
From: Hisaw, Melanie (SBOH)
Sent: 3/11/2025 10:53:45 AM
To: DOH WSBOH,Burns, Anna M (SBOH),Larson, Michelle L (SBOH)
Cc:
Subject: Public Comment on March 12, 2025 re: Pierce County DIY septic inspection

Anna and Michelle,

Dewey Gibson called our office today wanting to make sure his public comment came through that he sent yesterday. I didn't see it in the WSBOH inbox, and he was having troubles sending emails. So, I had him send his message to me, so hopefully this can be wrapped up into public comments later.

Should I make a copy of it so we have it available tomorrow? Let me know if you want me to do anything.

He wants to give verbal public comment at 9:50am, and he said he already registered. But he struggles with some IT, so I have his name down if needed.

Thanks!

Melanie Hisaw

Executive Assistant

Washington State Board of Health

melanie.hisaw@sboh.wa.gov <mailto:melanie.hisaw@sboh.wa.gov>

360-236-4104

360-688-3719 (cell)

Website
<https://gcc02.safelinks.protection.outlook.com/?url=https%3A%2F%2Fsboh.wa.gov%2F&data=05%7C02
, Facebook
<https://gcc02.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.facebook.com%2FWASBOH8
, Twitter
<https://gcc02.safelinks.protection.outlook.com/?url=https%3A%2F%2Ftwitter.com%2FWASBOH&data=0

From: Dewey Gibson <diysepticinspectpiercec@gmail.com>
Sent: Tuesday, March 11, 2025 10:44 AM
To: Hisaw, Melanie (SBOH) <Melanie.Hisaw@sboh.wa.gov>

Subject:

External Email

Yeah I live in Pierce County and I'm trying to get them to adopt a DIY septic inspection program so we can do it ourselves. I called and talked to Jeremy Simmons and asked him about the video you guys put out 3 years ago showing people how to inspect septics and to see if it was legit enough to be able to do and go inspect your own septics systems. He said yes as long as you were doing a gravity or a pressurized system, the video was legit enough for you to go do it and stand behind it.I watch a video and it seems pretty simple to me to be able to do so I'm not sure why it's taking so long for them to get something up and running? So that's what I'm trying to have Pierce County do but they're kind of making it sound like it's not good enough to be able to do but according to Jeremy Simmons it is. The next thing they're struggling with is figuring out a computer system to enter it in so they know who's doing what. So if you know what the other counties are using so I can let them know this is the program they need so we can get this up and running by this year. So I guess what I was looking for is maybe some help and explain to them how to get this up and running so it's not a burden for people to do, I'd appreciate it.You can either let me know how that's done and I'll let them know or you can call them directly and let them know at Pierce County Department of Health,

Thanks Have A Great Day

From: Dewey Gibson
Sent: 3/12/2025 11:47:57 AM
To: Hisaw, Melanie (SBOH)
Subject: Re: Getting DIY inspection program in Pierce County

External Email

Thank you. for all the help you did for me and here is the county I talked to that have DIY septic inspections
mason 360 427 5509 Andrea
thurston 360 867 2644 Leah
watcom 360 778 6000 Haley
jefferson 360 385 9444 Emma
skagit 360 416 1500 Greg
callam 360 417 2000 Hope And I didn't talk to Island county but they have one as well

On Wed, Mar 12, 2025 at 10:18 AM Hisaw, Melanie (SBOH) <Melanie.Hisaw@sboh.wa.gov <mailto:Melanie.Hisaw@sboh.wa.gov> > wrote:

Hi Dewey,

Glad you were able to connect this morning! Thank you for your testimony, I will pass it along to Board Staff.

Warmly,

Melanie Hisaw

Executive Assistant

Washington State Board of Health

melanie.hisaw@sboh.wa.gov <mailto:melanie.hisaw@sboh.wa.gov>

360-236-4104

360-688-3719 (cell)

Website <https://gcc02.safelinks.protection.outlook.com/?url=https%3A%2F%2Fsboh.wa.gov%2F&data=05%7C02
, Facebook <https://gcc02.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.facebook.com%2FWASBOH8
, Twitter <https://gcc02.safelinks.protection.outlook.com/?url=https%3A%2F%2Ftwitter.com%2FWASBOH&data=0

From: Dewey Gibson <diysepticinspectpiercec@gmail.com <mailto:diysepticinspectpiercec@gmail.com> >
Sent: Wednesday, March 12, 2025 10:08 AM
To: Hisaw, Melanie (SBOH) <Melanie.Hisaw@sboh.wa.gov <mailto:Melanie.Hisaw@sboh.wa.gov> >
Subject: Getting DIY inspection program in Pierce County

External Email

I'm here to try to get DIY septic inspection programs in Pierce County. At this time we don't have a program even though Washington State approved it back in 2000 to be able to inspect your own septic system.You made a video three years ago showing us how to inspect it. I talked to Jeremy Simmons who has 16 years of experience in the public health and environmental sectors, the Manager of the Wastewater Management Program. He said it's very accurate and stands behind it, if you have a gravity or a pressurized system and that they are pretty simple to do.I talked to multiple people at the Pierce County Department of Health to find out why we don't have it and all I got was bunch of excuses.They put out in the paper on March 2024 that it was on its way to the Key Peninsula.I talked to Neil's and he said it'd be done by the end of 2024 and all you have to do is watch a video and do the inspection. All this was misleading, misinformation or flat out lies and that's manipulation. When people do that they cannot be trusted in anything they say or do. I talked to Chantel and she said when she got hired in March of 2024 she was told that they were not going to do DIY septic inspections at all, but in the paper they said it's on its way the same month. I watched Pierce County Department of Health committee meetings where Chantel, Laurel and Jessica all gave misinformation about things. When I looked up what they said none of it was true. Council member Robyn Denson has tried to get them to get a program up and running the last 2 years, and still nothing, all they say is we're looking into the feasibility. When I told them that other Counties have a program up and running and that are successful. They tell me that these 8 other Counties have highly inaccurate programs and would never have a program like any of those counties do. I asked Jeremy about this and he said there were no programs and that they were accurate. I think every County should offer a DIY septic inspection, all it does is help people understand their septic systems and how they work. This really helps the people that are struggling out there like senior citizens, veterans, retirees on supplemental income, people with disabilities and the low income that can afford it making a burden on them. It feels like they think we're too stupid to be able to do it even though eight other counties are doing it already, so why not us. If there's anything you can do to get them to do this or to help get the ball rolling so we have this by this year so everyone can be in compliance with the state code without it being a burden.If this is what the taxpayers want this is what the taxpayer should get.

_____

From: Bob Runnells
Sent: 3/12/2025 9:27:53 AM
To: DOH WSBOH
Cc:
Subject: CDC Study from public Comments made to March 12 Board of Health

 *attachments\F6FD6A29621E4514_COVID-19 vaccines and AESI - Glob_PRDTOOL_NAMETOOLONG.pdf*

External Email

Hello,

Please see attached CDC study by Faksova et al that the Board of Health should read and share with all in the Department of Health regarding adverse events of special interest after COVID-19 shots.

Thank you,

Bob Runnells

Informed Choice Washington

Vaccine 42 (2024) 2200–2211

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

COVID-19 vaccines and adverse events of special interest: A multinational Global Vaccine Data Network (GVDN) cohort study of 99 million vaccinated individuals

K. Faksova [a,*], D. Walsh [b,c], Y. Jiang [b,c], J. Griffin [c], A. Phillips [d], A. Gentile [e], J.C. Kwong [f,g,h], K. Macartney [d,i], M. Naus [j,n], Z. Grange [k], S. Escolano [l], G. Sepulveda [m], A. Shetty [m], A. Pillsbury [d], C. Sullivan [k], Z. Naveed [j,n], N.Z. Janjua [j,n], N. Giglio [e], J. Perälä [o], S. Nasreen [f,p,x], H. Gidding [d,i], P. Hovi [q], T. Vo [r], F. Cui [s], L. Deng [d], L. Cullen [k], M. Artama [r], H. Lu [b,c], H.J. Clothier [c,m], K. Batty [t], J. Paynter [u], H. Petousis-Harris [c,u], J. Buttery [c,m,v], S. Black [c,u], A. Hviid [a,w]

[a] Department of Epidemiology Research, Statens Serum Institut, Copenhagen, Denmark
[b] Department of Statistics, University of Auckland, New Zealand
[c] Global Vaccine Data Network, Global Coordinating Centre, Auckland, New Zealand
[d] National Centre for Immunisation Research and Surveillance, Westmead, New South Wales, Australia
[e] Department of Epidemiology, Ricardo Gutierrez Children Hospital, Buenos Aires University, Argentina
[f] ICES, Toronto, Ontario, Canada
[g] Public Health Ontario, Toronto, Ontario, Canada
[h] Department of Family and Community Medicine, Temerty Faculty of Medicine and the Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario, Canada
[i] The University of Sydney, Australia
[j] British Columbia Centre for Disease Control, Vancouver, British Columbia, Canada
[k] Public Health Scotland, Glasgow, Scotland, United Kingdom
[l] Université Paris-Saclay, UVSQ, Inserm, CESP, High Dimensional Biostatistics for Drug Safety and Genomics, Villejuif, France
[m] Murdoch Children's Research Institute, Parkville, Victoria, Australia
[n] School of Population and Public Health, University of British Columbia, Vancouver, British Columbia, Canada
[o] Department of Health Security, Finnish Institute for Health and Welfare, Helsinki, Finland
[p] Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario, Canada
[q] Department of Public Welfare, Finnish Institute for Health and Welfare, Helsinki, Finland
[r] Faculty of Social Sciences, Tampere University, Finland
[s] School of Public Health, Peking University, China
[t] Auckland UniServices Limited at University of Auckland, New Zealand
[u] School of Population Health, University of Auckland, New Zealand
[v] University of Melbourne, Parkville, Victoria, Australia
[w] Pharmacovigilance Research Center, Department of Drug Design and Pharmacology, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark
[x] School of Public Health, SUNY Downstate Health Sciences University, Brooklyn, NY, USA

ARTICLE INFO

Keywords:
Vaccine safety surveillance
Pharmacovigilance
Adverse events following immunization
Adverse events of special interest
COVID-19
Observed vs. expected analysis

ABSTRACT

Background: The Global COVID Vaccine Safety (GCoVS) Project, established in 2021 under the multinational Global Vaccine Data Network™ (GVDN®), facilitates comprehensive assessment of vaccine safety. This study aimed to evaluate the risk of adverse events of special interest (AESI) following COVID-19 vaccination from 10 sites across eight countries.

Methods: Using a common protocol, this observational cohort study compared observed with expected rates of 13 selected AESI across neurological, haematological, and cardiac outcomes. Expected rates were obtained by participating sites using pre-COVID-19 vaccination healthcare data stratified by age and sex. Observed rates were reported from the same healthcare datasets since COVID-19 vaccination program rollout. AESI occurring up to 42 days following vaccination with mRNA (BNT162b2 and mRNA-1273) and adenovirus-vector (ChAdOx1)

* Corresponding author at: Department of Epidemiology Research, Statens Serum Institut, Artillerivej 5, Copenhagen S 2300, Denmark.
E-mail address: kfak@ssi.dk (K. Faksova).

https://doi.org/10.1016/j.vaccine.2024.01.100
Received 29 January 2024; Accepted 30 January 2024
Available online 12 February 2024

vaccines were included in the primary analysis. Risks were assessed using observed versus expected (OE) ratios with 95 % confidence intervals. Prioritised potential safety signals were those with lower bound of the 95 % confidence interval (LBCI) greater than 1.5.

Results: Participants included 99,068,901 vaccinated individuals. In total, 183,559,462 doses of BNT162b2, 36,178,442 doses of mRNA-1273, and 23,093,399 doses of ChAdOx1 were administered across participating sites in the study period. Risk periods following homologous vaccination schedules contributed 23,168,335 person-years of follow-up. OE ratios with LBCI > 1.5 were observed for Guillain-Barré syndrome (2.49, 95 % CI: 2.15, 2.87) and cerebral venous sinus thrombosis (3.23, 95 % CI: 2.51, 4.09) following the first dose of ChAdOx1 vaccine. Acute disseminated encephalomyelitis showed an OE ratio of 3.78 (95 % CI: 1.52, 7.78) following the first dose of mRNA-1273 vaccine. The OE ratios for myocarditis and pericarditis following BNT162b2, mRNA-1273, and ChAdOx1 were significantly increased with LBCIs > 1.5.

Conclusion: This multi-country analysis confirmed pre-established safety signals for myocarditis, pericarditis, Guillain-Barré syndrome, and cerebral venous sinus thrombosis. Other potential safety signals that require further investigation were identified.

1. Introduction

Since declaration of the COVID-19 pandemic by the World Health Organization (WHO) on March 11, 2020 [1] more than 13.5 billion doses of COVID-19 vaccines have been administered worldwide [2]. As of November 2023, at least 70.5 % of the world's population had received at least one dose of a COVID-19 vaccine [2]. This unparalleled scenario underscores the pressing need for comprehensive vaccine safety monitoring as very rare adverse events associated with COVID-19 vaccines may only come to light after administration to millions of individuals.

In anticipation of this unprecedented global rollout of COVID-19 vaccines, the Safety Platform for Emergency vACcines (SPEAC) initiative formulated a list of potential COVID-19 vaccine adverse events of special interest (AESI) in 2020 [3]. AESI selection was based on their pre-established associations with immunization, specific vaccine platforms or adjuvants, or viral replication during wild-type disease; theoretical concerns related to immunopathogenesis; or supporting evidence from animal models using candidate vaccine platforms [3].

One flexible approach for assessing AESI is the comparison of observed AESI rates following the introduction of a vaccine program with the expected (or background) rates based on historical periods pre-vaccine roll out [4,5]. Such comparisons can be executed rapidly and can play a key role in early detection of potential vaccine safety signals or when regulatory and public health agencies need rapid assessment of an emerging safety signal [4,6]. Observed versus (vs.) expected (OE) analysis was integral in identifying thrombosis with thrombocytopenia syndrome (TTS) as a safety signal, prompting the suspension of use of the ChAdOx1 (AstraZeneca COVID-19 vaccine) on March 11, 2021, in Denmark and Norway [7,8].

These evaluations are not only valuable early-on in large-scale vaccine deployment, but also as the vaccination program matures, especially if they can be conducted in a multi-country context. We conducted a global cohort study following the Observed vs. Expected Analyses of COVID-19 Adverse Events of Special Interest Study Protocol [9] with data from 10 sites across eight countries participating in the unique Global COVID Vaccine Safety (GCoVS) Project [10] of the Global Vaccine Data Network™ (GVDN®) [11]. The GCoVS Project, initiated in 2021, is a Centers for Disease Control and Prevention (CDC) funded global collaboration of investigators and data sources from multiple nations for the purpose of COVID-19 vaccine safety monitoring.

2. Methods

2.1. Study design

This retrospective observational study was designed to estimate the OE ratios of selected AESIs after COVID-19 vaccination in a multi-country population cohort.

2.2. Data source and study population

The GCoVS Project compiled electronic healthcare data on AESI related to COVID-19 vaccines from participants across multiple sites within the GVDN network, including Argentina, Australia – New South Wales, Australia – Victoria, Canada – British Columbia, Canada – Ontario, Denmark, Finland, France, New Zealand, and Scotland [10]. The healthcare data comprised of either individual- or population-level data, depending on the availability in the study sites (Supplementary Table 1).

Immunization registers containing individual-level vaccination data were utilized by the majority of study sites. These registers covered the same population and geographic region as the data sets used to calculate background rates. We also examined population-level data on vaccination uptake using regularly updated dashboards from the study sites. If the number of individuals vaccinated in specific age and gender groups was available, we converted those numbers into person-years based on the post-vaccination risk period. Unlike the registers with individual-level data, the age and sex strata used in this approach might not have matched the strata used in the background rates calculations.

Participants were individuals vaccinated with COVID-19 vaccines in the populations represented by the sites. To the extent possible, standardized methods were applied across sites. Patient types included hospital inpatients (Australia – New South Wales, France, New Zealand, Scotland), and combinations of inpatient and outpatient emergency department patients (Argentina, Australia – Victoria, Canada, Denmark, Finland). In countries without clearly defined patient types, hospital contact duration was used as a proxy for patient types. As an example, a contact duration of five hours or longer was used as a proxy for in-patients in Denmark. Site-specific characteristics of data sources and data are presented in Supplementary Table 1.

2.3. Study period and follow-up

The study periods varied across countries, commencing on the date of the site-specific COVID-19 vaccination program rollout, and concluding at the end of data availability (Table 1). In general, the study periods spanned from December 2020 until August 2023. The shortest study period observed occurred in Australia – New South Wales, including 11 months from February 2021 to December 2021. Argentina had the longest study period, from December 2020 to August 2023, encompassing a total of 32 months.

The risk intervals used after each dose were 0–7 days, 8–21 days, 22–42 days, and 0–42 days. For each vaccination dose, day 0 was denoted the day of vaccine receipt. For this manuscript, we present results for the risk interval of 0–42 days only. More data are presented on the GVDN dashboard with all latest updates from participating sites [12]. Outcome events that occurred outside the study period were not included. A 365-day washout period for outcome events was used to define incident outcomes. Outcome events were considered incident if

there was no record of the same outcome event during the preceding 365-day washout period. An individual may have contributed several outcome events on the condition they were separated in time by at least the washout period of 365 days.

2.4. Study variables and outcomes

2.4.1. Adverse events of special interest (AESI)

Thirteen conditions representing AESI of specific relevance to the current landscape of real-world vaccine pharmacovigilance were selected from the list compiled by the Brighton Collaboration SPEAC Project [3] and in response to the safety signals of thrombosis with thrombocytopenia syndrome [7,8] (Supplementary Table 2). The conditions chosen matched the AESI for which background rates were recently generated by GVDN sites [13]. AESI were identified using harmonized International Classification of Diseases 10th Revision (ICD-10) codes. Neurological conditions selected included Guillain-Barré syndrome (GBS), transverse myelitis (TM), facial (Bell's) palsy, acute disseminated encephalomyelitis (ADEM), and convulsions (generalized seizures (GS) and febrile seizures (FS)) as potential safety signals have been identified for some of these conditions [14–16]. Hematologic conditions included cerebral venous sinus thrombosis (CVST), splanchnic vein thrombosis (SVT) and pulmonary embolism (PE); the unusual site thromboses (CVST and SVT) were selected as markers of potential TTS that could be accurately identified using diagnostic codes [17,18]. Thrombocytopenia and immune thrombocytopenia (ITP) were also included due to their association with TTS and reports of ITP as an independent safety signal [7,19,20]. Myocarditis and pericarditis were included as cardiovascular conditions and the OE ratios were evaluated separately for each condition [21–23].

2.4.2. COVID-19 vaccines

As of November 2023, multiple vaccines against COVID-19 were in use by the GCoVS sites representing multiple platform types such as inactivated, nucleic acid-based (mRNA), protein-based, and non-replicating viral vector platforms (Table 2). For this manuscript, we focused on three vaccines that recorded the highest number of doses administered, Pfizer/BioNTech BNT162b2, Moderna mRNA-1273, and Oxford/Astra Zeneca/Serum Institute of India ChAdOx1 vaccines. The cumulative number of doses of other vaccines administered (n) across study sites were relatively low, with exceptions for the inactivated Sinopharm (n = 134,550) and Sinovac (n = 31,598) vaccines, the protein-based Novavax (n = 66,856) vaccine, and the adenovirus-vector Janssen/Johnson & Johnson (n = 1,137,505) and Gamaleya Research Institute/Sputnik (n = 84,460) vaccines. The total number of doses of each vaccine brand administered are outlined in Table 2. Exposure to COVID-19 vaccine by platform/type, brand, and dose data were available at the individual level to determine the number of observed cases by vaccine type/brand and dose profile and within the 0–42 days post-vaccination risk interval.

Table 2
Total number of vaccinations by brand.

Vaccine platform	Vaccine brand	Total doses
Inactivated	Covilo or SARS-CoV-2 Vaccine (Vero Cell) [Sinopharm (Beijing)]	134,550
	Covaxin [Bharat Biotech]	1,660
	CoronaVac or Sinovac [Sinovac Biotech]	31,598
	Inactivated (Vero cell) [Sinopharm (Wuhan)]	623
Nucleic acid-based	Comirnaty or Riltozinameran or Pfizer/BioNTech COVID-19 Vaccine Bivalent [Pfizer/BioNTech]	3,516,963
	Comirnaty or Tozinameran [Pfizer/BioNTech or Fosun-BioNTech]	183,677,660
	Comirnaty or Tozinameran Paediatric [Pfizer/BioNTech or Fosun-BioNTech]	2,439,086
	Spikevax bivalent Original/Omicron [Moderna]	2,750,476
	Elasomeran or Spikevax or TAK-919 Half Dose [Moderna or Takeda]	400,395
	Elasomeran or Spikevax or TAK-919 [Moderna or Takeda]	36,222,514
Protein-based	MVC-COV1901 [Medigen]	16
	Covovax or Nuvaxoid [Novavax or Serum Institute of India]	66,856
Non-replicating viral vector	Convidecia or Convidence [CanSino]	3,938
	Covishield or Vaxzevria [AstraZeneca or Serum Institute of India]	23,094,620
	Sputnik Light or Gam-COVID-Vac [Gamaleya Research Institute]	26
	Sputnik V [Gamaleya Research Institute]	84,460
	Janssen [Janssen/Johnson & Johnson]	1,137,505

2.5. Statistical analysis

2.5.1. Calculation of observed vs. expected ratios for each site

For each site, we calculated the observed number of events for each AESI in the risk interval after introduction of COVID-19 vaccination. To

Table 1
Population summary by site. (Only Pfizer/BioNTech BNT162b2, Moderna mRNA-1273, and Oxford/Astra Zeneca/Serum Institute of India ChAdOx1 vaccines and doses 1–4 included).

Characteristics		Argentina	Australia: NSW	Australia: Victoria	Canada: BC	Canada: Ontario	Denmark	Finland	France	New Zealand	Scotland
Study period		12/2020-08/2023	02/2021-12/2021	02/2021-06/2023	12/2020-05/2023	12/2020-03/2023	12/2020-02/2023	12/2020-06/2022	01/2021-12/2021	02/2021-09/2022	12/2020-05/2023
Vaccinated population	n	157,883	6,492,805	5,789,070	4,267,644	12,081,337	4,291,034	4,501,659	52,795,394	4,151,269	4,540,806
	Female (%)	78,374 (49.6)	3,289,381 (50.7)	2,925,886 (50.5)	2,183,666 (51.2)	6,192,991 (51.3)	2,179,415 (50.8)	2,324,067 (51.6)	27,216,365 (51.6)	2,100,071 (50.6)	2,346,694 (51.7)
	0-19 (%)	42,281 (26.8)	692,498 (10.7)	921,635 (15.9)	274,813 (6.4)	1,882,574 (15.6)	620,273 (14.5)	549,589 (12.2)	5,585,455 (10.6)	582,662 (14.0)	501,397 (11.0)
	20-39 (%)	58,567 (37.1)	2,125,624 (32.7)	1,858,706 (32.1)	1,386,513 (32.5)	3,421,403 (28.3)	1,100,566 (25.6)	1,159,303 (25.8)	14,517,426 (27.5)	1,321,332 (31.8)	1,218,142 (26.8)
	40-59 (%)	40,484 (25.6)	1,933,770 (29.8)	1,586,558 (27.4)	1,244,817 (29.2)	3,460,295 (28.6)	1,263,265 (29.4)	1,256,439 (27.9)	16,065,061 (30.4)	1,198,750 (28.9)	1,418,313 (31.2)
	60-79 (%)	15,167 (9.6)	1,433,446 (22.1)	1,139,623 (19.7)	1,103,315 (25.9)	2,706,343 (22.4)	1,063,018 (24.8)	1,234,825 (27.4)	12,997,416 (24.6)	865,928 (20.9)	1,142,053 (25.2)
	80+ (%)	1,384 (0.9)	307,467 (4.7)	282,548 (4.9)	258,186 (6.0)	610,722 (5.1)	243,912 (5.7)	301,503 (6.7)	3,630,036 (6.9)	182,597 (4.4)	260,901 (5.7)
BNT162b2	Dose 1		3,896,923 (60.0)	3,393,207 (58.6)	2,959,369 (69.3)	8,473,103 (70.1)	3,425,161 (79.8)	3,586,237 (79.7)	41,450,092 (78.5)	4,036,859 (97.2)	2,087,109 (46.0)
	Dose 2		3,837,153 (59.1)	3,313,758 (57.2)	2,778,036 (65.1)	7,382,893 (61.1)	3,480,685 (81.1)	3,594,661 (79.9)	38,876,671 (73.6)	3,990,353 (96.1)	1,967,726 (43.3)
	Dose 3		751,169 (11.6)	2,900,036 (50.1)	1,295,609 (30.4)	4,377,649 (36.2)	2,811,507 (65.5)	2,167,380 (48.1)	16,121,693 (30.5)	2,730,880 (65.8)	2,557,434 (56.3)
	Dose 4			969,442 (16.7)	259,228 (6.1)	1,469,297 (12.2)	1,609,558 (37.5)		54,905 (0.1)	595,269 (14.3)	358,410 (7.9)
mRNA-1273	Dose 1	2,850 (1.8)	134,960 (2.1)	199,865 (3.5)	940,656 (22.0)	2,100,866 (17.4)	507,031 (11.8)	554,076 (12.3)	5,853,595 (11.1)	3,255 (0.1)	205,528 (4.5)
	Dose 2	13,046 (8.3)	126,291 (1.9)	190,271 (3.3)	1,196,017 (28.0)	3,589,447 (29.7)	578,985 (13.5)	532,153 (11.8)	5,880,520 (11.1)	3,211 (0.1)	183,966 (4.1)
	Dose 3	45,712 (29.0)	117,804 (1.8)	617,724 (10.7)	1,482,817 (34.7)	2,965,640 (24.5)	61,548 (1.4)	812,002 (18.0)	4,676,771 (8.9)	2,184 (0.1)	970,917 (21.4)
	Dose 4			257,557 (4.4)	380,862 (8.9)	723,201 (6.0)	56,850 (1.3)		14,245 (<0.1)	134 (<0.1)	195,885 (4.3)
ChAdOx1	Dose 1	37,721 (23.9)	2,460,922 (37.9)	1,868,764 (32.3)	308,867 (7.2)	856,603 (7.1)	133,181 (3.1)	360,196 (8.0)	4,398,411 (8.3)	17,087 (0.4)	2,139,669 (47.1)
	Dose 2	36,164 (22.9)	2,433,046 (37.5)	1,835,469 (31.7)	132,111 (3.1)	221,118 (1.8)	1,780 (<0.1)	191,120 (4.2)	3,424,058 (6.5)	14,560 (0.4)	2,093,121 (46.1)
	Dose 3	28,255 (17.9)	7,483 (0.1)	57,841 (1)	1,757 (<0.1)		46 (<0.1)	306 (<0.1)	7,368 (<0.1)	2,058 (<0.1)	9,551 (0.2)
	Dose 4			13,693 (0.2)	76 (<0.1)				90 (<0.1)	212 (<0.1)	695 (<0.1)

Vaccines: Pfizer/BioNTech (BNT162b2), Moderna (mRNA-1273), and Oxford/Astra Zeneca/Serum Institute of India (ChAdOx1).

calculate the expected number of cases, we used pre-COVID-19 vaccination background rates data from 2015 to 2019 (2019–2020 for Denmark) collected in the GCoVS Background Rates of AESI Following COVID-19 vaccination study [13]. The observed follow-up period in person-years for a given vaccination profile and post-vaccination period was stratified according to age group and sex. Each of the age-sex stratified person-years were multiplied by the corresponding age-sex stratified background rate. This resulted in the expected number of cases in each stratum, which were then summed to give the total number of expected cases during the observed follow-up period.

The aggregated OE ratios by last dose were calculated by dividing the observed number of cases by the expected number of cases in the post-vaccination period, 95 % confidence intervals (CI) were derived using the exact Poisson distribution. We also calculated OE ratios for homologous schedules for BNT162b2, mRNA-1273, and ChAdOx1 vaccines up to four doses. Both the aggregated OE ratios and those specific to homologous schedules are presented.

We considered an OE ratio a potential safety signal of concern where the lower bound of the 95 % CI (LBCI) was greater than one and reached statistical significance [5]. However, we prioritised potential safety signals of concern for further evaluation where the LBCI was greater than 1.5, due to increased statistical evidence and the higher likelihood of being a true signal, based on expert opinion from the CDC and GVDN collaborators.

2.5.2. Combining results across sites

The results were aggregated across sites by summing the observed number of events for each AESI and the age-sex stratified person-years for a given vaccination profile and post-vaccination period. For each AESI, individual vaccine profiles were reported if the cumulative amount of follow up (in person-years) in the 0–42 days post-vaccination period was 10,000 or greater. The combined numbers of events and the OE ratio was calculated with 95 % CIs derived using the exact Poisson distribution. No event (i.e., zero) observed for a vaccine brand and dose profile was reported separately without CI.

2.5.3. Sensitivity analysis

Firstly, we conducted site-specific sensitivity analyses to further explore potential associations of the most significant safety signals identified in the main analysis. The observed rates reported by sites were considered in the analysis based on the following constraints. For each vaccine brand and dose profile, and post-vaccination period combination, the OE ratios and 95 % CI were suppressed if fewer than five events were observed. Secondly, we conducted supplemental analysis including other vaccines and doses administered across sites. The person-years threshold for reporting was lowered from 10,000 to 1,000 person-years compared to the main aggregated OE ratios analysis, allowing for broader scope of vaccines to be analysed.

2.6. Ethical approval

Approval from the relevant Human Research Ethics Committees was either acquired or an exemption obtained for all participating sites (Supplementary Table 3).

3. Results

The total vaccinated population across all sites comprised 99,068,901 individuals. Most vaccine recipients were in the 20–39 and 40–59-year age groups (Table 1). In total, 183,559,462 doses of BNT162b2, 36,178,442 doses of mRNA-1273, and 23,093,399 doses of ChAdOx1 were administered across all the sites in the study periods. The

Table 3
Aggregated OE Ratios by last dose, neurological conditions, period 0–42 days.

