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OHCOW CRITIQUE OF THE WSIB SCIENTIFIC REVIEW:

A RAPID REVIEW OF OCCUPATIONAL EXPOSURES AND SARCOIDOSIS.

WSIB OPERATIONAL POLICY BRANCH, JULY 28, 2022

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BACKGROUND

In 2021 Dr. Christine Oliver, MD, MPH, MSc, FACPM and Andrew Zarnke, PhD published a review in *Chest* entitled "Sarcoidosis: An Occupational Disease?"[1] In 2022 Dr. Oliver and OHCOW staff published a case series of sarcoidosis among members of the cohort of miners in the McIntyre Powder Project (MPP).[2] Both publications provided evidence in support of an association between occupational exposure to silica and sarcoidosis.

On July 28, 2022, the Policy Branch of WSIB prepared a Scientific Review entitled "A Rapid Review of Occupational Exposures and Sarcoidosis" that, although it is not an Operational Policy, is *"intended to assess the current state of the scientific evidence for occupational exposures and sarcoidosis in order to support decision making for sarcoidosis claims among Ontario workers across various industries including but not limited to mining and construction."*[3]

In August 2023, a paper entitled "Airborne occupational exposures associated with pulmonary sarcoidosis: a systematic review and meta-analysis" by Dr. C.C. Huntley et al was published in *Occupational and Environmental Medicine*.[4] Huntley et al used a systematic review (SR) and meta-analysis (MA) methodology rather than the rapid review (RR) methodology employed by the WSIB, and came to conclusions that differed in important respects from that of the WSIB. As a result, the WSIB RR is now out of date and urgently requires revision to incorporate the results from the Huntley et al paper.

Yet on May 22, 2024, the WSIB RR was published in the journal *Occupational Medicine* with the title "Occupational exposures and sarcoidosis: a rapid review of the evidence" without having been updated to include the methodologically stronger Huntley et al SR/MA or its conclusions, which differ significantly from the RR.[5]

On June 2, 2024, OHCOW submitted a Letter to the Editor of *Occupational Medicine* highlighting some of the shortcomings of the WSIB RR. Our letter has been accepted and is pending publication.[6]

The purpose of this document is to compare in more detail the July 28, 2022 WSIB RR internal Policy Branch paper with the August 2023 Huntley et al paper, explore important differences in their findings, and identify major shortcomings of the WSIB RR.

This document also recommends that the WSIB discontinue using the current RR for guidance in the adjudication of sarcoidosis claims until a more complete systematic review of the epidemiological literature, including the Huntley et al SR/MA, is carried out. It has come to our attention that the WSIB has summarized the findings of the RR into an Adjudicative Advice document dated September 30, 2022. that is being used by adjudicators in the Occupational Disease and Survivor Benefits Program (ODSBP) to deny claims for sarcoidosis.

Furthermore, we believe the continued use by WSIB of the RR methodology to assess the scientific evidence related to occupational diseases and workplace exposures will result in denied or delayed justice for Ontario workers.

MAJOR SHORTCOMINGS OF THE WSIB RAPID REVIEW

We believe that the following are major shortcomings of the WSIB RR that underscore the need to use full systematic review methodology for assessment of the epidemiological literature associated with occupational diseases.

Scope

The WSIB RR was unnecessarily narrow in scope. The 2023 SR/MA by Huntley et al is much broader in scope.[4] The search strategy used by the WSIB was much more limited; significantly fewer studies were included; and fewer potential exposures were considered (Tables 1-3).

Rationale

The rationale given by the WSIB lacks accuracy and foundation. It is described as follows:

"Currently we lack knowledge about the occupational risk factors associated with sarcoidosis. Existing reviews are primarily narrative in nature or dated and most have not completed an exhaustive and reproduceable search of the literature or critically appraised the scientific evidence prior to synthesizing the results. Rapid reviews can provide actionable and relevant evidence to make informed decisions in a less resource intensive way."[3]

To support this rationale, the WSIB RR references Tricco et al.[7,8] Tricco et al [2017] is a WHO publication that describes the potential of a RR in informing *"pressing health system decisions"* such as those affecting prevention and control of communicable diseases in Syria.[7] While a better understanding of occupational exposures as a risk factor for sarcoidosis is important to the present and future health of potentially exposed workers in Ontario, it is not the same kind of *"pressing health system decision."*

Tricco et al in an earlier publication [2015] note: *"Further research on rapid reviews is warranted. In particular, the consequences of various methodological shortcuts should be investigated. This could be examined through a prospective study comparing the results of rapid reviews to those obtained through systematic reviews on the same topic."*[8] To our knowledge, such a prospective study has not been published to date.

