

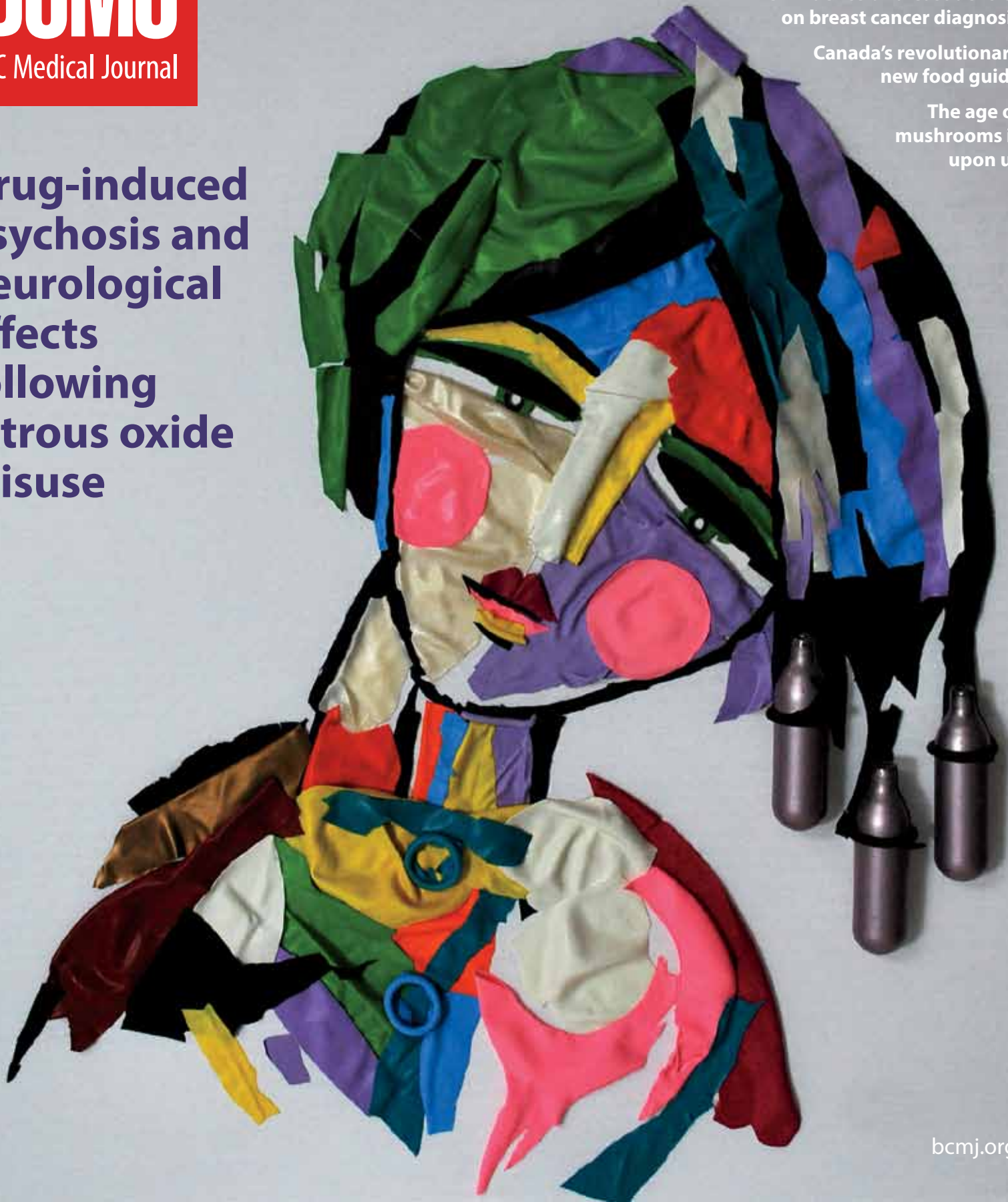
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ON THE COVER

Drug-induced psychosis and neurological effects following nitrous oxide misuse

Nitrous oxide is becoming a popular recreational drug all over the world. Users can easily obtain it by puncturing small cannisters used in whipped cream dispensers. Our case study on drug-induced psychosis following its misuse begins on page 385.

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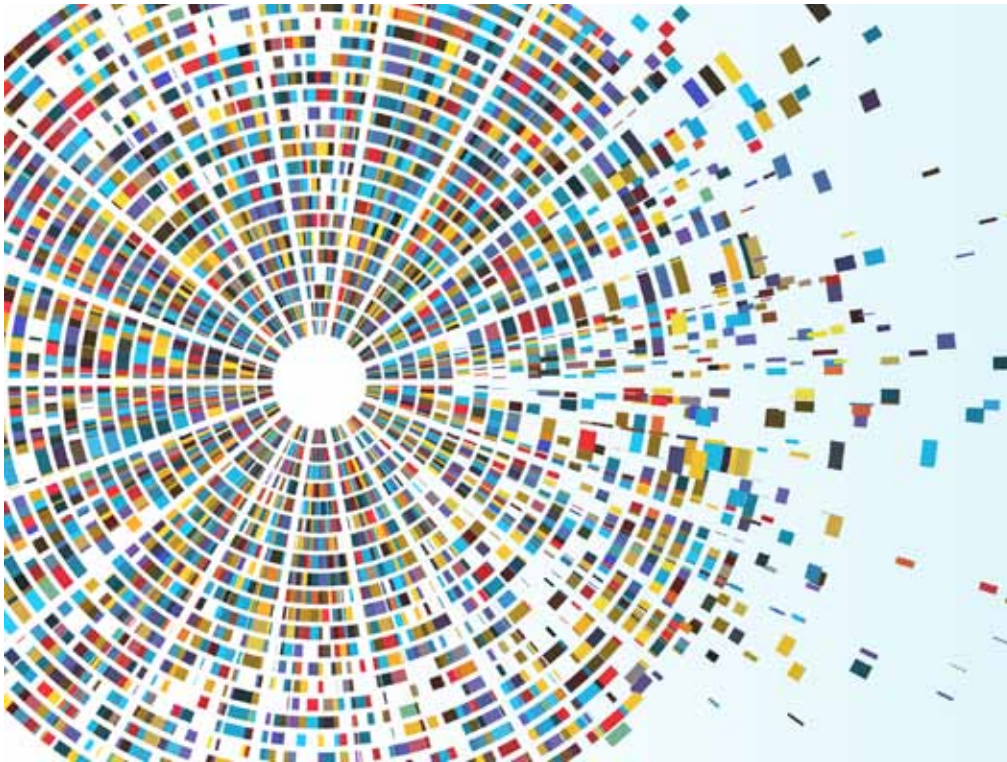
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My selfish Christmas wish

Christmas is a magical time for a child. Does anyone else remember the long-anticipated arrival of the Sears catalogue? My brothers and I would pour over the pages circling desired toys for my parents' later perusal. Unable to sleep on Christmas morning, we would lie in bed tortured by the slow movement of time until the anointed hour arrived and we were free to empty stockings and open presents. My parents seldom bought any of the circled items, explaining they looked cheap and wouldn't last. I am sure there was a lesson in there somewhere. Regardless, I was blessed to grow up in a home that could afford all the trappings of the holidays.

Over the years Christmas has become less about receiving and more about giving. The focus shifted to shopping for my spouse and children. This can be stressful, but the joy and happiness

reflected through a gift well chosen warms the heart. I would rather watch a loved one's reaction to opening a gift than open one myself. Being with family, sharing food and drink during this time, is about as perfect as it gets.

"All I want for Christmas is you!"

As another Yuletide approaches, I find myself in an interesting position. My children are grown and my parents have passed on. Grandchildren are awesome and I love spoiling them on Christmas; however, I find myself restless and longing for the good old days. Therefore, I have decided that this Christmas should once again be all about me and my wants (don't judge me). So, what does an editor desire for the year ahead? To paraphrase Mariah Carey, "All I want for Christmas is you!"

Our journal's circulation is roughly 14 000, which includes practising and retired physicians, students, and residents. I have heard that every person has at least one good novel in them. I would prefer to think that each of you has at least one good essay, opinion piece, scientific study, theme issue, letter, or back-page feature floating around in your consciousness. So, for Christmas, that is what I want. Write them down, type them up, finish that last paragraph, and send them in. Don't be intimidated. Our journal is written by the physicians of BC for the physicians of BC, so that means you. Please do your part to make this aging editor's dream a reality this Christmas. You all have something valuable to share and I want to read it.

Happy Holidays. ■

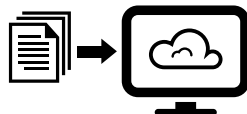
—David Richardson, MD

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New research on hormones and breast cancer: The headlines don't convey what women need to know

Researchers in the UK recently published the results of a worldwide analysis on menopausal hormone therapy and breast cancer risk in the *Lancet*.¹ The analysis included 58 studies, published between 1992 and 2018, of over 100 000 postmenopausal women with breast cancer. They found that women who had *ever* taken hormone therapy had a higher incidence of breast cancer than those who had not.

Now, these findings are significant and published in a reputable journal, but they are nowhere near as astonishing as the news media portrayed them to be.

Immediately after the results, sensational and fear-provoking interpretations appeared in the headlines. The *Telegraph* reported, "HRT raises breast cancer risks by a third, major Oxford study finds," and the *Guardian* read, "Breast cancer risk from using HRT is 'twice what was thought.'" The *Independent* conveyed, "Menopausal hormone therapy linked to greater breast cancer risk for more than a decade after use."²⁻⁴

These headlines might entice readers, but they certainly do not help women.

As doctors, we are continually challenged to interpret scientific research and then distill the relevant parts into language that our patients understand. Sometimes, however, we are merely a second opinion to the media. Like it or not, Dr Google has become the most accessible medical resource in the world. So when our patients get bad information online before they see us, it makes our job that much harder and, more importantly, it compromises their health care.

A brief history of menopause and hormone therapy is required to understand the impact of these recent titles. Menopause is a normal stage of life for women. A girl is born with a finite number of eggs that decrease over her lifetime until there are none left, and she enters menopause. On average this happens around 51 years old, but anywhere from 45 to 55 is normal.

While some women navigate this major life event without issue, 60% to 80% of women will encounter symptoms that worsen their quality of life.^{5,6} Hot flushes, night sweats, trouble sleeping, memory problems, and depressed mood are some of the most common concerns. These symptoms stem from the abrupt loss of

estrogen, normally produced by the ovaries, and the body's struggle to re-equilibrate. Although they are not life threatening, these complaints should not be dismissed as trivial.

For example, menopause in one of our patients, a lawyer, led to unpredictable sweats that caused her to appear distracted and nervous in the courtroom. She chose to take hormone therapy to help ease her body through the transition and credited it with keeping her fast-paced career on track. Another professional, a surgeon, could not practise because sweat from her face would drip into patients' open incisions. She also chose hormone therapy to allow her career to continue.

Hormone therapy mitigates menopausal symptoms by giving back a small dose of estrogen. Contemporary regimens most commonly involve an estrogen patch, gel, or tablet. Doctors individualize the amount to find the lowest effective dose for each woman. Unless the woman has had a hysterectomy, she would also be prescribed progesterone to limit the growth of the uterine lining, which could otherwise cause bleeding.

Dr Dunne is a co-director at the Pacific Centre for Reproductive Medicine in Vancouver and a clinical assistant professor at the University of British Columbia. She serves on the BCMJ Editorial Board. Dr Rowe is an associate professor at the University of British Columbia, former Editor-in-Chief of the Journal of Obstetrics and Gynaecology Canada, and a former BCMJ Editorial Board member. He is a recognized expert in menopause and hormone therapy.



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In the 1990s hormone therapy was common. After the results of the Women's Health Initiative (WHI) study in 2002 and 2004, however, the number of women starting hormone therapy dropped from 1 in 12 to 1 in 20.⁷⁻⁹ Furthermore, of the women already taking hormones when the WHI study was released, one in five stopped them. Among the main reasons they did so was media reporting.⁹

It is imperative that we step back and examine how we explain medical research to the public. Framing the results of a study with the appropriate context and magnitude can drastically change how people read them.

When we teach medical students about research, one of the most important principles of critical appraisal is interpreting the real-life risk. In statistical terms this is referred to as the absolute risk versus the relative risk. Relative risk is usually the less useful but more dramatic statistic—the one often cited in headlines. To

illustrate with a simple example, a headline that reads, “double the risk of dying” (a relative risk of 2.0) might actually be referring to an absolute risk of 1% going up to 2%.

In this UK study, the relative risk conveys how often the event (i.e., breast cancer) happened in the hormone therapy group versus the group that did not take hormones. Women 50 to 54 years old currently using hormones had a relative risk of 2.1, which can be interpreted as being *twice as likely* to get breast cancer. That sounds pretty scary to most people. Fortunately, doctors are trained to rely on the absolute risk. It is much more meaningful as it refers to the probability of breast cancer in a *population* of women exposed to hormone therapy.

The authors of the *Lancet* study actually did an excellent job of stating the absolute risks on the front page. Unfortunately, media headlines did not focus on that paragraph. The conclusion was that taking estrogen and progesterone for 5 years was associated with *one additional breast cancer in every 50 women*.¹ To put things in perspective, that is actually a smaller risk increase than drinking alcohol, not breastfeeding, or being overweight.⁵ Furthermore, as the North American Menopause Society emphasized, these results are observational associations rather than cause-and-effect conclusions, which are normally restricted to randomized controlled trial.^{4,10}

The problem, as with our periodic “pill scares” related to birth control pills, is that bad news grabs a reader’s attention but good news does not. In emphasizing an arguably small (and previously known) risk of breast cancer when framing a story about hormone therapy, we are missing the big picture. Menopausal women take hormone therapy because it makes their lives tolerable and their careers manageable, not because they really want to take it.

The commentaries that have appeared in response to this recent report all stress the importance of individualized decisions for women considering hormone therapy, and that’s as it should be.^{10,11} No menopausal woman should take hormone therapy without a careful assessment of her individual risk and the potential benefit, conducted with a knowledgeable care provider. Women and health care professionals should not be alarmed by the latest news. To


quote a recent statistician’s words in the *New Yorker*, “How impressed should we be by very strong evidence for a very weak effect?”¹² ■

—Caitlin Dunne, MD

—Timothy Rowe, MBBS, FRCS, FRCOG

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Strength in numbers: The power of cooperation

“We must use collegiality not to level people down, but to bring together their strength and creativity.” —Andy Hargreaves

As my year as Doctors of BC President reaches the halfway mark, I am reflecting on my mandate to date. In my inauguration speech, I spoke about leadership, professional culture, connectivity, change in our rapidly evolving world, and the need for courage. I am committed to supporting and building courage in physicians across our province. This courage enables them to lead the changes our health care system needs to be both comprehensive and sustainable moving into the future. To meet these goals I outlined back in June, I have been traveling across the province to begin to understand how my colleagues are defining, meeting, and resolving these challenging issues, and learning how Doctors of BC can support their work.

Those of us who have traveled, volunteered, or worked abroad understand that traveling and sharing experiences changes who we are at a fundamental level that can be hard to define. We understand that listening to stories and attempting to understand the experiences of others is transformative and goes a long way toward breaking down barriers. There is much we can glean through exposure to different methods of studying, coping, and ultimately addressing problems.

Being invited to attend local meetings with grassroots physicians and Doctors of BC staff who provide local support has been transformative for me personally. I have gained an amazing amount of direct knowledge in my engagement work, but what has been most striking to me is the power of collegiality, particularly in smaller communities. Our personal life experiences and (often unconscious) biases alter our interpretation of what we learn from every new encounter. In fact, people will often leave meetings with

very different interpretations of the same events. Maintaining and fostering this sense of professionalism and collegiality becomes even more crucial in this context.

When I sat down to write this column, I reflected on how I could best define *collegiality*. The *Merriam-Webster Dictionary* defines the word *colleague* as, “an associate or co-worker typically in a profession or in a civil or ecclesiastical office and often of similar rank or state: a fellow worker or professional.” I would suggest that the active definition of collegiality encompasses much, much more and includes the principles of respect, commitment to moral principles, and valuing the work of others. Collegiality builds trust. If we can respect each other’s work, viewpoints, and ideas, we can cooperate and provide the support needed to make necessary changes. If we are all committed to the same basic moral principles and values as physicians, and we understand the goals of our health care system, it makes it easier to work as a team where everyone is valued. Our shared commitment to understanding each other’s perspectives gives us the power to lead change.