		GBS		TRM		BP		ADEM		FSZ		GSZ	
Dose	Vaccine	OE Ratio	95%CI	OE Ratio	95%CI	OE Ratio	95%CI	OE Ratio	95%CI	OE Ratio	95%CI	OE Ratio	95%CI
1	ChAdOx1	2.49	(2.15,2.87)	1.91	(1.22,2.84)	0.98	(0.88,1.08)	2.23	(1.15,3.90)	0.93	(0.55,1.46)	0.86	(0.83,0.90)
	BNT162b2	0.90	(0.79,1.03)	0.74	(0.53,1.02)	1.05	(1.00,1.11)	1.28	(0.77,2.00)	0.73	(0.53,0.97)	0.92	(0.91,0.94)
	mRNA-1273	0.95	(0.65,1.34)	1.50	(0.77,2.62)	1.25	(1.11,1.39)	3.78	(1.52,7.78)	1.36	(1.02,1.77)	1.15	(1.10,1.20)
2	ChAdOx1	0.73	(0.54,0.96)	0.58	(0.21,1.26)	0.95	(0.85,1.06)	1.63	(0.70,3.21)	0.45	(0.20,0.89)	0.77	(0.74,0.81)
	BNT162b2	0.69	(0.60,0.79)	0.84	(0.62,1.11)	0.93	(0.88,0.97)	0.54	(0.23,1.06)	0.58	(0.42,0.79)	0.81	(0.80,0.83)
	mRNA-1273	0.84	(0.60,1.15)	1.27	(0.69,2.12)	1.02	(0.91,1.13)	1.21	(0.25,3.55)	1.44	(1.04,1.95)	0.97	(0.93,1.01)
3	ChAdOx1	3.99	(0.48,14.41)	0		0.75	(0.20,1.92)	0		2.88	(0.07,16.04	0.71	(0.44,1.10)
	BNT162b2	0.66	(0.54,0.79)	1.02	(0.68,1.46)	0.81	(0.76,0.87)	0.82	(0.30,1.79)	0.97	(0.69,1.33)	0.80	(0.78,0.82)
	mRNA-1273	0.68	(0.45,1.00)	0.92	(0.40,1.81)	0.83	(0.74,0.94)	0.64	(0.02,3.58)	0.58	(0.19,1.36)	0.69	(0.66,0.73)
4	BNT162b2	0.87	(0.56,1.29)	1.05	(0.39,2.29)	1.14	(0.99,1.29)	2.26	(0.06,12.62)	0.99	(0.43,1.94)	1.09	(1.04,1.14)
	mRNA-1273	0.88	(0.32,1.92)	1.25	(0.15,4.50)	1.08	(0.83,1.38)	0		0.85	(0.02,4.75)	1.00	(0.91,1.10)

AESI: GBS= Guillain-Barré syndrome, TRM= Transverse myelitis, BP= Facial (Bell's) palsy, ADEM= Acute disseminated encephalomyelitis, FSZ= Febrile seizures, GSZ= Generalised seizures
Vaccines: Pfizer/BioNTech (BNT162b2), Moderna (mRNA-1273), and Oxford/Astra Zeneca/Serum Institute of India (ChAdOx1)

Thresholds for statistical indications of potential signals:

Red: LBCI* >1.5, statistically significant safety signal

Yellow: LBCI* >1 and ≤1.5, statistically significant

Green: LBCI* ≤1.0, not statistically significant

*LBCI: Lower bound of confidence interval

Conditions applied to the analysis of aggregated OE ratios:

- PYRS ≥10000
- No censoring on observed counts

AESI: GBS = Guillain-Barré syndrome, TRM = Transverse myelitis, BP = Facial (Bell's) palsy, ADEM = Acute disseminated encephalomyelitis, FSZ = Febrile seizures, GSZ = Generalised seizures.
Vaccines: Pfizer/BioNTech (BNT162b2), Moderna (mRNA-1273), and Oxford/Astra Zeneca/Serum Institute of India (ChAdOx1).

Table 4
Aggregated OE Ratios by last dose, haematologic conditions, period 0–42 days.

		THR		ITP		PEM		CVST		SVT	
Dose	Vaccine	OE Ratio	95%CI	OE Ratio	95%CI	OE Ratio	95%CI	OE Ratio	95%CI	OE Ratio	95%CI
1	ChAdOx1	1.07	(1.03,1.12)	1.40	(1.24,1.58)	1.20	(1.16,1.24)	3.23	(2.51,4.09)	1.02	(0.89,1.16)
	BNT162b2	1.11	(1.08,1.14)	1.08	(1.01,1.16)	1.29	(1.26,1.32)	1.49	(1.26,1.75)	1.25	(1.17,1.34)
	mRNA-1273	1.33	(1.25,1.42)	1.13	(0.93,1.37)	1.33	(1.26,1.40)	1.48	(0.92,2.23)	1.23	(1.03,1.47)
2	ChAdOx1	0.96	(0.91,1.01)	1.02	(0.88,1.18)	0.96	(0.92,1.00)	1.15	(0.70,1.77)	0.95	(0.82,1.10)
	BNT162b2	0.92	(0.89,0.94)	0.93	(0.86,1.00)	0.99	(0.97,1.01)	1.25	(1.06,1.46)	1.03	(0.96,1.10)
	mRNA-1273	0.98	(0.92,1.04)	0.80	(0.65,0.97)	1.05	(0.99,1.10)	1.43	(0.95,2.06)	1.17	(1.01,1.36)
3	ChAdOx1	1.95	(1.29,2.84)	3.65	(0.75,10.67)	1.88	(1.32,2.58)	0		3.59	(0.43,12.96)
	BNT162b2	0.78	(0.75,0.81)	0.85	(0.77,0.93)	0.96	(0.93,0.98)	1.14	(0.89,1.44)	0.90	(0.82,0.99)
	mRNA-1273	0.73	(0.67,0.79)	0.72	(0.57,0.91)	0.97	(0.92,1.02)	0.94	(0.49,1.65)	0.94	(0.77,1.13)
4	BNT162b2	1.04	(0.95,1.13)	1.18	(0.99,1.41)	0.99	(0.94,1.04)	0.99	(0.47,1.81)	1.30	(1.06,1.59)
	mRNA-1273	1.08	(0.93,1.24)	0.96	(0.59,1.47)	1.03	(0.93,1.13)	0		1.53	(1.05,2.16)

AESI: THR= Thrombocytopenia, ITP= Idiopathic thrombocytopenia, PEM= Pulmonary embolism, CVST=Cerebral venous sinus thrombosis, SVT= Splanchnic vein thrombosis

Vaccines: Pfizer/BioNTech (BNT162b2), Moderna (mRNA-1273), and Oxford/Astra Zeneca/Serum Institute of India (ChAdOx1)

Thresholds for statistical indications of potential signals:

Red: LBCI* >1.5, statistically significant safety signal

Yellow: LBCI* >1 and ≤1.5, statistically significant

Green: LBCI* ≤1.0, not statistically significant

*LBCI: Lower bound of confidence interval

Conditions applied to the analysis of aggregated OE ratios:

- PYRS ≥10000
- No censoring on observed counts

AESI: THR = Thrombocytopenia, ITP = Idiopathic thrombocytopenia, PEM = Pulmonary embolism, CVST = Cerebral venous sinus thrombosis, SVT = Splanchnic vein thrombosis.
Vaccines: Pfizer/BioNTech (BNT162b2), Moderna (mRNA-1273), and Oxford/Astra Zeneca/Serum Institute of India (ChAdOx1).

highest numbers of doses were administered in France (120,758,419), followed by Canada – Ontario (32,159,817) and Australia – Victoria (15,617,627). In total, 23,168,335 person-years contributed to the OE ratios for the AESI following homologous schedules. The population summary is presented in Table 1, and more detailed information on the other administered vaccines are presented in Supplementary Table 4. In the results sections below, we provide both aggregated OE ratios (Tables 3–5) and detailed OE ratios for homologous schedules (Figs. 1–3), including the number of events and person-years. Overall, 95.8 % and 86.6 % of vaccinations were included in the aggregated and the homologous schedules analysis, respectively (Supplementary Table 5). The primary results from the individual sites as well as additional risk periods and meta-analyses for each AESI are available in the interactive GVDN Observed vs Expected (OE) Dashboard [12].

3.1. Neurological conditions

There was a statistically significant increase in GBS cases within 42 days after a first ChAdOx1 dose (OE ratio = 2.49; 95 % CI: 2.15, 2.87), indicating a prioritised safety signal (Table 3). Seventy-six GBS events were expected, and 190 events were observed (Fig. 1). The OE ratio for ADEM within 42 days after a first mRNA-1273 dose also fulfilled the significance threshold of a prioritised safety signal (3.78; 95 % CI: 1.52, 7.78), with two expected events compared with seven observed events (Fig. 1).

Statistically significant differences were also found for transverse myelitis (OE ratio = 1.91; 95 % CI: 1.22, 2.84) and ADEM (OE ratio = 2.23; 95 % CI: 1.15, 3.90) after a first ChAdOx1 dose. Bell's palsy had an increased OE ratio after a first dose of BNT162b2 (1.05; 95 % CI: 1.00, 1.11) and mRNA-1273 (1.25; 95 % CI: 1.11, 1.39). There were also increased OE ratios for febrile seizures following a first and second dose of mRNA-1273 (1.36, 95 % CI: 1.02, 1.77 and 1.44, 95 % CI: 1.04, 1.95, respectively), and for generalised seizures following a first mRNA-1273 dose (1.15, 95 % CI: 1.10, 1.20) and a fourth BNT162b2 dose (1.09, 95 % CI: 1.04, 1.14). No increased OE ratios were identified following a third dose of any vaccine. The results are concordant with the OE ratios of homologous schedules; however, an increased OE ratio for generalized seizures following a homologous schedule of four doses of mRNA-1273 (1.33; 95 % CI: 1.07, 1.63) was identified (Fig. 1). These outcomes did not meet the threshold for a prioritised safety signal following vaccination.

3.2. Hematologic conditions

The OE ratio of CVST was 3.23 (95 % CI: 2.51–4.09) within 42 days after a first dose of ChAdOx1, fulfilling the threshold of a prioritised safety signal (Table 4). In total, 21 events were expected, while 69 events were observed (Fig. 2).

Increased OE ratios were also identified for thrombocytopenia after a first dose of ChAdOx1 (1.07; 95 % CI: 1.03, 1.12), BNT162b2 (1.11; 95 % CI: 1.08, 1.14), and mRNA-1273 (1.33; 95 % CI 1.25, 1.42), as well as after a third dose of ChAdOx1 (1.95; 95 % CI: 1.29, 2.84). Immune thrombocytopenia also demonstrated increased OE ratios after a first dose of ChAdOx1 (1.40; 95 % CI: 1.24, 1.58) and BNT162b2 (1.08; 95 % CI: 1.01, 1.16). Pulmonary embolism OE ratios were increased following first doses of ChAdOx1 (1.20; 95 % CI: 1.16, 1.24), BNT162b2 (1.29; 95 % CI: 1.26, 1.32), and mRNA-1273 (1.33, 95 % CI: 1.26, 1.40), as well as after a third dose of ChAdOx1 (1.88; 95 % CI: 1.32, 2.58). The OE ratio of CVST was 1.49 (95 % CI: 1.26, 1.75) after a first dose and 1.25 (95 % CI: 1.06, 1.46) after a second dose of BNT162b2. An increased OE ratio for SVT was found after a first dose of BNT162b2 (1.25; 95 % CI: 1.17, 1.34) and mRNA-1273 (1.23; 95 % CI: 1.03, 1.47); a second dose of

Table 5
Aggregated OE Ratios by last dose, cardiovascular conditions, period 0–42 days.

		MYO		PER	
Dose	**Vaccine**	**OE Ratio**	**95%CI**	**OE Ratio**	**95%CI**
1	ChAdOx1	**1.36**	**(1.08,1.68)**	**1.29**	**(1.15,1.44)**
	BNT162b2	**2.78**	**(2.61,2.95)**	**1.54**	**(1.47,1.62)**
	mRNA-1273	**3.48**	**(3.00,4.01)**	**1.74**	**(1.54,1.97)**
2	ChAdOx1	**1.31**	**(1.01,1.68)**	**1.27**	**(1.12,1.43)**
	BNT162b2	**2.86**	**(2.70,3.03)**	**1.38**	**(1.32,1.45)**
	mRNA-1273	**6.10**	**(5.52,6.72)**	**1.67**	**(1.50,1.85)**
3	ChAdOx1	0		**6.91**	**(3.45,12.36)**
	BNT162b2	**2.09**	**(1.88,2.32)**	**1.19**	**(1.10,1.28)**
	mRNA-1273	**2.01**	**(1.60,2.49)**	**1.39**	**(1.20,1.59)**
4	BNT162b2	**2.06**	**(1.47,2.80)**	**1.55**	**(1.30,1.83)**
	mRNA-1273	**2.91**	**(1.45,5.21)**	**2.64**	**(2.05,3.35)**

AESI: MYO= Myocarditis, PER= Pericarditis

Vaccines: Pfizer/BioNTech (BNT162b2), Moderna (mRNA-1273), and Oxford/Astra Zeneca/Serum Institute of India (ChAdOx1)

Thresholds for statistical indications of potential signals:

Red: LBCI* >1.5, statistically significant safety signal

Yellow: LBCI* >1 and ≤1.5, statistically significant

Green: LBCI* ≤1.0, not statistically significant

*LBCI: Lower bound of confidence interval

Conditions applied to the analysis of aggregated OE ratios:

- PYRS ≥10000
- No censoring on observed counts

mRNA-1273 (1.17; 95 % CI: 1.01, 1.36); and a fourth dose of BNT162b2 (1.30, 95 % CI: 1.06, 1.59) and mRNA-1273 (1.53, 95 % CI: 1.05, 2.16). These outcomes did not meet the threshold for a prioritised safety signal following vaccination.

3.3. Cardiovascular conditions

Increased OE ratios fulfilling the threshold of prioritised safety signals for myocarditis were consistently identified following a first, second and third dose of mRNA vaccines (BNT162b2 and mRNA-1273) (Table 4). The highest OE ratio was observed following a first and second dose of mRNA-1273 (3.48; 95 % CI: 3.00, 4.01 and 6.10; 95 % CI: 5.52, 6.72, respectively). The OE ratio following a third dose of mRNA-1273 was 2.01 (95 % CI: 1.60, 2.49). The numbers of events for up to four doses of homologous schedules are shown in Fig. 3. The OE ratios of homologous schedules align with the aggregated OE ratios. The homologous OE for myocarditis following four doses of mRNA-1273 vaccine could not be estimated due to a lack of observed events.

Similarly, the OE ratio for pericarditis fulfilled the threshold of a prioritised safety signal following a first and fourth dose of mRNA-1273, with OE ratios of 1.74 (95 % CI: 1.54, 1.97) and 2.64 (95 % CI: 2.05, 3.35) respectively. An increased ratio of 6.91 (95 % CI: 3.45, 12.36), fulfilling the threshold of a prioritised safety signal, was also observed following a third dose of ChAdOx1. The aggregated OE ratios for pericarditis were increased following all doses of all the three vaccines presented (Table 4). The results are very similar to the ratios of homologous schedules (Fig. 3), except for the OE ratio of 1.23 (95 % CI: 0.45–2.69) after receipt of the fourth mRNA-1273 dose, which did not meet the threshold for a safety signal. The homologous OE ratio following a third dose of ChAdOx1 was not reported as only a small number of third doses of ChAdOx1 were given across study sites (Table1).

3.4. Sensitivity analysis

Secondary analyses were conducted to further explore GBS, ADEM, CVST, myocarditis, and pericarditis at the site-specific level. We report the aggregated OE ratios by last dose and site in the period 0–42 days after vaccination in Supplementary Tables 6–10. It was not possible to report results for all sites and study outcomes due to insufficient person-years or less than five events observed by site privacy criteria. The majority of identified safety signals following specific vaccine brand and dose combinations from the main analysis were, however, confirmed by individual sites where data were available. The supplementary analysis with person-years threshold of 1,000 and including other vaccines and doses administered within the GVDN sites, showed an increased OE ratio for some outcomes, e.g. for generalized seizures following a first dose of Gamaleya Research Institute/Sputnik vaccine (5.50, 95 % CI: 2.74, 9.84) (Supplementary Tables 11–13).

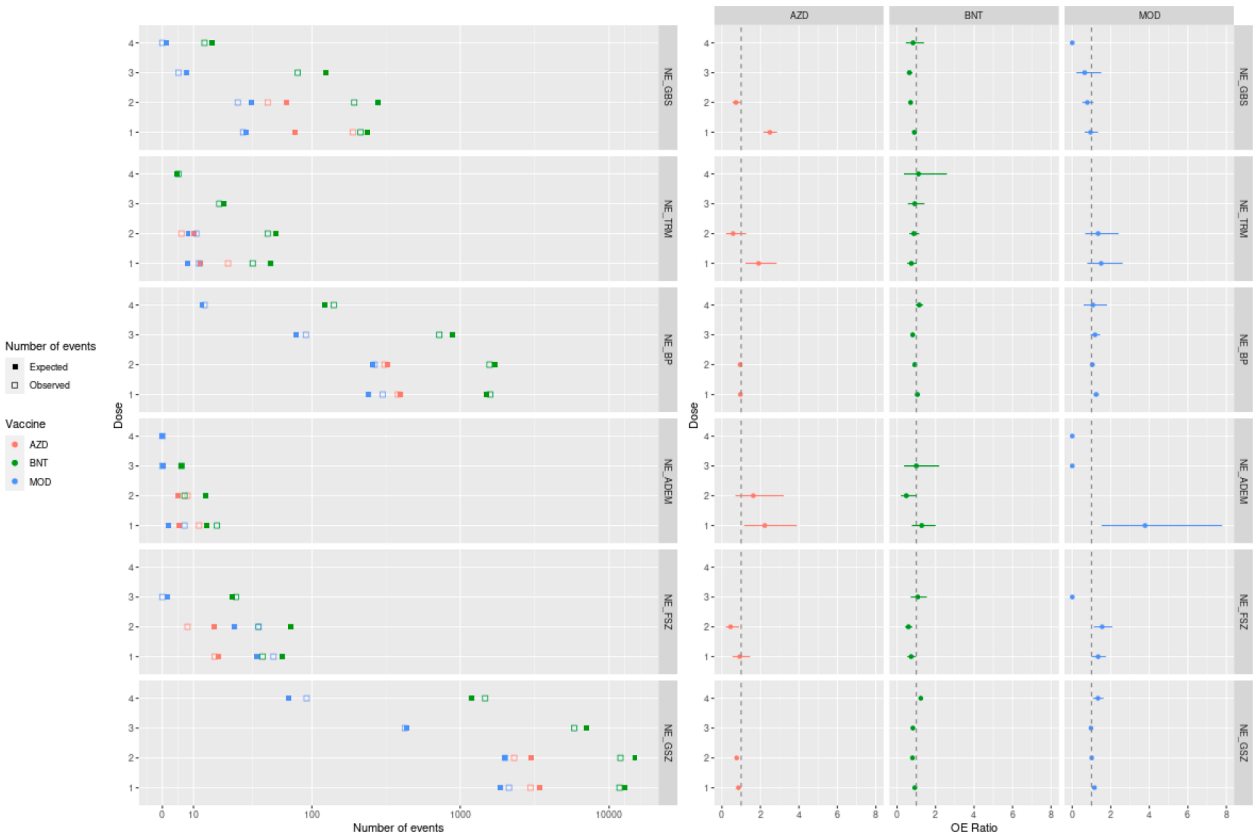

Fig. 1. Number of events and OE ratios (with 95 % confidence interval) for homologous schedules by dose 1–4, neurological conditions. AESI: GBS = Guillain-Barré syndrome, TRM = Transverse myelitis, BP = Facial (Bell's) palsy, ADEM = Acute disseminated encephalomyelitis, FSZ = Febrile seizures, GSZ = Generalised seizures. Vaccines: AZD = Oxford/Astra Zeneca/Serum Institute of India ChAdOx1, BNT = Pfizer/BioNTech (BNT162b2), MOD = Moderna (mRNA-1273).

4. Discussion

This multi-country cohort study was conducted in the unique setting of the GVDN. To date, the number of such large systematically coordinated studies across diverse geographical locations and populations is limited. However, several studies have previously assessed the risks of the identified safety signals following COVID-19 vaccination, primarily in single site settings. We investigated the association between COVID-19 vaccination and 13 AESIs comprising neurological, haematological, and cardiovascular conditions across 10 sites in eight countries including Europe, North America, South America, and Oceania. In this study including more than 99 million people vaccinated against SARS-CoV-2, the risk up to 42 days after vaccination was generally similar to the background risk for the majority of outcomes; however, a few potential safety signals were identified. We observed potential safety signals for GBS and CVST after the first dose of ChAdOx1 based on more than 12 million doses administered.

Overall, studies of the vector-based vaccines such as the ChAdOx1, have observed a higher incidence of GBS after vaccination compared with the background incidence; whereas, most studies of the mRNA vaccines, such as BNT162b2 and mRNA-1273, have not observed increases of GBS [14,15,24–27]. Atzenhoffer et al. [24] reported an elevated OE ratio > 2.0 for adenovirus-vectored COVID-19 vaccines, across countries contributing to VigiBase, an international database of adverse drug events and Patone et al. [27] reported 38 excess cases of GBS per 10 million exposed in the 1–28 days risk period following vaccination with ChAdOx1 in England. The authors did not observe an increased risk in those who received BNT162b2. In contrast, a study by Li et al. [28] showed no increased risk of GBS for ChAdOx1, while only SARS-CoV-2 infection was associated with a higher risk. The discrepancy, compared with the results of Patone et al. [27], could however be explained by a smaller sample size and different outcome measures. Overall, this evidence supports our findings of a GBS safety signal following ChAdOx1 vaccination. Although rare, this association was acknowledged by the WHO, the European Medicines Agency (EMA), and Therapeutic Goods Administration (TGA) of Australia, resulting in GBS being listed as a rare side effect following exposure to ChAdOx1 [15,29,30].

The identified increased risk of CVST following ChAdOx1 vaccination in this study is corroborated by multiple studies. An increased OE ratio was observed in a nationwide cohort study from Denmark and Norway, with increased rates of venous thromboembolic events, including CVST with an excess rate of 2.5 events per 100,000 vaccinations following ChAdOx1 [7]. Based on a variety of methodologies, other studies have also reported increased incidence of CVST after vaccination [31,32]. Ultimately, this rare but concerning safety signal led to the withdrawal of the ChAdOx1 vaccine from COVID-19 vaccine programs or implementation of age-based restrictions in multiple countries [8].

It is crucial to acknowledge the significance threshold of prioritised safety signals applied in this study (LBCI > 1.5). This threshold was selected based on expert opinion within the GVDN and at CDC, to focus on those outcomes most likely to be true signals. Some observed events, although not fulfilling this threshold, may still hold clinical importance and require further investigation. For instance, ITP with an OE ratio > 1.0 and LBCI of 1.2 following vaccination with ChAdOx1 aligns with findings reported in the literature as a potential signal. This concurrence is highlighted in a study conducted in Victoria, Australia, which observed a substantially higher than expected rate of ITP following ChAdOx1 vaccination [33].

Moreover, we observed significantly higher risks of myocarditis following the first, second and third doses of BNT162b2 and mRNA-1273 as well as pericarditis after the first and fourth dose of mRNA-

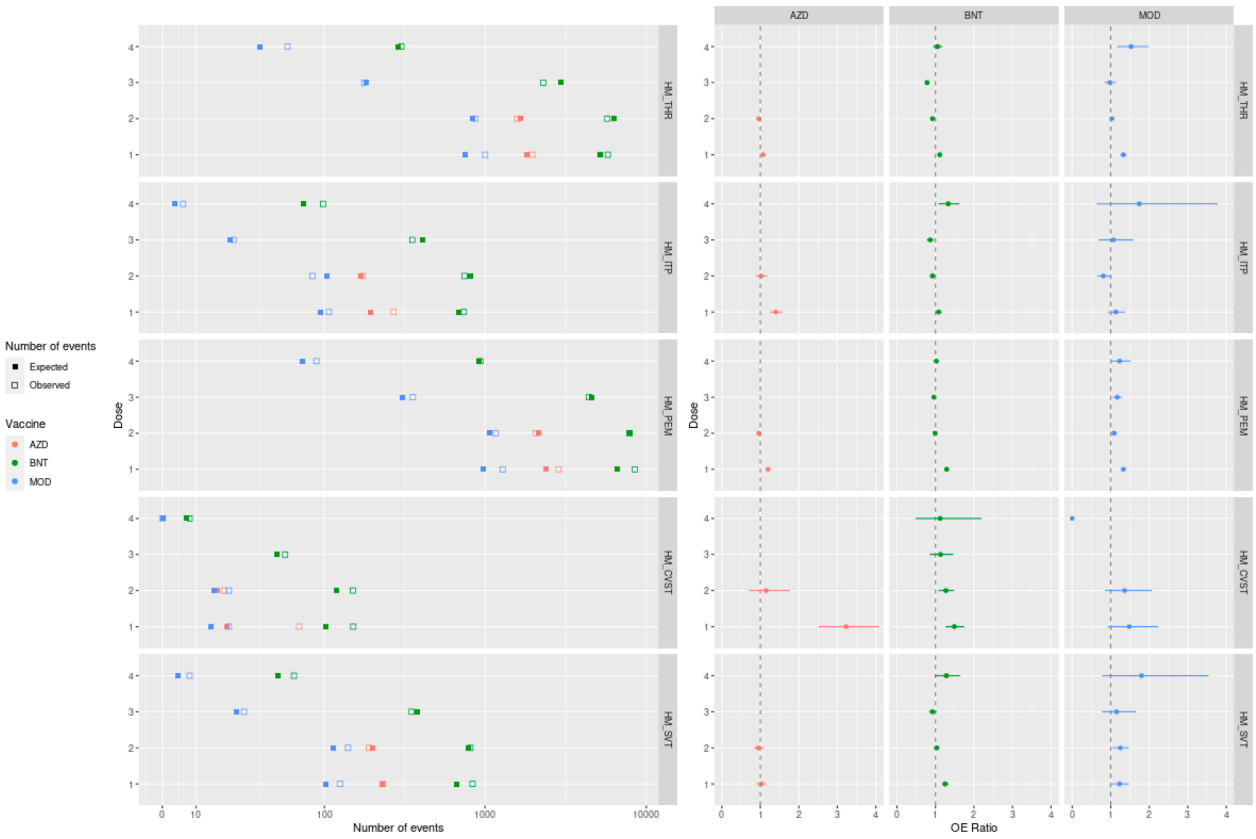

Fig. 2. Number of events and OE ratios (with 95 % confidence interval) for homologous schedules by dose 1–4, hematologic conditions. AESI: THR = Thrombocytopenia, ITP = Idiopathic thrombocytopenia, PEM = Pulmonary embolism, CVST = Cerebral venous sinus thrombosis, SVT = Splanchnic vein thrombosis. Vaccines: AZD = Oxford/Astra Zeneca/Serum Institute of India (ChAdOx1), BNT = Pfizer/BioNTech (BNT162b2), MOD = Moderna (mRNA-1273).

1273, and third dose of ChAdOx1, in the 0–42 days risk period. The elevated rates of pericarditis following ChAdOx1 vaccination identified in this study rely on a limited number of observed counts in the meta-analysis. The wide confidence interval underscores the substantial uncertainty of characterizing pericarditis as a safety signal following ChAdOx1 vaccination. However, our study confirms findings of previously identified rare cases of myocarditis and pericarditis following first and second doses of mRNA vaccines [21–23,34]. A large cohort study of 23.1 million residents across four Nordic countries revealed an increased risk of myocarditis among young males aged 16–24 years, based on 4–7 excess events in 28 days per 100,000 vaccinees after a second dose of BNT162b2, and between 9 and 28 per 100,000 vaccinees after a second dose of mRNA-1273 [22]. Similarly, studies from British Columbia, Canada reported cases of myocarditis to be higher among those receiving a second dose compared with a third dose, and for those who received a second dose of the mRNA-1273 vaccine compared with the BNT162b2 vaccine [35,36]. Patone et al. [37] estimated extra myocarditis events to be between one and 10 per million persons in the month following vaccination, which was substantially lower than the 40 extra events per million persons observed following SARS-CoV-2 infection period. A systematic review by Alami et al. [38] concluded that mRNA vaccinated individuals were twice as likely to develop myocarditis/pericarditis compared with unvaccinated individuals, with a rate ratio of 2.05 (95 % CI 1.49–2.82). Given the evidence, WHO issued updated guidance regarding these safety signals and mRNA COVID-19 vaccination, and EMA provided updates to the Product Information for BNT162b2 and mRNA-1273 vaccines [21,23]. TGA as well as the CDC continue to monitor and review data on myocarditis and pericarditis following COVID-19 vaccination [39,40].

Another potential safety signal was identified for ADEM after the first dose of mRNA-1273 vaccine, with five more observed than expected events based on 1,035,871 person-years and 10.5 million doses administered; however, the number of cases of this rare event were small and the confidence interval wide, so results should be interpreted with caution and confirmed in future studies. Although some case reports have suggested a possible association between COVID-19 vaccination and ADEM, there was no consistent pattern in terms of vaccine or timing following vaccination, and larger epidemiological studies have not confirmed any potential association [41–44]. Moreover, case reports may report on coincidental events and do not establish association nor indicate causality, thus larger observational studies are warranted to further investigate our finding. To address this, a follow-up study is currently being undertaken within the GVDN, focusing on a demographic not included in our analysis. Based on reports of rare ADEM cases to the European Database of Suspected Adverse Drug Reaction, EMA assessed the potential association of ADEM following vaccination with ChAdOx1 [45]. Frontera et al. [46] concluded that chances of having a neurological event following acute SARS-CoV-2 infection were up to 617-fold higher than following COVID vaccination, suggesting that the benefits of vaccination substantially outweigh the risks. A safety signal for generalized seizures was identified following Gamaleya Research Institute/Sputnik vaccination, however the number of vaccinations was relatively low compared with other vaccines in this study. Further studies are warranted to explore this potential safety signal.

Conducting a cohort analysis in the unique multi-country context of the GVDN leverages a vast and diverse data pool. Aggregating data from multiple countries on more than 99 million vaccine recipients has significantly increased the sample size and the statistical power compared with many previous safety studies. This enhances the ability to detect safety signals, especially for extremely rare adverse events, as the larger sample size provides greater precision in estimating observed rates.

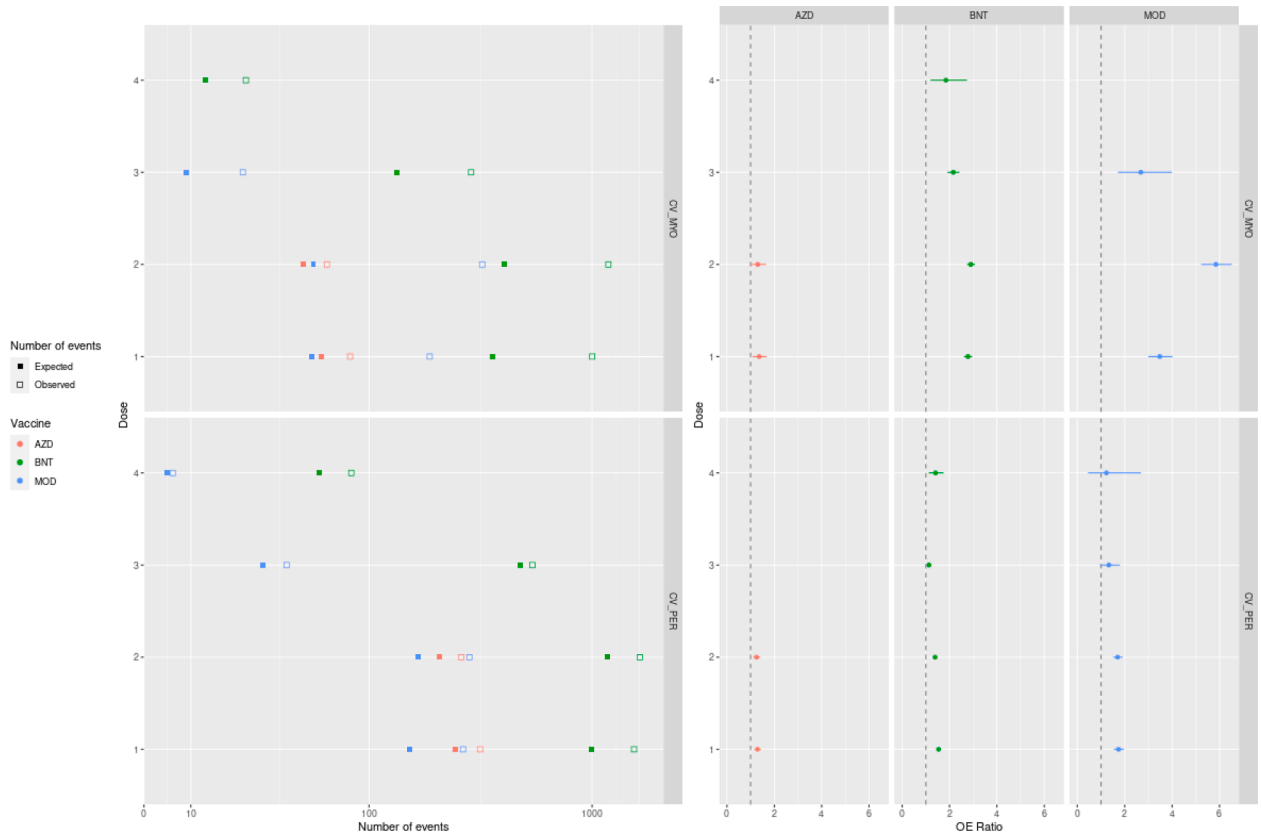

Fig. 3. Number of events and OE ratios (with 95 % confidence interval) for homologous schedules by dose 1–4, cardiovascular conditions. AESI: MYO = Myocarditis, PER = Pericarditis. Vaccines: Vaccines: AZD = Oxford/Astra Zeneca/Serum Institute of India (ChAdOx1), BNT = Pfizer/BioNTech (BNT162b2), MOD = Moderna (mRNA-1273).