Having decided to conduct an RR rather than a more comprehensive SR/MA, it is incumbent upon the WSIB to show that there is equivalency in terms of validity of outcome from these two types of reviews.

Transparency

The WSIB RR utilizes one of the "allowed" shortcuts of the RR approach, namely the use of 1 reviewer rather than the usual 2. The authors of the RR describe the single reviewer as an "*experienced reviewer*"; however, credentials and a description of his/her experience are not provided. Similarly, the second and third reviewers described under Screening and data extraction (pg. 7 of the WSIB RR) are not identified. The WSIB RR states that "the document was internally peer-reviewed"; again, there is no identification of the person(s) who performed the peer review.

Under the circumstances of this already "simplified or narrowed" review, this lack of transparency only further puts into question the reproducibility and degree of scientific rigor of the conclusions of this literature review. The experience of this single reviewer - to whom so much responsibility is given – cannot be verified. The affected Ontario worker and his/her family are asked to accept without evidence

the relevant experience of the single reviewer. The WSIB RR (page 22) suggests that the limitation of only one reviewer screening the citations and collecting the data is overcome by having a sample (10%) of the records checked by a second reviewer. The Huntley SR/MA used two independent reviewers, with differences resolved by discussion or by a third reviewer. Each is identified in the text of the review.

Lack of Updating

The WSIB RR is already out of date given the publication of the Huntley et al SR/MA. There does not appear to be a mechanism to update the RR and incorporate the findings from more recent studies. This falls short of the standard set for the WSIB by the Final Report of the Chair of the Occupational Disease Advisory Panel, which remains the foundational document setting out the WSIB's commitments in occupational disease policy-making and adjudication.[9] That report notes that in accordance with the Board's statutory duty under S. 161(3) to "monitor developments" in the scientific understanding of occupational diseases,

> WSIB staff must continuously evaluate and re-evaluate scientific studies being reported and must merge older and new information into a consistent set of evidence for use in scheduling, developing policy and adjudicating individual claims.[9]

Lack of transparency and clarity in the conduct and presentation of the results of the RR also hamper the ability of outside researchers to themselves add to the set of evidence in a consistent and reproducible way.

There is the risk that the present WSIB RR will set a precedent for the Board's future performance and use of RRs. These RRs may be produced in a similar manner and used to adjudicate occupational disease claims without scrutiny by external reviewers and organizations.

Study Selection

The WSIB RR excluded cross-sectional studies, case series, and case reports, without providing an adequate basis for this decision. Cross-sectional studies are not lower on the hierarchy of studies and can provide valuable information. They should not be excluded without cause. Case series often have high-quality exposure data that other reviews lack.

As a case series, the OHCOW 2022 article "Sarcoidosis in Northern Ontario Hard Rock Miners – a Case Series" was not considered in the WSIB RR analysis even though it was unique in its inclusion of semi-quantitative silica exposure data. However, it is listed at the end of the document under the heading *"Additional sarcoidosis documents of interest (not eligible for this rapid review – available by request)."*[3]

The WSIB RR also excluded studies of sarcoidosis in first responders exposed to World Trade Center Dust (WTC) dust. The reason given was that *"such exposures cannot be readily compared to exposures typically seen in Ontario workers."*[3] In their SR/MA of associations between occupational exposures and sarcoidosis, Huntley et al included cross-sectional studies, case series, case reports, and articles about first-responder exposure to WTC dust.

DIFFERENCES IN OUTCOME: WSIB RAPID REVIEW (2022) AND HUNTLEY ET AL (2023)

Results

As noted earlier there is a stark difference between the results found in the WSIB RR and the Huntley et al SR/MA.

The WSIB RR included 12 studies; only 2 were classified as being of acceptable quality based on analysis of bias. These were a cohort study by Jonsson et al and a case-control study by Graff et al.[10,11]

The Huntley et al SR/MA selected 81 studies for further review and meta-analysis was conducted for 12 occupational exposures.[4] Most commonly studied were silica (5 studies) and pesticides (3 studies). For mould or mildew, aluminum, nickel, and gold, 2 studies each were selected for meta-analysis. For silica, pesticides, and mould or mildew, statistically significant associations with sarcoidosis were observed. Single case-control studies revealed statistically significant associations with sarcoidosis for the following: organic dust, titanium, vegetable dust, radiation, and photocopier toner.

The Huntley et al SR/MA included 5 studies that were not included in the WSIB RR and excluded 4 studies included in the WSIB RR. Table 2 is a comparison of the 12 studies considered in the WSIB RR and the 12 studies considered in the Huntley et al SR/MA. Results of the Huntley SR/MA are summarized in Table 3.