I have witnessed firsthand the incredible collegiality of our colleagues across the province, as they truly value the professional skills they each bring to the table. I have seen their devotion to solving local issues in a way that supports, rather than tears down relationships across specialities, as they build processes that improve both the individual’s working life and

patient access to quality care. I have noticed the positive impact on relationships with our governing bodies, allied health, and public not-for-profits in improving on-the-ground resources and access to care.

I would like to challenge you all to take a moment, look at the work your colleagues do every day, and ask, “What can I do in my work that will improve the day-to-day work of my colleagues and foster a better system for all of us?” If you see nothing, then I encourage you to reach out and ask, as you may in fact not have the full picture.

There is no room for empire building or ego in this type of collegial work.

No matter how you as an individual apply the professional skills you have acquired to date, we are all an invaluable part of a much greater whole. There is power in supporting each other, and exploring new ways to deliver care that we simply cannot achieve working in silos. We are truly Better Together. ■

—Kathleen Ross, MD
Doctors of BC President

If we can respect each other’s work, viewpoints, and ideas, we can cooperate and provide the support needed to make necessary changes.

Colin Mar, MD, Janette Sam, MRT, Colleen E. McGahan, MSc, Kimberly DeVries, MSc, Andrew J. Coldman, PhD

The influence of breast density on breast cancer diagnosis: A study of participants in the BC Cancer Breast Screening Program

A screening participant's risk of being diagnosed with an interval breast cancer following a normal screening mammogram was found to increase with age and density, and to be roughly similar at 1 year for women at higher-than-average risk (first degree family history of breast cancer) to that at 2 years for women at average risk.

ABSTRACT

Background: Normal fibroglandular tissue appears white on a mammogram and is described as dense; fatty tissue appears dark and is described as non-dense. Increased breast density is associated with greater breast cancer risk. Increased breast density also reduces the sensitivity of mammography to reveal changes associated with cancer, a concern referred to as masking. Interval breast cancers are those diagnosed between screening visits and are more common in women with dense breasts. The effects of breast density have been the subject of

much research, but the results are often summarized in ways that do not facilitate understanding for referring physicians and screening participants. An analysis of data from the BC Cancer Breast Screening Program was proposed to assess the influence of breast density on the risk of cancer and on breast cancer prognostic factors.

Methods: Although density scores were not required prior to 2018, many BC Cancer Breast Screening Program centres assigned and recorded this information. Two study samples were abstracted from the Breast Screening Program database to achieve four study objectives. Sample 1 data included mammograms of participants age 40 to 74 obtained in 2017 using digital mammography and assigned density categories according to the Breast Imaging-Reporting and Data System (BI-RADS): A (least dense), B, C, or D (most dense). Sample 1 data were used to describe the distribution of BI-RADS breast density in the screening population (Objective 1). A subset of Sample 1 data was used to examine the stability of BI-RADS density categories assigned (Objective 2). Sample 2 data included mammograms performed from 2011 to

2015. Data from this period were used to examine the influence of density on the risk of breast cancer development (Objective 3) and the effect of density on prognostic factors such as tumor size and lymph node involvement (Objective 4). The 2011 to 2015 data collection period was chosen so that notification of any cancer cases to the BC Cancer Registry was complete and 5 years of data could be analyzed. The screening history of each participant in Sample 2 was assessed by screening rounds. Screening rounds that followed an abnormal result were excluded from the analysis as participants were likely subject to further testing prior to returning to screening, and their cases would not necessarily reflect the influence of density on mammography performance. A breast cancer was defined as screen-detected if it was diagnosed in the 12 months following an abnormal screening mammogram. All breast cancers not classified as screen-detected were defined as interval cancers. Rates of screen-detected breast cancer and interval cancer were calculated and rates were estimated for participants at average risk and higher-than-average risk (i.e., having a family history of breast cancer in a first-degree relative).

Dr Mar is medical director of the BC Cancer Breast Screening Program.

Ms Sam is operations director of the BC Cancer Breast Screening Program.

Ms McGahan is director of Cancer Surveillance and Outcomes, BC Cancer.

Ms DeVries is a biostatistician in Cancer Surveillance and Outcomes, BC Cancer.

Dr Coldman is an emeritus scientist in Cancer Control Research, BC Cancer.

This article has been peer reviewed.

Results: Breast density data analyzed for 208 925 BC Cancer Breast Screening Program participants were seen to vary by age, with a declining proportion of mammograms assigned BI-RADS C and D scores at increasing ages. Density also varied by ethnic group, with East Asian participants having denser breasts and First Nations participants the least dense breasts. Density did not vary by risk status. When 62 887 mammogram pairs from 2017 and earlier were compared, concordance was lowest for mammograms with a BI-RADS score of D. The majority of participants did not have both mammograms read by the same radiologist and concordance was lower when different radiologists read the mammograms than when the same radiologist read both mammograms. Cancer risk was evaluated by looking at 649 393 screening rounds for 388 576 participants. Predicted rates of interval and screen-detected cancer were calculated for women of average risk screened on a biennial (currently recommended) basis and for women of higher-than-average risk screened on an annual (currently recommended) basis. Risk of screen-detected cancer was seen to increase with age and to vary with BI-RADS density for both average-risk and higher-than-average-risk women. Risk of interval cancer also increased with BI-RADS density and with age for average-risk and higher-than-average-risk women. Prognostic factors were tabulated separately for biennial screen-detected cancers and interval cancers. Screen-detected cancers were smaller than interval cancers and less likely to have nodal involvement. Similarly, tumor size increased among interval cancers with increasing density, but the likelihood of nodal involvement did not.

Conclusions: Other studies report similar findings to those described here, with density declining with age, higher density seen in screening participants of East Asian heritage, instability in density categorization on consecutive mammograms, and instability increasing when mammograms are interpreted by different radiologists. When discussing breast screening, breast density alone should not be seen as the primary determinant of breast cancer risk. Following a normal screening mammogram, a screening participant's risk of being diagnosed with an interval breast cancer over the next screening round increases with age and density, and is roughly similar at 1 year for women at elevated risk

to that at 2 years for women at non-elevated risk. Further research is needed to elucidate the specific benefits of the increased cancer detection afforded by supplemental testing for screening participants found to have dense breasts.

Background

Breasts are composed of varying amounts of fibroglandular and fatty tissue. Normal fibroglandular breast tissue appears white on a mammogram and is described as dense, while fatty breast tissue appears dark and is described as non-dense. At the population level the average amount of dense tissue declines with increasing age and varies by ethnic group.^{1,2}

Radiologists of the BC Cancer Breast Screening Program (BCCBSP) assess breast composition using the Breast Imaging-Reporting and Data System (BI-RADS).³ A breast density category of A, B, C, or D is assigned based on the amount of fibrous and glandular tissue that appears on a mammogram, with A being least dense (most fatty) and D being most dense (has highest proportion of non-fatty tissue). Quantitative scales that assess the proportion of the breast that is dense⁴ are also common, and automated systems producing volumetric density estimates are available.⁵ The BCCBSP currently provides BI-RADS breast density scores with all screening mammography results.

Increased breast density is associated with greater breast cancer risk.⁶ Density also reduces the sensitivity of mammography to demonstrate changes associated with breast cancer, a concern referred to as masking.¹

There is considerable interest in the influence of breast density on mammography screening performance. Increased risk and masking act synergistically to increase rates of interval breast cancer that occur between screening visits after a normal screening mammogram.⁷ The primary objective of breast screening is to reduce the risk of breast cancer death in participants by diagnosing cancers when treatment

outcomes are considerably better than would pertain if they were diagnosed later.

Screening participants diagnosed with interval cancers have not benefited from screening since their time of diagnosis and stage of disease at diagnosis are unchanged by participation in screening. In many United States jurisdictions, legislation mandates the reporting of breast density to the referring health care provider and screening participant,⁸ and supplemental testing is offered to those with denser breasts (identified as BI-RADS C or D). Currently in British Columbia, breast density is reported to screening participants and their physicians. In Canada, the organization Dense Breasts Canada advocates for increased knowledge and awareness of the effects of breast density.⁹

Although the effects of breast density have been the subject of much research, the results are often summarized in ways that do not facilitate understanding for referring physicians and screening participants. Consequently, we proposed an analysis of BCCBSP data on density and subsequent breast cancer diagnoses with four objectives:

1. To describe the distribution of BI-RADS density categories within the population presenting to BCCBSP for routine breast screening.
2. To assess the stability of BI-RADS density categories assigned to screening participants.
3. To examine the influence of density on the risk of breast cancer in screening participants.
4. To examine the effect of density on breast cancer prognostic factors.

Methods

The BC Cancer Breast Screening Program maintains records of all examinations performed. Although density scores were not required prior to 2018, many screening centres assigned BI-RADS density scores and this

Increased breast density is associated with greater breast cancer risk. Density also reduces the sensitivity of mammography to demonstrate changes associated with breast cancer.

information was recorded in the BCCBSP database. This database contains details on the mammogram performed, including the result, and information on the participant (age, self-reported ethnic group, etc.). The British Columbia Cancer Registry (BCCR) records all cancers diagnosed in British Columbia residents, and it is routinely linked with the Breast Screening Program database so that all breast cancers occurring in screening participants are identified.

Two study samples were used to achieve the four study objectives.

Sample 1 data included mammograms of participants age 40 to 74 obtained in 2017 using digital mammography and reporting BI-RADS density [Figure 1]. Sample 1 data were used to describe the distribution of BI-RADS breast density categories in the screening population (Objective 1). A subset of Sample 1 data [Figure 1] was used to examine the stability of BI-RADS density categories assigned (Objective 2). The interval of 18 to 30 months between screening rounds was selected to encompass the usual range of rescreening times in participants recommended for biennial screening.

Sample 2 data included mammograms performed from 2011 to 2015 [Figure 2]. Sample 2 data were used to examine the influence of density on the risk of breast cancer (Objective 3) and the effect of density on prognostic factors such as tumor size, whether less than or more than 15 mm, and lymph node involvement (Objective 4). The 2011 to 2015 data collection period was chosen so that notification of any cancer cases to the BCCR was complete and 5 years of data could be analyzed.

The screening history of each participant in Sample 2 was assessed by screening rounds. A screening round started immediately after a mammographic examination and ended with the next screening visit, a diagnosis of cancer, or the end of the data collection period (31 December 2015). Each screening round had factors associated with it taken from the preceding screening visit. Screening rounds that followed an abnormal result were excluded from the analysis as participants were likely subject to further testing prior to returning to screening and their cases would not necessarily reflect the influence of density on mammography performance. Consequently, all screening

rounds commenced following a normal screening mammogram in the study period.

A breast cancer was defined as screen-detected if it was diagnosed in the 12 months following an abnormal screening mammogram. All breast cancers not classified as screen-detected that occurred within specified rescreening intervals (annual, biennial, or triennial) were designated as interval cancers.

Rates of screen-detected breast cancer and interval cancer were calculated and analyzed. Rates were estimated for screen-detected and

interval cancer for participants at average risk and higher-than-average risk.

The study was approved by the British Columbia Cancer Agency Research Ethics Board approval number H19-02530.

Results

Breast density data were analyzed for 208 925 BC Cancer Breast Screening Program participants age 40 to 74 who had a digital mammogram in 2017 [Figure 3]. Density was seen to vary by age, with an increasing proportion

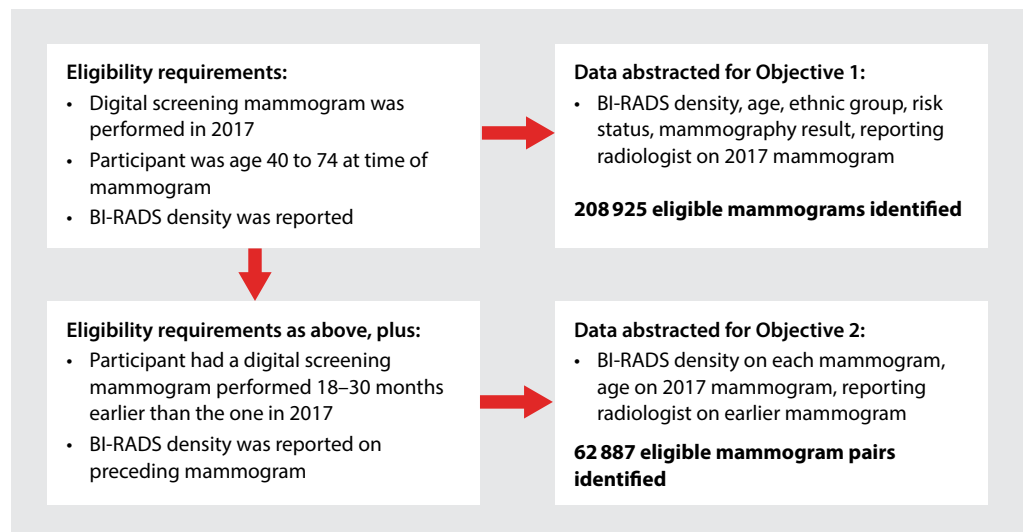


FIGURE 1. Sample 1 data used to examine BI-RADS breast density categories (Objective 1) and the stability of BI-RADS categories (Objective 2) in BC Cancer Breast Screening Program population.

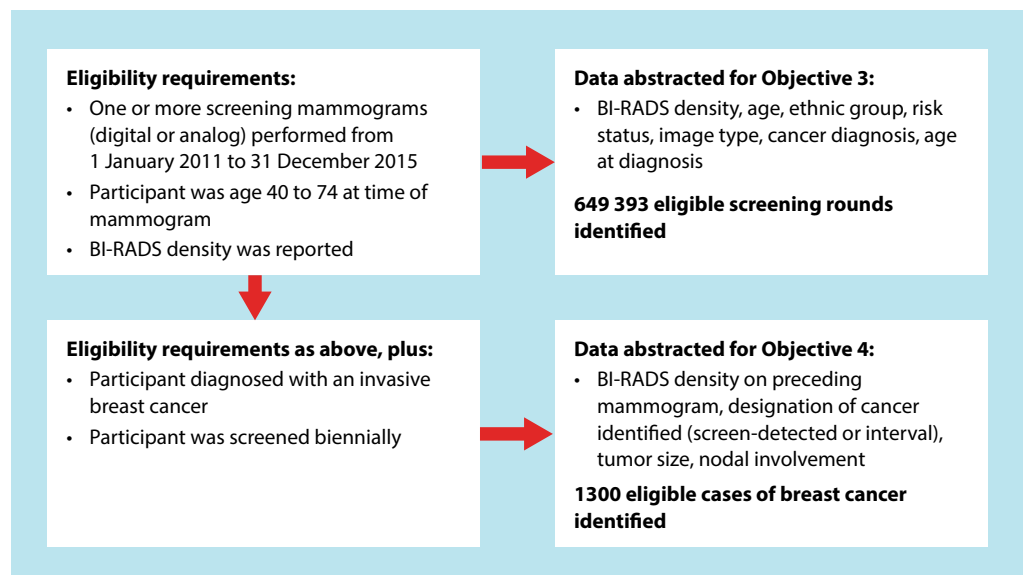


FIGURE 2. Sample 2 data used to examine the influence of density on the risk of breast cancer (Objective 3) and breast cancer prognostic factors (Objective 4) in BC Cancer Breast Screening Program population.

of BI-RADS A and B mammograms and a declining proportion of BI-RADS C and D mammograms at increasing ages. Density also varied by ethnic group, with East Asian participants having the densest breasts and First Nations participants the least dense. Density did not vary by risk status. Mammograms interpreted as abnormal were less likely in

BI-RADS category A (5.3%) than category B (9.4%), category C (10.5%), and category D (10.7%).

When 62 887 mammogram pairs from 2017 and earlier were compared, concordance was lowest for mammograms designated BI-RADS category D, with only 50.9% of mammograms designated as D on the first mammogram being

designated D subsequently [Table 1]. Concordance overall was 68.7% (same BI-RADS density on both mammograms) and 82.5% for categories C and D combined. The majority of participants (73.5%) did not have both mammograms read by the same radiologist and concordance was lower when different radiologists read the mammograms (65.5%) than

TABLE 1. BI-RADS breast density categories reported on 2017 mammograms compared with categories reported on earlier mammograms.