Results based on data across Europe, North and South America and Oceania offer stronger external validity, enabling findings to be more generalizable to a broader range of populations and healthcare settings participating in the global COVID-19 vaccination programme. Moreover, multi-country analyses facilitate comparisons between countries with varying vaccination strategies, population demographics, and healthcare systems, yielding insights into how these factors may influence vaccine safety profiles. Data used in our analysis were drawn from multiple databases, including healthcare databases, national immunization registries, and vaccination dashboards, allowing the identification of potential safety signals from various sources.

The results from our study should, however, be interpreted considering multiple limitations. Our analyses inherently involve heterogeneity in data collection, quality, and reporting standards across countries. These differences in healthcare infrastructure and surveillance systems can introduce bias and affect the comparability of results. The participating sites across the eight countries implemented varied vaccination strategies, including vaccine types, dosing schedules, and prioritization of vaccine recipients. Moreover, the multi-country analyses are susceptible to population confounding factors, such as differences in pre-existing health conditions, genetic factors, ethnic profiles, and behavioural patterns, which was not possible to adjust for in our analysis. We consider our approach suitable for application in large datasets representing average populations. However, age- and sex-specific historic background rates that are not adjusted for factors like prior disease may not provide a suitable comparison, for example, in the early stages of a vaccination campaigns where people with co-morbidities were vaccinated prior to other population groups.

Potential underreporting across countries may have led to an underestimation of the significance of potential safety signals. It is important to recognize the potential for false negatives, especially when detecting associations with lower confidence intervals below 1.5 that maintain statistical significance. The safety signals identified in this study should be evaluated in the context of their rarity, severity, and clinical relevance. Moreover, overall risk–benefit evaluations of vaccination should take the risk associated with infection into account, as multiple studies demonstrated higher risk of developing the events under study, such as GBS, myocarditis, or ADEM, following SARS-CoV-2 infection than vaccination. Finally, the use of ICD-10 codes is subject to considerations about specificity and sensitivity, and application may vary by country.

5. Conclusion

Observed vs. expected analyses in a multi-country context of the GVDN and the GCoVS Project offers a larger and more diverse dataset, enhanced generalizability, and improved statistical power over single site or regional studies. It also presents challenges related to data heterogeneity, population confounding factors, and variations in vaccination strategies and reporting systems. The involvement of researchers and data sources from diverse regions of the world promotes inclusivity, reduces potential biases, and fosters collaboration in the pursuit of a shared public health goal. While our study confirmed previously identified rare safety signals following COVID-19 vaccination and contributed evidence on several other important outcomes, further investigation is warranted to confirm associations and assess clinical significance. This could be addressed by conducting association studies specific to individual outcomes by applying methodologies such as the self-controlled case series (SCCS) to validate the associations [6].

Disclaimer

All analyses, inferences drawn, opinions, conclusions, and statements are those of the authors and do not necessarily represent the official views of, nor an endorsement by, CDC/HHS, or the U.S. Government. For more information, please visit cdc.gov.

Parts of this material are based on data and/or information compiled and provided by the Canadian Institute for Health Information and the Ontario Ministry of Health. The analyses, conclusions, opinions, and statements expressed herein are solely those of the authors and do not reflect those of the funding or data sources; no endorsement is intended or should be inferred. Parts of this material are based data and/or information provided by the British Columbia Ministry of Health. All inferences, opinions, and conclusions drawn in this manuscript are those of the authors, and do not reflect the opinions or policies of the Data Steward(s).

Funding statement

The GCoVS project is supported by the Centers for Disease Control and Prevention (CDC) of the U.S. Department of Health and Human Services (HHS) as part of a financial assistance award totalling US $10,108,491 with 100 % per cent funded by CDC/HHS.

The Ontario site contributing to this study was supported by Public Health Ontario and by the ICES, which is funded by an annual grant from the Ontario Ministry of Health. JCK is supported by a Clinician-Scientist Award from the University of Toronto Department of Family and Community Medicine.

CRediT authorship contribution statement

K. Faksova: Visualization, Writing – original draft, Writing – review & editing. **D. Walsh:** Data curation, Formal analysis, Investigation, Methodology, Software, Validation, Conceptualization, Writing – review & editing, Visualization. **Y. Jiang:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Software, Supervision, Validation, Visualization, Writing – review & editing. **J. Griffin:** Conceptualization, Writing – review & editing, Methodology. **A. Phillips:** Conceptualization, Methodology, Writing – review & editing, Investigation, Validation. **A. Gentile:** Data curation, Investigation, Supervision, Validation. **J.C. Kwong:** Data curation, Supervision, Validation, Writing – review & editing, Investigation, Methodology. **K. Macartney:** Data curation, Supervision, Validation, Writing – review & editing, Investigation, Methodology. **M. Naus:** Data curation, Supervision, Validation, Investigation, Methodology. **Z. Grange:** Data curation, Supervision, Validation, Conceptualization, Investigation, Methodology. **S. Escolano:** Data curation, Supervision, Validation, Investigation, Methodology, Writing – review & editing. **G. Sepulveda:** Data curation, Formal analysis, Software, Validation. **A. Shetty:** Data curation, Validation, Investigation, Methodology. **A. Pillsbury:** Data curation, Validation, Investigation, Methodology, Writing – review & editing. **C. Sullivan:** Data curation, Validation, Investigation, Methodology, Writing – review & editing. **Z. Naveed:** Data curation, Validation, Investigation, Methodology, Writing – review & editing. **N.Z. Janjua:** Data curation, Writing – review & editing. **N. Giglio:** Data curation, Investigation, Methodology, Validation. **J. Perälä:** Data curation, Investigation, Methodology, Validation. **S. Nasreen:** Conceptualization, Data curation, Validation, Writing – review & editing. **H. Gidding:** Conceptualization, Validation, Writing – review & editing, Investigation, Methodology. **P. Hovi:** Conceptualization, Validation, Writing – review & editing, Investigation, Methodology. **T. Vo:** Conceptualization, Validation, Formal analysis, Investigation, Methodology, Writing – review & editing. **F. Cui:** Conceptualization, Investigation, Methodology, Validation. **L. Deng:** Conceptualization, Investigation, Methodology, Validation, Writing – review & editing. **L. Cullen:** Conceptualization, Investigation, Methodology, Validation, Writing – review & editing. **M. Artama:** Conceptualization, Investigation, Methodology, Validation, Writing – review & editing. **H. Lu:** Data curation, Formal analysis, Software, Validation. **H.J. Clothier:** Conceptualization, Methodology, Validation, Writing – review & editing, Data curation, Formal analysis, Project administration. **K. Batty:** Conceptualization, Methodology, Project administration, Validation, Writing – review & editing. **J. Paynter:** Conceptualization, Methodology, Supervision, Data curation, Formal analysis, Writing – review & editing. **H. Petousis-Harris:** Conceptualization, Funding acquisition, Investigation, Methodology, Resources, Supervision, Writing – review & editing, Project administration. **J. Buttery:** Conceptualization, Funding acquisition, Investigation, Methodology, Resources, Supervision, Validation, Writing – review & editing, Project administration. **S. Black:** Conceptualization, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Writing – review & editing. **A. Hviid:** Conceptualization, Investigation, Methodology, Supervision, Validation, Writing – review & editing.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Jeffrey C. Kwong reports financial support was provided by Centers for Disease Control and Prevention. Naveed Z. Janjua reports financial support was provided by Centers for Disease Control and Prevention. Anders Hviid reports financial support was provided by Global Vaccine Data Network. Helen Petousis-Harris reports financial support was provided by New Zealand Ministry of Health. Steven Black reports a relationship with GSK that includes: consulting or advisory. Jeffrey C. Kwong reports a relationship with Canadian Institutes of Health Research that includes: funding grants. Jeffrey C. Kwong reports a relationship with Public Health Agency of Canada that includes: funding grants. Naveed Z. Janjua reports a relationship with AbbVie Inc that includes: consulting or advisory and speaking and lecture fees. Naveed Z. Janjua reports a relationship with Gilead Sciences Inc that includes: speaking and lecture fees. Anders Hviid reports a relationship with Independent Research Fund Denmark that includes: funding grants. Anders Hviid reports a relationship with Lundbeck Foundation that includes: funding grants. Anders Hviid reports a relationship with Novo Nordisk Foundation that includes: funding grants. Anders Hviid reports a relationship with VAC4EU that includes: consulting or advisory. Finnish Institute for Health and Welfare (THL) conducts Public-Private Partnership with vaccine manufacturers and has received research funding from Sanofi Inc. Petteri Hovi has been an investigator in these studies, but has received no personal remuneration. Helen Petousis-Harris has served on expert advisory boards and had speaking engagements for Pfizer and GSK. She has also received research funding from GSK. She has not received any personal honoraria. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The authors do not have permission to share data.

Acknowledgements

The Observed vs Expected Analyses Of COVID-19 Vaccine Adverse Events of Special Interest Study Protocol was developed by the Observed vs. Expected Work Group led by Anders Hviid[a,b]. Members of the Work Group were Nelson Aguirre Duarte[c], Miia Artama[d], Karin Batty[e], Steven Black[c,f], Hannah Chisholm[c], Hazel Clothier[g,h,i], Fuqiang Cui[j], Lucy Deng[k], Lucy Cullen[l], Heather Gidding[k,m,n], Petteri Hovi[o], Yannan Jiang[c], Janine Paynter[c], Helen Petousis-Harris[c], Anastasia Phillips[k], John Sluyter[c], Thuan Vo[d,o], and Daniel Walsh[c], Eric Weintraub[p].

Work group affiliations

a. Statens Serum Institut, Denmark; b. University of Copenhagen, Denmark; c. University of Auckland, New Zealand; d. Tampere University, Finland; e. Auckland UniServices Limited at University of Auckland, New Zealand; f. University of Cincinnati and Children's Hospital, USA; g. Victorian Department of Health, Australia; h. Murdoch Childrens Research Institute, Australia; i. Centre for Health Analytics, Melbourne Children's Campus, Australia; j. Peking University, Beijing, China; k. National Centre for Immunisation Research and Surveillance of Vaccine Preventable Diseases, Australia; l. Public Health Scotland, Glasgow, Scotland, United Kingdom; m. Kolling Institute, Northern Sydney Local Health District, Australia; n. University of Sydney Northern Clinical School, Australia; o. Finnish Institute for Health and Welfare, Finland; p. Vaccine Safety Datalink, Centers for Disease Control and Prevention.

The following individuals contributed as GVDN site leads: Anders Hviid (Denmark); Angela Gentile (Argentina); Sylvie Escolano (France); Eero Poukka (Finland); Jeffrey C. Kwong (Ontario, Canada); Kristine Macartney (New South Wales, Australia); Jim Buttery (Victoria, Australia); Monika Naus (British Columbia, Canada); Zoe Grange (Scotland); and Helen Petousis-Harris (New Zealand).

The following individuals contributed as GVDN site investigators: Gonzalo Sepulveda and Aishwarya Shetty (Victoria, Australia); Alexis Pillsbury (New South Wales, Australia); Christopher Sullivan (Scotland); Naveed Zaeema (British Columbia, Canada); Norberto Giglio (Argentina); Jori Perälä (Finland); Sharifa Nasreen (Ontario, Canada); Han Lu (New Zealand).

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2024.01.100.

References

[1] World Health Organization. WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020 2020. https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19—11-march-2020 (accessed October 13, 2023).

[2] Our World in Data. Coronavirus (COVID-19) Vaccinations - Our World in Data 2023. https://ourworldindata.org/covid-vaccinations (accessed October 13, 2023).

[3] Safety Platform for Emerging Vaccines S. D2.3 Priority list of adverse events of special interest: COVID-19. Brighton Collaboration; 2020. Available from: https://zenodo.org/records/6656179#.Y-0yxuyZOnN.

[4] van der Boom MDX, van Eekeren R, van Hunsel FPAM. Observed-over-Expected analysis as additional method for pharmacovigilance signal detection in large-scaled spontaneous adverse event reporting. Pharmacoepidemiol Drug Saf 2023; 32:783–94. https://doi.org/10.1002/pds.5610.

[5] Mahaux O, Bauchau V, Van Holle L. Pharmacoepidemiological considerations in observed-to-expected analyses for vaccines. Pharmacoepidemiol Drug Saf 2016;25: 215. https://doi.org/10.1002/PDS.3918.

[6] Li R, Stewart B, Weintraub E. Evaluating efficiency and statistical power of self-controlled case series and self-controlled risk interval designs in vaccine safety. J Biopharm Stat 2016;26:686–93. https://doi.org/10.1080/10543406.2015.1052819.

[7] Pottegård A, Lund LC, Karlstad Ø, Dahl J, Andersen M, Hallas J, et al. Arterial events, venous thromboembolism, thrombocytopenia, and bleeding after vaccination with Oxford-AstraZeneca ChAdOx1-S in Denmark and Norway: population based cohort study. BMJ 2021;373:n1114. https://doi.org/10.1136/bmj.n1114.

[8] European Medicines Agency. Signal assessment report on embolic and thrombotic events (SMQ) with COVID-19 Vaccine (ChAdOx1-S [recombinant])-Vaxzevria (previously COVID-19 Vaccine AstraZeneca) (Other viral vaccines). 2021.

[9] Global Vaccine Data Network. Observed vs. expected analyses of COVID-19 vaccine adverse events of special interest study protocol. Version 1.4. Auckland (NZ): Global Vaccine Data Network; 2022. Available from: https://www.globalvaccinedatanetwork.org/sites/globalvaccinedatanetwork.org/files/2024-01/GVDN-observed-vs.-expected-analyses-of-COVID-19-vaccine-AESI-V1.4.pdf.

[10] Global Vaccine Data Network. Global COVID Vaccine Safety (GCoVS). Auckland (NZ): Global Vaccine Data Network; 2022 [accessed 2023 October 13]. Available from: https://www.globalvaccinedatanetwork.org/global-covid-vaccine-safety-gcovs.

[11] Global Vaccine Data Network. Auckland (NZ): Global Vaccine Data Network; 2023 [accessed 2023 October 13]. Available from: https://www.globalvaccinedatanetwork.org/.

[12] Global Vaccine Data Network. GVDN: Observed vs expected (OE) dashboard. Auckland (NZ): Global Vaccine Data Network; 2023 [updated 2023 December 8; cited 2023 December 13]. Available from: www.globalvaccinedatanetwork.org/Data-Dashboards.

[13] Phillips A, Jiang Y, Walsh D, Andrews N, Artama M, Clothier H, et al. Background rates of adverse events of special interest for COVID-19 vaccines: a multinational Global Vaccine Data Network (GVDN) analysis. Vaccine 2023;41:6227–38. https://doi.org/10.1016/J.VACCINE.2023.08.079.

[14] Hanson KE, Goddard K, Lewis N, Fireman B, Myers TR, Bakshi N, et al. Incidence of Guillain-Barré syndrome after COVID-19 vaccination in the vaccine safety datalink. JAMA Netw Open 2022;5:E228879. https://doi.org/10.1001/JAMANETWORKOPEN.2022.8879.

[15] World Health Organization. Statement of the WHO Global Advisory Committee on Vaccine Safety (GACVS) COVID-19 subcommittee on reports of Guillain-Barré Syndrome (GBS) following adenovirus vector COVID-19 vaccines n.d. https://www.who.int/news/item/26-07-2021-statement-of-the-who-gacvs-covid-19-subcommittee-on-gbs (accessed October 23, 2023).

[16] Keizer RJ, Huitema ADR, Schellens JHM, Beijnen JH. Clinical pharmacokinetics of therapeutic monoclonal antibodies. Clin Pharmacokinet 2010;49:493–507. https://doi.org/10.2165/11531280-000000000-00000.

[17] World Health Organization. Global Advisory Committee on Vaccine Safety (GACVS) review of latest evidence of rare adverse blood coagulation events with AstraZeneca COVID-19 Vaccine (Vaxzevria and Covishield). Accessed October 23, 2023. https://www.who.int/news/item/16-04-2021-global-advisory-committee-on-vaccine-safety-(gacvs)-review-of-latest-evidence-of-rare-adverse-blood-coagulation-events-with-astrazeneca-covid-19-vaccine-(vaxzevria-and-covishield).

[18] Burn E, Li X, Kostka K, Stewart HM, Reich C, Seager S, et al. Background rates of five thrombosis with thrombocytopenia syndromes of special interest for COVID-19 vaccine safety surveillance: incidence between 2017 and 2019 and patient profiles from 38.6 million people in six European countries. Pharmacoepidemiol Drug Saf 2022;31:495–510. https://doi.org/10.1002/PDS.5419.

[19] Greinacher A, Thiele T, Warkentin TE, Weisser K, Kyrle PA, Eichinger S. Thrombotic thrombocytopenia after ChAdOx1 nCov-19 vaccination. N Engl J Med 2021;384:2092–101. https://doi.org/10.1056/NEJMOA2104840/SUPPL_FILE/NEJMOA2104840_DISCLOSURES.PDF.

[20] Hviid A, Hansen JV, Thiesson EM, Wohlfahrt J. Association of AZD1222 and BNT162b2 COVID-19 vaccination with thromboembolic and thrombocytopenic events in frontline personnel: a retrospective cohort study. Ann Intern Med 2022; 175:541–6. https://doi.org/10.7326/M21-2452.

[21] World Health Organization. COVID-19 subcommittee of the WHO Global Advisory Committee on Vaccine Safety (GACVS): updated guidance regarding myocarditis and pericarditis reported with COVID-19 mRNA vaccines. Accessed October 23, 2023. https://www.who.int/news/item/09-07-2021-gacvs-guidance-myocarditis-pericarditis-covid-19-mrna-vaccines.

[22] Karlstad Ø, Hovi P, Husby A, Härkänen T, Selmer RM, Pihlström N, et al. SARS-CoV-2 vaccination and myocarditis in a Nordic cohort study of 23 million residents. JAMA Cardiol 2022;7:600–12. https://doi.org/10.1001/JAMACARDIO.2022.0583.

[23] Gargano JW, Wallace M, Hadler SC, Langley G, Su JR, Oster ME, et al. Use of mRNA COVID-19 vaccine after reports of myocarditis among vaccine recipients: update from the advisory committee on immunization practices — United States, June 2021. MMWR Morb Mortal Wkly Rep 2021;70:977–82. 10.15585/MMWR.MM7027E2.

[24] Atzenhoffer M, Auffret M, Pegat A, Masmoudi K, Khouri C, Bertin B, et al. Guillain-Barré syndrome associated with COVID-19 vaccines: a perspective from spontaneous report data. Clin Drug Investig 2022;42:581. https://doi.org/10.1007/S40261-022-01164-4.

[25] Otero-Losada M, Petrovsky N, Alami A, Crispo JA, Mattison D, Capani F, et al. Disproportionality analysis of adverse neurological and psychiatric reactions with the ChAdOx1 (Oxford-AstraZeneca) and BNT162b2 (Pfizer-BioNTech) COVID-19 vaccines in the United Kingdom. Expert Opin Drug Saf 2023;22:343–9. https://doi.org/10.1080/14740338.2022.2120607.

[26] Walker JL, Schultze A, Tazare J, Tamborska A, Singh B, Donegan K, et al. Safety of COVID-19 vaccination and acute neurological events: a self-controlled case series in England using the OpenSAFELY platform. Vaccine 2022;40:4479–87. https://doi.org/10.1016/J.VACCINE.2022.06.010.

[27] Patone M, Handunnetthi L, Saatci D, Pan J, Katikireddi SV, Razvi S, et al. Neurological complications after first dose of COVID-19 vaccines and SARS-CoV-2 infection. Nat Med 2021;27:2144. https://doi.org/10.1038/S41591-021-01556-7.

[28] Li X, Raventós B, Roel E, Pistillo A, Martinez-Hernandez E, Delmestri A, et al. Association between covid-19 vaccination, SARS-CoV-2 infection, and risk of immune mediated neurological events: population based cohort and self-controlled case series analysis. BMJ 2022:376. https://doi.org/10.1136/BMJ-2021-068373.

[29] European Medicines Agency. Vaxzevria (previously COVID-19 Vaccine AstraZeneca) | European Medicines Agency. Accessed October 26, 2023. https://www.ema.europa.eu/en/medicines/human/EPAR/vaxzevria#product-information-section.

[30] COVID-19 vaccine weekly safety report - 09-12-2021 | Therapeutic Goods Administration (TGA). Accessed December 5, 2023. https://www.tga.gov.au/news/covid-19-vaccine-safety-reports/covid-19-vaccine-weekly-safety-report-09-12-2021#section-1298.

[31] Schulz JB, Berlit P, Diener HC, Gerloff C, Greinacher A, Klein C, et al. COVID-19 vaccine-associated cerebral venous thrombosis in Germany. Ann Neurol 2021;90: 627–39. https://doi.org/10.1002/ANA.26172.

[32] Andrews NJ, Stowe J, Ramsay ME, Miller E. Risk of venous thrombotic events and thrombocytopenia in sequential time periods after ChAdOx1 and BNT162b2

COVID-19 vaccines: a national cohort study in England. Lancet Reg Heal Eur 2022; 13. doi: 10.1016/J.LANEPE.2021.100260.
[33] Gordon SF, Clothier HJ, Morgan H, Buttery JP, Phuong LK, Monagle P, et al. Immune thrombocytopenia following immunisation with Vaxzevria ChadOx1-S (AstraZeneca) vaccine, Victoria. Australia Vaccine 2021;39:7052–7. https://doi.org/10.1016/J.VACCINE.2021.10.030.
[34] Buchan SA, Seo CY, Johnson C, Alley S, Kwong JC, Nasreen S, et al. Epidemiology of myocarditis and pericarditis following mRNA vaccination by vaccine product, schedule, and interdose interval among adolescents and adults in Ontario, Canada. JAMA Netw Open 2022;5:E2218505. https://doi.org/10.1001/JAMANETWORKOPEN.2022.18505.
[35] Naveed Z, Li J, Spencer M, Wilton J, Naus M, García HAV, et al. Observed versus expected rates of myocarditis after SARS-CoV-2 vaccination: a population-based cohort study. CMAJ 2022;194:1529–36. https://doi.org/10.1503/CMAJ.220676.
[36] Naveed Z, Li J, Wilton J, Spencer M, Naus M, Velásquez García HA, et al. Comparative risk of myocarditis/pericarditis following second doses of BNT162b2 and mRNA-1273 coronavirus vaccines. J Am Coll Cardiol 2022;80:1900–8. https://doi.org/10.1016/J.JACC.2022.08.799.
[37] Patone M, Mei XW, Handunnetthi L, Dixon S, Zaccardi F, Shankar-Hari M, et al. Risks of myocarditis, pericarditis, and cardiac arrhythmias associated with COVID-19 vaccination or SARS-CoV-2 infection. Nat Med 2021;28:410–22. https://doi.org/10.1038/s41591-021-01630-0.
[38] Alami A, Krewski D, Farhat N, Mattison D, Wilson K, Gravel CA, et al. Risk of myocarditis and pericarditis in mRNA COVID-19-vaccinated and unvaccinated populations: a systematic review and meta-analysis. BMJ Open 2023;13:e065687. https://doi.org/10.1136/BMJOPEN-2022-065687.
[39] COVID-19 vaccine safety report - 13-07-2023 | Therapeutic Goods Administration (TGA) n.d. https://www.tga.gov.au/news/covid-19-vaccine-safety-reports/covid-19-vaccine-safety-report-13-07-2023#myocarditis-and-pericarditis-after-covid19-vaccination (accessed December 5, 2023).
[40] Myocarditis and Pericarditis After mRNA COVID-19 Vaccination | CDC n.d. https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/myocarditis.html (accessed December 5, 2023).
[41] Brock K, Reyes SC, Conner C, Gillson N, Weiss M, Elfituri O, et al. Acute disseminated encephalomyelitis (ADEM)-like illness in a pediatric patient following COVID-19 vaccination. BJR | Case Rep 2023;9. https://doi.org/10.1259/BJRCR.20220097.
[42] Nimkar SV, Yelne P, Gaidhane SA, Kumar S, Acharya S, Gemnani RR. Fatal acute disseminated encephalomyelitis post-COVID-19 vaccination: a rare case report. Cureus 2022;14. https://doi.org/10.7759/CUREUS.31810.
[43] Permezel F, Borojevic B, Lau S, de Boer HH. Acute disseminated encephalomyelitis (ADEM) following recent Oxford/AstraZeneca COVID-19 vaccination. Forensic Sci Med Pathol 2022;18:74–9. https://doi.org/10.1007/S12024-021-00440-7.
[44] Khan S, Khan S, Waqar Z, Mobeen H, Khan N, Hassan M. Post Moderna Vaccine associated acute disseminated encephalomyelitis (ADEM) - a case report. Pak J Neurol Sci 2022;17. 10.56310/PJNS.V17I01.186.
[45] European Medicines Agency. *COVID-19 Vaccine Safety Update*.; 2021. https://www.ema.europa.eu/en/documents/covid-19-vaccine-safety-update/covid-19-vaccine-safety-update-vaxzevria-previously-covid-19-vaccine-astrazeneca-18-june-2021_en.pdf.
[46] Frontera JA, Tamborska AA, Doheim MF, Garcia-Azorin D, Gezegen H, Guekht A, et al. Neurological events reported after COVID-19 vaccines: an analysis of vaccine adverse event reporting system. Ann Neurol 2022;91:756–71. https://doi.org/10.1002/ANA.26339.

From: sue coffman
Sent: 3/12/2025 1:02:02 PM
To: DOH WSBOH
Cc:
Subject: Public Comment for March 12, 2025

attachments\6DF5367103E6408B_BOHcommentsActual.doc

External Email

Hello,

Here is the written version of what I gave today during the virtual Public Comment section for March's Board of Health meeting.

Thank you,

Sue Coffman

714-337-4331
CHDwa Chapter Co-Leader

https://wa.childrenshealthdefense.org/
<https://gcc02.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwa.childrenshealthdefense.org%2

ICWA Team Leader
Legislative District #24
https://informedchoicewa.org/
<https://gcc02.safelinks.protection.outlook.com/?url=https%3A%2F%2Finformedchoicewa.org%2F&data=

State BOH Testimony

STATE BOH
March 12, 2025
Tumwater, WA
9:50am Public Comment

Thank you for this opportunity to speak. My name is Sue Coffman, and I reside in Clallam County. It is so very important to me that the department of health understands where thousands of us stand when it comes to the health of our state and our nation.

As members of the Board of Health, your job is to advise us based upon the actual evidence uncovered. Due to the lack of transparency within the department, and your one-sided approach to public health, there is no true discussion about consent or the right to refuse. Additionally, there should be ongoing conversations about pesticides, toxins, and poor nutrition in our daily lives that contribute to our overall health.

I believe, as do so many others, that the position that RFK Jr now holds within Health & Human Services will finally open up the possibility of growing these conversations so that EVERYONE can have true informed consent. He is continually smeared by the press and by many government institutions with the hot-button title of "Anti-Vaxxer," when all he wants to do is uncover the corruption and get to the actual truth.

I deserve this attention, as do each of you, especially when it comes to imparting your opinion onto the citizens of this state. Do your own Due Diligence and uncover the reality of what is happening to us today, and stop spouting the lies that the lobbyists and pressure groups are insisting you say to your public.

Thank you for truly listening to my words. **1:25**

_____

From: Gerald Braude
Sent: 3/12/2025 12:49:02 PM
To: DOH WSBOH
Cc:
Subject: Gerald Braude public comment March 12, 20205

attachments\55ED8B7D09D64CBC_BOH Public Comment written March 12, 2025.docx

External Email

Dear Michelle: Attached is my public comment from this morning for the Board of Health to look over. Thank you for all you do. -- Gerald Braude

ICWA BOH Public Comment March 12, 2025

Did you know at last February's Franklin County of Commissioners meeting, all three commissioners voted to pass a resolution for the Benton Franklin County Health District Board to cease to provide, fund, or promote gene therapy vaccines—the COVID-19 thots—for infectious disease indications?

Before the passing of the resolution, an hour's worth of doctors and scientists spoke about the COVID-19 shots, and a few victims spoke about their COVID-19 shot injuries. After the resolution was passed, Commission Clint Didier turned his gaze to the presenters table and said, "Thank you, Dr. Cole and your team for coming out here. You're making a difference in the world. God bless you."

So, who is this Dr. Ryan Cole?

Board Certified physician as well as anatomic and clinical pathologist trained at the Mayo Clinic.

He was twice invited and spoke at Senator Ron Johnson's roundtable discussions in DC. He was invited and spoke at Marjorie Taylor Greene's congressional hearing as well as to members of the European Parliament at the International COVID-19 Summit. In all these presentations, he showed slides of the cells he examined in his pathology laboratory that illustrated the adverse events from the synthetic mRNA shots. As he said, "Cells don't lie."

So, why should this concern you? Because you stripped this Dr. Ryan Cole of his physician's license because of what he said in public about the COVID-19 shots.

WMC press release: In the order, the WMC found that Dr. Cole made demonstrably false and misleading statements in public presentations regarding the COVID-19 pandemic, COVID-19 vaccines, the use of ivermectin to treat COVID-19, and the effectiveness of masks.

Press Release

WASHINGTON Medical Commission
Licensing. Accountability. Leadership.

FOR IMMEDIATE RELEASE

Contact:
Stephanie Mason
Stephanie.Mason@wmc.wa.gov
Washington Medical Commission

WMC Disciplines Idaho Physician's License

OLYMPIA, WA – The Washington Medical Commission (WMC) issued an order restricting the license of physician Ryan N. Cole, MD (License #00048229). The order, issued following a five-day hearing, restricts Cole to the practice of pathology; he may not practice primary care medicine and may not prescribe medication. Cole practices in Boise, Idaho, but is licensed in both Idaho and Washington. The restrictions apply only to his practice in Washington.

In the Order, the WMC found that Cole made demonstrably false or misleading statements in public presentations regarding the COVID-19 pandemic, COVID-19 vaccines, the use of ivermectin to treat COVID-19, and the effectiveness of masks.

The WMC also found that Cole misrepresented his education and training in public presentations and to the WMC, publicly implied that a physician's death was due to the COVID-19 vaccine even though the physician died of a heart attack six months after getting vaccinated, and misrepresented facts to the WMC when stating that he had not advised patients or the general public to refrain from getting the COVID-19 vaccine.

The WMC also found that Cole provided substandard care to four Washington patients by prescribing ivermectin via telemedicine without seeing or examining the patients; failing to address other medical issues; and failing to document a history, medical decision-making, and informed consent.

In addition to the restrictions, Cole is required to take continuing medical education courses in COVID-19, pulmonary and respiratory diseases, medical-record keeping, and telehealth. Cole must also complete an ethics course, pay a fine of $5000, and write a paper addressing professionalism, truthfulness, and honesty in the practice of medicine.

Legal documents in this case are available online by visiting the DOH Provider Credential Search.

###

Remember the 520-page Congressional Report from the Select Subcommittee on the Coronavirus Pandemic I discussed with you at our last meeting? Here are two key findings in their little, green-shaded boxes.

1. **The Biden administration employed undemocratic and likely unconstitutional methods to fight what it deemed to be misinformation. Well, so did you people with Dr. Ryan Cole.**

2. **Public Health officials' arbitrary and overly broad mitigation measures and aggressive efforts to squash legitimate scientific debate unnecessarily exacerbated unemployment.**

FINDING:	The Biden Administration Employed Undemocratic and Likely Unconstitutional Methods to Fight What It Deemed to Be Misinformation.