Conclusions

The WSIB RR concluded:

- *"There is **limited** evidence for an association between silica exposure and sarcoidosis."*
- *"There is **inadequate** evidence for an association between other exposures (i.e., including, but not limited to, manufacturing, welding, agricultural occupations), in the absence of silica, and sarcoidosis."*[3]

As noted in the ODAP Chair's Report, "[a]ny review of the scientific evidence must begin with a consideration of the question one is attempting to answer using the evidence" (pg. 14).[9] A conclusion that the evidence for an association between silica exposure and sarcoidosis is "limited" elides the legally relevant question of whether the best actually available evidence tends to support the existence of a causal connection or not. Whether the evidence for such a connection should be considered settled or conclusive is relevant to prudential considerations around policy-making, but cannot be allowed to divert adjudicative decisions on individual claims from what the available evidence has to say and onto the speculative path of considering what the "missing" evidence of as yet non-existent research ***might*** say.

Such an approach would fall short of the WSIB's own commitments in this area. The law requires decision-makers to place the existing evidence for and against a causal connection between a disease and relevant exposures side by side and to judge which case is stronger. It does not allow for a decision that "the claimant has not presented enough evidence to prove his or her case or that the available evidence is insufficient to reach a decision" nor does it permit "allowing imported criteria to interfere with a just result" (p.10).[9] The finding of "inadequate" evidence for an association between sarcoidosis and other exposures falls outside this framework.

The WSIB RR also adds the following statement, casting doubt on its own conclusion that the limited evidence on silica exposure and sarcoidosis tends to support an association: *"Overall, the present body*

of evidence is small and inconsistent with methodological limitations that preclude the determination of a causal association including lack of evidence to determine a consistent threshold for duration, intensity, or quantity of exposure."[3] This is an imported criterion. It is neither a legal nor a scientific requirement and is in fact contraindicated as a relevant factor by the nature of the health condition being investigated. Sarcoidosis is an immunologically-mediated disease, like chronic beryllium disease. For such diseases, the dose of toxin required to produce the disease is variable and unpredictable. The WSIB RR assumes incorrectly that exposure thresholds have been shown to exist for such diseases and that an inability to determine these thresholds through consistent research findings fatally undermines the case for a causal association between the exposure and the disease in question, in this case sarcoidosis. This is the opposite of following the evidence where it leads.

In contrast, Huntley et al observed a statistically significant increase in risk for sarcoidosis associated with occupational exposures to silica, mould or mildew, and pesticides (Table 3).

Based on their findings, the authors concluded: *"Occupational silica, mould or mildew, and pesticide exposures are associated with increased odds of pulmonary sarcoidosis, while equipoise*[1] *persists with occupational metal and generic organic dust exposure. The number of exposures identified suggests that it is highly unlikely a single antigen is responsible for the onset of sarcoidosis – the onset is far more likely the result of a complex genetic-environment-immunological interaction."*[4]

The comprehensive nature of the Huntley et al SR/MA conclusions provides basis and room for a careful open-minded case-by-case consideration of sarcoidosis claims filed by workers in Ontario that is quite different from the restricted options offered by the WSIB RR.

RECOMMENDATIONS

1. OHCOW recommends that the WSIB discontinue using their current RR for guidance in the adjudication of sarcoidosis claims.

2. OHCOW recommends that the WSIB review and reconsider their decisions for all denied sarcoidosis claims that were adjudicated using their current RR and/or decisions that were made prior to the Huntley et al SR/MA.

3. OHCOW recommends that the WSIB use full systematic review methodology for future assessment of the epidemiological literature associated with occupational diseases.

4. OHCOW recommends that all WSIB reviews that assess the epidemiological literature associated with occupational diseases be registered with PRISMA.

[1] *Equipoise = equal distribution of weight; even balance or equilibrium*

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TABLES

Table 1: Comparison of 2022 WSIB "A Rapid Review of Occupational Exposures and Sarcoidosis" and Huntley et al 2023 "Airborne Occupational Exposures associated with Pulmonary Sarcoidosis: A Systematic Review and Meta-analysis"