Category	Number	Result on earlier mammogram		Result on 2017 mammogram		
		BI-RADS D	BI-RADS C or D	Same on both (%)	BI-RADS D on both (% of D on earlier)	BI-RADS C or D on both (% of C or D on earlier)
Age 40–49	8742	1520	5564	5872 (67.2%)	894 (58.8%)	4858 (87.3%)
Age 50–59	21 453	2119	10 587	14 729 (68.7%)	1034 (48.8%)	8708 (82.3%)
Age 60–69	23 318	1254	8109	16 168 (69.3%)	585 (46.7%)	6531 (80.5%)
Age 70–74	8165	340	2269	5623 (68.9%)	148 (43.5%)	1795 (79.1%)
Same reporting radiologist	16 690	1241	7234	12 913 (77.4%)	769 (62.0%)	6285 (86.9%)
Different reporting radiologist	46 197	4031	19 599	30 297 (65.5%)	1913 (47.5%)	15 840 (80.8%)
All	62 887	5272	26 833	43 210 (68.7%)	2682 (50.9%)	22 125 (82.5%)

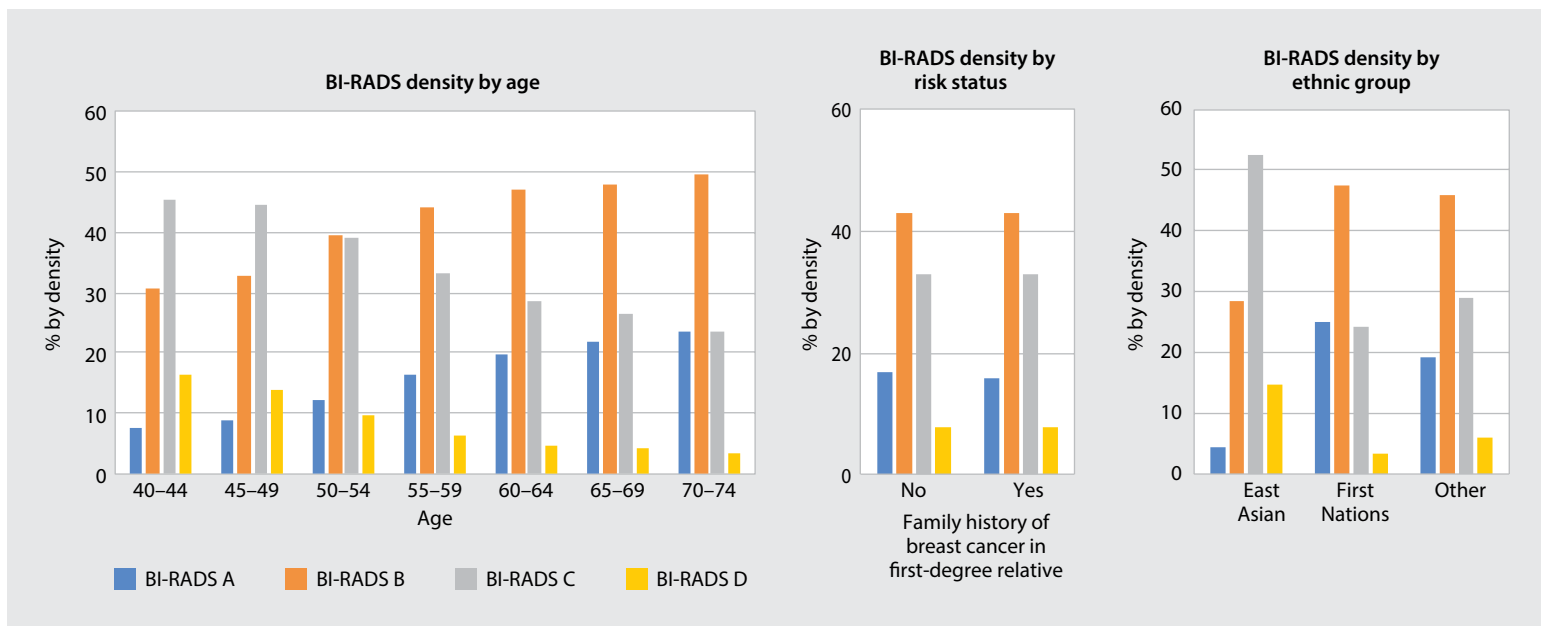


FIGURE 3. Breast density of participants screened in 2017 by age, risk status, and ethnic group.

TABLE 2. Screening round factors considered, including participant risk status, age, ethnic group, BI-RADS density category, and mode of detection for invasive breast cancers identified.

Factor		Number	%
First screening visit prior to round	No	582 337	89.7
	Yes	67 056	10.3
Higher-than-average risk	No	531 587	81.9
	Yes	117 806	18.1
Age at beginning of screening round	40–44	70 532	10.9
	45–49	106 729	16.4
	50–54	109 482	16.9
	55–59	112 096	17.3
	60–64	105 262	16.2
	65–69	87 763	13.5
	70–74	57 529	8.9
Image type of preceding mammogram	Analog	275 044	42.3
	Digital	374 349	57.7
Ethnic group	East/Southeast Asian	90 077	13.9
	First Nations	13 349	2.1
	Other	535 949	82.5
BI-RADS density at preceding mammogram	A	170 958	26.3
	B	243 738	37.5
	C	183 487	28.3
	D	51 210	7.9
Mode of detection for invasive breast cancer identified	Screen-detected	1513	58.9
	Not screen-detected	1057	41.1

when the same radiologist read both mammograms (77.4%).

Cancer risk was evaluated by looking at 649 393 screening rounds for 388 576 participants [Table 2]. The use of screening rounds resulted in the data being weighted by participants who attended screening more frequently. Within the study period, 3117 breast cancers were identified, of which 547 were ductal carcinoma in situ (DCIS). Most BC-CBSP screening centres (37 of 41 or 90%) recorded BI-RADS density for some screening rounds. Predicted rates of interval and screen-detected cancer were calculated for average-risk women screened on a biennial (currently recommended) basis [Figure 4] and for higher-than-average-risk women screened on an annual (currently recommended) basis [Figure 5]. Risk of screen-detected cancer was seen to increase with age and to vary with BI-RADS density for both average-risk women and higher-than-average-risk women. Risk of interval cancer also increased with BI-RADS density and with age for average-risk and higher-than-average-risk women. For women with BI-RADS category D density, however, a change from biennial screening to annual screening was found to have only a modest effect on the predicted proportion of interval cancer found at the next screening visit: a change from 58% (biennial) to 54%

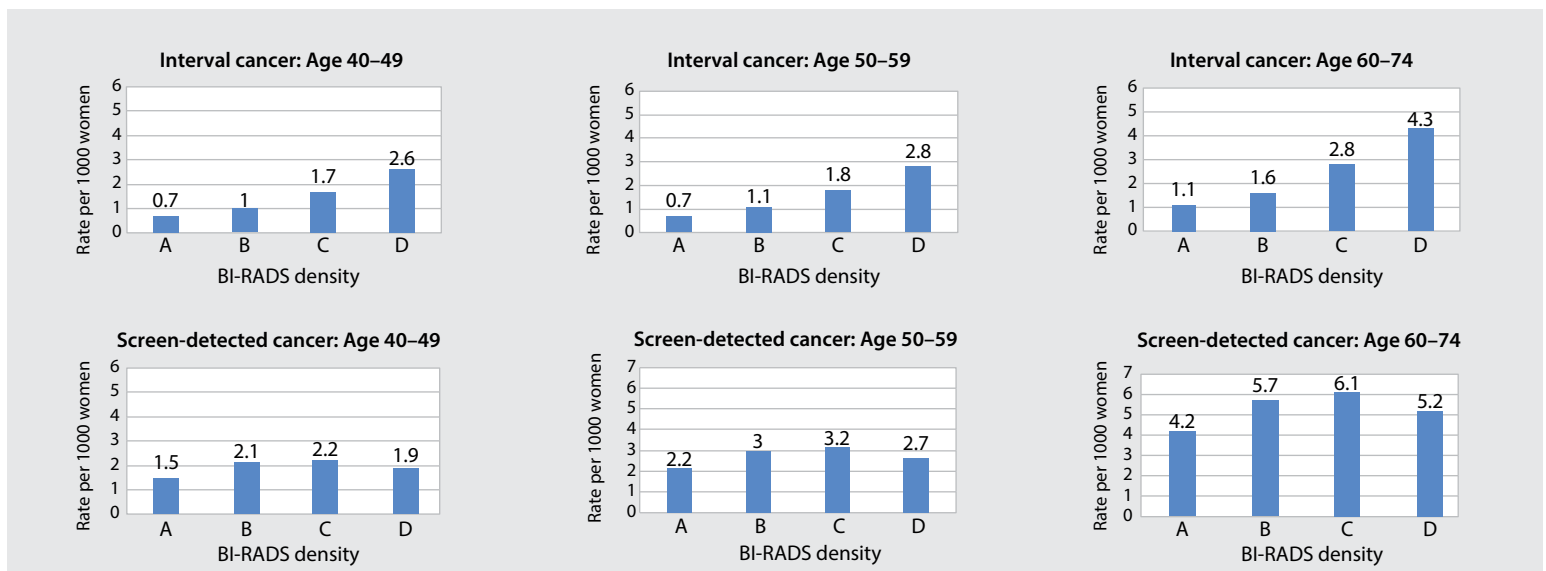


FIGURE 4. Predicted rate by age and density for average-risk women to be diagnosed with interval cancer in the next 2 years or screen-detected cancer at the next biennial screening visit following a normal mammogram.

(annual) for women age 40 to 49, from 51% (biennial) to 46% (annual) for women age 50 to 59, and from 45% (biennial) to 40% (annual) for women age 60 to 74.

Prognostic factors were tabulated separately for biennial screen-detected cancers and interval cancers [Table 3]. Tumors in screen-detected cancers were smaller than in interval cancers ($P < 10^{-5}$) and less likely to have nodal involvement ($P < 10^{-5}$). Within the screen-detected cancers, tumor size increased with increasing density (test for trend, $P = .005$), but the likelihood of nodal involvement did not increase ($P = 0.06$). Similarly, among interval cancers, tumor size increased with increasing density ($P = .0002$), but the likelihood of nodal involvement did not ($P = .19$).

Conclusions

The analysis of digital screening mammograms performed by the BC Cancer Breast Screening Program in 2017 showed that breast density decreased with age, was lower in First Nations and higher in East Asian participants, and did not vary by risk status. Examination of consecutive digital mammograms found that recorded density was not stable and that concordance (the same BI-RADS density reported on both mammograms) was less likely when different radiologists interpreted the two mammograms. Rates of screen-detected and interval invasive

breast cancers were found to vary with age and risk status. Rates of screen-detected cancer varied with density, although rates did not increase uniformly with increased density. In contrast, rates of interval cancer increased progressively with increasing density. Tumor size at diagnosis increased with increasing density, but the likelihood of nodal involvement did not change.

Other studies

Other studies report similar findings to those demonstrated here, with density declining with age¹⁰ and higher density seen in East Asians.¹¹ Similarly, other studies report instability in density categorization on consecutive mammograms¹² and instability increasing when

TABLE 3. Prognostic factors (tumor size and nodal involvement) for screen-detected, at 18–30 months, and interval, within 24 months, invasive breast cancers compared by BI-RADS density category.

Density	Mode of detection						Overall rates*	
	Screen-detected cancer diagnosed 18–30 months			Interval cancer diagnosed < 24 months				
	Number	% > 15 mm (95% CI)	% + node (95% CI)	Number	% > 15 mm (95% CI)	% + node (95% CI)	% > 15 mm (95% CI)	% + node (95% CI)
A	207	25.6 (20–32)	11.6 (8–17)	102	50.0 (40–60)	20.6 (14–29)	32	14
B	317	28.4 (24–34)	18.0 (14–23)	190	58.4 (51–65)	32.6 (26–40)	36	22
C	190	38.4 (32–46)	19.5 (14–26)	201	65.7 (59–72)	33.3 (27–40)	49	25
D	26	38.5 (22–57)	15.4 (6–34)	67	76.1 (65–85)	28.4 (19–40)	58	22
All	740	30.5 (27–34)	16.5 (14–19)	560	61.6 (58–66)	30.2 (27–34)		

*Obtained by weighting screen-detected and interval cancer rates per 1000 as shown in Figure 4.

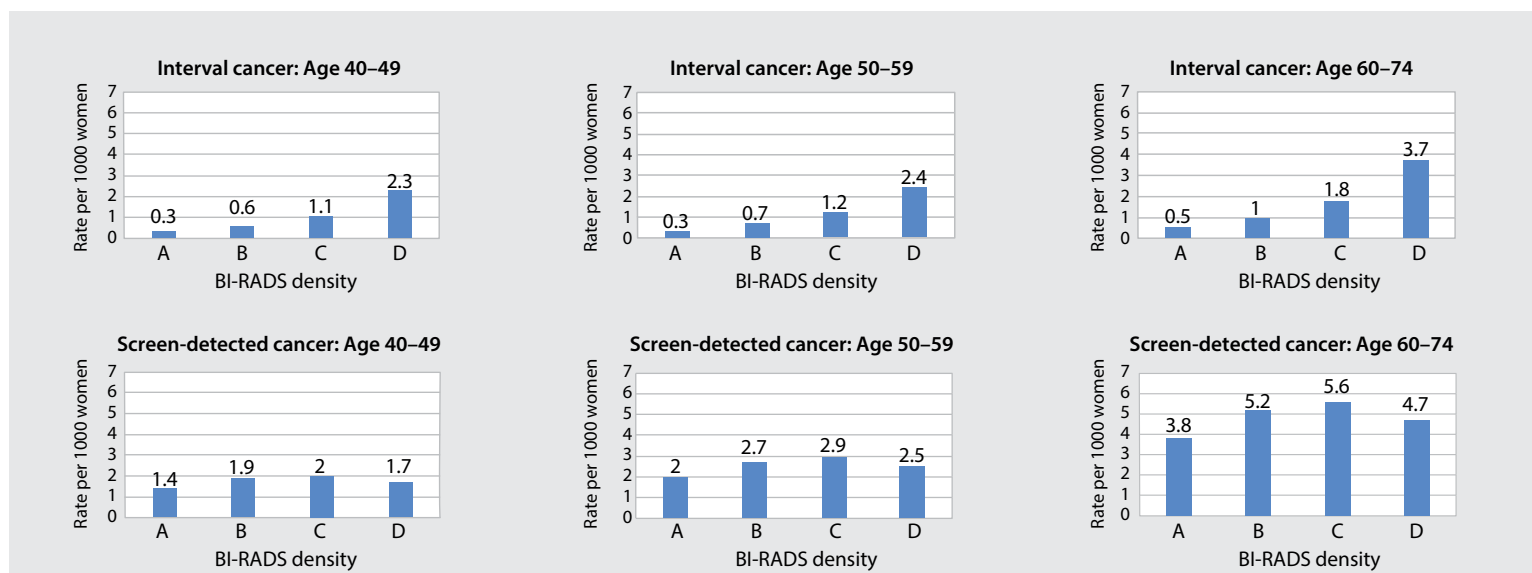


FIGURE 5. Predicted rate by age and density for higher-than-average-risk women to be diagnosed with interval cancer in the next year or screen-detected cancer at the next annual screening visit following a negative mammogram.

mammograms are interpreted by different radiologists.¹³⁻¹⁵ An increase in the rates of screen-detected and interval cancer with the length of the screening interval (annual, biennial, and triennial) is commonly observed.¹⁶ Other studies have also found that rates of screen-detected⁷ and interval¹⁷ cancer vary with reported density. In reporting relationships with screen-detected cancers, studies⁷ have used density recorded on the mammogram leading to screen detection rather than the preceding mammogram as done in this study. The reason for using the preceding mammogram here is so that reported rates of both screen-detected and interval cancers relate to the likelihood of future events in participants who have had a normal screening mammogram.