FINDING:	Public Health Officials' Arbitrary and Overly Broad Mitigation Measures and Aggressive Efforts to Squash Legitimate Scientific Debate Unnecessarily Exacerbated Unemployment.

As for this squashing of debate, it is only fitting that during Dr. Cole's presentation to the European Parliament, he showed a slide of a man holding a protest sign that read, "Of course, all scientists agree when you censor the scientists who don't."

As I've told you before, you've also performed this witch hunt on Dr. Renata Moon for her testimony at Ron Johnson's discussion and that's why she gave up her Washington license and moved to Florida. You did this kind of witch hunt on Doctors Richard Eggleston and Thomas Siler, too.

But there can be redemption on your part in all this. The Franklin County Commissioners invited Dr. Cole and his team to speak to them. You can do it, too.

Press Release

WASHINGTON Medical Commission
Licensing. Accountability. Leadership.

FOR IMMEDIATE RELEASE

Contact:
Stephanie Mason
Stephanie.Mason@wmc.wa.gov
Washington Medical Commission

WMC Disciplines Idaho Physician's License

OLYMPIA, WA – The Washington Medical Commission (WMC) issued an order restricting the license of physician Ryan N. Cole, MD (License #00048229). The order, issued following a five-day hearing, restricts Cole to the practice of pathology; he may not practice primary care medicine and may not prescribe medication. Cole practices in Boise, Idaho, but is licensed in both Idaho and Washington. The restrictions apply only to his practice in Washington.

In the Order, the WMC found that Cole made demonstrably false or misleading statements in public presentations regarding the COVID-19 pandemic, COVID-19 vaccines, the use of ivermectin to treat COVID-19, and the effectiveness of masks.

The WMC also found that Cole misrepresented his education and training in public presentations and to the WMC, publicly implied that a physician's death was due to the COVID-19 vaccine even though the physician died of a heart attack six months after getting vaccinated, and misrepresented facts to the WMC when stating that he had not advised patients or the general public to refrain from getting the COVID-19 vaccine.

The WMC also found that Cole provided substandard care to four Washington patients by prescribing ivermectin via telemedicine without seeing or examining the patients; failing to address other medical issues; and failing to document a history, medical decision-making, and informed consent.

In addition to the restrictions, Cole is required to take continuing medical education courses in COVID-19, pulmonary and respiratory diseases, medical-record keeping, and telehealth. Cole must also complete an ethics course, pay a fine of $5000, and write a paper addressing professionalism, truthfulness, and honesty in the practice of medicine.

Legal documents in this case are available online by visiting the DOH Provider Credential Search.

###

_____
From: bill teachingsmiles.com
Sent: 3/12/2025 2:36:53 PM
To: DOH WSBOH
Subject: Fetus and Infant harm

attachments\646F7E1BFC4E45D9_image.png

attachments\32A35516B86D41FE_Ko&Thiessen-critique of cost of CWF- 2 copy.pdf

External Email

Dear Board of Health,

My wife said I was not as clear as I could be in my illustration and presentation today at the Board meeting and I will do better here.

The panel members, based on comments and questions, do not understand the implications of the 3 studies they have considered over the last 8 hours of meetings. For example, harm to the developing brain as reported by National Toxicology Program and TSCA Court case was well done by Dr. Christie. The intent of my illustration was to tie those cases into practical terms, specifically for the fetus and infant.

We have about 0.01 ppm increase in mom's serum fluoride concentration from fluoridated water (CWF).
About 60% of maternal blood fluoride crosses the placenta (NRC p. 164)
Therefore, the fetus is exposed to about 0.006 ppm increase in fluoride concentration from fluoridated water which results in lower IQ. (Green et al, 2019) as measured in the child.

0.006 ppm or 6 parts per billion is extremely small amount and I assumed safe until the studies showed that tiny amount of fluoride lowers IQ. I was shocked.

The Board's webpage suggests 700 parts per billion, over 100 times more fluoride concentration is safe for an infant just after birth. No way. Entry of fluoride via the placenta is more than oral, probably.

However, neither the FDA, CDC, EPA nor the three largest fluoride raw product manufacturers under threat of perjury, said they had a single safety study on the developing brain. I doubt the Board or Department has a safety study or they would present the study to the Panel.

If 6 ppb is not safe for the fetus, how can 700 ppb be safe to make infant formula a few minutes after an infant is born if mom cannot breast feed? Mothers milk when detected has about 4 parts per billion. Very close to what the fetus gets from mother's blood.

My ppt slide below:

Does the panel have some of that science? Yes, but not enough to tie all the implications

together for judgment.

“Association Between Maternal Fluoride Exposure During Pregnancy and IQ Scores in Offspring in Canada.” JAMA 2019 GREEN The Journal of American Medical Association Editors speaking in a podcast said, "When I first saw this title my initial inclination was 'What the hell?'" That is still my reaction. Such a tiny amount of fluoride causes measurable harm.

I am requesting 4 hours of time with the panel and should have a couple of semesters for the courses. Yesterday the panel had a 32-minute presentation on the 2024 Cochrane report of fluoride's efficacy which was reasonably done. Then about 60 minutes of discussion before the meeting was adjourned. They could have asked me to start my presentation when they have time and perhaps saved an additional day of meetings.

The next meeting they will have 2 hours on "cost-benefit." However, such a presentation is premature. We cannot determine cost until we determine both benefit, costs saved less operating costs if any, and treatment of risks, if any.

The only study I know to have included the costs of treating the harm (side effects) of fluoride, was my published study Community Water Fluoridation a Cost-Benefit-Risk Consideration
<https://gcc02.safelinks.protection.outlook.com/?url=http%3A%2F%2Fdx.doi.org%2F10.1002%2Fpuh2.70
The closest before that was the study by Ko, attached.

I need to cover the best available science on the National Research Council's 2006 report to the EPA which listed 18 risks. Just 5 minutes on each is almost an hour and a half just for those streams of evidence. And more time needs to be spent on the teeth and on cost-benefit when risks are included and alternatives to fluoridation.

NRC 2006 reported:

cell function (mitochondria), harm to every cell of the body.
functional and cosmetic dental fluorosis
skeletal fluorosis,
arthritis,
chondrocyte metabolism,
reproductive fluorosis, an itsy bitsy chemical castration
developmental effects,
neurobehavioral effects,
harm to the endocrine system,
harm to the thyroid,
harm to the GI tract
harm to the kidneys
harm to the liver
harm to the immune systems,
genotoxicity,
Carcinogenicity—known carcinogen

Developmental neurotoxicity needs very little more panel time and a significant amount on harm to the teeth and lack of reasonable benefit is important. I am a dentist and I treated the harm from too much fluoride and made a significant amount of money selling fluoride.

But first, the panel members need to understand some basic tools to use when weighing the evidence. Some evidence is interesting, some evidence is significant, etc. How to judge the difference? And do we judge the evidence requiring absolute proof of harm or presumed harm or greater than 50/50 confidence of harm? And how to tie all the

streams of evidence together to weigh all risks is even more complex.

In addition, we should look at some alternatives to fluoridation, methods of protecting the most vulnerable and also what to do where naturally occurring fluoride is much higher. I am in full agreement with those telling the Board in public comment that dental caries can be a significant problem, although seldom fatal. Although I disagree that fluoridation is the answer to the problem, I agree with their concerns.

Please ask the panel to provide me with 4 hours. They have rejected having our experts present, so I need to cover the science.

Consider these sources:

RFK Jr and Makarey opposed to Fluoridation
Florida Surgeon General: CWF is "Public Health Malpractice" (requires greater than 50/50 confidence of harm)
Freedom for patient consent—police powers are used to mass medicate without patient consent
FDA "Do Not Swallow" referring to fluoride in an 11 oz of CWF
FDA warned WSBH: CWF would be Banned if NDA is applied for
FDA: CWF is Unapproved drug and Illegal drug
WA Board of Pharmacy "Legend Drug"
FDA, EPA, CDC & 3 F MFG Not one safety study
EPA Scientists: CWF "Boarders on Criminal Act"(2001 "beyond a reasonable doubt")
Fed Court: CWF "Unreasonable Risk"
NTP Moderate Confidence of lower IQ
CWF is ≈70 to175 times the dosage of Mom's milk
97% of Europe Fluoridation Free (drug regulatory authorities. Strong weight of evidence)

Cochrane (2024) Possibility of benefit or no benefit
Dosage for Benefit—Unknown
One Randomized Clinical trial: no benefit and no Randomized Controlled Trials needed for drug approval
Utah Bans Fluoridation
Not Everyone is in the "median." Harm is determined in a population based on a "statistical" mean, but individual harm can vary significantly.

Thank you for your encouraging the Department to give me 4 hours of time.

Bill Osmunson DDS MPH

The only source of F for the fetus Is Mom's Blood

Mother's serum F 0.006 ppm non-F water

0.016 ppm in CWF

CWF adds just 0.01 ppm to mom's blood

60% OF MATERNAL BLOOD FLUORIDE CROSSES THE PLACENTA NRC P. 164

erhaps 0.006 ppm more F gets to the fetu From CWF

Review

A critique of recent economic evaluations of community water fluoridation

Lee Ko[1], Kathleen M. Thiessen[2]

[1]Oakland, CA, USA, [2]Oak Ridge Center for Risk Analysis, Oak Ridge, TN, USA

Background: Although community water fluoridation (CWF) results in a range of potential contaminant exposures, little attention has been given to many of the possible impacts. A central argument for CWF is its cost-effectiveness. The U.S. Government states that $1 spent on CWF saves $38 in dental treatment costs.
Objective: To examine the reported cost-effectiveness of CWF.
Methods: Methods and underlying data from the primary U.S. economic evaluation of CWF are analyzed and corrected calculations are described. Other recent economic evaluations are also examined.
Results: Recent economic evaluations of CWF contain defective estimations of both costs and benefits. Incorrect handling of dental treatment costs and flawed estimates of effectiveness lead to overestimated benefits. The real-world costs to water treatment plants and communities are not reflected.
Conclusions: Minimal correction reduced the savings to $3 per person per year (PPPY) for a best-case scenario, but this savings is eliminated by the estimated cost of treating dental fluorosis.

Keywords: Water fluoridation, Economic evaluation, Cost of water fluoridation, Caries prevention, Cost benefit, Cost effectiveness, Effectiveness in adults, Dental fluorosis

Introduction

The USA and several other countries practice community water fluoridation (CWF), which has been promoted as the preferred solution to reduce caries for over half a century.[1] Approximately two-thirds of the U.S. population is treated in this manner according to the Centers for Disease Control and Prevention (CDC).[2] Community water fluoridation programs have increased water fluoride concentrations to 0.7–1.2 mg/l [0.7–1.2 parts per million (ppm)], although a 2011 proposed recommendation, if finalized, would decrease this to 0.7 mg/l.[3]

Community water fluoridation is a unique delivery mode of public health care in that fluoride is administered to everyone who drinks the water, regardless of dental status or needs, and at an amount proportional to the water consumed from the fluoridated source, which can range from zero to several liters per day.[4] At the same time, because most community water is not consumed by people, CWF results in dispersion of a regulated contaminant, fluoride, to the greater environment via wastewater treatment plants, storm sewer systems, and use on lawns and gardens. Fluoridation chemicals typically contain other regulated contaminants (e.g. arsenic), extending the possibility of human exposures and environmental dispersal.[5–8]

A central argument for using CWF to reduce tooth decay is the cost savings claimed by the CDC:[9] Every $1 invested in this preventive measure yields approximately $38 savings in dental treatment costs. This argument is repeated by the majority of state governments (Appendix 1) and is frequently cited by proponents to argue for initiating or maintaining CWF.

All $ signs in this paper refer to US$ unless otherwise indicated. However, statements such as $1 saves $38 are currency neutral.

The CDC's estimate is calculated from the per person per year (PPPY) savings reported by Griffin *et al.*:[10] With base-case assumptions, the annual per person cost savings resulting from fluoridation ranged from $15.95 in very small communities to $18.62 in large communities.[10i] Table 1 summarizes Griffin *et al.*'s results by population size. The CDC derived the $1-saves-$38 claim by scaling the $0.50 cost and the $18.62 savings estimate for large systems (>20,000 people) to get $0.50 : $18.62 ≈ $1 : $38. However, this derivation is not valid because it implies

Correspondence to: Kathleen M. Thiessen, Oak Ridge Center for Risk Analysis, 102 Donner Drive, Oak Ridge, TN 37830, USA. Email: kmt@orrisk.com

[i]CDC focused on the smallest and largest systems:[9] for a population <5,000 people, the net savings is $19.12 – $3.17 = $15.95; for a population >20,000 people, the net savings is $19.12 – $0.50 = $18.62.

DOI 10.1179/2049396714Y.0000000093

Table 1 Estimated costs and savings of community water fluoridation (CWF) for communities of various sizes from Griffin *et al.*[10]

Population size	Estimated cost* ($, PPPY)‡	Estimated savings*† ($, PPPY)‡
<5,000	3.17	15.95
5,000–9,999	1.64	17.48
10,000–20,000	1.06	18.06
>20,000	0.50	18.62

*Based on a 4% discount rate.
†Calculated with the base-case gross savings of $19.12.
‡Per person per year.

Table 2 Stated assumptions of Griffin *et al.*[10] and key inputs of the calculation of benefits

Stated assumptions	Key inputs
(1) The benefit is decay prevented and begins at age 6 years	(a) Benefit is the number of decayed tooth surfaces that would otherwise have been treated
(2) The benefit is constant over time	(b) Benefit in dollar amounts, or gross savings, is quantified in terms of averted dental fees for amalgam fillings and averted productivity losses due to a visit to a restorative dentist
(3) All decay is eventually treated	
(4) The adverse effects are negligible	
(5) Dental fees equal the cost of dental resources	(c) Every decayed surface results in a 1-hour dental visit for a single-surface restoration in the same year it occurs
(6) A decayed tooth surface will always receive a one-surface restoration	(d) The dental fee for a single-surface filling is $54, and the productivity loss from the visit is $18 (the U.S. average hourly wage)
	(e) A single-surface filling is replaced every 12 years with another single-surface filling, up to age 65 years
	(f) It takes one year of exposure for CWF to begin to prevent tooth decay
	(g) CWF averts 0.19 decayed tooth surfaces per person per year (PPPY) on average
	(h) The same rate of caries aversion applies from age 6 to 64 years

CWF: community water fluoridation.

scalability where scalability does not apply: spending more on CWF does not increase caries aversion or caries to be averted.

Griffin *et al.*[10] is the prime example of a body of work that attempts to evaluate the economics of CWF. As the most comprehensive and most cited work, it will be our focus. We limit our analysis to the smallest and largest systems in keeping with the CDC's report.[9] We also examined and comment on additional CWF cost-benefit analyses (Appendix 2).[ii]

Key steps in Griffin et al.*[10]*

A 1989 workshop[12] at the University of Michigan discussed the cost-effectiveness of CWF and other caries prevention programs, with cost estimates based primarily on data from Garcia.[13] A 1992 paper by Ringelberg *et al.*[14] improved upon Garcia's cost estimates, and Griffin *et al.*[10] produced their cost estimates (Table 1) by applying minor adjustments to the results of Ringelberg *et al.*,[14] as described later in this paper.

Griffin *et al.*[10] adopted a "societal perspective" and defined benefit as the cost of averted dental fees and associated productivity losses. They used a 4% discount rate for the main result of $19.12 gross savings. Griffin *et al.*'s stated assumptions and key intermediate results, organized into a set of key inputs, are provided in Table 2. Note that Input (c) differs from Assumption (3) in the timing of treatment — the authors' calculation was consistent with treatment in the same year. The following steps explain how Griffin *et al.* obtained their value:

Step 1: From Input (d), restoring one decayed tooth surface costs $54+$18=$72.

Step 2: As described by Input (e) the lifetime costs of a decayed surface include future replacement fillings; the number of replacements depends on when the decay occurs. Future replacement costs are discounted to arrive at a present value. The first avertable filling is discounted 1 year because of Input (f) in Table 2; replacements take place every 12 years up to age 65 years, based on Input (e).[iii] For example, for a child age 12.5 years, the lifetime cost at a 4% discount rate was estimated to be $159.61 as shown in the following equation:

[ii] These papers are technically cost-benefit analyses,[11] although the term cost-effectiveness is frequently used to refer to the degree that the value of benefit exceeds cost.

[iii] While cutting off replacement at age 65 years may appear to underestimate the benefit (cost of fillings), Griffin *et al.* appear to have overestimated by incorrectly or inconsistently applying the factors in the numerator, e.g. the expected lifetime costs of a decayed surface for age groups 55–59 and 60–64 years are both $69.23=$72/1.04 (Table 3), without the factor (which should be around 0.79) to account for fewer teeth at older ages. (Since Griffin *et al.* did not present these factors, except for the few that appear in the Equation (1) example, we are not able to recalculate and correct the numbers in Table 3.)

$$\$72\left(\frac{1}{1.04}+\frac{1}{1.04^{13}}+\frac{0.90}{1.04^{25}}+\frac{0.86}{1.04^{37}}+\frac{0.79}{1.04^{49}}\right) = \$159.61 \quad (1)$$

Thus the last replacement takes place at age $12.5+1+(4\times12)=61.5$ in this example. The cost for each filling or replacement filling is adjusted by a factor (the numerator of the term) representing the probability that the tooth remains at the replacement age.

Step 3: Calculate the national average, using the population distribution in Table 3. Use the midpoint to represent the group in each bracket, e.g. Equation (1) gives the lifetime benefit of an averted decay surface for the 6–19 age group, based on the midpoint, age 12.5 years.

Step 4: The calculation is repeated for each age bracket, except the first and the last age brackets as described by Input (h) in Table 2. Summing the weighted costs gives \$100.62 as the national average lifetime cost averted per decayed surface.

Step 5: As CWF averts 0.19 decayed surfaces PPPY, as described by Input (g), the benefit of CWF is thus

Gross saving $=\$100.62\times0.19=\$19.12$ PPPY

Costs

Griffin *et al.*[10] based their cost estimates for CWF on Ringelberg *et al.*,[14] except that the numbers were adjusted to 1995 dollars, and a different grouping of community sizes was used. Griffin *et al.* devote one paragraph to their cost estimates.[10]

Ringelberg et al.[14]

Ringelberg *et al.* used data for 44 Florida communities to estimate CWF costs. (Florida's phosphate industry is the largest U.S. producer of fluoridation chemicals.)[15,16] Ringelberg *et al.*'s improved estimates included costs for bulk storage and containment, labor, and opportunity costs of capital investment, and were based on a larger number of communities than previous estimates.[13] The estimated average cost increased from \$0.49 PPPY[13] to \$1.25 PPPY.[14] With phrases such as "allowable initial one-time costs … were documented by copies of actual invoices for equipment and services" Ringelberg *et al.*[14] appears detailed and based on actual data. However, these invoices were obtained from the Florida public health dental program, which has the authority to approve costs for communities seeking state grants to implement CWF,[17] and thus reflect costs allowed by the state dental program rather than actual costs.

Ringelberg *et al.*[14] used a 15-year life, with no remaining value, for initial implementation costs, and used 2.4% of the initial costs to calculate the maintenance and repair costs. Labor costs provided by CDC's fluoridation engineer were based on 1 hour per day for all systems and rates of \$7 per hour for small systems and \$9 per hour for medium and large systems. (Note that, in contrast, Input (d) in Table 2 uses \$18 per hour to calculate CWF benefit.) We will show that this is a simplistic and unrealistic view of what is involved in CWF operations.

Reality on the ground

In 2010, amid a budget crisis, the City of Sacramento, CA, instructed all departments to review programs and services. Mr. Marty Hanneman, then Director of the Department of Utilities, wrote in a memo to the City Council:[18]

> *The City of Sacramento has been fluoridating its water supplies just over 10 years. Within that time, the actual cost of operating and maintaining the fluoridation systems has proven to be considerably more than the initial estimate. … The fluoridation infrastructure at the E.A. Fairbairn Water Treatment Plant is overdue for replacement and will be very expensive to replace. … Fluoridating water is a very costly and labor intensive process and requires constant monitoring of fluoride concentrations to ensure proper dosages. … The chemical is very corrosive, so all equipment that is used in the fluoridation process has a very short life expectancy and needs to be replaced frequently. … but also causes frequent and complex system failures.*

This was echoed by Mr. René Fonseca of Carroll-Boone Water District in Eureka Springs, AR, which was required by a 2011 State mandate to begin CWF (Fonseca, 2012, private communication):

Table 3 Griffin *et al.*[10] weighted per person discounted lifetime cost of carious surface initially occurring at various ages

Age (years)	Discounted expected lifetime cost of decayed surface (\$)	1996 U.S. population (%)	Weighted cost (\$)
0–5		8.4	
6–19	159.61	20.4	32.56
20–24	146.95	6.8	9.99
25–29	144.86	7.2	10.43
30–34	128.24	8.3	10.64
35–39	127.76	8.5	10.86
40–44	105.12	7.7	8.09
45–49	105.55	6.6	6.97
50–54	106.42	5.2	5.53
55–59	69.23	4.2	2.91
60–64	69.23	3.8	2.63
65+		12.8	
Total		100	100.62

> *All of our chemical feed systems require regular maintenance which is routine but fluoride feed equipment often requires replacement and more frequent attention. … I have toured plants and seen in trade publications deteriorating pipes, steel doors and casing, electrical components, etc. There are millions of dollars spent yearly on infrastructure damage caused by fluoride in our industry.*

The realities expressed in these two quotes are not the exceptions. A water plant manager in Alberta, Canada, complained that the fumes from the acid etched the glass, paint, and computer screens of the water treatment plant.[19] Seven years after CWF began in 2001, Riverton, Utah, spent nearly $1.2 million for two new buildings "to get fluoride out of electrical and pump area."[20]

Several incidents of fluoride overfeeds at water-treatment plants have been investigated. Gessner *et al.*[21] described an accident that occurred in Hooper Bay, Alaska, in 1992, in which 296 residents suffered acute poisoning and a 41-year-old man died. Petersen *et al.*[22] reported on an overfeed incident in a residential Connecticut community in 1986. The fluoride caused gastroenteritis in 33% of those who drank the water and itching and skin rashes in those with dermal contact; the acidity leached copper from domestic plumbing. Penman *et al.*[23] investigated an outbreak of acute poisoning caused by a fluoride overfeed in a small rural community in Mississippi in 1993. Several people became ill and connected the onset of their illness to drinking tap water at the same restaurant. A community survey was performed, and the authors concluded that approximately one third of households in the town may have been affected, though the extent remains unknown.

Akiniwa[24] examined seven events of acute fluoride poisoning related to the fluoridation of drinking water that have been reported in the U.S. He estimated from these reports that acute fluoride poisonings have occurred at doses of 0.1–0.8 mg fluoride per kg of body weight. One fatal fluoride intoxication caused serious illness in 12 patients, 3 of whom died, in a hospital hemodialysis unit in Chicago in 1993.[25] Caused by failure of a widely used deionization system, this event would not have been catastrophic had the water not been fluoridated.

Other incidents reported in local media have included injuries to water plant workers, massive evacuation around an interstate highway, damages to water pipes or concrete floors, and environmental hazards to fish and ground. A number of these incidents are cited in Appendix 3.

An economic evaluation taking a societal perspective should have considered the societal costs from these inevitable consequences of CWF. However, comprehensive data needed to estimate such costs are lacking, because the government agencies that should track these incidents appear to have a conflict of interest in protecting and defending the CWF policy (e.g. Florida;[26] Layton;[27][iv] Appendix 1). Nevertheless, evidence presented here demonstrates that Ringelberg *et al.*[14] were unrealistic even considering only the direct costs of CWF to a water system.

Real-world estimates

In late 2010, Black and Veatch Corporation (Overland Park, KS USA) was retained through a competitive bid process to perform an objective evaluation of the fluoride program of the city of Sacramento, CA. After a comprehensive and detailed review, the study[28] observed that immediate and future upgrades would be needed to continue fluoridating and to achieve modest operational efficiency improvements. Noting that Sacramento's operational costs were within industry practice, the report developed detailed cost estimates and gave a different picture from Ringelberg *et al.*,[14] e.g. the labor cost was set at a rate of $100 per hour, in contrast to the $7/$9 per hour labor rate from the CDC. The city's engineer, Mr. Brett Ewart, explained (Ewart, 2012, private communication):

> *The 100/hr. is a hybrid rate used to represent the large variety of machinists, electrical staff, water quality staff, management, etc., that work on the program. The amount of staff time (and type of staff) dedicated to the fluoride program is flexible. Some maintenance activities are generally fixed, others are reactionary and difficult to predict in advance. The rate would include the employees' salary, benefits, and overhead to perform the work.*

Sacramento's water system consisted of the following: One large treatment plant supplying 44% of the water, whose fluoridation system had already been updated in 2007; a second large treatment plant (Fairbairn WTP) supplying 42% of the water, whose fluoridation system was in need of replacement; and 27 wells supplying 14% of the water, and whose fluoridation systems also required updates.[29] The overall cost estimates provided by Black and Veatch for the needed replacement and updates, annualized using a 2.5% discount rate over a 20-year planning horizon,[v] were $1 million for the 27 wells and $464,000 for the Fairbairn WTP.[29] The cost projection for the Fairbairn WTP is applicable for large water treatment plants, while the cost projections for the well upgrades are applicable for small systems.

[iv] In a letter to Davis County Health Department and others, the Mayor of Layton, Utah strongly protested that the costs of fluoridation to the citizens of Layton and Davis County were far greater than the costs portrayed by the Department when it "clearly knew better".[27]

[v] First 5 Sacramento, the organization that funded the study, may fund the capital update cost with a condition that requires the city to commit to CWF for 20 years, regardless of the city's future fiscal conditions.[18] In July 2012, the city accepted a grant from First 5 Sacramento to continue fluoridation until June 30, 2015, even though the grant will provide less than 10% of the system costs over the next 3 years.[30]

Table 4 Examples of fluoridation cost estimates

Water districts	Year Est	Pop (in thousands)	Reported implementation (I) and annual operation and maintenance (O) costs	PPPY ($) 15 years, 4% (I)
Napa, CA[34]	2003	77	I: $1M; O: $150,000	3.07
New York, NY[35]	2008	8,350	I: $12.57M (2 plants); O: $11.14M (chemicals)	1.45
San Jose, CA[36]	2011	1,000	I: $23M; O: $1.732M (Wells only)	3.72
Watsonville, CA[32]	2011	51	I: $50/person; O: $4/person	8.33
Portland, OR[37]	2012	900	I:$3.5M–$7.6M, O: $575,000	0.98–1.37
Carroll-Boone, AR[33,38]	2012	25	I: $894,000–$1.23M	3.09–4.26†
Davis, CA[39]	2013	67	I: $1.1M–$2.4M; O: $228,800–$240,700	4.84–6.69
Riverton, UT[20]	2000	35	I: $90,000 (estimate)	0.22†
	2001		I: $200,000 (actual)	0.49†
	2008		I: $1,174,278 (actual w/2 new buildings)	2.90†
Jordan Valley, UT[40]	2000	82	I: $56,000–$2.1M (estimates)	0.06–2.22†
	2004		I: $2.45M; O: $297,000 (actual)	6.21

†Estimates do not include operation and maintenance costs.

To calculate the PPPY costs, we allocated the total population of Sacramento, 466,000 people (2010 U.S. Census), to the 27 wells and to the Fairbairn WTP using the percentages of total water supplied of 14% and 42%, respectively. The allocated populations are 65,000 and 196,000, respectively. Dividing the total costs by population and number of injection sites, we obtain a cost estimate of $15.38 and $2.37 PPPY for a single-injection point water system serving 2,400 and 196,000 people, respectively. (Systems serving 2,400 people are not rare. Of the 44 systems in Ringelberg *et al.*[14] three systems had smaller populations and seven systems had smaller populations per injection site.)

We considered whether to adjust for the cost of living in Sacramento and determined that there was no need. The cost of living for Sacramento is 8% higher than the U.S. average.[31] This differential, however, is easily offset by other considerations, e.g. the use of a 2.5% instead of 4% discount rate. The cost projection also assumes that the Health Department continues to waive a requirement for certain standard equipment. In addition, actual bids for construction may turn out to be much higher than the engineer's estimates.[32,33] Finally, it was unknown whether implementing the recommendations would solve the city's fluoridation issues.[29]

A small water system serving more than 2,400 people is expected to cost less than $15.38 PPPY. Similarly, many large systems serve less than 196,000 people and are expected to cost more than $2.37 PPPY. (Note that large water districts serving more than 196,000 people will not necessarily cost much less than $2.37 PPPY, because such water districts often have multiple treatment plants and/or auxiliary wells, which make them equivalent to a smaller single-injection point system). Therefore, reasonable cost estimates for the smallest (<5,000 people) and largest (>20,000) systems in Table 1 would be about $10 and $3 PPPY, respectively.

Strictly speaking the annual cost projections provided by Black and Veatch are 20-year financing costs. At the end of the 20-year period, components such as new buildings may still have value. However, given the ability of the chemicals to degrade concrete (Appendix 3 items 17 and 19), significant annual maintenance and repair costs after the financing period are expected. In addition, circumstances could require a water system to implement major infrastructure changes to their fluoridation facilities. Sacramento is such an example. Despite implementing fluoridation comparatively late (around 2000), the city has already endured major infrastructure adjustments and is considering more, long before the 20-years projection period. Finally, it is possible that a system may discontinue CWF; in that case, buildings constructed specifically for CWF may hold little value.

Other estimates

The Black and Veatch report cited above is valuable in that it is recent, comprehensive, detailed, and authored by a firm that has consulted on other fluoridation programs. In general, reliable cost information for CWF programs is difficult to obtain, and information provided in response to a request is often limited to the cost of the fluoride chemicals. In Table 4, we present additional cost information and estimates collected from various sources.[20,32–40] The majority of these are cost estimates prior to implementation; New York and some Utah figures show actual costs. Costs are reported either for implementation (*I*) or for annual operation and maintenance (*O*). For convenience, we calculate a PPPY cost by annualizing the implementation cost (*I*) using a 4% discount rate over 15 years[vi] (meaning $100 annualizes to $8.65) and normalizing the total, i.e., dividing the annualized *I* plus *O*, if available, by

[vi] The service life of fluoridation equipment depends very much on the component and on the service conditions. According to Black and Veatch,[29] only a few components in indoor setups can expect a service life of 15 years or more, and some components have a service life of only 5–10 years in an outdoor setup.

population. (Population figures are taken from the CDC website or the U.S. Census Bureau if they are not reported in the source article.)

Many of the cost estimates shown in Table 4 are incomplete or partial, or the values are underestimated. Several (denoted with †) do not include operation and maintenance (O&M) costs. The New York numbers consist of costs to rehabilitate CWF facilities in two plants, and only chemicals are included in O&M. The San Jose numbers provided in a Black and Veatch study were for wells that provide only half of the water for the city, which imports the other half. The preliminary estimates for Napa, CA are from about the time that Sacramento began its fluoridation program and probably suffer from similar underestimates of costs.[18] The estimates for Portland, OR were provided by the Water Bureau after a meeting with representatives from the CDC and the organizations pushing to fluoridate the city. The $575,000 O&M figure appears unrealistic — Sacramento already paid over $400,000 back in fiscal year 2008/2009 for hydrofluorosilicic acid (HFSA) to fluoridate 86% of their water; this translates to about $1 PPPY for the cost of HFSA alone. In addition, the O&M estimate excluded costs of additional caustic or other corrosion control chemicals to bring the pH back to an appropriate level, and the cost of additional capital improvements needed to mitigate water quality impacts were not included in the estimated capital costs.[37]

Community water fluoridation proponents have a poor track record for cost estimates. For example, the county health board of Davis County, UT, provided a cost estimate of $1.38–$2 PPPY prior to a vote in 2000, but the true implementation cost was $4.29 PPPY.[41] This is also seen in the estimates/observed figures for the two Utah systems in Table 4. In 2001, Arkansas state legislators passed a state mandate to fluoridate community drinking water. They were partially motivated by an offer from Delta Dental of Arkansas to donate $500,000 total toward startup costs for the 32 water systems affected.[42] Later Delta Dental pledged $2 million for 34 systems and soon found itself needing to raise another $6–$10 million.[43] (State mandates in California and Arkansas both require the initial implementation costs be funded by outside sources.)