	WSIB Rapid Review	**Huntley systematic review and meta-analysis**
Primary authors, expertise, affiliations	Undisclosed	**Primary author:** Dr. Christopher Huntley- Physician, West Midlands Respiratory Medicine Registrar with a specialist interest in Interstitial and Occupational Lung Diseases; Institute of Applied Health Research, University Hospitals, Birmingham, UK **5 co-authors** also have affiliations with the University of Birmingham Hospitals or Medical School
Publication Date	July 28, 2022	Aug 28, 2023
Methodology	Rapid review following PRISMA[2] guidelines	Systematic review & meta-analyses following PRISMA and MOOSE[3] guidelines
Search Strategy - databases & publication range	PubMed, CINAHL (ESBCO host) from database inception to April 2022	Medline, Embase, ZETOC, Cochrane Library, PROPERO, Open Grey from Jan 1,1958 to December 31, 2022
Number of full text articles assessed for eligibility	n=2916 titles & abstracts screened for relevance & 64 full text articles assessed for eligibility	n=7773 titles & abstracts screened & 348 full text articles assessed for eligibility
Number of eligible studies included for data extraction	n=12 excluded cross-sectional studies & case series	n=76 included cross-sectional studies, case series & case reports
Number of studies included in the review	n=12 (8 case-control, 3 cohort studies, & 1 systematic review of non-cancer occupational health risks including sarcoidosis in firefighters)	76 studies were eligible for inclusion in the compendium of occupational causes of sarcoidosis.

[2] PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses
[3] MOOSE = Meta-analysis Of Observational Studies in Epidemiology

Number of studies that examined individual occupational exposures associated with sarcoidosis	n=11: silica n=6 multiple occupational or environmental exposures (metal/wood dusts, insecticides, mold or jobs in teaching, manufacturing, welding & navy enlisted personnel) n=5	n=83: silica n=33 iron n=13 aluminum n=12 WTC dust n=9 chromium n=8 titanium n=8
Number of studies included in the meta-analyses	Not applicable as no meta-analysis was done	n=12 silica n=5 (4 case-control, 1 cohort) pesticides n=3 case-control mold & mildew n=2 case-control gold n=2 case control aluminum n=2 case-control nickel n=2 case-control
Risk of bias & quality assessment	Scottish Intercollegiate Guidelines Network (SIGN) and AMSTAR-2 (assess systematic reviews of occupational exposures)	Newcastle-Ottawa scale adapted for cross-sectional, cohort & case-control studies & Joanna Briggs Institute critical appraisal tool adapted for case series & case reports

Table 2: Comparison of Cohort or Case-Control Studies Considered in the Reviews

	Studies included in the WSIB Rapid Review (2022)	**Studies included in the meta-analysis portion of the Huntley et al paper (2023)**
Cohort Studies		
Gorham et al (2014)	✔	x
Jonsson et al (2019)	✔	✔
Vilborg et al (2017)	✔	x
Case-Control Studies		
Graff et al (2020)	✔	✔
Barnard et al (2005)	✔	✔
Rossman et al (2009)	✔	x
Newman et al (2004)	✔	✔
Rafnsson et al (1998)	✔	✔
Kucera et al (2003)	✔	✔
Bejer et al (2020)	✔	✔
Calvert et al (2003)	✔	x
Catinon et al (2018)	x	✔
Jordan et al (2011)	x	✔
Kajdasz et al (2001)	x	✔
Rjbicki et al (2004)	x	✔
Levin et al (2018)	x	✔
TOTAL STUDIES	**11**	**12**

Table 3: Results from Huntley et al Systematic Review and Meta-Analysis (2023)*		
Occupational Exposure	**Studies**	**Meta-Analysis Summary Risk Estimate**
Silica	Bejer et al (2020), Kucera et al (2003), Graff et al (2020), Jonsson et al (2019), Rafnsson et al (1998)	**OR=1.26; 95% CI 1.02-1.56**
Pesticides	Kajdasz et al (2001), Kucera et al (2003), Newman et al (2004)	**OR=1.42; 95% CI 1.09-1.85**
Mould or mildew	Kucera et al (2003), Newman et al (2004)	**OR=1.52; 95% 1.21-1.91**
Aluminum	Kucera et al (2003), Levin et al (2018)	OR=1.89; 95% CI 0.72-4.95
Nickel	Bejer et al (2020), Kucera et al (2003)	OR=1.18; 95% CI 0.65-2.14
Gold	Kucera et al (2003), Newman et al (2004)	OR=0.39; 95% CI 0.14-1.09
		Single Case Control Study Risk Estimate
Organic dust	Barnard et al (2005)	**OR=2.57; 95% CI 1.35-5.16**
Titanium	Kucera et al (2003)	**OR=3.15; 95% CI 1.02-9.68**
Vegetable dust	Kucera et al (2003)	**OR=1.82; 95% CI 1.01-3.27**
Radiation	Newman et al (2004)	**OR=1.83; 95% 1.00-3.46**
Photocopier toner	Rybicki et al (2004)	**OR=2.91; 95% CI 1.71-4.94**
Welding fume	Newman et al (2004)	OR=0.40; 95% CI 0.16-0.96

statistically significant risk estimates in bold