Risk

Many factors other than age, family history, and breast density have been found to influence breast cancer risk. These include ethnicity, age at menarche, menopause status, history of pregnancy, body mass index, activity level, alcohol consumption, tobacco consumption, and history of benign breast disease.¹⁸ Individual risk is not indicated by a single factor alone and tools have been developed to provide estimates using some of these factors.^{19,20} Using single factors to predict risk is further complicated by negative correlations between some risk factors (e.g., breast density and body mass index). When discussing breast screening, breast density alone should not be seen as the primary determinant of breast cancer risk.

Study challenges

Although breast density reporting was not required by the screening program during the study, the majority of BC screening centres did report density voluntarily and provided these data to the program. BI-RADS density was not reported to physicians or patients undergoing screening and was not used for routine clinical care, meaning that the results may not be representative of density when reported for use in clinical care.

For the evaluation of density category stability, only digital mammography results were used. This was not the case for evaluation of breast cancer risk, where 42% of the studies were performed using analog mammography.

Digital mammography has been found to show higher sensitivity in the presence of density,²¹ suggesting that the relationships with interval cancers reported here could change if all screening for this study had been conducted using digital mammography. The breast cancer risk portion of this study used data from 2011 to 2015. During this period the BI-RADS density assessment system was updated to its fifth edition,³ a change that is reported to have resulted in differential classification of mammographic density.²²

**Breast density
decreased with age, was
lower in First Nations
and higher in East Asian
participants, and did
not vary by risk status.**

Prior to February 2014, British Columbia screening policy recommended annual screening for women age 40 to 49 and biennial screening for women age 50 to 79. After 2014, biennial screening was recommended for average-risk women age 50 to 74 and 40 to 49 (if electing screening), and annual screening for women with a family history of breast cancer in a first-degree relative. Consequently, many of the rates presented in **Figure 4** and **Figure 5** represent screening practice not recommended for part of the data collection period, and observed rates may have been influenced by factors not captured in the analysis.

Sensitivity is commonly used to measure the accuracy of diagnostic tests. However, as usually defined, this sensitivity measure cannot be assessed in screening participants because of the absence of an accepted gold standard for identifying breast cancer in asymptomatic women. Consequently, alternate measures are used. The most common of these is period sensitivity,²³ which is equal to the ratio of screen-detected to screen-detected-plus-interval cancer rates over the screening period. Several studies have reported period sensitivity with density and have found that it declines with increasing density.²⁴ Period sensitivity was not calculated using the

results presented in **Figure 4** and **Figure 5** because the rate of screen-detected cancer is from the following screen and not the current screen. Nevertheless, the ratio of screen-detected to screen-detected-plus-interval cancer declines with increasing density as has been seen elsewhere. It must also be kept in mind that the rates presented in **Figure 4** and **Figure 5** do not include in situ breast cancers or breast cancers detected at a first screening visit; inclusion of such cases would increase the ratio of screen-detected to screen-detected-plus-interval cancers.

Study implications

The relationship between higher density and future interval cancer risk is of concern because it suggests that screening participants with the densest breasts may benefit less from screening. On an absolute scale, those with the lowest density likely benefit the least from screening since they have the lowest rate of breast cancer detected at screening. However, those with the highest density have elevated interval cancer rates before the next screening visit and may thus represent the greatest opportunity for potential cancer detection improvement. Importantly, though, all age, risk, and density subgroups are diagnosed with screen-detected and interval cancers. There is no national standard defining what risk threshold, if any, is sufficient to consider altering screening recommendations. Indeed, mammography remains the primary screening tool regardless of breast density. Current Canadian breast screening recommendations do not indicate further breast screening in addition to routine mammography.²⁵ In the United States, where most screening is performed annually, it has been suggested¹⁷ that an annual interval cancer risk threshold of 1 per 1000, which is exceeded for women with BI-RADS D, is an appropriate threshold to consider additional screening interventions. However, the US Preventive Services Task Force considers evidence to be insufficient to recommend any adjunctive screening on the basis of breast density alone.²⁶

In Europe and Australia, breast screening policy does not vary with breast density. In Canada, several provinces increase the mammography frequency from biennial to annual for average-risk participants with the densest

breasts (generally those categorized BI-RADS D). However, our results for women with BI-RADS category D density show that a change from biennial to annual screening has only a modest effect on the predicted proportion of interval cancers. In the US, despite the absence of supporting guidelines, it is common to offer breast ultrasound and possibly breast magnetic resonance imaging to women with BI-RADS C or D breast density following a normal screening mammogram. Many studies have shown that the addition of breast ultrasound results in the identification of mammographically occult breast cancer and a recent systematic review²⁷ concluded that it increases the screen-detection rate by an average of 40% of that detected at mammography. A randomized clinical trial in Japanese women aged 40 to 49 is currently comparing adding ultrasound to mammography and clinical breast examination.²⁸ The first round of this study found a 55% increase in screen-detected cancer with a similar proportional increase across breast densities,²⁹ and a 37% reduction in interval invasive breast cancer in those receiving ultrasound screening. While it is unlikely that screening can produce further reductions in breast cancer mortality among existing participants without substantially reducing interval cancer rates, reductions in interval cancers alone do not guarantee a reduced risk of death. Reductions would also be required in the overall frequency of advanced cancers (screen-detected-plus-interval).

The previous discussion concerns the detection of invasive breast cancer, but overall approximately 22% of cancers detected on screening mammography are DCIS, which in BC is seen to decline with age. In 2017 DCIS represented 33% of cancer diagnoses in participants aged 40 to 49 and only 15% of those 70 to 79.³⁰ The proportion of DCIS detected by breast ultrasound following a normal mammogram is lower than that for mammography. For example, in the J-START trial, 37% of cancers detected by mammography were DCIS versus 16% of cancers detected by breast ultrasound in those with a normal screening mammogram.²⁸ Given an estimated conversion rate of DCIS to invasive disease of less than 1% per year³¹ a lower proportion of cancers detected by breast ultrasound than by mammography may not be

disadvantageous. Reported false-positive rates for breast ultrasound are variable²⁷ and can be comparable to those associated with screening mammography. In the J-START trial, where participating centres received specific training on the performance and interpretation of screening ultrasounds, 6.6% of participants had an abnormal screening mammogram result. Among those with a normal screening mammogram, 5.7% had an abnormal screening ultrasound result. The positive predictive

Rates of interval cancer increased progressively with increasing density. Tumor size at diagnosis increased with increasing density, but the likelihood of nodal involvement did not change.

value for breast cancer detection was 4.8% for the screening mammogram and 3.6% for the screening ultrasound.²⁸

Summary

Based on findings reported in the literature and the data presented here, physicians with patients enrolled in the BC Cancer Breast Screening Program can expect the following:

- Younger patients are more likely to have denser breasts since breast density tends to decrease with age.
- Women of East Asian heritage are more likely than other screening participants to have denser breasts, although their risk of breast cancer is lower on average.
- Screening participants with a first degree family history of breast cancer are not more likely to have dense breasts.
- The breast density categorization of many screening participants will change on consecutive mammograms.
- Other factors (e.g., body mass index) will influence both breast density and breast cancer risk.

Following a normal screening mammogram, a screening participant's risk of being diagnosed with an interval breast cancer over the next screening round increases with age and breast density, and is roughly similar at 1 year for women at elevated risk to that at 2 years for women at non-elevated risk.

These findings are intended to facilitate a discussion of breast density, breast cancer risk, the role of mammography in screening, and the role of supplemental testing. Breast density is one of multiple breast cancer risk factors to be considered, and its greatest impact is on the risk of interval cancer. While women age 40 to 74 with the densest breasts (BI-RADS D) but of otherwise average risk may benefit the most from additional testing, annual mammography was not found to offer a significant improvement.

The benefits and limitations of supplemental ultrasound should always be considered. Evidence indicates that ultrasound does detect additional cancers but is accompanied by the additional probability of false-positive studies and the need for biopsy.

Further research is needed to elucidate the specific benefits of the increased cancer detection afforded by supplemental testing for screening participants found to have dense breasts. ■

Competing interests

All authors are affiliated with the BC Cancer Breast Screening Program. Dr Coldman serves as a consultant for the BC Cancer Breast Screening Program and was paid for drafting this report.

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Matthew Mo Kin Kwok, MD, CCFP(EM), FCFP, Jane de Lemos, PharmD, MSc Epid,
Mazen Sharaf, BSc Pharm, ACPR

Drug-induced psychosis and neurological effects following nitrous oxide misuse: A case report

The case of a 20-year-old female who experienced auditory and visual hallucinations after inhaling nitrous oxide she obtained legally in “whippits”—canisters used in whipped cream dispensers—highlights the need to report such adverse events to appropriate authorities so that data can be collected about the dangers associated with commercially available products and the number of misuse cases in Canada.

ABSTRACT: Nitrous oxide (N₂O) is an increasingly popular recreational drug globally. Users commonly inhale the gas from punctured canisters known as “whippits” that are designed for use in whipped cream dispensers. A surge in N₂O use has been reported in the UK, with a self-report recreational drug survey finding an increase in use from 20% in 2014 to 31% in 2017. The survey found that when nicotine, alcohol, and caffeine were excluded, N₂O was the seventh most common drug used by respondents. The accessibility

of N₂O as a consumer good contributes to misuse, as seen in the case of a 20-year-old female who presented to the emergency department complaining of visual and auditory hallucinations. The patient had no history of psychiatric or medical illness before experiencing symptoms, and results from laboratory investigations and physical examinations revealed no abnormalities. The patient reported inhaling nitrous oxide on a daily basis, however, and had recently increased her use of legally obtained whippits. A psychiatrist, a neurologist, and an addictions medicine specialist assessed the patient in consultation and agreed that her psychosis was the result of N₂O misuse. This case illustrates the need to increase awareness regarding the possible sequelae of nitrous oxide misuse and address current reporting limitations and the ease of access consumers have to nitrous oxide products.

Nitrous oxide (N₂O), commonly known as “laughing gas,”¹ has historically been used for medicinal purposes such as anesthesia, analgesia, and sedation.² It is also available as a consumer product in canisters known as “whippits” that are used in whipped cream dispensers.

An increasing number of publications and the Global Drug Survey (GDS), a self-report survey of recreational drug use, suggest N₂O is being misused by those seeking the dissociative state produced by puncturing whippits and inhaling the gas or “nanging.” The GDS found that when nicotine, alcohol, and caffeine were excluded, N₂O was the seventh most common drug used by 130 000 respondents.³

Whippits are readily available through storefront and online suppliers with no restriction on age of purchaser, medical history, quantity desired, or intended use. As long as the purchaser can pay for the product there is no barrier to obtaining whippits.

Each whippit contains 8 g of 100% N₂O, on average. The duration of action is short-lived (1 to 2 minutes)⁴ after the canister is punctured and the gas is released into an inflatable or an enclosed object for inhalation.¹

N₂O that is chemically identical to the N₂O in whippits is also sold with a drug identification number (DIN) for medicinal purposes. When used as an inhalational anesthetic, N₂O has analgesic and sedative effects. In accordance with federal legislation, N₂O is classified by Health Canada as an “ethical” product that

Dr Kwok is an emergency physician at Richmond Hospital and a clinical assistant professor in the Department of Emergency Medicine at the University of BC. Dr de Lemos is a clinical pharmacist at Richmond Hospital and a clinical professor in the Department of Pharmaceutical Sciences at UBC. At the time of writing, Mr Sharaf was a pharmacy practice resident at Lower Mainland Pharmacy Services. Currently, he is a clinical pharmacist at Children's and Women's Health Centre of BC.

This article has been peer reviewed.

“does not require a prescription, but that is generally prescribed by a medical practitioner. Ethical products are unscheduled non-prescription professional use products.”⁵

Case data

A 20-year-old female presented to the emergency department with visual and auditory hallucinations, agitation, and gait disturbance. She voiced concerns about a “transmitting” device in her throat. She believed that this device was making her legs weak and affecting her walking. She also heard voices from the device telling her to kill herself. She had come to the emergency department because she was worried for her safety.

The patient had no history of psychiatric or medical illness. She reported inhaling nitrous oxide on a daily basis. She had increased her use recently and was inhaling gas from approximately 100 whippits per day. The patient stated that she bought the canisters legally with a shopping app and showed the physician the website she used to make her purchases. She reported no other recreational or prescription drug use.

The patient was a slim and slightly built Asian female. She appeared anxious but not distressed. She was cooperative and her vital signs at triage were stable. On examination she showed no sign of head trauma. Her pupils were equal and reactive to light. Her speech and her gait were normal. Her neck was supple and her thyroid examination revealed no abnormalities. Respiratory, cardiac, and abdominal findings were unremarkable. Her neurological examination results were normal with no lateralizing sign, and her mental status exam revealed normal affect.

Laboratory investigations included an ECG that revealed normal sinus rhythm and a QTC of 399. CBC, electrolyte, blood urea nitrogen, and creatinine levels were all within normal limits. ASA, acetaminophen, and ethanol levels were normal. Her vitamin B12 level was also normal.

A psychiatrist, a neurologist, and an addiction medicine physician assessed the patient in consultation and agreed that she was psychotic as a result of N₂O misuse. The patient was kept in hospital until her symptoms resolved and she was discharged without incident.

Discussion

This case illustrates the need to consider the possible sequelae of nitrous oxide misuse (whether acute or chronic), the current reporting limitations, and N₂O accessibility issues.

Possible sequelae

Beyond symptoms of psychosis, N₂O misuse has been associated with myeloneuropathy and neurological effects, which are mentioned in a growing number of reports.^{1,2,6-8} These adverse effects can result from both acute and chronic exposure. A systematic review from 2016 that focused exclusively on N₂O misuse revealed that the users in 72 of 91 cases experienced some sort of neurological adverse effect,

Nitrous oxide can be readily obtained as a commercial product without any restrictions.

predominantly myelopathy, myeloneuropathy, and subacute combined degeneration.² Less common presentations included psychiatric symptoms as seen in our case. Additionally, 29 cases of nitrous-oxide-related death were reported.² Although the systematic review was unable to establish a dose-related toxicity because of unreliable data, the majority of cases involved the daily use of whippits.

The mechanism of these adverse effects is not well understood. N₂O is thought to be associated with low vitamin B12 levels. N₂O-induced oxidation converts vitamin B12 from a reduced to an oxidized form, which inhibits the activity of methionine synthase, leading to impairment of methylation reactions and DNA synthesis. This in turn leads to the accumulation of homocysteine.^{2,6} Clinical syndromes have been reported with both acute and chronic nitrous oxide use.

Reporting limitations

Health care providers play an important role in reporting adverse events from nitrous oxide misuse to the appropriate authorities. In the case described here it was initially difficult to

determine which authority should receive the report. When N₂O with a DIN⁵ is used for a medicinal purpose, the appropriate authority is the Canada Vigilance Program, which operates the adverse reaction online database. When the N₂O comes from a product marketed for making whipped cream, the appropriate authority is Health Canada Consumer Products and Cosmetics. A member of our health care team submitted a report to both authorities to ensure appropriate actions could be taken.

In response to our report, a Health Canada representative explained that Consumer Products and Cosmetics would document the misuse but only take further action if the N₂O canister had faults or hazards regarding its intended use, which is making whipped cream.

To our surprise, no cases of N₂O misuse have been reported to Health Canada Consumer Products and Cosmetics, and only one case of substance abuse of N₂O had been reported to the Canada Vigilance Program.

We also contacted the BC Drug and Poison Information Centre (DPIC) and learned that the provincial toxicology call centre received 14 calls regarding N₂O toxicity from misuse of whippits or similar commercial products between 2015 and 2019. Since our investigation determined that Health Canada received only one report of N₂O misuse in this period, many incidents appear to have gone unreported.

The number of N₂O cases described in the literature, the calls made to BC DPIC, and news stories of misuse⁹ all suggest that current reporting does not reflect the magnitude of the toxicity problem.

N₂O accessibility issues

Nitrous oxide can be readily obtained as a commercial product without any restrictions. In the case described here, the patient purchased canisters from a reputable online shopping website and had them shipped directly to her.

Whippits come in different sizes and can be purchased in bulk. At the time of writing, a package of 100 canisters could be purchased online for less than \$100.00 (\$1.00 per canister).¹⁰ Because the canisters are not sold for inhalation, there is no regulation that mandates

providing information on the risks or possible sequelae of N₂O misuse, nor are sellers qualified to provide this information.