Overall, reported costs of CWF are consistent with our real-world estimates and not with those estimates[10,14] commonly cited by fluoridation proponents.

Costs of dental fluorosis

Griffin *et al.*'s Assumption (4) in Table 2, that the adverse effects of CWF are negligible,[10] is common to most cost-benefit analyses of CWF. It is inexplicable that neither Griffin *et al.*[10] nor other similar studies (Appendix 2) mention dental fluorosis, defective enamel in permanent teeth due to childhood overexposure to fluoride.[44,45] Community water fluoridation, in the absence of other fluoride sources, was expected to result in a prevalence of mild-to-very-mild (cosmetic) dental fluorosis in about 10% of the population and almost no cases of moderate or severe dental fluorosis.[46] However, in the 1999–2004 NHANES survey, 41% of U.S. children ages 12–15 years were found to have dental fluorosis, including 3.6% with moderate or severe fluorosis.[47]

As an increased prevalence of dental fluorosis became evident, there were attempts to shift attention to other sources of swallowed fluoride, such as toothpaste.[48] However, 1/4 liter (or about 8 oz) of fluoridated water at the "optimal" concentration of 1 mg/l contains the same amount of fluoride as a bead of toothpaste (0.15% w/v fluoride ion) 0.68 cm in diameter. Regarding other sources of ingested fluoride, Szpunar and Burt[49] state that the factor that differentiates the studied communities with respect to the prevalence of caries and fluorosis is the fluoride concentration in the community water supply.

Dental fluorosis had been dismissed as cosmetic by CWF promoters and government agencies in the U.S. until the National Research Council (NRC) concluded that "severe dental fluorosis" qualified as an adverse health effect due to increased risk of caries and loss of dental function.[44] When an economic evaluation is framed as having a societal perspective, it should include effects that result in social costs, regardless of whether the effects are cosmetic or systemically harmful. In a later paper, Griffin *et al.* indicated that some people may want "esthetic restorative procedures" to treat fluorosis, but treatment costs were not estimated.[50] We next provide a high level estimate of the minimal costs of treating dental fluorosis.

Dental fluorosis is classified by the severity of the discoloration, the presence of pitting, and the extent of the tooth surfaces affected.[44,45vii] Although bleaching and microabrasion can be used to improve the appearance of milder cases of fluorosis, moderate and severe dental fluorosis can require extensive treatment to improve the cosmetic appearance and prevent further loss of enamel.[44,45] Treatment options include applications of veneers or crowns. Porcelain veneers may cost more than composite resin veneers ($800–$2,500 vs. $250–$1,500), but they require less frequent replacement (10–15 vs. 5–7 years).[52,53]

[vii] Dean's classification for very mild, mild, moderate, severe and very severe dental fluorosis: at least two teeth contain mottled surface area covering less than 25%, between 25 and 50%, between 50 and 100%, 100% (with discrete pitting), and 100% (with confluent pitting) of the tooth surface, respectively[51]

Crowns are "usually used as a last resort because they can be a threat to tooth vitality."[44]

For this analysis, we assume that each moderate or severe fluorosis tooth receives a porcelain veneer treatment. We further assume that a child with the condition gets the first treatment at age 13.5 years, and the veneers are replaced every 12 years. The lifetime cost of a veneer is calculated using equation (1), except the \$72 is replaced by the cost of a veneer, for which we use a lower-end number of \$1,000. This gives a lifetime cost of \$2,217. Dean's Enamel Fluorosis Index, the most widely used classification of dental fluorosis, is assigned on the basis of the two most-affected teeth.[44] Thus, the lifetime cost of veneers for a child with moderate or severe fluorosis would be at least \$4,434.

Beltrán-Aguilar *et al.*[47] reported that 3.6% of U.S. children ages 12–15 years in 1999–2004 had moderate or severe dental fluorosis, but did not provide information on the fluoridation status of the affected children. At most about 60% of the U.S. population received fluoridated water during the time period when these children were susceptible to development of fluorosis.[viii] Both the prevalence and the severity of dental fluorosis are correlated with the fluoride concentration in drinking water.[45,49,55] If all of the cases of moderate and severe dental fluorosis occurred in fluoridated rather than nonfluoridated areas, then at least 6% of children in fluoridated areas would have moderate or severe fluorosis.[ix] For our calculations, we have assumed that 5% of children in fluoridated areas have moderate or severe fluorosis. From Table 3, the percentage of children at age 13.5 years is about 20.4% / 14 = 1.46%. Thus the minimum cost of treating dental fluorosis is estimated to be \$4,434 × 1.46% × 5% = \$3.24 PPPY.

Other costs

There are other costs missing from the conventional cost-benefit analyses of CWF (Appendix 2). The NRC's 2006 report on fluoride exposures and toxicity found that the U.S. Environmental Protection Agency's (EPA) drinking water standard for fluoride was not protective of human health.[44] The NRC did not evaluate CWF for safety or efficacy, but the report showed that the average fluoride exposures associated with adverse health effects are within the expected range of fluoride intake for populations with fluoridated water, especially for infants, young children, and people with high water intake.[44,56x] Peckham and Awofeso's recent review specifically concluded that fluoridation has "significant costs" in relation to adverse effects on human health, although these costs were not quantified.[57]

Health risks to water plant operators are not included in most discussions of CWF, but these individuals may receive substantial occupational exposures to fluoride if the safety infrastructure or training is not adequate or if equipment malfunctions.[58,59]

Most of the fluoridation chemicals used in the U.S. are byproducts of the phosphate fertilizer industry in North America or Asia.[15,16,60] Since only a small percentage of municipal water is actually consumed by people, the practice results in wide dispersion of a regulated pollutant into the environment via local water districts. Fluoride pollution may result in serious ecological risks to aquatic organisms.[61]

Fluoride is regulated by the U.S. EPA as a contaminant in drinking water[62] and as an air pollutant.[63] A number of fluoride compounds are considered hazardous substances with assigned Reportable Quantities.[64] In addition, fluoridation chemicals often contain other regulated contaminants.[5–8] Hirzy *et al.*[65] estimated that the typical concentration of arsenic in the major fluoridation chemical (HFSA) could be responsible for several excess lung and bladder cancers per year in the U.S. and the consequent costs of treatment.

Political costs have at times been acknowledged but not included in CWF analysis.[10] This category goes beyond costs associated with fluoridation referenda to include government expenditures for promoting fluoridation programs, costs associated with lobbying elected officials on this issue, legal challenges to fluoridation programs, and possible personal injury litigation involving workers or members of the public.[66–70]

There are also costs associated with avoiding fluoridated tap water, either by need or by choice. These are all societal costs of CWF that should not simply be excluded or assumed negligible without examination.

Benefits

The primary benefit attributed to CWF is prevention of caries, although a major review in the United Kingdom reported no relevant studies of "evidence level A (high quality, bias unlikely)" and expressed surprise that little high quality research had been undertaken.[71] Caries prevention is commonly assessed in terms of a reduction of decayed, missing, or filled

[viii] Infants and young children are most at risk for exposures leading to dental fluorosis.[45] Children ages 12–15 years when surveyed between 1999 and 2004 were born between 1984 and 1992. Centers for Disease Control and Prevention's data indicate that 53–60% of the U.S. population between 1984 and 2002 received fluoridated water.[54]

[ix] 3.6 / 53% = 6.8% and 3.6 / 60% = 6%.

[x] People with high water intake include athletes, outdoor workers, military personnel, and people with medical conditions such as diabetes insipidus or diabetes mellitus.[44] People with impaired kidney function may have high water intake and might also have reduced urinary excretion of fluoride.[44]

teeth (DMFT), DMF tooth surfaces (DMFS), or their variations.[xi] Estimation of averted caries is obviously central to a cost-benefit analysis.

Griffin *et al.*[10] relied on the theory that caries averted by CWF can be considered in terms of two factors as shown in the following equation

$$\text{Averted caries} = \text{Incidence} \times \text{Effectiveness} \quad (2)$$

where Incidence is the per person annual caries increment without CWF, and Effectiveness is the percentage reduction in caries due to CWF.

Before we explain and critique how Griffin *et al.*[10] derived their values for Incidence and Effectiveness, it is worthwhile to examine the concepts of incidence and effectiveness in the context of CWF.

Incidence

Griffin *et al.*[10] treat the reported caries incidence in selected nonfluoridated areas as the caries incidence in the absence of CWF. However, they have not accounted for the decline in caries rates over time apart from CWF or the variability in caries rates among various areas, independent of CWF.

It has been known for decades that tooth decay prevalence has been declining in developed countries regardless of CWF status, i.e., the "secular decline".[11] Diesendorf[72] listed over 20 studies which reported substantial temporal reductions in caries in unfluoridated areas. In many cases, the magnitudes of the reduction were comparable to those attributed to fluoridation in some fluoridated areas; it was also pointed out that fluoride toothpaste or supplement could not have accounted for many of the reductions.

That fluoride is not needed for dental health is not surprising. A 1952 NRC report[73] described studies reporting that the teeth of ancient peoples and modern primitive peoples were relatively free from dental caries, in a striking contrast to the teeth of modern people. However, primitive peoples had increased rates of caries when brought into contact with a modern diet. This is consistent with the fact that caries are rare in animals in the wild. Finn[73] also described the significant geographic and temporal variability of caries prevalence, citing Hagan[74] for demonstrating how caries prevalence may vary within narrow geographic limits, as well as fluctuating within the same area from time to time.

Hagan[74] studied 12 communities in Georgia, including 24,092 children, and reported the following by community: The average annual caries increments were 0.18–0.90 for children up to 16 years old; the DMFT ranged from 0.40–2.44 at age 7 years to 1.41–10.64 at age 16 years; the percentage of children with at least 1 DMFT ranged from 23–77% at age 7 years to 58–100% at age 16 years. The ranges of DMFT for a given age in these pre-CWF situations approach or exceed the differences reported between fluoridated and nonfluoridated locations in more recent years. For example, Heller *et al.*[55] reported mean DMFS values ranging from 2.53 (0.7–1.2 ppm F) to 3.08 (<0.3 ppm F), with a mean DMFS of 2.75 for the entire sample (18,755 U.S. schoolchildren ages 5–17 years with a history of a single residence). The percentage of caries-free children ranged from 52.5% (>1.2 ppm F) to 57.1% (0.3–0.7 ppm F), averaging 54.6% for the entire sample. McDonagh *et al.*[71] reported that, among 15 studies analyzed, the mean differences in dmft or DMFT ranged from 0.5 to 4.4 (median 2.25).

Other historical data contradicting the idea that fluoride is needed for dental health have been reported. Using data from New Zealand Health Department records of 5-year-olds' tooth decay from 1930 to 1990, fluoridation coverage, and fluoride toothpaste sales, Colquhoun[75] showed that the dramatic decline in tooth decay started long before water fluoridation, fluoride toothpaste, or application of fluoride. Another paper noted that the DMF rate in children ages 12–15 years in Taiwan was as low as 1/3 to 1/6 of that in children of the Western countries where water fluoridation had been in effect for 8–11 years.[76]

Studies that attributed differences in tooth decay rates between selected communities to CWF may have only observed these geographic or temporal variabilities, independent of any effect of CWF. Other studies (see Appendix 5) found that non-fluoridated cities also experienced rapid reductions in tooth decay rates without installing CWF, even though these cities had previously been compared with fluoridated cities as evidence that CWF reduces caries. Hence the concept of a no-fluoridation caries incidence rate has little meaning.

Effectiveness

Griffin *et al.*[10] derived their estimate of effectiveness from Brunelle and Carlos,[77] who reported on the second of two large-scale National Institute of Dental Research (NIDR) surveys, completed in 1980 and in 1987, respectively. Each survey sampled and examined approximately 40,000 U.S. school children aged 5–17 years.

Community water fluoridation effectiveness has been variously reported in the literature. The unit of measure can be variations of DMFT, DMFS for permanent teeth, the corresponding measures for deciduous teeth, or the percentage of children with no caries. They could be for a single age or for an age range. Information about length of exposure to CWF

[xi] DMFS counts the number of decayed (untreated), missing, filled tooth surfaces and DMFT counts teeth instead of surfaces. (An adult without wisdom teeth has 28 permanent teeth and 128 tooth surfaces.) Capital letters refer to permanent teeth and lower case letters (dmfs, dmft) to deciduous teeth.

may or may not be included. Study parameters are often poorly defined and confounding factors not typically examined.

Often a percentage value is produced from some relative differentials and referred to as CWF effectiveness, despite that the percentages come from different situations. Some may argue that since all the different kinds of studies point to similar ranges of effectiveness, it is proof that the effectiveness estimates are robust. However, the premise of this argument is false.

First: Units. Units of measures do affect the results. An independent investigation of the 1987 NIDR data using DMFT instead of DMFS led to the conclusion of no effectiveness.[78] When asked about results for teeth, Brunelle was quoted to have said that they "are in a box somewhere" and she "could not remember what exactly the results were" and that the decay rate for teeth "is rather low so that there is very little difference in most anything."[79] Truman *et al.*[80] estimated effectiveness in units of teeth from data reported in a number of studies (Table 5) even if a study reported data in both teeth and surfaces.

Studies reporting results in teeth were more common in the past. The focus shifted toward surfaces as the prevalence of caries dropped and caries became concentrated in a small subset of the population.[81] Measuring caries in units of surfaces gives heavy weight to the small percentage of people with high levels of decay.[xii]

Second: Lengths of exposure. There are two relevant exposures: exposure to carious influence and exposure to CWF.

Exposure to caries is determined in part by the time a tooth erupts. Usually age is used as a surrogate for the length of this exposure. If a study examines subjects of a range of ages and one effectiveness number is to be presented, which age is selected or how different age groups are weighted to calculate an average can produce different results. Appendix 4 provides examples of studies showing differences in caries experience that were attributed to CWF exposures, when the results may be better explained by differences in age distributions of the populations being compared.

Exposure to CWF is often handled by comparing only those with lifetime exposure to those with no exposure. However, if a result is contingent on excluding partial exposure it weakens the argument for CWF as a public policy. More importantly, this approach introduces a probable bias if the two exposures (to caries and to CWF) are not independent. Evidence indicates that ingested fluoride may delay tooth eruption,[44,45,85] which would affect caries scoring by giving the appearance of less decay for a given age.[44,45] Komárek *et al.*[86] used data for actual tooth eruption time and found no convincing effect of fluoride intake on caries development. Weaver[87] indicated that "the caries inhibitory property of fluorine seems to be of rather short duration," consistent with a delay in the exposure of permanent teeth to a cariogenic environment.

Third: Methods. The methods of determining an effectiveness value are even more problematic, especially in regard to policy references. This is best demonstrated by an examination of Truman *et al.*,[80] which was co-authored by Griffin, other CDC personnel, and a Task Force appointed by the Director of the CDC. The Task Force was established by the U.S. Department of Health and Human Services (HHS) in 1996 to provide recommendations for community preventive services, programs, and policies. Reported in 2000, the findings of the Task Force's systematic review[88] became the main results of Truman *et al.*[80] on CWF effectiveness, as well as the basis for Healthy People[xiii]2010's goal of increasing CWF in the U.S. to cover 75% of the population.[91] Healthy People 2020[92] continues with a goal of increasing coverage to 79.6%.

Truman *et al.*[80] based their conclusion on 14 studies in three groups (Table 5):[76,93–105]

- Studies starting or continuing CWF with before and after measurements (Group A-On)
- Studies stopping CWF with before and after measurements (Group A-Off)
- Studies starting or continuing CWF with only post measurements (Group B-On)

They calculated a number of "estimates of effectiveness" from the studies using two formulas, one for Group A (before-and-after) and one for Group B (post measurements only). The measures were mostly DMFT or dft.

The median of estimates was taken to represent the CWF effectiveness for each study type; the results were 29.1% for Group A-On, 50.7% for Group B-On, and 17.9% for Group A-Off. (The 29.1% and 50.7% figures were presented by the Task Force.)[88] With these numbers the authors concluded "strong evidence shows that CWF is effective." This conclusion is not valid. We describe three areas of problems below (details provided in Appendix 5).

[xii] Proponents often appeal to sympathy for young children with high levels of tooth decay to argue for CWF.[82] However, early childhood caries (ECC) is not prevented by fluoride.[83,84]

[xiii] CDC's "Healthy People" series "provides science-based, national goals and objectives with 10-year targets designed to guide national health promotion and disease prevention efforts to improve the health of all people in the United States."[89] One goal of Healthy People 2000, 2010, and 2020 has been to "increase the proportion of the U.S. population served by community water systems with optimally fluoridated water."[90–92]

Selection of studies: Studies of higher quality and relevance such as the NIDR surveys or other U.S. studies were not included. Many studies on the effect of cessation of CWF (Group A-Off) were omitted even though this group had only three studies. Not all included studies are relevant for CWF or meet the stated criteria.

Selection of estimates: The number of estimates selected from each study appears arbitrary. Fewer estimates were selected from large-scale studies reporting findings in detail than from small studies reporting few findings. Sometimes the selected estimate did not fit the group it was placed in. Selection of arbitrary numbers of estimates from an arbitrary set of studies does not lead to confidence in the reported median.

Selection of formula: Within the limited set of studies and estimates selected, the authors failed to apply their formula consistently. In addition, the results from the application of the formula can be misleading. Upon examination of the data, some purported positive outcomes are revealed as purely an artifact of the formula — the never-fluoridated communities had a dramatic reduction in caries without the help of CWF.

The incidence and effectiveness in Griffin et al.[10]

Three estimates for Incidence were compiled from several unrelated sources while three estimates for Effectiveness were derived from a single source. They are paired by magnitude and substituted in Equation (2) to arrive at three cases of averted DMFS as shown in Equation (3).

$$\begin{aligned} \text{best case}: &\ 1.16 \times 29\% = 0.34 \\ \text{base case}: &\ 0.76 \times 25\% = 0.19 \\ \text{worst case}: &\ 0.33 \times 12\% = 0.04 \end{aligned} \tag{3}$$

The base-case averted DMFS of 0.19 is the key input (g) in Table 2. (Note that not all studies cited by the authors measured DMFS, and the differences were not always pointed out.) We next examine how the numbers on the left-hand side were derived.

Table 5 The studies, the age of children examined, group placed, and number of estimates calculated by Truman *et al.*[80] to evaluate CWF effectiveness

Study	Age	Group/no. Est.
Arnold and Dean[93]	4–15	A-On/4
Beal and James[94]	5	A-On/2
Beal and Clayton[95]	5,8,12	A-On/4
Loh[96]	7–9	A-On/2
Evans *et al.*[97]	5	A-On/3, B-On/1
Guo *et al.*[76]	4–15	A-On/2, B-On/3
Künzel and Fischer[98]	6–15	A-On/4, A-Off/2
Attwood and Blinkhorn[99]	10	A-Off/1
Kalsbeek *et al.*[100]	15	A-Off/2
Brown and Poplove[101]	14–17	B-On/4
Fanning *et al.*[102]	3–6	B-On/3
Hawew *et al.*[103]	6,12	B-On/4
Provart and Carmichael[104]	5	B-On/2
Rugg-Gunn and Nicholas[105]	5	B-On/3

The Incidence

Griffin *et al.*[10] obtained three sets of annual caries increments in nonfluoridated communities as Incidence; they are reproduced in Table 6. The sources were, respectively, published studies cited in Garcia,[13] the National Survey of Oral Health (NSOH) in U.S. Schoolchildren and a separate NSOH in Employed Adults and Seniors, and the First and Third National Health and Nutrition Examination Survey (NHANES I, 1971–1974 and NHANES III, 1989–1994).

For the best case, the authors used the controls in Garcia's review[13] of published studies of clinical and community trials. For the base case, the incidence for children was imputed by dividing the difference in mean DMFS for 6-year-olds and 17-year-olds living in communities without fluoridation by 11. Unrelated to the children's survey, the adult NSOH survey was measured in DFS (without M, missing surface) and was not stratified by community fluoridation status. Hence, they imputed the incidences by using the least fluoridated region (Pacific). They scaled the mean DFS by the ratio of average numbers of teeth in the two age points to adjust for missing teeth. They also added root caries incidences from other studies. For the worst case, the authors imputed the incidence using data from two NHANES surveys, which did not report fluoridation status. A major difference from the base case was that they tried to use data on the same birth cohort over time. Additional adjustment was applied because earlier NHANES data measured DFT instead of DFS.

The source of the best case, Garcia,[13] was the basis for discussion of CWF in the 1989 Michigan Workshop. Workshop participants were critical of the numbers. "Most work groups felt that the estimates of caries incidence in Garcia's report were generally too high and reduced them by several decimal points, though some reduced them further."[12] Griffin *et al.*[10] also stated in their discussion that the samples were probably not representative of the general population. Thus, the best case is invalid.

Griffin *et al.*[10] also admitted that the base case was overestimated. They remarked that, given the secular decline in caries, using cross-sectional data to impute

Table 6 Griffin *et al.*'s estimates of annual caries increment (tooth surfaces) from selected studies, by age[10]

	Age (year)			
Source	6–17	18–44	45–65	Avg.
Published studies (best case)	1.40	0.83	1.24	1.16
NSOH (base case)	0.77	1.09	0.43	0.76
NHANES (worst case)	0.49	0.49	0.00	0.33

caries increment from the NSOH would overestimate current increment. Secular decline[11,72] refers to the widespread decline in caries observed in nonfluoridated areas. It means that when a 6-year old living in a nonfluoridated area today grows up to be 17 years old, he will likely have fewer caries than his 17-year old neighbor has today. Thus using the latter to represent the former (cross-sectional data) overstates the incidence of caries.

The Effectiveness

As with the Incidence, Griffin *et al.*[10] presented three cases for Effectiveness, all essentially from Brunelle and Carlos.[77] The 1987 NIDR Survey examined 39,206 children, of whom about 92% had complete residence histories. Brunelle and Carlos[77] analyzed data from 16,398 children with either lifelong exposure or no exposure to CWF and presented mean DMFS by age (see Table 12) and by region (Table 7). The national averages from this subset of data showed a difference of 0.6 DMFS, or 18%, between the two exposure groups. By further restricting their sample to a subset of 5,954 children (reportedly by removing all data points with any supplemental fluoride exposure), the 18% difference was raised to 25%. No age or regional distribution was shown for this restricted set of data. Griffin *et al.*[10] took this 25% as the base-case Effectiveness.

Brunelle and Carlos[77] ignored 58% of the total data (or 55% of those with complete residence histories), despite that partial exposure data from this national survey can be analyzed and are informative.[78] It is therefore questionable if the 18% reduction in DMFS represents the findings of the survey. Even more troublesome is the 25% adopted as the base-case Effectiveness, as it ignores 85% of the survey data.

The best- and worst-case Effectiveness, 29% and 12%, respectively, were supposed to be calculated from the best three and the worst four effective regions. However, the worst four regions (I, II, III, and V in Table 7) would average closer to 6% than 12% using regional population data found elsewhere.[106] It appears that Griffin *et al.*[10] may have removed Region III (Midwest) from the calculation given the comment: "The negative effectiveness value in the Midwest may have been due to small sample size because few children living in this region actually received nonfluoridated water." This criticism would equally apply to the highest-effectiveness Region VII (Pacific), as few children in this region received fluoridated water, but it was not considered a problem.

Lack of evidence for adults

Assumption (2) and Input (h) in Table 2 assume the same CWF benefit to age 64 years, despite that estimates of Effectiveness were derived from a children's survey. Two adult studies[51,107] were cited to support this extrapolation. However, the data presented in Grembowski *et al.*[107] do not support its conclusion, and Eklund *et al.*[51] appear to be mis-cited in addition to the fact that the concentrations involved, 3.5 versus 0.7 mg/l, are irrelevant to an evaluation of CWF. We examine each of these studies below.

That few adult studies are available has been noted elsewhere. Garcia[13] stated that very limited information exists in the literature about caries incidence in adults, and Newbrun[108] identified only seven adult studies; he commented that very few acceptable data exist and that the comparison was either between those living in low-fluoridated and high-fluoridated (greater than optimal) communities or between those living in optimally fluoridated and high-fluoridated communities. Thus, it is not surprising that Truman *et al.*[80] included "What is the effectiveness of CWF among adults aged $\geq$ 18 years?" among important unanswered questions.

More recently Slade *et al.*[109] presented an analysis of Australian data from a 2004–2006 survey, and Griffin *et al.*[110] did a meta-analysis of several earlier studies. We examine these papers in detail in Appendix 4. Among other problems, both articles (and several studies included in the latter) failed to properly account for different age distributions.

Grembowski *et al.*[107]

This study examined Washington state employees and spouse-dependents aged 20–34 years living in Olympia, Seattle, or the Pullman, WA/Moscow,

Table 7 Mean DMFS of each U.S. region by CWF status (1986–1987) from Brunelle and Carlos[77]

Region	Lifelong exposure	No CWF exposure	Population with CWF (%)	Relative Diff (%)
I	3.11	3.45	55	9.9
II	3.08	3.42	49	9.9
III	2.86	2.69	74	–6.3
IV	2.75	3.60	54	23.6
V	2.49	2.71	59	8.1
VI	2.36	3.07	34	23.1
VII	1.42	3.61	19	60.7
U.S.	2.79	3.39	53	17.7

DMFS: decayed, missing, or filled tooth surfaces; CWF: community water fluoridation.

Table 8 Average number of decayed and filled surfaces by period of fluoridated exposure in lifetime from Grembowski *et al.*[107]

Period of fluoridation exposure in lifetime	No. of adults	Average age	College degree (%)*	Average DFS
No exposure in lifetime	226	30.4	35	27.9
Pre-eruptive exposure patterns (ages 0–5 only or ages 0–14 only)	40	30.1	40	20.0
Post-eruption exposure patterns (ages 15–34 only)	266	30.7	78	22.2
Exposed most of life	63	31.0	72	15.7

*Includes those with a college degree and those with graduate work or a graduate degree.

Idaho area. The data presented in this study are reproduced in Table 8.

Griffin *et al.*[10] paraphrased Grembowski *et al.*[107] claiming that the average 30-year-old adult with continuous lifetime exposure to fluoridated water had 8.7 fewer decayed or filled surfaces, or a 31% reduction compared with 30-year-old adults with no CWF exposure. However, based on the data (Table 8), it is unclear how these figures were estimated.

There are additional problems with Grembowski *et al.*[107] For example, it was stated that "1,066 … formed the data base for this analysis"; but the paper shows results for only 595 participants, and makes no mention of the other 471 participants. In other words, 44% of the data are unaccounted for.

Grembowski *et al.* described calculating the years of fluoridation exposure for the age ranges: 0–5, 6–14, 15–19, and 20–34 years, to "explore systemic and topical effects." However, Table 8 has a group described as having an exposure pattern, meaning exposure to CWF for the majority of time during the period of "ages 0–5 only or ages 0–14 only" — it appears to be a hastily created grouping to avoid showing results from the original design. Indeed only 40 adults were in this group, so that they had to qualify their conclusion that "exposure to fluoridated water during childhood has lifetime benefits" with "These results are tentative, however, because the pre-eruptive sample size was small."

The four groups differed in their education levels as well as their fluoride exposure (Table 8), with the no-exposure group having the lowest percentage with a college degree. The CDC has reported that oral health disparities are associated with lower education level.[111xiv] Although Grembowski *et al.* pointed out the difference in education level, they did not evaluate the possible impact of this difference on their findings.[107]

Grembowski *et al.* revealed that people in the nonfluoridated sites had less untreated decay than in the fluoridated sites. They also pointed out that the filled component of DFS is influenced by dentists' treatment decisions. They noted that dentists in nonfluoridated areas may restore teeth in adults more frequently, and that use of identical treatment criteria would "slightly reduce" their estimates of fluoridation's benefits.

They claimed to offer evidence that exposure to fluoridated water during childhood has a lifetime benefit and concluded that their findings provide support for health officials to continue and expand this public health program. Their data do not support the conclusion.

Eklund *et al.*[51]

This study examined the communities of Lordsburg and Deming, New Mexico, with fluoride concentrations of 3.5 and 0.7 mg/l in the drinking water supply, respectively. Subjects were approximately 30–60 years of age, had been born and lived at least the first 6 years of life in the city, and had an unequivocal water history. The main results were summarized in two tables, one for dental fluorosis and one for caries, reproduced in Tables 9 and 10, respectively.

Griffin *et al.*[10] wrote that this work found adults who received a high fluoride concentration experienced 20% fewer carious *surfaces*. The 20% number was an interpretation from two numbers, 7.0 and 8.7, found at the upper right corner of Table 10. (Note: the unit of measure was teeth, not surfaces.) The authors, however, were less inclined to draw the kind of conclusion that Griffin *et al.*[10] did. They wrote:

> *The picture is less obvious for dental caries. … The assessment of dental caries in an adult population is difficult. … First, it is often difficult to determine why missing teeth were removed. … Second, it is not*

Table 9 Number and percent of subjects by city and fluorosis classification from Eklund *et al.*[51]

Fluorosis	Lordsburg (n=164)		Deming (n=151)	
Normal			104	(68.9%)
Questionable			23	(15.2%)
Very mild	1	(0.6%)	17	(11.3%)
Mild	1	(0.6%)	2	(1.3%)
Moderate	37	(22.6%)	5	(3.3%)
Severe	63	(38.4%)		
Very severe	62	(37.8%)		

[xiv] "Disparities [in dental health] were noticed across all age groups, among racial/ethnic groups, persons with lower education and income, and by smoking status."[111]

Table 10 Comparison of mean decayed, missing, or filled teeth (DMFT) and selected components by city and age of lifelong resident adults from Eklund *et al.*[51]

	Decayed		Missing		Filled		DMFT	
Age group	L	D	L	D	L	D	L	D
All	0.8	0.6	2.8	2.4	2.9	5.4	7.0	8.7
27–40	0.4	0.7	1.3	1.6	3.6	4.4	5.9	6.9
41–50	1.5	0.5	2.4	3.7	2.4	6.6	7.1	11.1
51–65	0.6	0.2	5.6	3.3	2.2	7.3	8.8	11.1

L: Lordsburg; D: Deming

possible to determine whether all filled teeth had a carious lesion as defined by the diagnostic criteria.

In contrast, they concluded that differences between the communities are ''obvious and unequivocal'' for dental fluorosis. Indeed, no one from Lordsburg escaped dental fluorosis and 76% of them were severe or very severe. At the lower concentration of 0.7 mg/l, Deming had 16% dental fluorosis, including some moderate cases.

Table 10 shows that the higher DMFT in Deming was due to a much higher filled component across all age groups. As with Grembowski *et al.*,[107] Eklund *et al.*[51] noted that the filled component is influenced by dentists' treatment decisions. On the other hand, the oldest age group in Lordsburg had many more missing teeth, similar to other studies that found a relationship between high fluoride exposure and tooth loss.[112,113]

Costs of dental treatments

Costs of dental treatments consist of dental fees and lost productivity. Griffin *et al.*[10] used survey data for the dental charge,[114] which may differ from the charge in a competitive market, and therefore not be representative of the resource costs. Assumption (6) holds that all fillings are single-surface fillings. This overestimates dental costs, since a three-surface cavity does not require three times more resources than a one-surface cavity requires, in terms of either time lost or dentist's effort. In fact, the fees in the survey were $53.60 and $83.27 for one- and three-surface amalgam fillings, respectively.[114] Griffin *et al.* used the U.S. average hourly wage for the productivity cost. Average hourly wage overestimates productivity cost, since another central argument for CWF is equity, i.e. it is supposed to be particularly beneficial to low-income people.

Minimal corrections

In this section, we show how the defects in the derivation of CWF benefits, or gross savings, discussed above can be corrected.

