experienced hair loss faced a 2.5 times greater likelihood of reporting hair loss than those whose fathers did not experience hair loss[7]. Other studies have confirmed the association between the patient's hair loss and positive family history for first-degree relatives[8]. Approximately 80% of androgenic alopecia is accounted for by family history[1]. Similarly, 20% of patients with alopecia areata have a positive family history[9].

The experience of growing up in a household where balding is commonplace is one that is all too familiar for patients suffering from alopecia. Male androgenic alopecia has an autosomal dominant heredity and affects 30-50% of men by the age of 50[1]. Most males from my maternal and paternal family tree began losing their hair in their teens and twenties. Awaiting a similar fate as them is a source of anxiety for me. The distress that many patients face once the process of hair loss begins is understandable and requires empathy from healthcare professionals.

Not Limited to Adolescence

While acne has been linked with adolescence, the prevalence of adult acne is increasing[6]. Analogous to adolescent acne, adult acne commonly affects the face and can lead to scarring or pigmentation[7,8]. With an increasing presence and potential complications, adult acne also warrants attention from the medical community.

Psychological Consequences

With such negative societal views towards acne, it is not surprising that the condition is associated with mental health implications. In adolescents, acne is linked to depression, anxiety, and attention deficit hyperactivity disorder. Among adults, depression, anxiety, psychosis, and obsessive-compulsive disorders are associated with psychiatric comorbidities. These disorders may be due to the sense of insecurity, fear of public shaming, and social withdrawal experienced by acne-prone individuals. The psychiatric impacts may be greater in adults, with up to 40% experiencing psychiatric comorbidities[9].

Is Pharmacologic Theraphy Enough?

Historically, healthcare providers have turned to pharmacologic options to control acne severity, excoriations, and flares. While doing so, the psychological and social aspects of acne have often been overlooked. Nevertheless, acne requires a well-rounded approach that extends beyond the skin alone. For instance, severe forms of acne share a similar social, emotional and psychological burden as other chronic conditions including asthma and diabetes[10,11]. Recent studies have also shown that acne-prone individuals are at higher risks of experiencing conflicts with family members and peers[12]. Considering the multifaceted consequences of acne, more holistic approaches are warranted for its treatments.

Various efforts have been made to deliver holistic approaches to care for other conditions. Already, there are centers for atopic dermatitis patients where whole families can participate in educational programs. These are run under a multidisciplinary team consisting of dermatologists, psychologists, nurse practitioners, and nutritionists catering to the different needs of each patient. In addition to the formal services offered, families can also interact with one another while sharing their experiences and tips. These programs are present in Europe, Asia, and the United States, and have been met with positive feedback by participants[13-14].

In 2018, the first acne educational program for high school students was launched by the Acne and Rosacea Society of Canada, under the name "Skin Confident."[15] Aimed at students in grades 10 and 11, this consists of a free online 1-hour presentation discussing the biology behind acne, and recommendations towards managing skin care and self-esteem[15]. Similar programs could target acne-prone individuals in other age groups, including younger students and adults. In addition, efforts should be made to implement offline sessions hosted by healthcare providers, and to include family members, caregivers, and individuals living or working with individuals experiencing acne. To our knowledge, "Skin Confident" is unique in its place of Canadian educational programs dedicated to acne.

In the interim, more widespread use of psychological treatments should be advocated for acne. These include cognitive-behavioral, interpersonal, and group therapies to address the psychological burden accompanied by acne. A 2019 systematic review found cognitive behavioral therapies to be effective for moderate-to-severe psoriasis, and similar treatment modalities should be further explored for acne[16].

Moreover, the stigma directed towards acne can be targeted through public health educational programs. These should be aimed at altering the societal perception towards acne so that the stigma will be lessened. The cumulative effects of reduced social repercussions and improved overall well-being of acne-prone individuals will be synergistic.

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