Medicinal products with a drug identification number are classified by Health Canada according to different schedules that determine how accessible the product is to the public and the circumstances that require a health care provider (e.g., physician or pharmacist) to be involved in acquiring the product.¹¹ The safety and the complexity of the product and the harm the product may cause patients when used are all considered. Health Canada will reassess access to a medicinal product if new information arises, such as reports of adverse reactions, and may choose to further restrict or to ease access to the public.

Health Canada considers nitrous oxide to be an “unscheduled non-prescription professional use” product.⁵ This raises an important question: if N₂O used medicinally is deemed to require health care provider involvement, why is the purchase of N₂O used commercially not restricted in any way given the potential impact on consumers?

Summary

A case of nitrous oxide misuse by a 20-year-old female that resulted in drug-induced psychosis and neurological effects illustrates the need for clinicians to recognize N₂O as a potential substance of abuse and a possible cause of unexplained psychiatric or neurological symptoms.

In addition, this case highlights the need to report N₂O-related adverse events to appropriate authorities. The lack of N₂O misuse reports going to Health Canada means data are not

being collected about the dangers associated with commercially available products or the number of misuse cases in Canada.

Increased awareness is needed regarding N₂O toxicity and the more serious adverse drug effects that are possible. Solutions to misuse might include restricting access, adding safe-

Health Canada considers nitrous oxide to be an “unscheduled non-prescription professional use” product. This raises an important question: if N₂O used medicinally is deemed to require health care provider involvement, why is the purchase of N₂O used commercially not restricted in any way given the potential impact on consumers?

guards to minimize harm, and encouraging intervention from authorities to prevent product misuse. ■

Competing interests

None declared.

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The role of genetics in medicine: A future of precision medicine

Detailing the current role of genomics/genetics in medicine and expanding on its future applications and implications.

Yue Bo Yang, BSc

Alexis and Noah Beery were misdiagnosed and mistreated for cerebral palsy for 14 years, until genetic sequencing led to a proper diagnosis of dopa-responsive dystonia in 2010 and cured them of the symptoms that had plagued their childhood.¹ However, despite the power of genetic sequencing in medicine, it is still emerging in translation and is reserved for certain subsets of patients. Sequencing the first human genome was a 13-year international collaborative effort costing US\$3 billion.² Today, it can be completed for US\$1000 in under 24 hours³ due to advancements in biotechnologies. This opens the door to the exciting prospect of routine whole-genome sequencing (genomic sequencing) for the standard patient, bringing forth an era of precision medicine, which tailors the prevention and management of illness to an individual patient using their detailed genomic data in combination with their environment, lifestyle, and background.

Current uses of genetics in medicine

Prenatal screening tests are the most widely offered genetic tests across North America, whereby fragments of placental DNA fragments drawn from maternal blood are sequenced for genetic abnormalities. In recent years, cancer therapy has focused on using tumor-specific antigens⁴ elucidated by sequencing as the targets of biologic therapies. For example, ado-trastuzumab is a monoclonal chemotherapy combination drug that has reduced the 3-year disease-free remission rate of HER2-positive breast

cancer by 11.3% from the prior standard of treatment.⁵ Let us not forget that the sequencing of factors VIII, IX, and insulin were the foundation of pharmacologic management of hemophilia and diabetes respectively.

Cancer therapy has focused on using tumor-specific antigens elucidated by sequencing as the targets of biologic therapies.

Pharmacogenomics, the optimization of drug response in relation to genetics, is another promising emerging field and is a cornerstone of current genetic medicine. Ivacaftor is a potentiator of the CFTR channel and is the most effective cystic fibrosis medication on the market; however, it is only applicable to the 4% to 5% of the patient population who are homozygous for the *F508del* mutation.⁶ In Canada, genetic testing is offered to patients only under specific circumstances, such as having a lineage of Huntington disease or a high index of suspicion for *BRCA1/2* mutations. Otherwise, patients may access fee-based genotyping through private biotechnology companies such as 23andMe⁷ that profile patients' genomes for specific genes of interest. Whole-genomic sequencing is currently not widely available for typical consumers outside of specific research circumstances. Nevertheless, genomics has its place in current medicine and is poised to expand vastly in the next decade.

The future of genomics in medicine

Clinician leaders visualize two primary future roles for preventive whole-genome sequencing:

1. As a noninvasive screening test for preventive medicine.
2. As a test to improve diagnostic capabilities.⁸

In effect, similar to how the identification of *BRCA1/2* mutation carriers led to prophylactic mastectomy and oophorectomies, early detailed genomic data would lead to valuable insight into future disease risks spanning diverse specialties from oncology⁹ to psychiatry¹⁰ and would aid in their prevention. In order to accomplish this feat, there is a worldwide push for "big data" in genomic medicine, where millions of reference sequences, individualized patient factors, and phenotypic expression are collected and coalesced into a multifactorial database and

Mr Yang is a medical student in the class of 2021 at the University of British Columbia Faculty of Medicine. In his spare time he enjoys playing badminton and eating at buffets.

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algorithm where individually sequenced genomes can be compared. To reach this goal, President Barack Obama launched the National Institutes of Health's All of Us campaign in 2015, mandating the collection of 1 million sequenced genomes, complementing environmental factors, and demographic information from US citizens.¹¹ Currently, over 600 000 have been collected.¹² This is a multinational effort; countries such as the United Kingdom and China have launched similar initiatives. The Global Alliance for Genomics and Health (GA4GH) predicts 60 million genomes will be sequenced worldwide by 2025. Just as radiological imaging has increased the positive predictive value of suspected diagnoses based on clinical signs and symptoms, and has decreased the rates of exploratory surgical procedures, genomics in medicine is poised to augment this further and add another layer of confidence to diagnostic approaches.

Conclusion

It is exciting to hypothesize how the expanding role of genomics in medicine will impact our understanding and classification of disease. Perhaps purely clinical diagnoses such as trigeminal neuralgia, major depressive disorder, or atopic dermatitis will reform in light of underlying genetic origins. Ultimately, this will better classify our understanding of illnesses and improve treatment strategies and research.

Lastly, we cannot turn a blind eye to the barriers to precision medicine. With much of the world's population still deplete of basic resources and health care, genomics and precision medicine would primarily be a resource for developed countries in the next decade. The ethics of storing identifiable genetic information, the rights of patients to knowledge of such data, and the potential effects on stakeholders at all levels of health care are additional complex issues. However, given the current funding status and international attention garnered by precision medicine and genomics, it will certainly have its place in the future of medicine. ■

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Competing interests

None declared.

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The age of mushrooms is upon us in medicine

Psychedelic medications, including mushrooms, are on the verge of becoming mainstream practice.

Mark Elliott, MD

Some of us will remember turn-on-tune-in-drop-out Timothy Leary, the psychologist whose work on then-legal psychedelics in the 1960s got him fired from Harvard University. His subsequent arrest and the government's attempt to stamp out the counterculture anti-Vietnam movement led to the US federal government banning the manufacture and sale of all psychedelic drugs.

But the tide has turned, and psychedelic drugs are currently having a huge resurgence.

Indications

Psychedelics will soon be routine for treating opioid addiction,¹ PTSD,² and refractory depression,³ as well for use in palliative care settings.⁴

Mycology review

Fungi is the generic term for the group of eukaryotic organisms that include molds, yeast, and mushrooms. Mushrooms are spore-bearing fruit of the fungus and the roots are called *mycelium*. Mycelium are thread-like branchings that can become enormous. A mycelium mat in Oregon was found to be 2500 acres in size.⁵ What is so fascinating about mycelium is that fungi branched off from the human evolutionary tree perhaps 600 million years ago. At this point, animals internalized their digestive systems but fungi left theirs externalized. These mycelium threads in the ground are separated from the external world, teeming with bacteria and viruses, by a skin only one cell thick (animal skin, in contrast, is many cell layers thick). There is a constant war between the mycelia who need to eat the microorganisms and the microorganisms who want to eat the mycelia—so that fungi have extensive antiviral and antibacterial properties that are now beginning to be investigated. Mycelia are the decomposers of the world's forests.

Dr Elliott is a staff anesthesiologist at Providence Healthcare in Vancouver.

This article has been peer reviewed.

The reason that antifungal agents in medicine are so toxic in humans is that fungi are much closer to humans than bacteria.

Pharmacology review

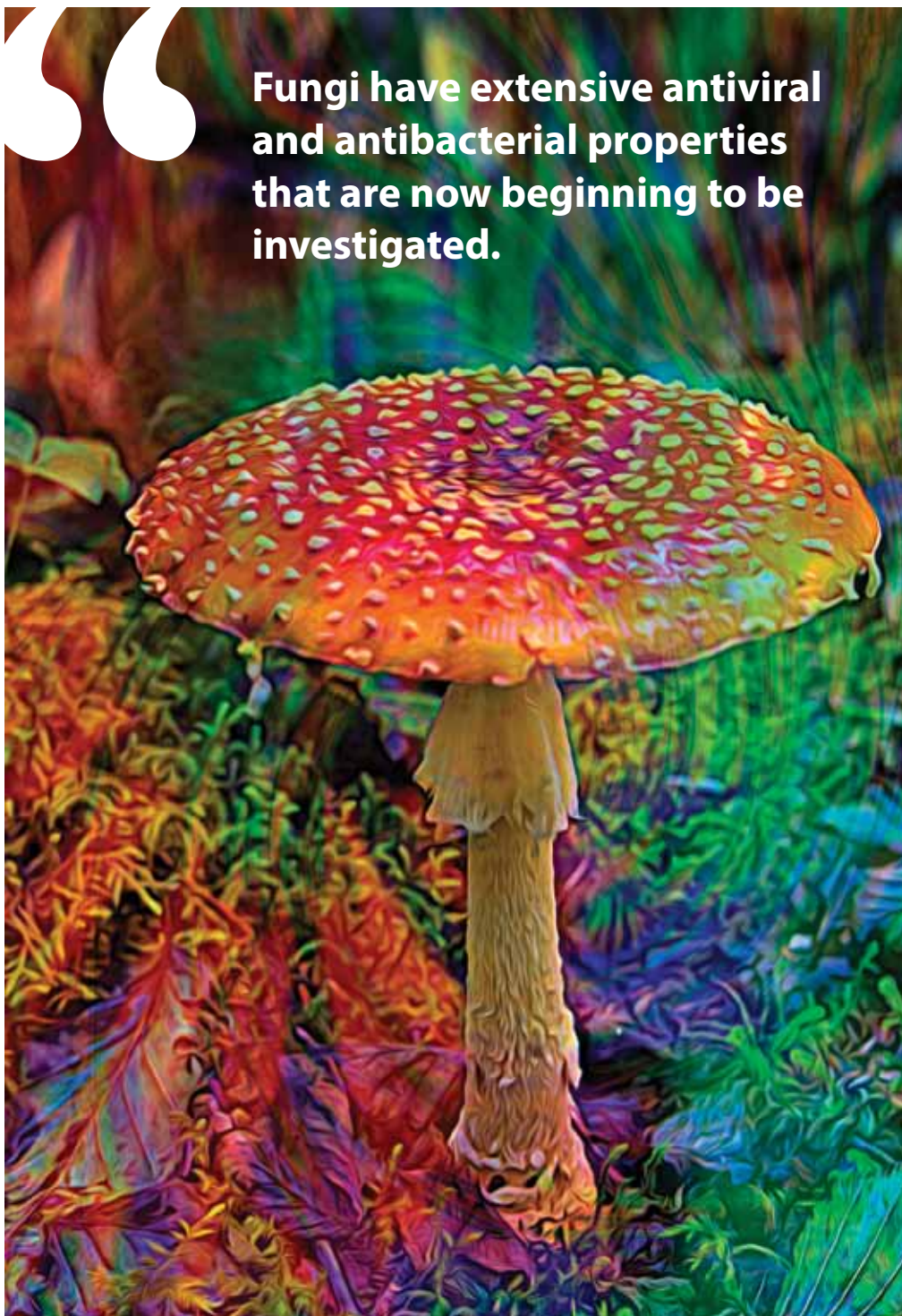
Psychedelics—whether one is referring to psilocybin (found in more than 200 species of mushrooms), mescaline (from the peyote cactus), LSD (a refined form of lysergic acid extracted from the ergot fungus), or ayahuasca (a brewed mixture of substances from vines traditionally found in the Amazon basin)—seem to affect serotonin and/or monoamine oxidase (MAO) receptors in the brain. As research ramps up there undoubtedly will be other receptors with cool-sounding acronyms. These drugs cause the brain to light up on an fMRI. As this “neuronal crosstalk” increases, so does the patient’s “ego dissolution,” usually with accompanying feelings of bliss and a sense of oneness.

The uses that seem to be generating the most press are for opioid and smoking addiction, end-of-life care issues, refractory depression, and PTSD. In October 2018, the US Food and Drug Administration granted “breakthrough therapy” designation to psilocybin for depression. In May 2019, Denver, Colorado, voters passed a ballot to decriminalize psychedelic mushrooms. This year US congresswoman Alexandria Ocasio-Cortez filed legislation to remove the legal restrictions surrounding clinical research of these compounds in the name of assisting veterans with PTSD.

The guru of mycology, Paul Stamets,⁶ who lives nearby on the Olympic Peninsula in Washington, has a very interesting evolutionary take on this subject, which is basically a promotion of the older Stone Age hypothesis of Terence McKenna.⁷ In essence, it says that something amazing happened to the homo sapiens brain about 200 000 years ago; a massive increase in cognitive ability allowed humans to conquer the planet by cooperating. This theory goes on to say that early hominids coming out of the trees and onto the savannah came across large amounts of mushrooms growing like weeds from animal dung. Over many millennia these early humans got to know which mushrooms were for calories, which ones were poisonous, and which ones were “magic”—that is, contained psilocybin. As McKenna writes, “Homo sapiens ate its way to a higher

This year US congresswoman Alexandria Ocasio-Cortez filed legislation to remove the legal restrictions surrounding clinical research of psilocybin in the name of assisting veterans with PTSD.

Fungi have extensive antiviral and antibacterial properties that are now beginning to be investigated.



consciousness,” and, “It was at this time that religious ritual, calendar making, and natural magic came into their own.”⁷

The future

The trend to acceptance of these drugs is now about where cannabis was 10 years ago, but

things change faster now. German millionaire Christian Angermayer has started a company called Compass Pathways that is buying the intellectual property rights for the manufacture of psychedelics with the backing of Silicon Valley billionaire Peter Thiel. Food guru Michael Pollan has a recent book on the virtues of the

psychedelics.⁸ The Multidisciplinary Association for Psychedelic Studies run by researcher and TED Talks speaker Rick Doblin is a not-for-profit research organization dedicated to psychedelics also getting a lot of attention.^{9,10}

The age of mushrooms is upon us! ■

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Physician engagement gains traction across BC

Meaningful physician engagement is essential to a health care organization's ability to deliver high-quality, cost-effective patient care. But for the past 2 decades—as BC's health authorities were regionalized and doctors in hospitals became even busier with capacity and wait-list pressures—doctors and administrators have been challenged to build effective collaborative processes that ensure physicians are included in decision making about their work environment and patient care.

But now that's changing. The Specialist Services Committee's Facility Engagement Initiative supports physicians who work in acute care facilities across BC to establish formal structures that increase their voice and influence in their hospital and region.

Since Facility Engagement was introduced 4 years ago, 72 medical staff associations (MSAs) have partnered with their health authorities to build a new foundation for collaboration. With funding available for MSA administrative and management support and physician sessional time, MSAs are setting priorities, renewing relationships with health authority leaders, and initiating collaborative activities—more than 1400 to date.

Thanks to these efforts, the tide is starting to turn.

This article is the opinion of the Specialist Services Committee and has not been peer reviewed by the BCMJ Editorial Board.

Facility Engagement in action

As a first step to creating a foundation for collaboration, many MSAs have improved physician-to-physician relationships. This is the most notable change associated with Facility Engagement to date, as reported in the 2019 evaluation of the initiative (www.facilityengagement.ca/evaluation). Two examples of the 160-plus activities with this goal are:

• The BC Cancer Agency's new medical staff association created a common forum for all physicians providing cancer care to collaborate across disciplines and regions, allowing them to connect with each other, and discuss care of their patients and personal well-being.

• Internists and family doctors working at the University Hospital of Northern British Columbia in Prince George met to better understand each other's pressures and needs, improve communication, and explore ways to increase inpatient coverage, leading to collaboration with Northern Health to create a general internal medicine unit.