Costs of dental treatments

The resource value of a treatment is best represented by the allowable charge from a widely accepted insurance fee schedule. Fee schedules may vary for a number of reasons, but the relative values among closely related procedures tend to be stable.

Table 11 shows the allowable charges for amalgam fillings from two large payers, one from a public payer[115] and one from the largest commercial payer (private communication). The payments are not proportional to the number of surfaces involved, and Assumption (6) in Table 2 clearly overestimates the dental charges. Using these relativities and two assumptions a new gross savings estimate will be provided.

Our first assumption is that the average number of decayed surfaces per filling is two and the average dental fee is about that of a two-surface filling. For example, a 40% : 30% : 20% : 10% distribution of one-, two-, three-, and four-or-more-surface fillings, respectively, produces such averages using the relativities in Table 11. Our second assumption is that each equivalent two-surface filling costs 1 hour in lost wages.

Brown and Lazar[114] reported that there were more two-surface fillings than one-surface fillings in the 1990 survey and that the number of one-surface fillings has been dropping faster despite a vastly increased number of examinations. Since the more the distribution is weighted toward more-surface decays the less gross savings there are, our first assumption likely overestimates gross savings.

Table 11 Allowed charges and their relativities for amalgam fillings from two insurance fee schedules

Surfaces	Denti-Cal (CA Medicaid, $)	Delta Dental (San Diego area, $)
One	39 (1)	72 (1)
Two	48 (1.23)	87 (1.21)
Three	57 (1.46)	108 (1.50)
Four or more	60 (1.54)	118 (1.64)

Using the more generous 1.23 factor from Denti-Cal to calculate a correction, the average cost per carious surface, \$54+\$18, in Step 1 is changed to

$$(1.23 \times \$54 + \$18)/2 = \$42.21 \quad (4)$$

The \$54 fee for a one-surface amalgam filling was based on a survey of about 5% of U.S. dentists in private practice.[114] We argue that the allowed charge from a major commercial dental insurer better represents the true cost of resources, and we have an actual allowable charge of \$72 from the San Diego area (Table 11). The cost of living in San Diego is 1.43 relative to the U.S. average.[31] Using that index would give a one-surface amalgam cost of \$72/1.43=\$50.35 today. It is reasonable then to keep the national average assumption at \$54, which is 38% higher than the current California Medicaid payment rate.

The \$18 opportunity cost was a U.S. average hourly wage. The 2010 U.S. median and mean hourly wages are reported to be \$12.68 and \$19.21, respectively.[116] As equity is the other strongest appeal of CWF, the median wage is more appropriate than the mean wage for representing productivity loss. Substituting the \$12.68 for the \$18 in equation (4) to obtain an updated average cost per carious surface gives

$$(1.23 \times \$54 + \$12.68)/2 = \$39.55 \quad (5)$$

This value replaces the \$72 in equation (1) in Step 2. The final result is that the \$19.12 PPPY gross savings in Step 5 changes to

$$\$19.12 \times (\$39.55/\$72) = \$10.50 \text{ PPPY} \quad (6)$$

Averted caries — a consistent approach

Calculating averted caries as a product of no-CWF Incidence and CWF Effectiveness is fundamentally unsound. Griffin *et al.*[10] could have derived a self-consistent averted caries directly from Brunelle and Carlos,[77] the results from which are summarized in the first six columns in Table 12.

As it was assumed that CWF benefit begins at age 6 years and the caries aversion begins after 1 year of exposure [Inputs (f) and (h) in Table 2], the first annualized data point (difference in DMFS) is at age 7 years with 1 year of exposure. This procedure provides 11 data points, as illustrated in the last three columns in Table 12. Taking the mean of the 11 data points gives the average annual DMFS difference (0.11), which can be used as the averted tooth decay surfaces PPPY.

Thus a self-consistent derivation yields an averted DMFS PPPY of 0.11, not 0.19. Applying this correction to the previous adjustment, the gross savings is further reduced to

$$\$10.50 \times (0.11/0.19) = \$6.08 \text{ PPPY} \quad (7)$$

Lack of evidence for adults

Since there is no real evidence that CWF prevents caries in adults, we present hypothetical scenarios; each scenario assumes that the caries aversion rate extends to a given age.

To calculate the estimate for each scenario, Step 4 is modified by summing the weighted costs to the cut-off age. Thus, if CWF is effective to age 19, 29, 39, or 64 years, the national average lifetime cost averted per decayed surface becomes \$32.56, \$52.98, \$74.48, or \$100.62, respectively, prior to the corrections. The ratio of each of the lifetime costs to \$100.62 is how the gross savings is reduced in each age scenario.

Table 12 Summary data from Brunelle and Carlos,[77] differences between no exposure and lifelong exposure groups, and estimate of averted caries based on the data

Age		Lifelong exposure		No exposure		Years after age 6	Difference in mean DMFS	
	U.S. population	Children examined	Mean DMFS	Children examined	Mean DMFS		Cumulative	Annual
5	2,552,751	227	0.03	229	0.10			
6	3,980,732	705	0.14	645	0.14			
7	3,578,063	764	0.36	780	0.53	1	0.17	0.17
8	3,211,415	782	0.64	757	0.79	2	0.15	0.08
9	3,332,326	766	1.05	811	1.33	3	0.28	0.09
10	3,357,708	802	1.64	710	1.85	4	0.21	0.05
11	3,179,166	716	2.12	756	2.63	5	0.51	0.10
12	3,206,386	649	2.46	687	2.97	6	0.51	0.08
13	3,229,289	616	3.43	613	4.41	7	0.98	0.14
14	3,473,894	590	4.05	600	5.18	8	1.13	0.14
15	3,552,049	504	5.53	559	6.03	9	0.50	0.06
16	3,581,737	529	6.02	551	7.41	10	1.39	0.14
17	3,045,456	515	7.01	535	8.59	11	1.58	0.14
Total	43,280,972	8,165	2.66	8,233	3.24		Average =	0.11

DMFS: decayed, missing, or filled tooth surfaces.

Thus the gross savings of $6.08 PPPY becomes $1.97, $3.20, $4.50, or $6.08 PPPY if the CWF benefit extends to age 19, 29, 39, or 64 years, respectively.

Discussion

Corrected net savings

In the previous section, we showed how several defects in the derivation of the $19.12 PPPY estimate of CWF benefit can be corrected. The corrected gross savings estimate is $1.97, $3.20, $4.50, or $6.08, if the CWF benefit extends to age 19, 29, 39, or 64 years, respectively.

As described earlier, the cost estimates of $0.50 for large water systems and $3.17 for small systems[10] were not based on reality. We used a detailed engineering projection report prepared for a system that has a decade of CWF experience and has characteristics of both large and small systems to obtain a more reasonable estimate of $3 and $10 PPPY, respectively.

The net savings are summarized in Table 13. In short, there is minor savings only if the caries aversion attributed to CWF extends to old ages and only in large systems. Thus minimal correction to several methodological problems eliminates most of the savings. When we include the estimated cost of treatment of dental fluorosis of at least $3.24 PPPY, there are no savings left in any scenario in Table 13.

Topical effect

There is a question whether any savings for averted caries are real, because the mechanism by which fluoride is thought to help prevent caries is topical. Griffin *et al.*[10] explained that Assumption (1) in Table 2 was due to the benefit from water fluoridation being primarily "topical and post-eruptive." The CDC[1] states that fluoride prevents dental caries predominantly after eruption of the tooth into the mouth, and its actions are primarily topical. Both articles referenced Featherstone,[117] who stated that the effect of ingested fluoride on caries is minimal.

Current official justification for continuing promotion of CWF is that fluoride in tap water provides teeth with continuous exposure from water, beverages, and foods prepared with tap water, and that a constant low concentration of fluoride is maintained in the dental plaque and saliva all day.[118] The first point can be left to common sense. The second point contradicts current oral hygiene recommendations concerning plaque and has been refuted concerning saliva. The concentrations of fluoride in ductal saliva, approximately 0.016 ppm in fluoridated areas and 0.006 ppm in nonfluoridated areas, are "not likely to affect cariogenic activity."[119]

In addition, fluoride, by ingestion or by contact, negatively affects enamel remineralization in individuals with low calcium and magnesium in teeth enamel (usually due to undernutrition).[57] Hence, CWF may increase caries in people with poor nutritional status.

Equitable?

That CWF particularly helps the poor at a very low average cost to all has been an integral argument for CWF. We briefly examine the equity aspect.

A major review of the effectiveness of CWF states "There is some evidence [strength of evidence=C] that water fluoridation reduces inequality in dental health across social classes in 5- and 12-year-olds [in England] … The small quantity of studies, differences between these studies, and their low quality rating, suggest caution in interpreting these results."[71]

In Appendix 5, we point out two studies missing from the review of Truman *et al.*[80] In the first study Szpunar and Burt[49] reported that a fluoride concentration of 1.0 or 1.2 mg/l prevented caries, but 0.8 mg/l did not. (The current CWF range is 0.7–1.2 mg/l, and HHS proposed to decrease it to 0.7 mg/l.)[3] This study chose a predominately white township bordering Detroit, instead of the largely black and long fluoridated Detroit, to represent a fluoridated community. Burt *et al.*[120] reported that only 0.2% of low-income adults in Detroit in the 14–35 age group (born after CWF started in 1967) were caries free (compared to 55% of children up to age 12+ in the unfluoridated community in Szpunar and Burt).[49]

In the second study, Shiboski *et al.*[121] found that the prevalence of early childhood caries was not affected by fluoridation status. Among Head Start (low income) children, the most fluoridated ethnic group (Asians, with 69% in fluoridated areas) had the worst tooth decay status. Among non-Head Start children, the most fluoridated ethnic group (Asians, with 81% in fluoridated areas) had tooth decay rates similar to those of white Head Start children, with 12% in fluoridated areas.

Truman *et al.*[80] stated: "The current burden of poor oral health continues to disproportionately

Table 13 Present-day, corrected estimates of net savings ($) per person per year from water fluoridation

			CWF benefit extends to age			
			19	29	39	64
System size	Cost ($)	Benefit ($) ⇒	1.97	3.20	4.50	6.08
Large	3		–1.03	0.20	1.50	3.08
Small	10		–8.03	–6.80	–5.50	–3.92

affect communities with large numbers of African Americans, American Indians, Hispanics, the poor, and the disabled of any race or ethnic group." (See also CDC.)[111] This was not the case historically. Citing many studies published between 1933 and 1947, Finn[73] stated that blacks had less caries than whites. On the other hand, recent data indicate that dental fluorosis is more prevalent among blacks and Hispanics,[47,111] suggesting that lack of fluoride is not an explanation for their poorer oral health.

Conclusion

For decades, the U.S. federal and state governments have promoted CWF to improve dental health of residents at low costs. Yet, in spite of the presumed savings in dental costs to Americans due to widespread use of CWF, employment of dentists is projected to grow by 16% between 2012 and 2022 (vs. 11% for all occupations),[122] and cosmetic dentistry in the U.S. has grown to be a multi-billion dollar industry.[123] We have shown that the promise of reduced dental costs was based on flawed analyses. In particular, the primary cost-benefit analysis used to support CWF in the U.S. assumes negligible adverse effects from CWF and omits the costs of treating dental fluorosis, of accidents and overfeeds, of occupational exposures to fluoride, of promoting CWF, and of avoiding fluoridated water. In assessing the benefits, it ignores important large data sets and assumes benefits to adults that are unsupported by data. Thus this analysis, as well as other economic analyses of CWF (Appendix 2), falls short of reasonable expectations for a cost-benefit analysis from a societal perspective. Minimal correction of methodological problems in this primary analysis of CWF gives results showing substantially lower benefits than typically claimed. Accounting for the expense of treating dental fluorosis eliminates any remaining benefit.

Disclaimer Statements

Contributors Both authors have contributed substantially to conception of the study, analysis and interpretation of data, drafting of the article, and critical revision of the article. Both authors have given final approval to the article as submitted.

Funding No outside funding was received for this project.

Conflicts of interest The authors have no conflicts of interest to declare.

Ethics approval Ethical approval was not required.

Acknowledgements

The authors wish to thank the reviewers for their helpful comments and a number of individuals for providing information.

Appendix 1: State governments repeating the $1 saves $38 claim

This appendix gives a list of U.S. State governments, other U.S. government agencies, and Canadian sources that repeat the claim that $1 saves $38. Mississippi and Oregon did not repeat CDC's claim of $1 saves $38. We include them in the list because they repeat the net savings PPPY estimated by Griffin *et al.*[10] Mississippi provided its own cost estimate ($1 to $2 PPPY), but the estimated net savings are from Griffin *et al.*[10] All URLs were last accessed on August 13–15, 2013, except Canadian sources, which were last accessed on October 15, 2013. † indicates state legislative records. The list may not be exhaustive.

1. *Alabama*: "For most cities, every $1 invested in fluoridation saves $38 in dental treatment costs." http://medicaid.alabama.gov/documents/2.0_Newsroom/2.5_Presentations/2.5_Medical_Services_Presentations/2.5_OHCA_Goode_Fluoridation_9-23-10.pdf
2. *Alaska*†: "It is one of the most efficient ways of providing cost effective preventative health care; every $1 spent on fluoridation saves $37 in future dental expenses." http://www.legis.state.ak.us/basis/get_single_minute.asp?session=24&beg_line=00787&end_line=00956&time=1605&date=20060228&commHES&house=H
3. *Arizona*: "Research shows that every $1 invested in water fluoridation saves $38 in unnecessary costs for dental treatment." http://directorsblog.health.azdhs.gov/?p=1072
4. *Arkansas*: "Fluoridation saves money. According to the the Centers for Disease Control and Prevention (CDC), every $1.00 spent on fluoridation prevents $38 in dental treatment." http://www.healthy.arkansas.gov/programsServices/oralhealth/Documents/FactSheetFluoridation.pdf
5. *California*: "Every $1 spent on fluoridation saves $38 in dental treatment costs." http://www.cdph.ca.gov/programs/Pages/FluoridationInformation.aspx
6. *Colorado*: "Fluoridation is proven to reduce tooth decay over a person's lifetime, and is a cost-effective prevention strategy, saving $38 for every $1 invested and preventing up to 40 percent of tooth decay." Select "The State of Health – Full report" on http://www.colorado.gov/cs/Satellite/HealthCareReform/CBON/1251641417543
7. *Connecticut*: "Every dollar spent on fluoridation saves $38 in avoided dental bills." http://www.ct.gov/dph/lib/dph/drinking_water/pdf/Water_Fluoridation_Fact_Sheet.pdf
8. *Delaware*: "In fact, every $1 invested in fluoridation saves at least $38 in costs for dental treatment." http://www.dhss.delaware.gov/dhss/pressreleases/2013/cdcfluoridationaward-021313.html
9. *Florida*: "The return on investment is tremendous — with various studies reporting $38–$80 in dental treatment cost savings for each dollar invested in community water fluoridation." http://www.doh.state.fl.us/family/dental/perspectives.pdf
10. *Georgia*: "Water fluoridation has been shown to reduce dental decay by 20–40% in fluoridated communities, and results in a savings of $38 in future

dental expenditures for each $1 invested in fluoridation." http://www.dph.ga.gov/programs/oral/index.asp

11. *Illinois*: "Studies have shown that for every dollar invested in fluoridation, as much as $38 is saved in dental treatment costs." http://www3.illinois.gov/PressReleases/PrintPressRelease.cfm?RecNum=2846
12. *Indiana*: "CDC data shows that for every dollar spent on water fluoridation, $38 are saved in reduced costs for dental care." http://www.in.gov/isdh/23287.htm
13. *Iowa*: "In fact, every $1 invested in water fluoridation saves $38 in dental treatment costs." http://publications.iowa.gov/6430/1/may_jun2008%5B1%5D.pdf
14. *Kansas*: "For most cities, on average, every $1 spent toward community water fluoridation saves $38 in dental treatment costs." http://www.kdheks.gov/ohi/download/Burden_of_oral_disease_in_Kansas.pdf
15. *Louisiana*: "Each $1 spent saves $38 in future dental treatment costs." http://new.dhh.louisiana.gov/assets/oph/Center-EH/operator/04-FlouridePresentation_Exercise.pdf
16. *Maine*: "In fact, for every dollar spent on community water fluoridation up to $42 is saved in treatment costs for tooth decay." http://www.maine.gov/dhhs/mecdc/population-health/odh/water-fluoridation.shtml
17. *Maryland*: "For most cities, every $1 invested in community water fluoridation saves $38 in dental treatment costs." http://phpa.dhmh.maryland.gov/oralhealth/docs1/community-water-fluoridation.pdf
18. *Massachusetts*: "In fact, for every dollar spent on community water fluoridation, up to $38 is saved in treatment costs for tooth decay." http://www.mass.gov/eohhs/docs/dph/com-health/oral-fluoride-community-water-factsheet.pdf
19. *Michigan*: "For most cities, every $1 invested in water fluoridation saves $38 in dental treatment costs." http://www.michigan.gov/documents/mdch/2012_MOHC_CWF_Tool_Kit_395210_7.pdf
20. *Minnesota*: "Recently published CDC studies have indicated that, for most cities, every $1 invested in water fluoridation saves $38 in dental treat ment costs." http://mn.gov/health-reform/images/WG-PPH-2012-04-Public-Comments-Minnesota-Fluoridation-Plan.pdf
21. *Mississippi*: "In Mississippi, the cost of water fluoridation is usually between one and two dollars per person per year and saves $16 – $19 per person per year in dental treatment costs." http://www.msdh.state.ms.us/msdhsite/_static/resources/1067.pdf
22. *Missouri*: "For most cities, every $1 invested in water fluoridation saves $38 in dental treatment costs." http://health.mo.gov/living/families/oralhealth/pdf/oralhealthbrochure.pdf
23. *Nevada*: "It has been estimated that for every one dollar invested in community water fluoridation there is a savings of approximately $38 or more in averted dental treatment costs." http://health.nv.gov/PDFs/OH/BurdenOfOralDisease2012.pdf
24. *New Jersey*†: "An analysis by the CDC has found that, in communities of more than 20,000 people where it costs about 50 cents per person to fluoridate the water, every one dollar invested yields $38 savings in dental treatment costs." ftp://www.njleg.state.nj.us/20082009/A4000/3709_I1.DOC
25. *New York*: "Every dollar spent on fluoridation on average saves $38 in avoided dental bills." http://www.health.ny.gov/prevention/dental/fluoridation/cost.htm
26. *North Carolina*: "For every dollar spent on community water fluoridation, approximately $38 is saved in treatment costs for tooth decay." http://www.ncdhhs.gov/dph/oralhealth/services/fluoride.htm
27. *North Dakota*: "According to the U.S. Centers for Disease Control and Prevention, for every dollar spent on community water fluoridation, up to $38 is saved in treatment costs for tooth decay." http://www.ndhealth.gov/oralhealth/Publications/2012-2017_Oral_Health_State_Plan.pdf
28. *Ohio*: "Every dollar spent on fluoridation saves more than $40 in dental care." http://www.odh.ohio.gov/features/odhfeatures/PublicHealthWeek/Friday.aspx
29. *Oklahoma*: "For most cities, every $1 invested in water fluoridation saves $38 in dental treatment costs." http://www.ok.gov/health/Child_and_Family_Health/Dental_Health_Service/Community_Water_Fluoridation_Program/
30. *Oregon*: "Saves per person per year: $15.95 in small communities; $18.62 in large communities." http://public.health.oregon.gov/PreventionWellness/oralhealth/Documents/fluoride-program-module1.pdf
31. *Pennsylvania*†: "However, for most cities, every $1.00 invested in water fluoridation saves $38.00 in dental treatment costs." http://www.legis.state.pa.us/WU01/LI/CSM/2009/0/25_X.pdf
32. *Rhode Island*: "For every dollar spent on community water fluoridation, up to $38 is saved in treatment costs for tooth decay." http://www.health.ri.gov/healthyliving/oralhealth/about/fluoridation/
33. *South Carolina*: "For most cities, every $1 invested in community water fluoridation saves $38 in dental treatment costs." http://www.scdhec.gov/health/mch/oral/docs/water_fluoridation_flyer.pdf
34. *Tennessee*: "Every dollar spent on fluoridation saves $38 in avoided dental bills." http://health.tn.gov/oralhealth/communityBenefits.html
35. *Texas*: "A CDC study found that for communities with 20,000+ residents, every $1 invested in community water systems with fluoridation yields $38 in savings from fewer cavities treated." http://www.dshs.state.tx.us/dental/Oral-Health-in-Texas-2008-Report.doc
36. *Utah*: "… in most communities, every $1 invested in fluoridation saves $38 or more in treatment costs." http://health.utah.gov/oralhealth/resources/oralHealthReport_2011webFinal.pdf
37. *Vermont*: "For every dollar spent on fluoridation, up to $38 is saved in costs associated with dental care." http://healthvermont.gov/family/dental/fluoride/
38. *Virginia*: "CDC recommends water fluoridation as a safe, effective, and inexpensive method of preventing decay; every $1 invested in fluoridation saves approximately $38 in costs for dental treatment." https://www.vdh.virginia.gov/news/PressReleases/2011/110411FlouridationAward.htm
39. *Washington*: "For most communities, every $1 invested in water fluoridation saves $38 in dental

treatment costs." http://www.doh.wa.gov/Portals/1/Documents/Pubs/160-021_Fluoridate_Facts.pdf
40. *West Virginia*: "For every one dollar invested in community water fluoridation, $38 in dental treatment costs are saved." http://www.wvdhhr.org/mcfh/icah/wv_oral_health_plan_2010.pdf
41. *Wisconsin*: "For most cities, every $1 invested in water fluoridation saves $38 in dental treatment costs." http://www.dhs.wisconsin.gov/publications/P0/p00457.pdf
42. *Indian Health Service*: "Cost savings — for every $1 spent, $38 saved." http://www.ihs.gov/doh/clinicmanagement/ohpgdocs/chapter4/community%20water%20fluoridation.doc
43. *National Institute of Dental and Craniofacial Research*: "An economic analysis has determined that in most communities, every $1 invested in fluoridation saves $38 or more in treatment costs." http://www.nidcr.nih.gov/OralHealth/Topics/Fluoride/StatementWaterFluoridation.htm
44. *Chief Dental Officer of Canada*: "Cooney said the Center for Disease Control estimates every $1 invested in fluoridation saves $38 of dental treatment." http://www.insidehalton.com/news-story/2895950-fluoride-to-stay/
45. *New Brunswick*: "A study from the Centre for Disease Control in the United States estimated that for every $1 invested in community water fluoridation saves $38 in costs for dental treatment." http://www2.gnb.ca/content/dam/gnb/Departments/h-s/pdf/en/HealthyEnvironments/FluorideStatement.pdf
46. *Ontario*: "The CDC estimates $38 in avoided costs for dental treatment for every $1 invested in community water fluoridation." http://www.health.gov.on.ca/en/news/bulletin/2011/hb_20110404_2.aspx
47. *Quebec*: Institut national de santé publique du Québec. "According to the CDC, US$38 could be saved for every dollar invested in fluoridation in a community of 20,000 inhabitants." http://www.inspq.qc.ca/pdf/publications/705-WaterFluoration.pdf
48. *Saskatchewan*: "Every $1 invested in water fluoridation saves $38 in dental treatment costs." http://www.health.gov.sk.ca/Default.aspx?DN=7d4df43c-3e21-49cf-9ef2-4b1feca2b4fd
49. *Winnipeg*: "It is also the most cost-effective means of fluoride delivery, with every dollar spent on water fluoridation saving an estimated $38 in treatment costs for tooth decay." http://www.wrha.mb.ca/wave/2011/11/fluoride-facts.php

Appendix 2: Other cost-benefit studies

Earlier economic evaluations of CWF have been reviewed by White *et al.*[11] Mariño *et al.*[124] summarize a number of studies for caries prevention programs but do not discuss those studies in detail. Griffin and Jones[125] reviewed Mariño *et al.* Other studies examined dental insurance data and did not find CWF to be associated with lower utilization or costs of dental services.[126,127]

In this appendix, we comment on several additional recent CWF cost-benefit studies: Campain *et al.*[128] assessed the impact of changing dental needs over time on the cost savings from CWF in Australia. O'Connell *et al.*[129] estimated the cost savings associated with CWF in Colorado and potential savings if the unfluoridated communities were to implement CWF. Wright *et al.*[130] investigated whether it would be cost-effective to fluoridate water supplies that were not fluoridated in New Zealand. Kroon and van Wyk[131] examined whether water fluoridation is still a viable option to reduce dental caries in South Africa by addressing concerns about cost and effectiveness. Tchouaket *et al.*[132] estimate the cost savings in Quebec resulting from CWF; since this is a 2013 paper claiming to use an "innovative approach" we will comment on it separately.

Costs

As with Griffin *et al.*,[10] both O'Connell *et al.*[129] and Kroon and van Wyk[131] based their cost estimates on Ringelberg *et al.*[14] Wright *et al.*[130] hypothetically estimated capital and annual operating costs "by consulting equipment providers and operators of fluoridation systems." These studies all adopt the assumption of a 15-year replacement schedule except Kroon and van Wyk,[131] who are more detailed in the cost aspect and have a separate replacement schedule of 8 years for mechanical and electrical plant. On the other hand, Campain *et al.*[128] used a simple A$0.27 PPPY but provided no details.

Estimates of averted caries

O'Connell *et al.*[129] essentially used the base case from Griffin *et al.*[10] They used the 25% value for Effectiveness. For Incidence, they used the base case (middle row in Table 6 in the main text) with minor changes: They reduced the 0.77 and 1.09 values by 20.9% for the secular trend, but decided that the 0.43 value for age 45–65 years was too low; instead they used 1.08 and 1.31 for ages 45–64 years and ages 65 years and older, respectively, through consultation with Griffin. The resulting average averted caries is 0.2 DMFS, almost the same value (0.19 DMFS) as in Griffin *et al.*,[10] but O'Connell *et al.* applied it to all ages from age 5 years.

Campain *et al.*[128] assumed uniform but changing effectiveness for all ages from age 6 years. They picked a value within the range of numbers reported from a set of references, including several discussed in this article.[77,107,108,133] Thus they assumed that CWF effectiveness was 50% in the 1970s, 30% in the 1980s, and 25% in the 1990s. For Incidence they constructed a matrix of year versus age range from their literature search and imputed values where information was missing.

Kroon and van Wyk[131] cited the 15% Effectiveness from Petersen *et al.*,[134] and also modeled the benefit using 30% and 50%. This Effectiveness is applied to teeth, not surfaces as in the other studies. For Incidence they used local survey data by city. The

method, according to Kroon and van Wyk,[135] is to divide the DMFT survey of, say, 15-year-olds by 15–6 = 9 and assume it is the same for people of all ages, including those age 6 years and less. The authors noted that the mean DMFT for 12-year-old South African children decreased from 1.73 in 1988–1989 to 1.05 in 1999–2002 in this unfluoridated country.

Wright *et al.*[130] did not try to estimate a value for Effectiveness. For children aged 4–13 years, they compared treatment data for restorations and extractions for both deciduous and permanent teeth to calculate savings on dental fees. They used 1996 Wellington and Canterbury data without supporting the selection, since such data are available for all New Zealand and for all years. For ages 14–34 years, they used a 0.29 averted DFS number from Grembowski *et al.*[107] (but increased it to 0.59 surfaces for Maori) and assumed no effectiveness after age 34 years.

Costs of dental treatments

On productivity loss, Campain *et al.*[128] and O'Connell *et al.*[129] used approaches similar to Griffin *et al.*[10] Wright *et al.*[130] and Kroon and van Wyk[131] did not include productivity cost. Below, we note the variations in the methods of estimating dental fees in these studies.

Kroon and van Wyk[131] estimated caries in DMFT and used the average cost of two-surface fillings for the dental charge for each DMFT. Wright *et al.*[130] used the treatment database from Wellington and Canterbury for children ages 4–13 years and included both deciduous and permanent teeth. For those ages 14–34 years, they calculated the cost of a single-surface filling using an average dentist hourly rate (with inflation) and the 15 minutes time needed to put in the filling. They assumed that fillings are replaced every 8 years.

Campain *et al.*[128] and O'Connell *et al.*[129] attempted to include more-surface fillings, composite fillings, and crown or extraction costs. However, the calculations lack transparency, and there are questions as to whether the interaction between extractions and restorations is handled properly in the latter. The most serious problem with the two studies is that they calculated the dental fees plus productivity cost on a *per visit* or *per service* basis, rather than normalizing that cost to a *per surface* basis, because one visit or service may treat more than one surface. By multiplying the estimated averted DMFS by a cost per visit or service rather than a cost per surface, they overestimated the averted costs of dental services. In addition, crowns or extractions are not always due to caries, but may have other causes. Thus these approaches lead to a far worse overestimation than Assumption (6) in Griffin *et al.*'s analysis.[10]

Tchouaket et al.[132]

A paper by Tchouaket *et al.* claims to use an "innovative approach" to assess the economic value of water fluoridation for Quebec, in which only 2.7% of the population is fluoridated.[132] The presentation lacks critical information and contains fundamental errors. The authors claim that their analysis "adopted a societal perspective that allowed us to track all the costs and effects of the intervention." However, they did not include or mention the costs of treating dental fluorosis or any of the costs we discussed under "Other costs." All $ signs in this section are Canadian dollar, C$.

Tchouaket *et al.* produced $1.93, $2.05, or $2.25 PPPY as the costs of CWF, using information from the few fluoridated municipalities in Quebec. Supposedly, the three values correspond to using 3%, 5%, or 8% to amortize the subsidies received by these municipalities over 20 years. They listed several salary rates but provided no other quantitative information, thus readers are not able to repeat any calculations or confirm the numbers.

For CWF benefits, Tchouaket *et al.* did not try to estimate averted caries. Instead, they estimated the yearly costs associated with restorative dental treatments in Quebec to be $532.08, $532.87, or $534.05 PPPY, depending on discount rates. They compared these with the cost values above at various hypothetical values of CWF effectiveness, and claimed that CWF is cost-effective even at 1% effectiveness and that Quebec saves more than $560 million a year at an "expected average effectiveness of 30%."

It should be noted that the $532–$534 PPPY *restorative* expense exceeds the actual per capita spending on *all* dental services in Canada, which was reported to be $380.83 in 2009 and $399.10 in 2011.[136,137] Tchouaket *et al.* confused untreated tooth decay and dmft/DMFT (decayed, missing, or filled teeth) — only untreated decay ("d" or "D" in dmft/DMFT) requires a restoration service. A filled tooth might need a replacement at some point in the future, but definitely not every year.

The authors calculated the number of teeth restored in a year by multiplying the number of persons who used dental services within the past year, by age group, times the dmft/DMFT index for that age group. First, the average dmft/DMFT values given in the paper are clearly cumulative, not an annual increment. Only a small percentage of these would correspond to untreated decay that requires a restoration service.[xv] Second, Tchouaket *et al.*

[xv] While the level of caries experience is very high in Quebec adults aged 35–44 years, only 1.8 out of 148 surfaces are decayed (in need of treatment), on the average, and more than half of the people (55.5%) have no decayed surfaces.[138]

apparently failed to recognize that routine dental cleaning and examinations are common in developed countries, thus having used dental services does not equate to having had a tooth restored.

Data in the paper indicate that 25–61% of children (depending on age) were caries free, while 78–91% had visited a dentist in the past year; thus many of the children utilizing dental services had not had any restorations, that year or previously. The 35–44 age group had an average 20 DMFT, and 69% used dental services in the past year. Tchouaket *et al.*'s calculations assumed that each of the 69% (724,000 people) had 20 restorations in 1 year. The correct interpretation of the data is that the average Quebecer 35–44 years old had accumulated 20 DMFT between the age of about 6 and the time of the survey, about 29–38 years, or approximately 0.5–0.7 new DMFT on average per year. This is consistent with the increments of 0.2–0.6 dmft/DMFT for children that can be derived from other information in the paper.