Improved communication with health authorities is another notable change. Physicians, administrators, and health authority executives are meeting regularly and establishing collaborative processes. More physicians are taking on leadership roles. Progress to date is illustrated by dozens of examples, such as:

• In Comox-Campbell River, Facility Engagement opened the door to dialogue and a new working relationship between the physicians and the health authority, which led to the resolution of congestion

issues during the opening of new hospital campuses.

- At Providence Health Care in Vancouver, six physician leads were selected to represent the voice of medical staff and work alongside senior health authority executives to carry out the organization's new 7-year strategic priorities and clinical/master planning. More than 120 physicians were engaged to provide ideas and perspectives to help create the plan.

Physicians are also looking to improve their work environment and patient care, initiating more than 200 collaborative projects with hospital administrators, front-line staff, and regional health authority leaders.

- Last year, physicians at Trail's Kootenay Boundary Regional Hospital engaged the entire hospital—from specialists to administrators to cleaners—in an extraordinary effort that reduced surgical site infections to well below the national average, and the overall hospital infection rate by 50%.
- At Lions Gate Hospital in North Vancouver, an emergency room physician engaged clinical and support staff and administration in a collaborative effort to reorganize space, processes, and manpower in the department. The changes improved patient flow and wait times, communication between doctors and nurses, and reduced in nonphysician tasks.

Physicians have also taken the opportunity to explore how they can reduce the risk of burnout and provide patient care in a healthier way. Physician health is a common theme for MSA's facility engagement work, with more than 100 related activities underway across BC.

- A region-wide collaborative effort to stimulate action and elevate medical staff well-being as a strategic organizational/system priority is underway in Fraser Health,

representing 12 acute care sites as well as divisions in the community.

- The Physician Wellness Committee at Royal Inland Hospital in Kamloops has identified a number of strategies and actions to support physician health, including a peer group that provides a safe, confidential environment for physicians to discuss challenges and critical incidents.

Facility Engagement is also supporting medical staff engagement in the implementation of electronic health records, starting with Lower Mainland hospitals that are adopting the Cerner system.

Moving forward

There is more work to be done to achieve sustained change, and further evaluation of the Facility Engagement Initiative will determine its ongoing impact. Meanwhile, physicians and health authority leaders from many parts of the province report they are making headway. They are building trust and having constructive conversations about plans and decisions that impact their hospitals, programs, and patient services.

A sense of optimism is fueling the initiative across BC as physicians enjoy renewed teamwork and make positive changes that make a difference to their work culture and their patients' experience and care.

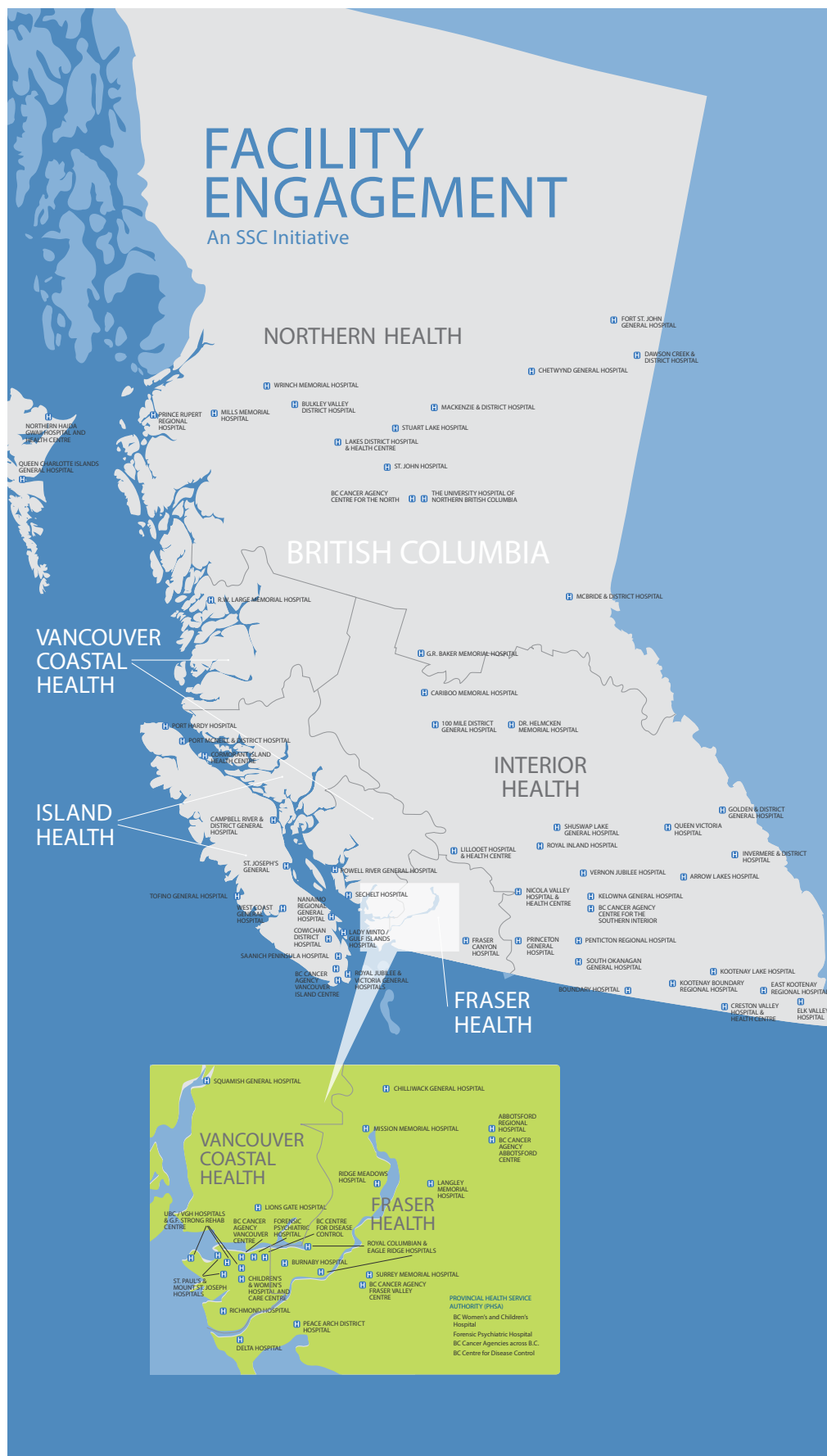
Read what physicians are saying about Facility Engagement at www.facilityengagement.ca/whatschanging. Read more examples of progress at www.facilityengagement.ca/stories. ■

—Sam Bugis, MD

Vice President, Physician Affairs and Specialist Practice

—Cindy Myles

Director, Facility Physician Engagement, Specialist Services Committee



Shared decision making and breastfeeding: Supporting families' informed choices

British Columbia has the highest rates of breastfeeding initiation in Canada, but there is a sharp decline in breastfeeding in the weeks or months after birth.¹ Supporting families in making difficult infant feeding choices in a nonjudgmental way can support the health of infants and may help increase breastfeeding rates by improving the therapeutic relationship with health care professionals. While promotion of exclusive human-milk feeding is well intentioned and based on evidence that it confers more health benefits for parents and infants compared to formula,² a family's context and choices are sometimes overlooked. Breastfeeding may not be the optimal choice at a given time due to early return to work, history of smoking or drug use, and other far-reaching socioeconomic reasons.^{3,4} When families choose infant feeding options other than exclusive human milk, they frequently experience guilt, shame, and failure, which can create mistrust with their health care professionals.⁵ In this context, health care professionals may need more support to engage in complex discussions that promote breastfeeding while simultaneously offering safe, informed choices of alternate feeding options.

Developing health care professionals' skills in shared decision making is one solution. Shared decision making is a form of non-directive counseling where the professional and

patient come together as experts, in clinical evidence and lived experience respectively. This division of power shifts the conversation from *giving* patient education to *exchanging* information to help the family reach their goals.⁶ The ideal result of a shared decision-making process

is a patient decision that is informed, consistent with their personal values, and acted upon.⁷

The BC Centre for Disease Control, in partnership with researchers from UBC and the Centre for Health Evaluation and Outcome Sciences, has been developing shared

decision-making skills education for health care professionals to better support infant feeding choices. To date, our interview study and literature review have explored BC health care professionals' and families' needs in making infant feeding decisions from pregnancy to 6-months postpartum.

We learned that BC health care professionals begin infant feeding discussions with questions to gain information about the family ("Do you plan on breastfeeding?"), not for the family to gain clarity about their goals and what matters most to them. They also centred the conversation on newborn health, such as weight gain milestones, which can ignore related concerns that influence parents' infant feeding choices. Existing communication and counseling approaches used by BC health care professionals (e.g., trauma-informed care, motivational interviewing) can underpin the development of shared decision-making skills.

Training in shared decision making for health care professionals is well established in other parts of Canada, and in the next phase

of our collaboration we will bring a program to BC. It will include experiential learning, practical cases, cultural safety techniques, strategies for building rapport with families, and educational credits. ■

—Sarah Munro, PhD

UBC, Centre for Health Evaluation and Outcome Sciences (CHÉOS)

—Cynthia Buckett, MBA, RD
BCCDC

—Julie Sou, MSc
CHÉOS

—Nick Bansback, PhD
UBC, CHÉOS

—Henry Lau, RD
BCCDC

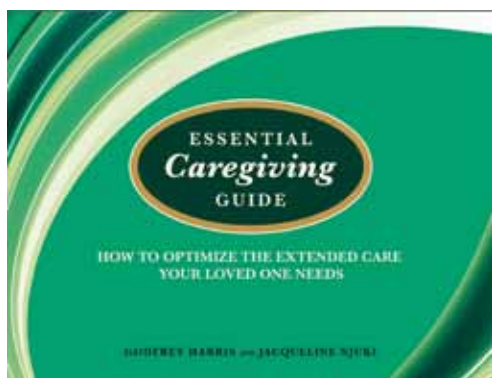
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This article is the opinion of the BC Centre for Disease Control and has not been peer reviewed by the BCMJ Editorial Board.

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Book review: *Essential Caregiving Guide: How to optimize the extended care your loved one needs*



By Godfrey Harris and Jacqueline Njuki. Los Angeles: The Americas Group, 2019. ISBN-13: 978-0935047905. Paperback, 68 pages. US\$15.95

The concerned and loving daughter notices her 72-year-old mother is showing early signs of dementia. She approaches her family physician for advice on how best to bring a caregiver into her mother's life, how to help the caregiver set appropriate goals, and how to supervise the caregiver's work. The family physician may suggest that the daughter read this recently published booklet: *Essential Caregiving Guide*.

The booklet is short on text; it is filled with various forms to be used to record pertinent information or to take inventory. The family completes forms about the patient's personal

and health data, medication lists, current daily routines, grooming, bathroom needs, and very importantly, likes and dislikes. The caregiver's forms include a list of caregiving goals and, as the caregiver begins to assist the patient, they report accomplishments, changes, and anomalies along with periodic summaries. There is a separate form for the caregiver's evaluation.

No individual forms can provide a complete picture of a patient's or a family's situation; a continuum to care is needed. For example, part-time or a short period of assistance may be needed postsurgery; 24-hour care may be required in advanced cases of dementia or other major disorders. Some of the forms in this booklet could be filled out by a patient with adequate ability to communicate; others may be too simplistic for complex situations.

The family doctor may wish to emphasize that caregiving may extend to many issues—safety, administration of medications, companionship, food and feeding, locomotion and muscle-strength maintenance when appropriate, skin care, general cleanliness, and bowel and urinary care. The kinds of forms needed

BC's top family physician of 2019

The College of Family Physicians of Canada (CFPC) and the Foundation for Advancing Family Medicine (FAFM) have selected the 2019 Family Physicians of the Year as the recipients of the Reg L. Perkin Awards. Each year 10 recipients (one from each province) are nominated by their peers, colleagues, and the CFPC's chapters for their leadership, contributions to patient care, and commitment to family medicine teaching and research. The 2019 Family Physician of the Year from British Columbia is Dr Catherine Textor, MD, CCFP (EM), from Prince George.

Dr Textor has worked as a full-service family doctor in Prince George for the past 16 years. She is one of four partners who own a group family practice providing comprehensive care that includes obstetrical, palliative, and long-term care; home visits; surgical assists; and in-hospital care for their patients. Obstetrical care is a special area of interest for the practice, and they take referrals from colleagues in Prince George and outlying rural communities in the region. They also teach medical students and residents in their practice and in the hospital. For 11 years Dr Textor also did part-time work in the emergency department at the University Hospital of Northern British Columbia (UHNBC).

As the physician lead at the Prince George Division of Family Practice, Dr Textor is currently spearheading two large initiatives. The first involves preserving longitudinal family medicine in the community, including a new approach to the care of unattached patients and opening a new primary care medical unit at UHNBC in partnership with Northern Health. The second is developing a model for the delivery of mental health and substance use services in Northern British Columbia.

Growing up in a small town on Vancouver Island, the only exposure Dr Textor had to the medical system was her family doctor. As she went through rotations in medical school, she found it difficult to pick just one specialty. She loves her job for the variety it brings and the privilege it offers of sharing in the most intimate moments of her patients' lives.

The complete list of recipients and each recipient's biography is available at <https://fafm.cfpc.ca/fpoy-2019>.



Dr Catherine Textor

to record details such as these are not included in the booklet and may have to be devised separately.

Further, managerial or supervisory requirements from the family depend on the caregiver's compassion and experience, and on the circumstances under which the caregiving takes place.

The booklet's text is not inspiring, but the forms do serve as introductory guides for the family and the caregiver. I think it is a good start as a way to get organized.

Caveat: The book is written with the United States' public health services in mind, but virtually all comments about caregiving are just as relevant in Canada.

—George Szasz, MD

Hear from patients: New GPSC Patient Experience Tool

Family doctors and teams can now hear from their patients about their experiences and interactions with a practice using a new tool developed by the General Practice Services Committee (GPSC). The Patient Experience Tool is a tablet-based survey that asks patients about topics such as wait times, office hours, and coordination of care. More than 6000 patients have completed the survey, initially piloted by 39 clinics throughout BC since 2016.

The Patient Experience Tool data can inform quality improvement activities in a practice, and practices can opt to share aggregated data with their local division. Practice team

members can access responses in real time using an easy-to-use, web-based dashboard. The secure platform automatically anonymizes and randomizes the responses upon receipt before the data are reported in the dashboard. For more information, visit www.gpsc.bc.ca.

Mushroom poisonings on the rise in BC

The BC Centre for Disease Control's Drug and Poison Information Centre is urging British Columbians to use extreme caution when foraging or consuming wild mushrooms. Poison Control received 201 mushroom poisoning calls as of 30 September 2019, well on track to being one of the most active years in recent history.

Amanita phalloides, also known as the death cap mushroom, has been increasingly popping up throughout BC, including in Victoria and South Vancouver Island, the Gulf Islands, Metro Vancouver, and the Fraser Valley region. The death cap is the most poisonous mushroom in the world, most often found in urban areas here. There have been no reported human deaths from BC death cap mushrooms since 2016 when a child passed away; however, two dogs have died due to possible death cap poisoning in 2019.

Facts about the *Amanita phalloides* (death cap):

- Death cap mushrooms are believed to kill more people worldwide than any other mushroom.

- Death caps are particularly dangerous because of their resemblance to edible varieties of mushrooms. They can be mistaken for edible puffballs when young or the Asian Straw mushroom when older.
- Toxins found in death caps include amatoxins, phallotoxins, and virotoxins.
- Symptoms of poisoning include nausea, vomiting, watery diarrhea, low blood pressure, liver failure, and kidney failure.
- Illness begins 8 to 12 hours after ingestion, beginning with gastrointestinal symptoms like vomiting and diarrhea, followed by apparent recovery.
- Gastrointestinal symptoms recur and damage to the kidney and liver progresses over the next 3 to 6 days.

Tips to stay safe while mushroom hunting:

- If you are unsure, don't eat it!
- Only pick and eat mushrooms that are well known to be edible and easy to distinguish from poisonous varieties.
- If you suspect you've consumed a poisonous mushroom, call the Drug and Poison Information Centre 24-hour phone line at 1 800 567-8911 and seek medical attention immediately.
- Only hunt for mushrooms in safe terrain and exercise extreme caution if in remote areas.
- Save one of each kind of mushroom so their identities can be confirmed should symptoms develop.