Tchouaket *et al.* summarized fees for treatment of one cavity, including transportation costs and lost wages. A total fee for each of three categories (by type of tooth and age group) was not provided. The text and table in the paper disagree on the calculation of transportation costs, and some information in the summary table is not explained. The text indicates that those age 14 years or older require two separate trips, one for a complete examination and one for the restoration to treat one cavity. However, fees for routine dental exams should not be counted toward costs that can be saved by CWF.

The authors appear to have taken their calculated number of teeth restored for a given age group times the cost per restoration for that age group to obtain the total cost of restorations in one year for that age group. The combined total cost for the three age groups included in the analysis (5–8, 11–14, 35–44; 1.7 million people total) appears to have been averaged over the entire population of Quebec (7.9 million people) to obtain their final average of $532–$534 PPPY. This brings up the question of whether other age groups (9–10, 15–34, and 45+) were assumed to have no restorations. However, averaging (incorrectly) over the entire population rather than over the relevant age groups compensates partly for the great overestimation in the number of restorations per year.

The three values $532.08, $532.87, or $534.05 supposedly differ in the different discount rates (3%, 5% and 8%) used to calculate repeat treatment. Estimating the dental cost for replacement services is not new, but the scant description provided in two sentences does not show what the authors have done or allow readers to understand why the three results are so close.

Tchouaket *et al.* admitted that basing the 2010 economic value on caries prevalence data more than a decade old is a limitation. This is a legitimate concern due to the well known "secular decline" of caries in developed countries.[72] However, the authors argued that because the percentage of the Canadian population with at least one dental cavity has remained stable at 96%, the average DMFT in Quebec likely has remained the same or even increased. Actually, the 96% figure applies only to dentate adults aged 20–79 years. For children aged 6–11 years and adolescents aged 12–19 years, the corresponding national figures are less than 60%.[136] Factual error aside, this argument reflects their confusion with the differences between cumulative DMFT and new caries and with properly defined populations.

Appendix 3: Accidents, overfeeds and damages

A number of accidents, overfeeds, and damages caused by CWF are summarized in Table 14.

Table 14 Examples of accidents, overfeeds and damages from CWF

Location and date	Description
1. Deltona, FL September, 1994	"A tanker truck cracked open on I-4 near Deltona … and released 4,500 gallons of fluorosilicic acid in one big whoosh." It was "one of the worst chemical spills in Volusia county's history." 2,300 people were evacuated, and more than 50 people were sent to hospitals with complaints of skin and respiratory irritations, including some hours after the spill. Motorists were instructed not to wash off the chemical film with water as that could cause respiratory problems to anyone nearby. EPA officials felt it was "a significant health hazard as far as ground water." The agency ordered around-the-clock cleanup on I-4 that lasted days.
2. Lowell, AR December, 1996	Beaver Water District fluoridated Fayetteville with fluorosilicic acid and Springdale with sodium fluorosilicate powder prior to 1992. When CWF was resumed in 1996, adding Rogers and Bentonville, the decision was made to use the powder, as fumes from the liquid had severely damaged the injection facility in the past.
3. Malvern, AR March, 1997	A water plant operator at the Kimzey Regional water plant was sprayed by fluorosilicic acid at work. According to his 2012 personal account, he became 100% disabled for almost 14 years and still requires large amounts of pain medicine. He suffered permanent health damage, including losing all his teeth.
4. Charleston, SC August, 2000	A worker accidentally put the wrong chemical in the fluoride tank in the Hanahan Water Treatment Plant. The chemical "reacted; it released a large amount of heat; the fiberglass essentially melted; the gas flowed; it just burst." This resulted in a 20,000-gallon acidic mess. The total bill for cleanup and repairs was about $250,000.

Table 14 Continued

Location and date	Description
5. Wakefield, MA August, 2000	An overdose of fluoride seeped into the town water supply. Officials made door-to-door warnings around the pumping station. The public became aware only after a local news station called the town. Authorities said there were no reports of illness; but Linda Collins disagreed, ''I was crazy dizzy and I had the runs. I think it was woefully inadequate the way they notified us,'' she said. ''Because they didn't.''
6. Coos Bay, OR October, 2000	At least 3.5 million gallons of partially treated sewage has spewed into the Coos Bay after 400 gallons of fluorosilicic acid flowed into a sewage treatment plant, killing its bacteria-munching organisms.
7. Fort Wayne, IN February, 2001	About 6,000 gallons of fluorosilicic acid drained from the lower level of the filtration plant into the sewer. The fluoride tank overflowed, and caustic fumes filled the area causing difficulty breathing, chest pains, severe headache and sore eyes in plant workers. Four workers were treated in the hospital.
8. Marlboro, MA October, 2003	A valve malfunction allowed a concentrated level of fluoride to flow into the water system. Workers went door to door to alert nearby customers, flushed water mains, and shut down the plant for some time. Residents and businesses were advised to take extreme care when flushing their pipes, and not to come into contact with the water, which could cause burning, skin irritation, or both.
9. Westminster, MA November, 2005	Emergency crews responded to a chemical spill at the Regional Water Treatment Facility after one of the storage tanks leaked about 750 gallons of fluorosilicic acid. An operator and two colleagues were transported to the hospital.
10. Moncks Corner, SC April, 2006	In the Santee Cooper water treatment plant, a water plant security guard became sick after she walked through a cloud of sodium fluorosilicate. The complaints included having trouble breathing, feeling like something was constantly caught in her throat, and ''in the following weeks, Morris's hair started falling out, she developed a rash on her arms and back, and she continued to be wracked with convulsive fits of coughing.''
11. Nashville, TN March, 2007	Valve malfunctions caused a fluoride overfeed in Harpeth Valley Utilities District. The Incident Event Log showed that an operator noted abnormal measurements starting at 12:40 a.m. 9 March 2007. Plant workers went through the facility shutting off equipment, conducted frequent water samplings and measurements, performed aggressive and continuous flushing, and contacted authorities. They also prepared for door to door public notifications, fielded incoming calls, responded to media requests, and continued sampling throughout the distribution systems until 17 March 2007. They also retained an outside engineering service to review and provide recommendations for the chemical feed systems.
12. Salt Lake City, UT August, 2007	A fluoride tank overflowed at a water treatment plant. Fluoride (1,500 gallons) spilled into a pond, resulting in an advisory to avoid Parleys Creek for several days. Utility workers used sandbags and a makeshift earthen dam to contain the chemical. Four hazmat teams worked to keep the fluoride from flowing beyond a park at the base of Parleys Canyon. Water was released from a reservoir to flush the chemical from the creek.
13. Conway, AR July, 2008	A 42-inch water pipe corroded to the point of failure, due to the fluoride injection port being mounted too close to a chlorine injection port, necessitating the shutdown of a portion of the plant that was completed only in 2005.
14. Chesterfield, MO February, 2009	Approximately 200 gallons of fluoride spilled from a ruptured tanker truck, which was carrying 4,000 gallons of the chemical at Missouri American Water's central plant. The truck's driver and two employees from the plant were taken to an area hospital.
15. Anchorage, AK April, 2010	A system malfunction at Fort Richardson Water Treatment Plant caused excess fluoride in the drinking water supply. Officials warned ''anyone who lives, works on or visits the two posts in Anchorage not to drink the water … The water also should not be used to brush teeth and wash or cook food. Any ice cubes … should be thrown out.''
16. Asheboro, NC June, 2010	Tank malfunction caused approximately 60 gallons of fluoride to be dispersed into the water system. The news release said: ''Residents who consumed a large quantity of water during this period may possibly experience short-term effects such as an upset stomach, vomiting, or diarrhea. The temporary effect from skin contact, such as showering, might include slightly irritated skin.''
17. Rock Island, IL March, 2011	Hazmat crews were called to the Rock Island water treatment plant for a spill of hydrofluorosilicic acid from a tanker truck. As plant employees evacuated, crews began suiting up, working quickly to stop the leak that had begun eating through concrete.
18. England, AR April, 2011	A worker mistakenly poured about 10 to 20 gallons of fluoride into a container holding around 150 gallons of bleach. It created a dangerous gas and led to an evacuation of several businesses near the water treatment plant. The worker and an employee from a nearby business were treated for breathing problems. The county Hazmat team cleaned up the area 3 hours later.
19. Hickory, NC August, 2011	The City transferred $106,713 from capital reserve to maintenance and repair to pay for refurbishing the chemical room and to replace two fluoride tanks. The tanks leaked enough fluoride to degrade the concrete around the containment area and floor.
20. Martinsville, VA February, 2012	The city had to pay $16,450 in penalties after about 1,000 gallons of fluorosilicic acid leaked from a tank at the city water treatment plant. The spill caused the deaths of an estimated 4,445 fish. Officials said that the ground near the spill absorbed quite a bit of the acid, and how much went into the creek was unknown. ''Fluorosilicic acid is 'a very strong acid … with a very corrosive effect on any metals it touches,' and corrosion caused the pump to fail.''
21. Memphis, TN July, 2012	Fluorosilicic acid tank failure along with containment failure caused approximately 1,500 gallons of the acid to be released onto ground at the public utility. Approximately 1.5 acres were impacted. Workers cordoned off the area and placed berm along the west property line to prevent further runoff. The impacted area was to be excavated and soil properly disposed of.

CWF: community water fluoridation.

Additional incidents of acute poisoning have been described elsewhere.[139,140]

Below are the sources, which are mostly media reports, often reproduced in secondary sources, except for the following: Item 3 is a first-person account; Item 11 is an internal log of the water district obtained by request; Item 19 is a city council record; and Item 21 is a report in the National Response Center database. A compilation of other reports in this database up to February 2005 can be found in ActionPA.[141] All URLs for the sources were last accessed on August 20, 2013, except those in Item 4 that were accessed on April 10, 2014.

1. Deltona, FL. 1994. Spills snarls traffic, lives — The acid closed the road into the night, forced 2,300 from homes and sent 50 to hospitals. Agency orders around-the-clock cleanup on I-4. Orlando Sentinel. http://www.fluoridealert.org/news/fluorosilicic-acid-spill-on-florida-highway/
2. Lowell, AR. 1996. Adding fluoride costly. Carroll County News. http://www.carrollconews.com/story/print/1778486.html and phone conversation with Beaver Water District personnel.
3. Malvern, AR. 1997. The Joe Walls Story by Joe and Jodee Walls, 2012. http://arkansas.securetherepublic.com/www/archiveviewer.php?post_id=1464&post_year=2012
4. Charleston, SC. 2000. Water plant loses fluoride. The Post & Courier. http://nl.newsbank.com/nl-search/we/Archives?p_action=doc&p_docid=111F18B49B49D318&p_docnum=35 and CPW offi cials treated to plate of headaches. The Post & Courier. http://nl.newsbank.com/nl-search/we/Archives?p_action=doc&p_docid=111F1DB9C2FEDC68&p_docnum=33
5. Wakefield, MA. 2000. Norfolk could teach Wakefield about posting water alerts. Boston Herald. http://www.fluoridefreefairbanks.org/Fluoridation%20Accidents%20Local%20Coverage.html
6. Coos Bay, OR. 2000. Fluoride Spill in Oregon. The Oregonian. http://www.fluoridealert.org/news/fluoride-spill-in-oregon/
7. Fort Wayne, IN. 2001. Fluoride Spill in Fort Wayne, Indiana. The Journal Gazette. http://www.fluoridealert.org/news/fluoride-spill-in-fort-wayne-indiana/
8. Marlboro, MA. 2003. Marlboro water flooded with fluoride — Stuck valve in treatment plant caused toxic release. Worcester Telegram & Gazette. See Item 5 for URL.
9. Westminster, MA. 2005. Two water-treatment workers in hospital after fluorosilicic acid spill. Sentinel & Enterprise. http://www.fluoridealert.org/news/2-water-treatment-workers-in-hospital-after-fluorosilicic-acid-spill/
10. Moncks Corner, SC. 2006. Former water plant guard says chemical cloud made her sick. The Post & Courier. http://www.fluoridealert.org/news/former-water-plant-guard-says-chemical-cloud-made-her-sick/
11. Nashville, TN. 2007. Fluoride overfeed incident event log (March 9–17) and water advisory. Harpeth Valley Utilities District.
12. Salt Lake City, UT. 2007. Fluoride spill taints Parleys Creek. People, dogs warned to avoid stream. The Salt Lake Tribune. http://archive.sltrib.com/printfriendly.php?id=6773022&itype=NGPSID
13. Conway, AR. 2008. Conway Corp. approves funds for fluoridation. The Cabin. http://thecabin.net/stories/071608/loc_0716080001.shtml
14. Chesterfield, MO. 2009. Chesterfield: workers contain spill of approximately 200 gallons of fluoride. St. Louis Post-Dispatch. http://www.fluoridealert.org/news/workers-contain-chemical-spill-of-estimated-200-gallons-of-fluoride-in-chesterfield/
15. Anchorage, AK. 2010. Excess fluoride taints water at Anchorage military bases — Poisonous: High levels can lead to stomach ailments and even death. Anchorage Daily News. http://www.adn.com/2010/04/28/1254268/military-bases-water-supply-overloaded.html
16. Asheboro, NC. 2010. City reports over-release of fluoride. Courier-Tribune. See Item 5 for URL.
17. Rock Island, IL. 2011. Rock Island: hydrofluorosilicic acid spill at Rock Island water-treatment plant. WQAD TV. http://www.fluoridealert.org/news/hazmat-crews-respond-to-chemical-spill-at-rock-island-water-treatment-plant/. Also available in a video at http://www.youtube.com/watch?v=Hvttwsc5lh8.
18. England, AR. 2011. England: mix-up with chemicals at Arkansas water plant causes evacuation; drinking water not threatened. Associated Press reported in The Republic. http://www.fluoridealert.org/news/england-mix-up-with-chemicals-at-arkansas-water-plant-causes-evacuation-drinking-water-not-threatened/
19. Hickory, NC. 2011. City Council Action Agenda. Hickory, NC. http://www.hickorync.gov/egov/documents/1312385507_796722.pdf
20. Martinsville, VA. 2012. Council will pay penalty over spill. Martinsville Bulletin. http://www.martinsvillebulletin.com/article.cfm?ID=32276
21. Memphis, TN. 2012. Spill of 1500 gallons FSA in Memphis, TN. National Response Center Incident Report. Incident Report # 1017173 http://www.nrc.uscg.mil/reports/rwservlet?standard_web+inc_seq=1017173

Appendix 4: More on CWF effectiveness in adults

We examine two recent articles claiming to show effectiveness of CWF for adults: Slade *et al.*[109] applied SAS procedures on data from a 2004–2006 Australian survey of adults. Griffin *et al.*[110] performed a meta-analysis of 20 studies that sought to "examine the effectiveness of self- and professionally applied fluoride and water fluoridation among adults."

Slade *et al.*[109] concluded that high lifetime fluoridation exposure was associated with 11% and 10% lower DMFT (or 30% and 21% DFS) among pre-1960 and 1960–1990 birth cohorts. We show that what is attributed to CWF is better explained by differences in age distributions.

Griffin *et al.*[110] combined CWF with self- and professionally applied fluoride, which are topical treatments

and very different from CWF in many respects, e.g. the applications or dosages are controllable; it does not appear reasonable to combine them in a meta-analysis. They "used a random-effects model, which assumes that each study was randomly selected from a hypothetical population of studies," without discussing the applicability of the model. We focus on the CWF-related studies. These authors concluded that the CWF effectiveness was a 27.2% reduction in caries. We are not able to reproduce this result, which was based on four studies reporting DMFT and one study reporting DMFS; there was no explanation how the different units were handled. As with Slade *et al.*,[109] Griffin *et al.*[110] failed to adequately account for different age distributions.

Slade et al.[109]

Thirty dentist-examiners conducted the oral examination in this national survey. For participants aged <45 years, only teeth extracted because of dental caries or periodontitis were counted as missing, but all absent teeth for older people were counted. Fluoridation exposure was determined by residential history, and a value of 0, 0.5, or 1 was assigned if the fluoride concentration at the location was less than 0.3, between 0.3 and 0.7, or greater than 0.7 mg/l, respectively. A value of 0.5 was assigned to all localities in New Zealand, Canada, or the U.S. and 0 to all other foreign localities, without regard to the actual CWF status of the locality.

A significant portion of CWF exposure status was imputed: 3,779 people were considered to have valid exposure data (Complete case), meaning less than 50% of the person's residential data were missing; the missing years were assumed to be their average observed fluoridation exposure. The exposure status of the remaining 1,726 people with more than 50% missing residential data was imputed by substituting with the status of a random sample from the 3,779 people who belonged to the same geographical stratum and 10-year age group.

Samples were divided into four levels of CWF exposure, i.e. <25% (negligible), 25 to <50%, 50 to <75%, and ≥75% (prolonged) of lifetime. Given the way CWF exposure was determined, the accuracy of this classification is questionable.

Slade *et al.* use unspecified linear regression models to "age-adjust" caries experience and fluoridation exposure. They draw the main conclusion of effectiveness by comparing the "age-adjusted" DMFT/DFS scores of the "prolonged" and "negligible" groups for the cohorts born before 1960 and those born between 1960 and 1990, respectively. The observed DMFT/DFS scores are not provided. The "age-adjusted" DMFT/DFS scores are given by birth cohort and exposure group (Table 15).

Table 15 "Age-adjusted" DMFT and DFS from Slade *et al.*[109]

	% of Lifetime exposed to CWF			
	<25%	25–50%	50–75%	≥75%
Pre-1960 birth cohort				
DMFT	21.75	20.90	21.62	19.21
DFS	37.90	35.83	37.00	29.97
1960–1990 birth cohort				
DMFT	8.91	9.53	8.88	7.61
DFS	15.89	18.01	15.65	12.41

CWF: community water fluoridation; DMFT: decayed, missing, or filled teeth.

The scores reported in Table 15 are not consistent with the conclusion that CWF exposure is effective. The scores for the two middle exposure levels were interpreted as "suggested a dose-response relationship." This is an unreasonable explanation, as an apparent difference in DMFT/DFS is lacking among the first three exposure categories. In addition, exposure levels were defined by cumulative residential status relative to age. For example, a person who lived in places with a fluoride concentration of 1 mg/l for 50 years and 0.25 mg/l for 20 years (treated as 0 mg/l, as 0.25 is less than 0.3) would have been assigned to the 50 to <75% exposure group, which, according to their results, gets no benefit relative to someone living all 70 years in nonfluoridated areas.

There are also questions regarding the validity of their use of linear regression models to "age-adjust." Calculation from data provided by Slade *et al.* (shown in Table 16) reveals that some cells have few or no people. In particular, the category of ≥75% exposure level is clearly much younger than the other three exposure categories. Given the large difference in DMFT/DFS between the pre-1960 and 1960–1990 birth cohorts (Table 15), and the large difference in age distributions between the first three exposure categories and the fourth category (Table 16), it is not surprising that the ≥75% exposure category would have lower DMFT/DFS scores than the other exposure categories. Hence the differences in caries attributed to CWF between the <25% and

Table 16 Number of people and age distributions in the 2004–2006 Australian National Survey (calculated from information in Slade *et al.*[109])

	% of lifetime exposed to CWF				
	<25	25–50	50–75	≥75	All categories
15–24	65	10	17	154	246
25–34	91	19	39	268	416
35–44	174	103	187	301	765
45–54	177	143	365	108	792
55–64	212	236	394	0	842
≥65	192	393	134	0	718
Total	910	903	1,135	831	3,779

CWF: community water fluoridation.

≥75% exposure groups are probably due to inappropriate handling of age distributions.

There are other unexplained discrepancies. For example, the differences in DMFT or DFS between the <25% and ≥75% exposure groups given in the text are not consistent with the numbers reproduced in Table 15. In particular, the DFS difference in the pre-1960 cohort was said to be 11.10 or 30%, but the numbers indicate 7.93 or 21%.

Griffin et al.[110]

This 2007 article included nine CWF studies (Table 17).[51,107,133,142–147] Few, if any, of the studies can be considered high quality studies appropriate for examining the effects of CWF. Four studies involved concentrations greater than those used for CWF (0.7–1.2 mg/l).[51,133,143,145] In all, but one study,[146] the examiners were probably not blind to the location of a subject's residence. Eight studies were cross-sectional, and the towns compared may have simply differed for reasons having nothing to do with CWF. The one study categorized as "prospective" is in essence a cross-sectional study that compares caries increment over an 18-month period, since no "intervention" was started or changed at the onset of the period.[143]

Only four of the nine studies were conducted in the U.S. Of these, two were examined earlier in this paper.[51,107] Below we offer a few general remarks, followed by comments on the remaining studies, especially the other two U.S. studies.[142,143]

As we discussed earlier, assessment of dental caries in adults is difficult. Wiktorsson *et al.*[144] described difficulties in judging caries prevalence based on fillings (due to practices such as preventive fillings for discolored fissures on occlusal surfaces) and in defining new caries incidence, since the majority of the primary caries lesions are only enamel lesions, possibly arrested caries in many cases.

In some studies,[133,145,146] the reported age distributions suggest that the low fluoride groups were older than the fluoride groups. Griffin *et al.*[110] do not seem to have considered this difference in the age distributions in their analysis.

In the context of testing the hypothesis that adults benefit by continuing to drink fluoridated waters, the progression of the differences in caries is important. Englander and Wallace,[142] Murray,[133] and Stamm *et al.*[145] each reported narrowing of the differences in mean DMFT between the low fluoride and fluoride groups with increasing ages for lifetime residents. The logical conclusion is that drinking fluoridated water is not helpful beyond a certain age.

Englander and Wallace[142] examined 896 and 935 adults aged 18–59 years from two Illinois towns, Aurora (1.2 mg/l) and Rockford (0.1 mg/l, referred to as "fluoride deficient"). All subjects were examined by the first author. The caries experience was found to be significantly less in the subjects from Aurora, which was attributed to the different fluoride levels in their drinking water. We offer some observations that disagree with that conclusion.

The differences in mean DMFT presented for the two towns were 5.22, 8.14, 6.62, 5.59, and 5.76 for the 18–19, 20–29, 30–39, 40–49, and 50–59 years old age groups, respectively. The mean years of consuming the respective waters in either city were increased by about 10 years for each additional 10 years age group. However, the difference in mean DMFT decreased for age groups above 29 years (for DMFS, the corresponding differences in the means decreased slightly for ages 30–39 years, but decreased substantially for ages >39 years). If the caries difference is to be attributed to fluoride, are we to conclude that after age 29 years, consuming water with 1.2 mg/l fluoride increases caries?

The study groups from the two cities were said to have similar socioeconomic structures, but there are questions as to how similar the two groups really were. Almost everyone in Aurora (pop. 65,000) and more than half the population of Rockford (pop. 130,000) were contacted. It was found that 2% of those in Aurora over 20 years old were toothless, yet the figure was 14% for Rockford. (Anyone with less than 10 teeth was not invited to participate. The percentages of people contacted who had 1–9 teeth were not given.) A sevenfold difference in the toothless population may indicate an economic difference. Even though the edentulous people were not included in the study, the authors appeared to consider the figures representative, as they tried to adjust the measurements by adding the

Table 17 Summary of community water fluoridation (CWF) studies included in Griffin *et al.*[110]

Study	Study location	Type of study	High fluoride (>1.2 mg/l)
Eklund *et al.*[51]	USA	Cross-sectional	3.5 mg/l
Grembowski *et al.*[107]	USA	Cross-sectional	
Murray[133]	Great Britain	Cross-sectional	1.5–2.0 mg/l
Englander and Wallace[142]	USA	Cross-sectional	
Hunt *et al.*[143]	USA	"Prospective"	0.7–1.5 mg/l
Wiktorsson *et al.*[144]	Sweden	Cross-sectional	
Stamm *et al.*[145]	Canada	Cross-sectional	1.6 mg/l
Thomas and Kassab[146]	Great Britain	Cross-sectional	
Morgan *et al.*[147]	Australia	Cross-sectional	

2% and 14% toothless figures into the DMFT figures to raise the total percentage difference.

Englander and Wallace[142] reported their results in DMFT as well as in DMFS. (They wrote that differences in dental caries experience were more striking when evaluated by means of DMF tooth surfaces.) Griffin *et al.*[110] chose to use the numbers in DMFS. (The ratio of DMFT between the two towns appears to be similar to the ratio of DMFS according to Griffin *et al.*,[110] but that is because they incorrectly listed the value for the filled component instead of the DMF for Aurora.)

Hunt *et al.*[143] reported new caries incidence over an 18-month period for 424 adults aged 65 years and older from a "narrowly defined geographical area" in two rural Iowa counties. Of these subjects, 174 were lifelong residents of "fluoride deficient" nonfluoridated communities, and 250 had lived in fluoridated communities (0.7–1.5 mg/l) for various lengths of time. Those who had 5–30 years of residence in fluoridated communities had comparable or worse new caries incidence compared to the lifelong nonfluoridated subjects. The authors thus focused on the remaining 101 persons with more than 30 years of residency in fluoridated communities (40% of the fluoridated sample) to draw the conclusion of effectiveness. Griffin *et al.*[110] used only the 77 persons with more than 40 years of residency in fluoridated communities (31% of the fluoridated sample). As mentioned above, one would be tempted to conclude from Englander and Wallace[142] that drinking fluoridated water after age 29 years does not work. Here, we learn that drinking it for less than 30 or 40 years does not work.

Hunt *et al.*[143] used a cross-sectional approach to compare baseline characteristics of the two groups for those with more than 30 years of residence. After at least 30 years of exposure to fluoridated water, no statistically significant difference in DFS (coronal or root caries) was noticed. In fact, Hamasha *et al.*, describing the same study population, did not even mention fluoride as a possible factor in the long-term caries experience.[148] Apparently, only in this 18-month period was a difference observed and attributed to fluoride. In a companion paper from the same study, Hunt *et al.* indicated no significant correlation between tooth loss and residence in a nonfluoridated community.[149]

Murray[133] reported on two towns in Great Britain, one with high fluoride (1.5–2 mg/l) and one with low fluoride (0.2 mg/l). Data were reported in 5-year age groups for general samples and for dentate samples. One interesting finding was that the prevalence of edentulous persons by age was strikingly similar between the two towns, reaching about two-thirds by age 60–65 years. In the author's terms, the "M" component of the DMFT score was similar in both groups. However, one way to look at this is that fluoride ingestion had little or no effect on the likelihood that a person would have a full set of dentures by age 60–65 years. The difference in mean DMFT was fairly constant in the earlier age groups and significantly narrowed from around age 40 years in the general sample. (The pattern of narrowing difference in DMFT persists after removing edentulous samples.) Murray's samples differed greatly in their age distributions, with the high fluoride group having approximately twice the fraction (33.2% vs. 16.5%) of people in the 20–24 age group and a substantially smaller fraction (27.1% vs. 44.3%) in the 40–65 age groups. Griffin *et al.*[110] apparently included these samples without considering that it might not be appropriate.

Wiktorsson *et al.*[144] compared adults 30–40 years old in Swedish towns with 1 or 0.3 mg/l fluoride. Griffin *et al.*[107] indicate blinded examiners and unspecified fluoride concentrations, but these descriptions do not fit the actual paper — a single examiner performed examinations in the respective communities and was unlikely to have been blind to subjects' geography. Persons with non-representative water sources were not examined. After discussing difficulties in scoring caries in adults, Wiktorsson *et al.*[144] report that the community with "optimal" fluoride had "significantly better" dental health status. However, without summary data for age subgroups, the picture is not entirely clear — the presented scatter plots for filled surfaces and for decayed surfaces (for ages 31–43 years) do not appear to suggest a benefit for continuing consumption of fluoridated water. (This study reports in tooth surfaces only and uses linear regression analysis.)

Stamm *et al.*[145] deal with 1.6 and 0.2 mg/l fluoride in Canada, and the examiners were not blind to their subjects' place of residence. The study excluded people with fewer than eight teeth. Griffin *et al.*[110] included the 17–19 year old group in the total sample from Stamm *et al.*,[140] although the 15–19 year olds in Murray[133] were excluded. The low fluoride group included only 1.5% in that age group, versus 6% in the fluoride group. Ages 60+ years made up nearly 18% of the low fluoride group but only 12% of the fluoride group. With respect to progression, the differences in mean DMFT between the high and low fluoride groups decreased with the older age groups, from 5.1 at ages 30–39 years to 1.7 for ages 60+ years.

Thomas and Kassab[146] included only females up to 32 years old, while they were hospitalized to give birth. A single hospital was used by women from a fluoridated island community (Anglesey) and several nonfluoridated mainland communities in Wales (United Kingdom); lifelong residents were included in the study. Although the authors indicate no

significant differences in age group structure of the samples from the two areas, the data show that Anglesey had more in the youngest (<20) age group, 24.1% versus 12.9% and fewer in the oldest (25–29 and 30–32) age groups, 30.0% and 5.9% versus 36.5% and 9.6%. The island of Anglesey was chosen for a demonstration fluoridation study in the 1950s. The experiment was terminated after only 5 years and the whole island was fluoridated based on the mean dmft index for 5-year-old children.

Morgan *et al.*[147] analyzed data for a group of Royal Australian Navy recruits, mostly males, ages 15–24 years, and with limited education. Griffin *et al.*[110] used only the results (mean DMFT scores by fluoride history) for 20–24 year olds (208 recruits). Morgan *et al.* indicated only that approximately 20% and 30% of the total sample (1,100 recruits) were considered "fluoridated" and "nonfluoridated" (determined by residential history), respectively, and included in the calculation of the mean DMFT scores. Griffin *et al.* used the percentages to impute the sizes of the "fluoridated" and "nonfluoridated" groups to be 42 and 62, respectively.

Appendix 5: More on the CWF effectiveness in Truman *et al.*[80]

Despite a reference to 21 papers, Truman *et al.*[80] based their conclusion of CWF effectiveness on 14 studies grouped into three groups:

- Studies starting or continuing CWF with before and after measurements (Group A-On)
- Studies stopping CWF with before and after measurements (Group A-Off)
- Studies starting or continuing CWF with only post measurements (Group B-On)

They calculated a number of "estimates of effectiveness" using two formulas:

Group A (before-and-after):
$$\{(NoF_{pre} - NoF_{post}) - (F_{pre} - F_{post})\} \,/\, NoF_{pre}$$
Group B (post measurements only):
$$(F_{post} - NoF_{post}) \,/\, NoF_{post}$$

The measures were mostly DMFT or dft. See Table 5 for summaries.

The median of the estimates thus calculated for each group was taken to represent the CWF effectiveness for each type of studies, even though median can be sensitive to the studies or estimates included in the set. The results were 29.1% for Group A-On (based on 21 estimates from 7 studies), 50.7% for Group B-On (based on 20 estimates from 7 studies), and 17.9% for Group A-Off (based on 5 estimates from 3 studies). With these numbers the authors concluded that "strong evidence shows that CWF is effective." Below, we discuss a number of problems.

Selection of studies: Of the 14 studies, only one 1956 article is a U.S. study.[93] The two large-scale, multimillion dollar NIDR surveys were not included, peculiar as this review was to be the basis for setting goals for U.S. public policies. Szpunar and Burt,[49] a study co-authored by the organizer of the 1989 Michigan Workshop, was not included, nor was Shiboski *et al.*,[121] a CDC-funded study examining caries in California children by ethnicity and head-start (or low income) status. One would expect the authors of Truman *et al.*[80] to make particular efforts to include this study because (1) the Pacific Region was the least fluoridated region and hence the main target of a new push for CWF and (2) they posed "What is the effectiveness of CWF in reducing socioeconomic or racial and ethnic disparities in caries burden?" as an important unanswered question.

Among the included studies, Loh[96] is a review article providing partial information from a 1970 paper; it failed to meet the authors' stated criteria for inclusion. Another inappropriate inclusion was Hawew *et al.*,[103] a Libyan study with the goals of demonstrating feasibility of collecting data and recording the caries prevalence in Benghazi (0.8 mg/l). The paper also reports data for a small rural area with 1.8 mg/l fluoride concentration, but the comparison of 0.8 (within the CWF range of 0.7–1.2 mg/l) versus 1.8 mg/l (above the CWF range) is not relevant to demonstrating the effectiveness of CWF.

Some authors of the included studies have published other CWF studies, e.g. Attwood co-authored Downer *et al.*,[150] which could be a B-On study. Künzel *et al.*[151] and the many studies cited therein could be in group A-Off. These omissions are particularly surprising since group A-Off has only three studies and five estimates.

Selection of estimates: Group A-Off contains three studies and five imputed estimates: 17.9% from Attwood and Blinkhorn,[99] 29.1% and 31.7% from Kalsbeek *et al.*,[100] and –1.1% and –42.2% from Künzel and Fischer.[98] Thus the median is 17.9%.

Kalsbeek *et al.*[100] reported measurements for 15-year-olds taken in different years. Of the two before-and-after estimates imputed from this study, one was not a before-and-after comparison — the fluoridated town had stopped CWF about 6 or 7 years before the "before" point.

Künzel and Fischer[98] reported measurements for every age from 6 to 15 years. This was a large-scale multiyear study, and the sizes of each age group are significant. But instead of imputing multiple estimates from selected single-age data, as was done with some other studies, all single-age data were ignored, and only two age-range summaries were used to impute two estimates. Had Truman *et al.*[80] been consistent in the selection of estimates, the median for Group A-Off would have shifted to a negative value and changed the conclusion to no CWF effectiveness.

In contrast, four estimates were imputed from the much smaller Libyan study[103] — for each of the two ages reported, the public school data from the rural town were used twice to impute two estimates by comparing them with the public school data and, separately, with the private school data from Benghazi.

Selection of formula: Within the limited set of studies and estimates selected, the authors failed to apply their formula consistently. Two estimates for deciduous teeth from Guo *et al.*[76] were included in group A-On and two for permanent teeth in group B-On. The study clearly belongs to group A-On, as it reported before-and-after measurements for all ages and for both deciduous and permanent teeth. Instead of following their stated method and including the estimates of 300%, 211%, and 208% for the permanent teeth of the three selected age groups, they ignored the before measurements and treated them as if there were only post measurements for permanent teeth. Similarly, Evans *et al.*[97] reported measurements for 5-year-olds divided into three social classes. Truman *et al.*[80] included three Group A-On estimates, one for each social class; but the combined total for all social groups was treated as a post-only study and contributed another estimate in Group B-On.

The results from the application of the formula can be misleading. For example, the three positive estimates[99,100] in group A-Off are presented as estimates of how much CWF prevents caries. In fact, the data in these two studies, as well as other studies involving cessation of CWF, showed that there were no increases in caries after stopping fluoridation, aside from possibly a temporary and small increase shortly afterward, which could simply be reflecting the removal of the delayed eruption effect. (Within the 6-year period in Attwood and Blinkhorn,[99] the mean DMFT decreased by 0.54 in the never-fluoridated town and increased by 0.06 in the town that stopped fluoridation at the midpoint of the period. In the 9-year period that sandwiched the cessation of CWF in Kalsbeek *et al.*,[100] the DMFT decreased by 3.7 in the never-fluoridated town and increased by 0.4 in the fluoridated town; 8 years later, it further decreased by 5.6 in the former and decreased by 2.3 in the latter town.) Thus the purported positive outcomes were purely an artifact of the formula — the never-fluoridated communities had a dramatic reduction in caries without the help of CWF.

References

1 Centers for Disease Control and Prevention. Fluoridation of drinking water to prevent dental caries. MMWR. 1999;48:933–40.
2 Centers for Disease Control and Prevention. 2010 Water fluoridation statistics. 2011 [cited 2013 Aug 20]; Available from: http://www.cdc.gov/fluoridation/statistics/2010stats.htm
3 Federal Register. Proposed HHS recommendation for fluoride concentration in drinking water for prevention of dental caries. Fed Regist. 2011;76(9):2383–8.
4 U.S. Environmental Protection Agency. Estimated Per Capita Water Ingestion and Body Weight in the United States — An Update. Washington, DC: U.S. Environmental Protection Agency, Office of Water, EPA-822-R-00-001; 2004.
5 Brown RA, Cornwell DA, MacPhee MJ. Trace contaminants in water treatment chemicals: Sources and fate. J AWWA. 2004;96(12):111–25.
6 Weng C-N, Smith DB, Huntley GM. Treatment chemicals contribute to arsenic levels. Opflow. 2000;10:6–7.
7 Casale RJ. Improving chemical handling procedures can help reduce associated treatment problems. J AWWA. 2001;93(9): 95–106.
8 Mullenix PJ. A new perspective on metals and other contaminants in fluoridation chemicals. Int J Occup Environ Health. 2014;20(2):157–66.
9 Centers for Disease Control and Prevention. Cost savings of community water fluoridation. 2013 [cited 2013 Aug 8]; Available from: http://www.cdc.gov/fluoridation/factsheets/cost.htm
10 Griffin SO, Jones K, Tomar SL. An economic evaluation of community water fluoridation. J Public Health Dent. 2001; 61:78–86.
11 White BA, Antczak-Bouckoms AA, Weinstein MC. Issues in the economic evaluation of community water fluoridation. J Dent Educ. 1989;53(11):646–57.
12 Burt BA, editor. Proceedings for the workshop: cost effectiveness of caries prevention in dental public health. Results of Workshop. J Public Health Dent. 1989;49:331–7.
13 Garcia AI. Caries incidence and costs of prevention programs. J Public Health Dent. 1989;49:259–71.
14 Ringelberg ML, Allen SJ, Brown LJ. Cost of fluoridation: 44 Florida communities. J Public Health Dent. 1992;52:75–80.
15 Florida Institute of Phosphate Research. Public and environmental health. 2010 [cited 2014 Mar 31]; Available from: http://www.fipr.state.fl.us/research-area-public-health.htm
16 Centers for Disease Control and Prevention. Temporary shortages of fluoridation additives: FAQs. 2013. [cited 2014 Mar 31]; Available from: http://www.cdc.gov/fluoridation/faqs/engineering-shortages.htm
17 Florida Department of Health. The Florida fluoridation project. [cited 2014 Apr 16]. Available from: http://www.floridahealth.gov/healthy-people-and-families/community-health/dental-health/fluoridation/_documents/grant.pdf
18 Hanneman M. Memo to the Mayor and the City Council of Sacramento regarding fluoridation of the city's water supply. 2010 [cited 2013 Aug. 11]; Available from: http://fluoridefreesacramento.org/html/budget_for.html
19 Jeffery A. Water plant manager speaks on fluoride. Drayton Valley Western Review. 2008 [cited 2013 Aug 8]; Available from: http://www.fluoridealert.org/news/Water-plant-manager-speaks-on-fluoride/
20 Hill S, Olson S. Riverton City, e-mail to Lorna Rosenstein. February 6, 2009. Supplied by Waterwatch of Utah.
21 Gessner BD, Beller M, Middaugh JP, Whitford GM. Acute fluoride poisoning from a public water system. N Engl J Med. 1994;330:95–9.
22 Petersen LR, Denis D, Brown D, Hadler JL, Helgerson SD. Community health effects of a municipal water supply hyperfluoridation accident. Am J Public Health. 1988;78(6): 711–3.
23 Penman AD, Brackin BT, Embrey R. Outbreak of acute fluoride poisoning caused by a fluoride overfeed, Mississippi, 1993. Public Health Rep. 1997;112:403–9.
24 Akiniwa K. Re-examination of acute toxicity of fluoride. Fluoride. 1997;30(2):89–104.
25 Arnow PM, Bland LA, Garcia-Houchins S, Fridkin S, Fellner SK. An outbreak of fatal fluoride intoxication in a long-term hemodialysis unit. Ann Intern Med. 1994;121(5):339–44.
26 Florida Department of Health. Policy statement on community water fluoridation. 2012 [cited 2014 Apr 16]; Available from: http://www.floridahealth.gov/healthy-people-and-families/community-health/dental-health/fluoridation/_documents/policy-text.pdf

27 Stevenson J. Mayor of Layton, Utah, letter to Davis County Commission and others. March 31, 2003. Supplied by Waterwatch of Utah.
28 Sacramento. Fluoride best practices study report. Department of Utilities, City of Sacramento. April 2011 [cited 2013 Aug 8]; Available from: http://sacramento.granicus.com/MetaViewer.php?view_id=22&clip_id=2620&meta_id=362729
29 Black and Veatch. Fluoride best practices study report. 2011 [cited 2013 Aug 8]. Available from: http://sacramento.granicus.com/MetaViewer.php?view_id=22&clip_id=2620&meta_id=362730
30 Lillis R. Sacramento City Council extends fluoride program despite rising costs. The Sacramento Bee. 2012 [cited 2013 Aug 8]; Available from: http://www.sacbee.com/2012/07/30/4672955/sacramento-city-council-extends.html
31 Sterling. Cost of Living in Sacramento, CA, and in San Diego, CA. Sterling's Best Places. 2012 [cited 2013 Aug 16]; Available from: http://www.bestplaces.net/cost_of_living/city/california/sacramento and http://www.bestplaces.net/cost_of_living/city/california/san_diego
32 Jones D, Fessenden M. Watsonville fluoride battle 10 years after approval: Backers fight back as support wanes. Santa Cruz Sentinel. 2011 [cited 2013 Aug 11]; Available from: http://www.santacruzsentinel.com/ci_19416925
33 Lucariello K. Bid tabled for fluoride facility due to high cost. 2013 [cited 2014 Feb 2]; Available from: http://www.carrollconews.com/story/print/2029229.html
34 Lovell CM. Napa resists putting fluoride in its water supply. Napa Valley Register. 2012 [cited 2013 Aug 11]; Available from: http://napavalleyregister.com/news/local/napa-resists-putting-fluoride-in-its-water-supply/article_17765df6-7d4a-11e1-a426-001a4bcf887a.html
35 Capetanakis A. City of New York, Department of Environmental Protection. Letter to P.S. Beeber, 1 February 2009. Available from: http://www.scribd.com/doc/18235930/NYC-Fluoridation-Costs-2008-Feb-2-2009-Letter-Page-1 and http://www.scribd.com/doc/18235931/NYC-2008-Fluoridation-Costs-Page-2-Feb-2009-Letter
36 Black and Veatch. Fluoridation Study. Executive Summary. 2011. San Jose Water Company Project Number 169146. [cited 2014 April 14]; Available from: http://cf.valleywater.org/About_Us/Board_of_directors/Board_meetings/_2011_Published_Meetings/MG43358/AS43360/AS43364/AI43480/DO43520/DO_43520.PDF
37 Schmidt B. Fluoride would cost $5 million and take 5-plus years. OregonLive.com. 2012 [cited 2013 Sep 14]; Available from: http://blog.oregonlive.com/portlandcityhall/2012/08/fluoride_would_cost_5_million.html
38 Gillette B. Fluoride costs rising. Carroll County News. 2012 [cited 2013 Aug 11]; Available from: http://www.carrollconews.com/story/print/1830366.html
39 Niederberger H, Jensen D. City of Davis Water Fluoridation Staff Presentation. 2013 [cited 2014 Apr 8]; Available from: http://city-council.cityofdavis.org/Media/Default/Documents/PDF/CityCouncil/CouncilMeetings/Agendas/20131001/06-Fluoridation-Staff-Presentation.pdf
40 Forsyth BA. Jordan Valley Water Conservancy District, letter to S. Olsen, Citizens for Safe Drinking Water, Salt Lake City, UT. 21 April 2004. Supplied by Waterwatch of Utah.
41 Saxton B. Fluoride costs brush officials wrong way – Totals mount up as implementation figures trickle in, *Standard Examiner*. 14 August 2004.
42 Crozier S. Arkansas success. State passes fluoridation law; coalition credited with victory, *ADA News*. 2011 [cited 2013 Aug 8]; Available from: http://www.ada.org/news/5572.aspx
43 KHBS. Arkansas Foundation trying to trim fluoridation costs. KHBS-TV. 2012. [cited 2013 Aug 11]; Available from: http://www.4029tv.com/Ark-Foundation-Trying-To-Trim-Fluoridation-Costs/-/8898190/14699548/-/ryhaqx/-/index.html
44 National Research Council. Fluoride in drinking water: a scientific review of EPA's standards. Washington, DC: National Academy Press; 2006.
45 Limeback H, Robinson C. Fluoride therapy. In: Limeback H, editor. Comprehensive preventive dentistry, Ch. 16. Ames, Iowa, West Sussex, and Oxford: John Wiley & Sons, Ltd; 2012. p. 251–82.
46 National Research Council. Health effects of ingested fluoride. Washington, DC: National Academy Press; 1993.
47 Beltrán-Aguilar ED, Barker L, Dye BA. Prevalence and Severity of Dental Fluorosis in the United States, 1999–2004. NCHS Data Brief 53. Hyattsville, MD: National Center for Health Statistics; 2010 [cited 2013 Aug 8]; Available from: http://www.cdc.gov/nchs/data/databriefs/db53.htm
48 Horowitz HS. The need for toothpastes with lower than conventional fluoride concentrations for preschool-aged children. J Public Health Dent. 1992;52(4):216–21.
49 Szpunar SM, Burt BA. Dental caries, fluorosis, and fluoride exposure in Michigan schoolchildren. J Dent Res. 1988;67(5):802–6.
50 Griffin SO, Beltrán ED, Lockwood SA, Barker LK. Esthetically objectionable fluorosis attributable to water fluoridation. Community Dent Oral Epidemiol. 2002;30:199–209.
51 Eklund SA, Ismail AI, Burt BA, Calderon JJ. High-fluoridated drinking water, fluorosis and dental caries in adults. JADA. 1987;114:324–8.
52 American Association of Cosmetic Dentistry. Veneer Infographic. 2013 [cited 2013 Aug 20]; Available from: http://www.aacd.com/veneerinfographic
53 Johnstone G. Dental Veneers Cost and Procedure Details. Consumer Guide to Dentistry. [undated] [cited 2013 June 15]; Available from: http://www.yourdentistryguide.com/veneer-procedure/
54 Centers for Disease Control and Prevention. Reference Statistics on Water Fluoridation Status. 2013 [cited 2014 July 29]; Available from: http://www.cdc.gov/fluoridation/statistics/reference_stats.htm
55 Heller KE, Eklund SA, Burt BA. Dental caries and dental fluorosis at varying water fluoride concentrations. J Public Health Dent. 1997;57:136–43.
56 National Research Council. Emergency and continuous exposure guidance levels for selected submarine contaminants, Vol. 3. Washington, DC: National Academy Press; 2009.
57 Peckham S, Awofeso N. Water fluoridation: a critical review of the physiological effects of ingested fluoride as a public health intervention. Scientific World Journal. 2014;2014:293019.
58 Centers for Disease Control and Prevention. Engineering and administrative recommendations for water fluoridation. MMWR. 1995;44(RR–13):1–40.
59 Lauer B, Rubel F. Water fluoridation principles and practices, 5th edn. Denver, CO: American Water Works Association; 2004.
60 Henderson JL, Raucher RS, Weicksel S, Oxenford J, Mangravite F. Supply of critical drinking water and wastewater treatment chemicals. Denver, CO: Water Research Foundation; 2009 [cited 2013 Aug 20]; Available from: http://www.waterrf.org/PublicReportLibrary/91264.pdf
61 Camargo JA. Fluoride toxicity to aquatic organisms: a review. Chemosphere. 2003;50:251–64.
62 U.S. Environmental Protection Agency. 2012 edition of the drinking water standards and health advisories. Washington, DC: U.S. Environmental Protection Agency, Office of Water, EPA 822-S-12-001; 2012.
63 U.S. Environmental Protection Agency. Definition of regulated air pollutant for purposes of Title V. 1993 [cited 2013 Aug 8]; Available from: http://www.epa.gov/ttn/caaa/t5/meta/m17434.html
64 Code of Federal Regulations. Title 40, Chapter I, Section 302.4 – Designation of hazardous substances; 2012 July 1 Edition.
65 Hirzy JW, Carton RJ, Bonanni CD, Montanero CM, Nagle MF. Comparison of hydrofluorosilicic acid and pharmaceutical sodium fluoride as fluoridating agents — a cost-benefit analysis. Environ Sci Policy. 2013;29:81–6. Corrigendum. Environ Sci Policy. 2014;38:282–4.
66 Centers for Disease Control and Prevention. Funding Opportunity Number: CDC-RFA DP07-710. 2007 [cited 2013 Oct 14]; Available from: http://www.cdc.gov/od/pgo/funding/DP07-710.htm
67 Centers for Disease Control and Prevention. Oral Health Program Strategic Plan 2011–2014. 2011 [cited 2013 Oct 14]; Available from: http://www.cdc.gov/OralHealth/pdfs/oral_health_strategic_plan.pdf
68 American Dental Association. The state of fluoridation. 2012 [cited 2012 Jul 17]; Available from: http://www.ada.org/en/publications/ada-news/2012-archive/july/the-state-of-fluoridation
69 American Dental Association. American Dental Political Action Committee 2012 Annual Report. 2013 [cited 2013 Oct 14]; Available from: http://www.ada.org/sections/advocacy/pdfs/ADA_2012AnnualReport_FINAL_090913_SinglePage.pdf

70 Graham JR, Morin PJ. Highlights in North American litigation during the twentieth century on artificial fluoridation of public water supplies. J Land Use Environ Law. 1999;14(2):195–242.
71 McDonagh MS, Whiting PF, Wilson PM, Sutton AJ, Chestnutt I, Cooper J, *et al*. Systematic review of water fluoridation. BMJ. 2000;321:855–9.
72 Diesendorf M. The mystery of declining tooth decay. Nature. 1986;322:125–9.
73 Finn SB. Prevalence of dental caries. In: A survey of the literature of dental caries. Washington, DC: National Academy of Sciences; 1952. p. 117–73. Publication 225.
74 Hagan TL. Dental caries prevalence and tooth mortality. A study of 24,092 Georgia children in 12 communities. Public Health Reports. 1947;62:1757–72.
75 Colquhoun J. Fluorides and the decline in tooth decay in New Zealand. Fluoride. 1993;26:125–34.
76 Guo MK, Hsieh CC, Hong YC, Chen RS. Effect of water fluoridation on prevalence of dental caries in Chung-Hsing New Village, Taiwan, after 9 years. J Formosa Med Assoc. 1984;83:1035–43.
77 Brunelle JA, Carlos JP. Recent trends in dental caries in U.S. children and the effect of water fluoridation. J Dent Res. 1990;69:723–7.
78 Yiamouyiannis JA. Water fluoridation and tooth decay: Results from the 1986–1987 national survey of U.S. schoolchildren. Fluoride. 1990;23(2):55–67.
79 Hileman B. New studies cast doubt on fluoridation benefits. Chemical & Engineering News. 1989 [cited 2013 Aug 8]; Available from: http://www.slweb.org/NIDR.html
80 Truman BI, Gooch BF, Sulemana I, Gift HC, Horowitz AM, Evans CA, *et al*. Reviews of evidence on interventions to prevent dental caries, oral and pharyngeal cancers, and sports-related craniofacial injuries. Am J Prev Med. 2002;23:21–54.
81 Macek MD, Heller KE, Selwitz RH, Manz MC. Is 75 percent of dental caries really found in 25 percent of the population? J Public Health Dent. 2004;64(1):20–5.
82 Santa Clara County Public Health Department. Water Fluoridation in Santa Clara County. 2009 [cited 2014 Apr 20]; Available from: http://www.sccagingcollaborative.org/documents/WaterFluoridation.pdf
83 Harris R, Nicoll AD, Adair PM, Pine CM. Risk factors for dental caries in young children: a systematic review of the literature. Community Dent Health. 2004;21(1):71–85.
84 Barnes GP, Parker WA, Lyon TC, Drum MA, Coleman GC. Ethnicity, location, age, and fluoridation factors in baby bottle tooth decay and caries prevalence of Head Start children. Public Heath Reports. 1992;107(2):167–73.
85 Feltman R, Kosel G. Prenatal and postnatal ingestion of fluorides — fourteen years of investigation — final report. J Dent Med. 1961;16(4):190–8.
86 Komárek A, Lesaffre E, Härkänen T, Declerck D, Virtanen JI. A Bayesian analysis of multivariate doubly-interval-censored dental data. Biostatistics. 2005;6:145–55.
87 Weaver R. The inhibition of dental caries by fluorine. Proc R Soc Med. 1948;41(5):284–90.
88 Community Preventive Services Task Force. Preventing dental caries: community water fluoridation. Community Preventive Services Task Force. 2000 [cited 2013 Aug 8]; Available from: http://www.thecommunityguide.org/oral/fluoridation_archive.html
89 Centers for Disease Control and Prevention. Healthy people. 2013 [cited 2014 July 29]; Available from: http://www.cdc.gov/nchs/healthy_people.htm
90 USDHHS. Healthy People 2000. National Health Promotion and Disease Prevention Objectives. Washington, DC: DHHS Publication No. (PHS) 91-50212; 1991.
91 U.S. Department of Health and Human Services. Healthy people 2010. 21. Oral Health; 2000. Available from: http://www.healthypeople.gov/2010/document/HTML/Volume2/21Oral.htm
92 U.S. Department of Health and Human Services. Healthy people 2020. Oral Health: Objectives; 2013. Available from: http://www.healthypeople.gov/2020/topics-objectives/topic/oral-health/objectives
93 Arnold FJ, Dean HT. Effect of fluoridated public water supply on dental caries prevalence. Public Health Reports. 1956;71:652–8.
94 Beal JF, James PM. Dental caries prevalence in 5-year-old children following five and a half years of water fluoridation in Birmingham. Br Dent J. 1971;130:284–8.
95 Beal JF, Clayton M. Fluoridation. A clinical survey in Corby and Scunthorpe. Public Health. 1981;95:152–60.
96 Loh T. Thirty-eight years of water fluoridation — the Singapore scenario. Community Dent Health. 1996;13(Suppl 2):47–50.
97 Evans DJ, Rugg-Gunn AJ, Tabari ED, Butler T. The effect of fluoridation and social class on caries experience in 5-year-old Newcastle children in 1994 compared with results over the previous 18 years. Community Dent Health. 1996;13:5–10.
98 Künzel W, Fischer T. Rise and fall of caries prevalence in German towns with different F concentrations in drinking water. Caries Res. 1997;31:166–73.
99 Attwood D, Blinkhorn AS. Trends in dental health of ten-year-old school children in south-west Scotland after cessation of water fluoridation. Lancet. 1988;2:266–7.
100 Kalsbeek H, Kwant GW, Groeneveld A, Dirks OB, van Eck AA, Theuns HM. Caries experience of 15-year-old children in the Netherlands after discontinuation of water fluoridation. Caries Res. 1993;27:201–5.
101 Brown H, Poplove M. The Brantford-Sarnia-Stratford fluoridation caries study: Final survey, 1963. Can J Public Health. 1965;56:319–24.
102 Fanning EA, Cellier KM, Somerville CM. South Australian kindergarten children: effects of fluoride tablets and fluoridated water on dental caries in primary teeth. Aust Dent J. 1980;25:259–63.
103 Hawew RM, Ellwood RP, Hawley GM, Worthington HV, Blinkhorn AS. Dental caries in children from two Libyan cities with different levels of fluoride in their drinking water. Community Dent Health. 1996;13:175–7.
104 Provart SJ, Carmichael CL. The relationship between caries, fluoridation and material deprivation in five-year-old children in County Durham. Community Dent Health. 1995;12:200–3.
105 Rugg-Gunn A, Nicholas K. Caries experience of 5-year-old children living in four communities in North East England receiving differing water fluoride levels. Br Dent J. 1981;150:9–12.
106 Ripa LW. A half-century of community water fluoridation in the United States: review and commentary. J Public Health Dent. 1993;53:17–44.
107 Grembowski D, Fiset L, Spadafora A. How fluoridation affects adult dental caries. JADA. 1992;123:49–54.
108 Newbrun E. Effectiveness of water fluoridation. J Public Health Dent. 1989;49(5):279–89.
109 Slade GD, Sanders AE, Do L, Roberts-Thomson K, Spencer AJ. Effects of fluoridated drinking water on dental caries in Australian adults. J Dent Res. 2013;92(4):376–82; and appendices.
110 Griffin SO, Regnier E, Griffin PM, Huntley V. Effectiveness of fluoride in preventing caries in adults. J Dent Res. 2007;86(5):410–5; and appendices.
111 Centers for Disease Control and Prevention. Surveillance for dental caries, dental sealants, tooth retention, edentulism, and enamel fluorosis — United States, 1988–1994 and 1999–2002. MMWR. 2005;54(No. SS–3):1–44.
112 Zimmermann ER, Leone NC, Arnold FA Jr. Oral aspects of excessive fluorides in a water supply. JADA. 1955;50:272–7.
113 Russell AL. Fluoride domestic water and periodontal disease. Am J Public Health. 1957;47:688–94.
114 Brown LJ, Lazar V. Dental procedure fees 1975 through 1995: how much have they changed? JADA. 1998;129:1291–5.
115 California Department of Health Care Services. 2012 Denti-Cal Schedule of Maximum Allowances. In: Medi-Cal Dental Program Provider Handbook. California Department of Health Care Services; 2012. p. 5–112.
116 Johnston DC. First look at US pay data, it's awful. 2011 [cited 2013 Aug 8]; Available from: http://blogs.reuters.com/david-cay-johnston/2011/10/19/first-look-at-us-pay-data-its-awful/
117 Featherstone JD. Prevention and reversal of dental caries: Role of low level fluoride. Community Dent Oral Epidemiol. 1999;27:31–40.
118 Centers for Disease Control and Prevention. Community Water Fluoridation: Questions and Answers. 2013 [cited 2013 Aug 8]; Available from: http://www.cdc.gov/fluoridation/factsheets/cwf_qa.htm
119 Centers for Disease Control and Prevention. Recommendations for using fluoride to prevent and control dental caries in the United States. MMWR. 2001;50(RR–14):1–42.

120 Burt BA, Kolker JL, Sandretto AM, Yuan Y, Sohn W, Ismail AI. Dietary patterns related to caries in a low-income adult population. Caries Res. 2006;40(6):473–80.
121 Shiboski CH, Gansky SA, Ramos-Gomez F, Ngo L, Isman R, Pollick HF. The association of early childhood caries and race/ethnicity among California preschool children. J Public Health Dent. 2003;63(1):38–46.
122 Dentists. Job Outlook. 2014 [cited 2014 Aug 5]; Available from: http://www.bls.gov/ooh/healthcare/dentists.htm#tab-6
123 American Association of Cosmetic Dentistry. Cosmetic Dentistry Continues to Surge – Market Estimated at $2.75 Billion. 2007 [cited 2013 Aug 8]; Available from: http://www.aacd.com/index.php?module=cms&page=723
124 Mariño RJ, Khan AR, Morgan M. Systematic review of publications on economic evaluations of caries prevention programs. Caries Res. 2013;47:265–72.
125 Griffin SO, Jones K. Quality of reporting in economic evaluations of interventions to prevent dental caries needs improvement. J Evid Base Dent Pract. 2013;13:109–10.
126 Grembowski D, Milgrom P. The influence of dentist supply on the relationship between fluoridation and restorative care among children. Med Care. 1988;26:907–17.
127 Maupomé G, Gullion CM, Peters D, Little SJ. A comparison of dental treatment utilization and costs by HMO members living in fluoridated and nonfluoridated areas. J Public Health Dent. 2007;67(4):224–33.
128 Campain AC, Mariño RJ, Wright FA, Harrison D, Bailey DL, Morgan MV. The impact of changing dental needs on cost savings from fluoridation. Aust Dent J. 2010;55:37–44.
129 O'Connell JM, Brunson D, Anselmo T, Sullivan PW. Costs and savings associated with community water fluoridation programs in Colorado. Prev Chronic Dis. 2005;2:A06.
130 Wright JC, Bates MN, Cutress T, Lee M. The cost-effectiveness of fluoridating water supplies in New Zealand. Aust N Z J Public Health. 2001;25(2):170–8.
131 Kroon J, van Wyk PJ. A retrospective view on the viability of water fluoridation in South Africa to prevent dental caries. Community Dent Oral Epidemiol. 2012;40(5):441–50.
132 Tchouaket E, Brousselle A, Fansi A, Dionne PA, Bertrand E, Fortin C. The economic value of Quebec's water fluoridation program. J Public Health. 2013;21:523–33.
133 Murray JJ. Adult dental health in fluoride and non-fluoride areas. 1. Mean DMF values by age. Br Dent J. 1971;131:391–5.
134 Petersen PE, Lennon MA. Effective use of fluorides for the prevention of dental caries in the 21st century: The WHO approach. Community Dent Oral Epidemiol. 2004;32:319–21.
135 Kroon J, van Wyk PJ. A model to determine the economic viability of water fluoridation. J Public Health Dent. 2012;72(4):327–33.
136 Canadian Dental Association. Dental Health Services in Canada. Facts and Figures. 2010. [cited 2014 Jan 14]; Available from: http://www.med.uottawa.ca/sim/data/Dental/Dental_Health_Services_in_Canada_June_2010.pdf
137 Canadian Dental Association. Highlights. Dental care expenditures in Canada in 2011. 2012 [cited 2014 Jan 17]; Available from: http://www.cda-adc.ca/en/services/fact_sheets/dental_expenditures_12.asp
138 Brodeur JM, Payette M, Benigeri M, Gagnon PF, Olivier M, Chabot D. Dental caries in Quebec adults aged 35 to 44 years. J Can Dent Assoc. 2000;66:374–9.
139 Fluoride Action Network. Acute Poisonings from Water Fluoridation. 2002 [cited 2013 Aug 8]; Available from: http://www.fluoridealert.org/articles/fluoridation-accidents/
140 Carton R. Middletown Maryland Latest City to Receive Toxic Spill of Fluoride in their Drinking Water. The Townsend Letter for Doctors. 1994 [cited 2013 Aug 8]; Available from: http://www.fluoridealert.org/articles/carton-1994/
141 Action PA. Fluoridation chemical accidents. 2005 [cited 2013 Aug 8]; Available from: http://www.actionpa.org/fluoride/chemicals/accidents-us.html
142 Englander HR, Wallace DA. Effects of naturally fluoridated water on dental caries in adults. Public Health Rep. 1962;77:887–93.
143 Hunt RJ, Eldredge JB, Beck JD. Effect of residence in a fluoridated community on the incidence of coronal and root caries in an older adult population. J Public Health Dent. 1989;49:138–41.
144 Wiktorsson AM, Martinsson TR, Zimmerman M. Caries prevalence among adults in communities with optimal and low water fluoride concentrations. Community Dent Oral Epidemiol. 1992;20:359–63.
145 Stamm JW, Banting DW, Imrey PB. Adult root caries survey of two similar communities with contrasting natural water fluoride levels. JADA. 1990;120:143–9.
146 Thomas FD, Kassab JY. Fluoridation in Anglesey: a clinical study of dental caries in mothers at term. Br Dent J. 1992;173:136–40.
147 Morgan MV, Stonnill A, Laslett AM. Dental caries amongst Royal Australian Navy recruits, 1988. Aust Dent J. 1992;37:201–4.
148 Hamasha AA-H, Warren JJ, Hand JS, Levy SM. Coronal and root caries in the older Iowans: 9- to 11-year incidence. Spec Care Dentist. 2005;25(2):106–10.
149 Hunt RJ, Hand JS, Kohout FJ, Beck JD. Incidence of tooth loss among elderly Iowans. Am J Public Health. 1988;78(10):1330–2.
150 Downer MC, Blinkhorn AS, Holt RD, Wight C, Attwood D. Dental caries experience and defects of dental enamel among 12-year-old children in north London, Edinburgh, Glasgow and Dublin. Community Dent Oral Epidemiol. 1994;22:283–5.
151 Künzel W, Fischer T, Lorenz R, Brühmann S. Decline of caries prevalence after the cessation of water fluoridation in the former East Germany. Community Dent Oral Epidemiol. 2000;28(5):382–9.