Dr Gerald Stewart, past president of Doctors of BC, was one of the first recipients of the CCFP designation.

Celebrating a family medicine milestone and 1969 trailblazers

Fifty years ago a pioneering group of 12 family physicians successfully completed the first ever Certification Examination in Family Medicine and earned the Certification in the College of Family Physicians of Canada (CCFP) special designation. They were introduced to recognize the rigorous assessment required for two key priorities: to support the broad scope of skills and knowledge required of family physicians in their central role caring for patients, and to help advance family medicine in Canada.

Among the class members is Gerald Stewart, MD, CCFP, FCFP, LM, from Kelowna, BC. Dr Stewart graduated from the UBC Medical School and cared for the people of Kelowna and mentored new generations of family physicians for nearly 60 years. He retired from medicine in 2018. Dr Stewart is also a past president of Doctors of BC, having served in 1984/1985.

For the complete list of the class of 1969, visit www.cfpc.ca/meet-some-of-the-members-of-the-class-of-1969.

Learn more

Visit the BCCDC's information page on the death cap mushroom to familiarize yourself with what it looks like and what to do if sighted or ingested: www.bccdc.ca/health-info/prevention-public-health/death-cap-mushrooms.

There are many other varieties of wild mushrooms that are less toxic than death caps but can also cause severe illness. Search for "wild mushrooms" on www.bccdc.ca for additional resources.

For information on which mushrooms in BC are edible and which are poisonous, visit UBC's Mushrooms Up! database: www.zoology.ubc.ca/~biodiv/mushroom.

For more information on the Vancouver Mycological Society and their resources on poisonous mushrooms, visit www.vanmyco.org/about-mushrooms/poisonous.

Naloxone kits encouraged for those who smoke or snort

The BC Centre for Disease Control (BCCDC) is advising people who use drugs to get trained in overdose response and pick up a Take Home Naloxone kit, regardless of how they choose to consume, after new research revealed that people who smoke or snort drugs are half as likely to carry lifesaving naloxone medication. The warning stems from results of a 2018 survey of people who use drugs in BC and research published recently in the journal *Drug and Alcohol Dependence*. The survey, conducted by the harm reduction team at the BCCDC, found that people who reported smoking or snorting drugs as their preferred method of drug use were half as likely to carry naloxone as those who preferred injecting. This was true even after taking several factors into account, including gender, age, and type of drug used.

The unpredictability of the street drug supply puts people at risk. Data in BC show that people who smoke or snort opioids are experiencing overdoses and dying. While uncommon, there have also been reports of fentanyl-related deaths among people using stimulants, such as cocaine and methamphetamine.

The BCCDC is also advising anyone who is around people who use drugs and who may

witness an overdose to get trained and get a kit so they can respond. Take Home Naloxone kits are available free of charge at hundreds of locations across the province and can be found using the site finder on <https://towardtheheart.com>.

Learn more about the 2018 Harm Reduction Client Survey findings at www.bccdc.ca/health-professionals/data-reports/harm-reduction-and-substance-use.

New international exercise guidelines for cancer survivors

For the rising number of cancer survivors worldwide, there's growing evidence that exercise is an important part of recovery. But how much and what type of exercise is needed?

A recent review of research, conducted by an international group of experts led by the University of British Columbia, has resulted in the development of new exercise guidelines for cancer survivors. The updated recommendations, published in *Medicine and Science in Sports and Exercise*, outline specific "exercise prescriptions" to address common side effects, such as anxiety and fatigue, associated with cancer diagnoses and treatment.

In general, the new guidelines recommend survivors perform aerobic and resistance training for approximately 30 minutes per session, 3 times a week. This is a departure from earlier guidelines, published nearly a decade ago, which advised cancer survivors to meet the general public health guidelines for all Americans (150 minutes of exercise a week).

The new recommendations are based on a substantive review and analysis of the growing body of scientific evidence in the field. Since the first guidelines were put forward in 2010, there have been more than 2500 published randomized controlled exercise trials in cancer survivors (an increase of 281%).

The new paper ("Exercise guidelines for cancer survivors") is one of three papers published that summarize the outcomes of an international roundtable that explored the role of exercise in cancer prevention and control. The paper's lead author, Dr Kristin Campbell, associate professor in UBC's Department of Physical Therapy, and director of the Clinical Exercise Physiology Lab, served as the Canadian representative on the roundtable, working

alongside the Canadian Society for Exercise Physiology, one of 17 partner organizations. The roundtable brought together a group of 40 international, multidisciplinary experts from various organizations who conducted a thorough and updated review of the evidence on the positive effects of exercise in preventing, managing, and recovering from cancer. Together, the three papers offer new evidence-backed recommendations for incorporating exercise into prevention and treatment plans and introduce a new Moving Through Cancer initiative (https://www.exerciseismedicine.org/support_page.php/moving-through-cancer/), led by the American College of Sports Medicine, to help clinicians worldwide implement these recommendations.

The new recommendations include:

- For all adults, exercise is important for cancer prevention and specifically lowers risk of seven common types of cancer: colon, breast, endometrial, kidney, bladder, esophagus, and stomach.
- For cancer survivors, incorporate exercise to help improve survival after a diagnosis of breast, colon, and prostate cancer.
- Exercising during and after cancer treatment improves fatigue, anxiety, depression, physical function, quality of life, and does not exacerbate lymphedema.
- Continue research that will drive the integration of exercise into the standard of care for cancer.
- Translate into practice the increasingly robust evidence base about the positive effects of exercise for cancer patients.

For more information and links to all three papers visit www.acsm.org/read-research/newsroom/news-releases/news-detail/2019/10/16/expert-panel-cancer-treatment-plans-should-include-tailored-exercise-prescriptions.

Patients with mood, anxiety disorders share abnormalities in brain's control circuit

New research published in *JAMA Psychiatry* shows for the first time that patients with mood and anxiety disorders share the same abnormalities in regions of the brain involved in emotional and cognitive control. The findings hold promise for the development of new

treatments targeting these regions of the brain in patients with major depressive disorder, bipolar disorder, posttraumatic stress disorder, and anxiety disorders.

Mood and anxiety disorders account for nearly 65% of psychosocial disability worldwide and represent a major public health challenge. In Canada, one in three people (approximately 9.1 million) will be affected by mental illness during their lifetime, according to Statistics Canada. The defining symptoms of these disorders are persistent or recurring negative feelings, mainly depression and anxiety.

Dr Sophia Frangou is the study's senior author and a psychiatry professor at UBC. Dr Frangou recently joined UBC as the President's Excellence Chair in Brain Health at the Djavad Mowafaghian Centre for Brain Health. She started this research as head of the research team at the Icahn School of Medicine at Mount Sinai, New York.

For the study, Dr Frangou and her research team analyzed more than 9000 brain scans from previously published studies that compared the brain activity of healthy adults to

those diagnosed with a mood or anxiety disorder, ranging from major depression to post-traumatic stress disorder.

They found that patients exhibited abnormally low activity in the inferior prefrontal and parietal cortex, the insula, and the putamen—regions that are key parts of the brain circuit for emotional and cognitive control and are responsible for stopping ongoing mental activities and switching to new ones. They also discovered hyperactivity in the anterior cingulate cortex, the left amygdala, and the thalamus, which work together to process emotional thoughts and feelings.

Following her move to UBC, Dr Frangou plans to pursue further research to leverage these findings toward more targeted interventions, such as noninvasive stimulation of specific regions of the brain, which could improve outcomes for those living with mood and anxiety disorders.

The study is believed to be the largest analysis of brain scans of patients with mood and anxiety disorders to date. It was funded by the National Institute of Mental Health in the US, the German research funding organization Deutsche Forschungsgemeinschaft, and the European Union's Horizon 2020 Research and Innovation Programme.

The study, "Shared neural phenotypes for mood and anxiety disorders" is available at online at <https://jamanetwork.com/journals/jamapsychiatry/fullarticle/2753513>.

New DNA "clock" could help measure development in young children

Scientists have developed a molecular "clock" that could reshape how pediatricians measure and monitor childhood growth and potentially allow for an earlier diagnosis of life-altering developmental disorders. The research, published in *Proceedings of the National Academy of Sciences*, describes how the addition of chemical tags to DNA over time can potentially be used to screen for developmental differences and health problems in children.

The study was led by researchers at BC Children's Hospital, the University of British Columbia, and the University of California,

Los Angeles. It is the first study to describe a method specifically designed for children, called the Pediatric-Buccal-Epigenetic (PedBE) clock, which measures chemical changes to determine the biological age of a child's DNA.

Small chemical changes to DNA, known as epigenetic changes, alter how genes are expressed in certain tissues and cells. Some of these changes happen as a person ages and others may be in response to a person's environment or life experiences. In adults, these patterns of epigenetic changes are well established. They can be used to accurately predict a person's age from a DNA sample or, if a person's epigenetic age differs from their actual age, the clock can point to differences in health, including age-related diseases and early mortality.

The PedBE clock was developed using DNA methylation profiles from 1032 healthy children whose ages ranged from a few weeks old to 20 years. The researchers found 94 different sites in the genome that, when tested together, could accurately predict a child's age to within about 4 months. The team also found that children who spent longer in the womb showed an accelerated rate of DNA change by 3 months, demonstrating that this tool could be used to indicate an infant's developmental stage. The analysis can be done cheaply and efficiently on cells collected from a cheek swab.

In a small pilot study, the researchers also found that children with autism spectrum disorder (ASD) showed a higher PedBE "age" than those considered to be developing typically, suggesting that the clock could be used to screen for ASD.

The researchers made the tool freely available along with the publication of this study so other research teams are able to use and experiment with the tool right away.

The study, "The PedBE clock accurately estimates DNA methylation age in pediatric buccal cells," is available online at www.pnas.org/content/early/2019/10/09/1820843116.



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Obituaries

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Dr Donald Wilson Lang
1931–2019

Dr Donald Wilson Lang died peacefully at the Comox Valley Hospital surrounded by family. He is survived by his wife of 63 years, Mary Louise; their four children, Susan, Andrea, Barbara (Blair MacLean), and Graham (Caroline Berka); 11 grandchildren; and twin great-granddaughters.

Don and Mary Lou were born and raised in Edmonton and married soon after they graduated from the University of Alberta in 1955 (Mary Lou with a BSc in public health nursing). They settled first in Barrhead, Alberta, where Don started his career in the era before universal health care. From 1959 to 1960 they lived in Bristol, England, and Don pursued further medical training. On their return to Canada, Don joined a family practice in Kimberley, BC.

Although the initial plan was to stay for a short time, Don and his family spent 18 happy years in the “Bavarian City of the Rockies” enjoying wonderful friends and a marvelous outdoor life. In 1971, Don arranged for a unique and memorable 1-year practice exchange with a physician in Bowral, Australia.

In 1978 the family moved to North Vancouver, where Don transitioned from being a small community GP to having an urban practice in Lynn Valley and working at Lions Gate Hospital. In 1995 Don and Mary Lou relocated to the Comox Valley where Don did some locums before fully retiring. Don used to say, “It’s not how long you live, it’s how well you live,” and he lived well!

—Lang Family
Comox Valley



Dr Pascualito Aquino Seminiano
1947–2019

Dr Pascualito Seminiano passed away from this life to eternal life on 25 September 2019 at Langley Memorial Hospital, surrounded by his family.

Dr Seminiano was best known by his family and friends as Lito. He was born on 23 May 1947 in Donsol Sorsogon, Philippines. He completed his medical degree from the Far Eastern University in the Philippines in 1972 and immigrated to Canada in 1979.

Lito completed his psychiatric residency at the University Hospital in Saskatoon. After obtaining his FRCPC, he practised in Moose Jaw and Regina, Saskatchewan. In 1991 Lito moved to Langley, BC, with his family and started working as a consultant psychiatrist at Langley Memorial Hospital and at Langley Mental Health Centre, and also opened his private practice. Lito was very involved with the development and growth of psychiatric services in Langley. He was a warm, jovial, kind person and was very dedicated to his profession. Lito was always willing to help others, and whenever his patients and colleagues were in need, he was always available and helpful. He retired in December 2016 when he was diagnosed with pancreatic cancer.

Lito was married to Emy for 40 years. He adored Emy, and she was a source of joy and comfort throughout his life. Lito was a loving father to his daughter, Andrea; son, Joshua; daughter-in-law, Marielle; and grandfather to Mason. He was also a caring brother to his siblings and warmhearted uncle to his many nieces and nephews. Spending time with family and friends was very important to Lito, and he brought a lot of fun and laughter into their lives.

Lito had a deep and committed faith and was very devoted to his church. He was a member of Bukas Loob sa Diyos (Catholic Covenant Community) and served in different ministries. He was also a member of the Legion of Mary (Our Lady of the Woods) at the St. Nicholas Parish in Langley. Traveling was one of Lito’s passions, and he often went on cruises and visited many countries around the world. He was dedicated to a regular fitness program and would go to the gym regularly, even after becoming ill.

Lito is survived by his wife, Emy; his children, Andrea, Joshua, and daughter-in-law Marielle; his grandson, Mason; his sisters, Nimfa Diguangco and Elena Andrews; his brother, Amado Jr. Seminiano; and their families. Lito’s presence and big booming laugh will also be missed by his colleagues and patients in Langley.

—N.G. Nair, MBBS, FRCPC
Langley

—Shilpa C. Shete, MBBS, FRCPC
Langley

Obituaries continued on page 400



Mr James (Jim) Edward Gilmore
1930–2019

On 24 October 2019, the medical profession lost one of its most loyal and dedicated supporters. Mr James Edward Gilmore, retired director of communications and one of the few non-physician honorary members of the BC Medical Association (as Doctors of BC was formerly called) died at the age of 89 years in Victoria.

Jim was born on 19 April 1930 in Vancouver, where he lived most of his life. He is survived by his sister (Gerry), two children (Tracy and Dan), three grandchildren, four great-grandchildren, and a number of adopted children from previous marriages. Jim’s career in the communications industry began as copy boy at the *Province* at age 15, and subsequently as a sportswriter and columnist at the *News Herald* and *Vancouver Sun*. He branched out into the public relations field as executive director

of the California Optometric Association and acquired an interest in politics. He returned to Canada and became the chief of staff for federal cabinet minister, the Hon. Ronald (Ron) Basford, and later become the first public relations manager for the Royal Bank in BC.

In the early 1970s the BCMA was suffering attacks from both within and without the organization, and a decision was made to hire a public relations expert to regain public support for organized medicine and offset the government’s public relations offensive. The BCMA hired Jim in 1973 as its first director of communications.

Jim had a transformative impact on organized medicine during his 20-year tenure at the BCMA. He convinced BCMA leaders that the profession would get nowhere if it dedicated its resources to reacting to crises whenever the government imposed its power against the profession. Although individual British Columbians (including politicians, bureaucrats, journalists, academics, and others) had immense trust and support for their own individual doctors, that was not generally the case for doctors as a group. Jim obtained BCMA budget support to establish a superb Department of Communications that developed ongoing campaigns demonstrating to the public that organized medicine was an important segment of society, particularly in the development of public policy for the betterment of British Columbians. Jim’s multi-faceted communication programs, both internally and externally facing, became the envy of other medical associations across Canada and outside Canada, winning many public relations awards. This strategy, along with the work of the



Jim in his favorite deerstalker hat.

Economics Department, was very effective in improving the financial situation for BC doctors, and the payment schedule rose to become the highest in Canada on an overall basis and remained there throughout most of Jim’s 20 years as director of communications.

In addition to the honorary membership bestowed upon him by the BCMA, Jim was also given the Pat Monk Memorial Award for his contributions to public relations by the Canadian Public Relations Society. Those interested in learning more about Jim’s storied career should read Dr Brad Fritz’s article in the January/February 2017 issue of the *BC Medical Journal* online at www.bcmj.org/special-feature/mr-jim-gilmore%E2%80%94one-good-guys.

Doctors of BC owes a great debt to Mr James Edward Gilmore.

—Norman D. Finlayson, MD
Former Executive Director, BCMA (1986–98)

—Dan Gilmore

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PSP supports for quality improvement activities: Refreshed compensation policy, simplified certification process

The GPSC recognizes that doctors and health care team members invest significant time to ensure that practices run smoothly and efficiently. As family practice teams expand, practices are increasingly focused on quality improvement (QI) activities. To better support this work, the Practice Support Program (PSP) has updated how it compensates and certifies family physicians and eligible team members who engage in eligible QI activities.

Refreshed compensation policy

Based on physician feedback, PSP has refreshed the way GPs and team members are compensated for QI activities. Effective 15 June 2019, each eligible team member in a practice can receive compensation for up to 15 hours of work for participating in any eligible QI activity (for information on eligible and non-eligible QI activities visit www.gpsc.bc.ca/what-we-do/professional-development/psp). Team members eligible for compensation for QI activities include MOAs, allied health providers in private practice, and allied health providers employed by a GP practice. Team members who are employed or compensated by a health authority are ineligible.

For increased efficiency, doctors can now submit one form to claim a sessional payment for the hours spent on QI activities, and PSP team members are available to support doctors and practice teams to track their time throughout the process.

This article is the opinion of the GPSC and has not been peer reviewed by the BCMJ Editorial Board.

Simplified certification process

Effective 1 November 2019, PSP introduced a simplified certification process to replace the existing process for PSP learning modules, PSP small group learning sessions, and the GPSC patient medical home assessment (doctors currently participating in these services will not be affected). The new process will offer more credits, increased flexibility, and alignment with PSP's updated compensation policy, detailed above.

The process will enable family doctors to earn up to three credits per hour, for up to 15 hours (maximum of 45 Mainpro+ credits) for activities including in-practice visits with an RST or physician peer mentor, development and implementation of action plans, and participation in PSP's learning sessions.

In-practice coaching and mentoring

PSP Regional Support Teams (RST) and physician peer mentors are available to guide practices through a facilitation cycle that supports them in undertaking QI activities covered by the new compensation policy and new certification process. The facilitation cycle can help practices maximize efficiencies through activities like identifying changes in practice workflow, developing proactive patient recalls for common tests, and using data (including patient experience data) to inform practice improvements.

For more information contact a PSP Regional Support Team (see box), or email psp@doctorsofbc.ca. ■

—Alana Godin

Director, Community Practice and Quality,
Doctors of BC

PSP Regional Support Teams


Fraser Health: psp@fraserhealth.ca

Interior Health: psp@interiorhealth.ca

Northern Health: liana.doherty@northernhealth.ca

Vancouver Coastal: pspsupport@vch.ca

Vancouver Island Health: rsp@viha.ca




Building Capacity

Customized support to optimize family practices


Through PSP, doctors can build practice capacity, practice more efficiently, focus more on clinical care and patient relationships, and adopt the attributes of the patient medical home in BC.

PSP offers doctors and other practice team members:


LEARNING OPPORTUNITIES



COACHING AND MENTORING



DATA TOOLS



Canada's revolutionary new food guide

Earlier this year the federal government released a revised and dramatically different version of Canada's Food Guide. This is the ninth iteration of a document that has played a central role in informing what health professionals, the media, and the government tell Canadians about what foods to eat and how to eat it. Initially referred to as Canada's Official Food Rules, the 1942 document was released during wartime rationing, and it was intended to prevent nutritional deficiencies and improve the health of Canadians. The concept of food groups was introduced and specific amounts of foods from each group were suggested for daily consumption.

This information was promulgated through the media and government publications, and later editions were incorporated into school curricula across the country. Limited amounts of processed foods were available before the 1960s and consumption of whole grains and other whole foods were specifically encouraged through the food guide. The 1961 edition reflected the beginning of a revolution in food processing, storage, and transportation, and the widespread availability of processed, canned, and packaged convenience foods. The 1977 revision was colorfully illustrated and brochure-like. The involvement of stakeholders from the food and agricultural industries in this edition paralleled the dramatic shift in Canadians' diets toward more highly processed foods.

By 1992 the food guide was considered the bible of nutrition, with 24 million copies distributed nationwide. Canada's Food Guide

This article is the opinion of the Nutrition Committee, a subcommittee of Doctors of BC's Council on Health Promotion, and is not necessarily the opinion of Doctors of BC. This article has not been peer reviewed by the BCMJ Editorial Board.

had become the nutritional backdrop for Canadian society, informing the education of dietitians and forging government policy. Although it was heavily promoted and widely adopted, it was also increasingly criticized by health professionals and nutritional scientists who expressed concern about the heavy involvement of the agri-foods industry in this pivotal document. Prior to the release of the 2007 edition, this criticism became palpable for what was perceived by some as a wholesale adoption of unhealthy, highly processed foods and beverages in the face of an emerging epidemic of obesity and other diseases that were heavily influenced by dietary factors. In one *CMAJ* article, the 2007 guide was referred to as an "obesogenic recipe for dramatic increases in premature death."¹ Yoni Freedhoff, a well-known obesity medicine physician, called it "Canada's Food Guide to Unhealthy Eating."²

In the years leading up to the 2019 edition, influential elements of the government began to recognize the need to promote major shifts in the diets of Canadians. The 2016 Senate Standing Committee report, *Obesity in Canada*, stated that "Canada's Food Guide has been at best ineffective, and at worst enabling, with respect to the rising levels of unhealthy weights and diet-related chronic diseases in Canada."³ The committee recommended that the Minister of Health immediately undertake a complete revision of the guide in order for it to better reflect the current state of scientific evidence: "The revised food guide must: Be evidence-based; Apply meal-based rather than nutrient-based principles; Effectively and prominently describe the benefits of fresh, whole foods compared to refined grains, ready-to-eat meals and

processed foods; and Make strong statements about restricting consumption of highly processed foods."³ In this report the committee recommended that the Minister of Health revise the food guide on the guidance of an advisory body that "comprises experts in relevant areas of study, including but not limited to nutrition, medicine, metabolism, biochemistry, and biology; and does not include representatives of the food or agriculture industries."³ Remarkably, the health minister acted on all of these recommendations, and the current Canada's Food Guide gradually came to life.

Based on the "healthy eating plate" concept,⁴ the 2019 guide focuses on eating whole, unprocessed foods, and has a large emphasis on healthy food behaviors like eating mindfully, cooking from scratch at home, enjoying wholesome food, and eating meals with others. Although it has been heavily criticized by the

food industry and a few health care professionals, most of us on the front lines of obesity medicine consider it one of the premier triumphs of democracy, science, and common sense. In my practice, Canada's Food Guide and its many associated resources now play a central role in helping me guide patients toward an enjoyable diet based on real food, perhaps for the first time in their lives. ■

—Michael Lyon, MD

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Workplace exposure to rabies

Occupations identified as high risk for rabies exposure and infection include veterinarians, animal control workers, rabies diagnostic lab workers, spelunkers exploring caves, bat biologists and other wildlife biologists, pest control workers, and workers traveling to countries endemic for canine-mediated rabies. While transmission to health care workers caring for a patient infected with rabies has not been documented, theoretically transmission could occur through direct contact of broken skin or mucosa with saliva, tears, oropharyngeal secretions, cerebrospinal fluid, or neural tissue of an infected individual. Rabies is a reportable disease under the Canada Food Inspection Agency (CFIA) Health of Animals Act.¹

Causes

Rabies is a rare zoonotic disease caused by a Lyssavirus of the Rhabdoviridae family. In Canada, the disease is usually found in wild animals such as raccoons, skunks, bats, and foxes. Domesticated animals can become infected if they are bitten by an animal with rabies or come in contact with its saliva. Canine rabies remains endemic in many countries. Globally, dog bites provide the greatest risk of rabies transmission.²⁻⁵ In BC, bats are the only known reservoirs for the rabies virus.²

The rabies virus is carried in the saliva and neural tissue of an infected animal and can be transmitted to humans via the animal's bite or scratch, or through an individual's open wounds or mucus membranes. While very rare, transmission via nonbite routes, such as airborne transmission from bat secretions⁶ or direct human-to-human transmission through organ transplants⁷ has been reported.

This article is the opinion of WorkSafeBC and has not been peer reviewed by the BCMJ Editorial Board.

Disease progression

The incubation period is usually 3 to 8 weeks, although rarely can be as short as a few days to as long as several years.² After an initial period of nonspecific symptoms such as fever, malaise, or anxiety, frank neurological signs ranging from hyperactivity (encephalitis) to paralysis appear before the person lapses into a coma. Death typically occurs within 10 days from the onset of symptoms.²

Prevention

For workers in occupations that are high risk for rabies infection, pre-exposure prophylaxis with rabies vaccine is recommended, followed by a booster dose in the event of exposure.^{2,6}

For health care workers, routine precautions, including wearing gowns, goggles, masks, and gloves, are recommended when providing care to persons suspected of having clinical rabies.⁸ In the event of an exposure, public health officials follow specific criteria to identify high-risk contacts and provide postexposure prophylaxis.^{2,3}

Workers should seek immediate medical attention if they suspect they have been exposed to rabies. In BC, any worker who has had direct contact with a bat should seek medical attention, and the attending physician should call the local public health authority for guidance. Public health will conduct a risk assessment to determine whether rabies postexposure prophylaxis is indicated.

Treatment

Postexposure prophylaxis for rabies includes thorough wound washing, a series of rabies vaccines, and where indicated, rabies immunoglobulin (RIG). Given promptly,² rabies post-exposure prophylaxis is effective.³

When a worker is exposed to a bite or scratch of an infected source, rabies immunoglobulin is used to infiltrate the wound, or to infiltrate the exposed area when a bite or scratch cannot be ruled out. BC Centre for Disease Control has released new interim guidelines on postexposure prophylaxis and rabies immunoglobulin.^{2,9} Tetanus-diphtheria vaccine should also be updated as required.

If your patient suspects they have been exposed to rabies at work, encourage them to file a claim with WorkSafeBC. Providing all the relevant clinical information on a Form 8/11 is important to help your patient with their claim.

For assistance

If you have questions about a workplace rabies exposure or claim, please contact a medical advisor in Occupational Disease Services at 604 231-8842 or in your nearest WorkSafeBC office, or call the Medical Advisor Hotline at 1 855 476-3049. ■

—**Geetha Raghukumar, MBBS, DLSHTM, MSc, CIC, CCFP, FRCPC**
WorkSafeBC Medical Specialist, Occupational Disease Services

—**Olivia Sampson, MD, CCFP, MPH, RCPSC**
WorkSafeBC Manager of Clinical Services

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CME calendar

Rates: \$75 for up to 1000 characters (maximum), plus GST per month; there is no partial rate. If the course or event is over before an issue of the *BCMJ* comes out, there is no discount. **Deadlines:** ONLINE: Every Thursday (listings are posted every Friday). PRINT: The first of the month 1 month prior to the issue in which you want your notice to appear, e.g., 1 February for the March issue. The *BCMJ* is distributed by second-class mail in the second week of each month except January and August. **Planning your CME listing:** Advertising your CME event several months in advance can help improve attendance; we suggest that your ad be posted 2 to 4 months prior to the event. **Ordering:** Place your ad at www.bcmj.org/cme-advertising. You will be invoiced upon publication. Payment is accepted by Visa or MasterCard on our secure online payment site.

CME ON THE RUN

VGH and various videoconference locations, 31 Jan–5 Jun (Fri)

CME on the Run sessions are held at the Paetzold Lecture Theatre, Vancouver General Hospital and there are opportunities to participate via videoconference from various hospital sites. Each program runs on Friday afternoons from 1–5 p.m. and includes great speakers and learning materials. Dates and topics: 31 Jan (Psychiatry). Topics include: Bipolar II update on treatment; When too much wine becomes a problem; Adult ADD diagnosis and management; Where are we with benzodiazepines? The good, the bad, and the ugly; Sleeplessness beyond the sedatives; Smoking addiction: How can we do better?; Adjunctive therapies for depression; Counseling on cannabis and the implications on the developing brain. The next sessions are: 3 Apr (infectious disease and travel); 1 May (prenatal, pediatric, and adolescents); 5 Jun (internal medicine). To register and for more information visit ubccpd.ca, call 604 675-3777 or e-mail cpd.info@ubc.ca.

GP IN ONCOLOGY TRAINING

Vancouver, 3–14 Feb (Mon–Fri)

The BC Cancer's Family Practice Oncology Network offers an 8-week General Practitioner in Oncology training program beginning with a 2-week introductory session every spring and fall at the Vancouver Centre. This program provides an opportunity for rural family physicians, with the support of their community, to strengthen their oncology skills so that they may provide enhanced care for local cancer patients and their families. Following the introductory session, participants complete a further 30 days of customized clinic experience at the

cancer center where their patients are referred. These can be scheduled flexibly over 6 months. Participants who complete the program are eligible for credits from the College of Family Physicians of Canada. Those who are REAP-eligible receive a stipend and expense coverage through UBC's Enhanced Skills Program. For more information or to apply, visit www.fpon.ca, or contact Jennifer Wolfe at 604 219-9579.

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Advertisements are limited to 700 characters. Rates: Doctors of BC members: \$50 + GST per month for each insertion of up to 350 characters. \$75 + GST for insertions of 351 to 700 characters. Nonmembers: \$60 + GST per month for each insertion of up to 350 characters. \$90 + GST for insertions of 351 to 700 characters. Deadlines: Ads must be submitted or canceled by the first of the month preceding the month of publication, e.g., by 1 November for December publication. Visit www.bcmj.org/classified-advertising for more information. Ordering: Place your classified ad online at www.bcmj.org/classified-advertising. Payment is required at the time that you place the ad.

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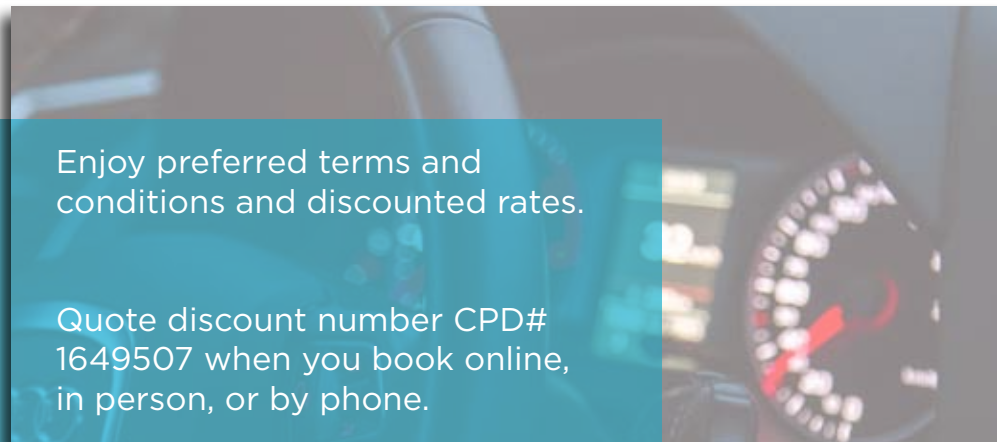
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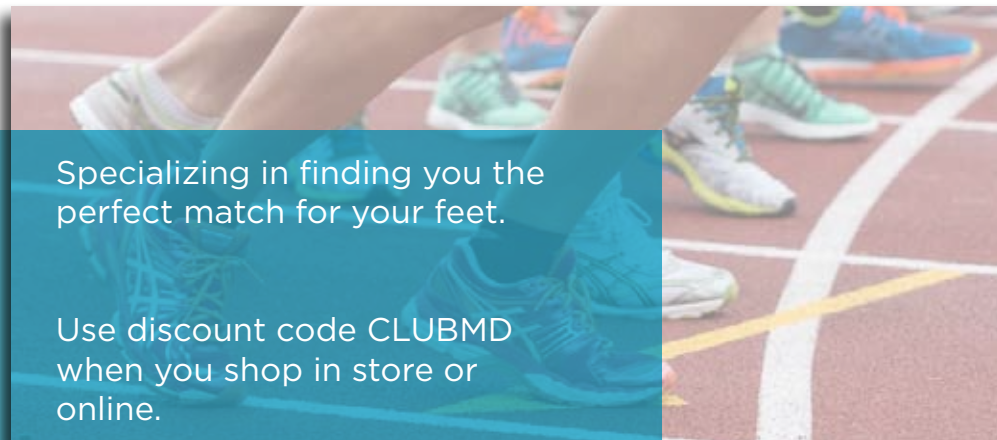
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