

**Evidence-Based Practice Group Answers to Clinical
Questions**

**Blue Light from
Digital Screens Used at Work**

A Rapid Systematic Review

By

WorkSafeBC Evidence-Based Practice Group

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September 2018



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About this report

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Published: September 2018

About the Evidence-Based Practice Group

The Evidence-Based Practice Group was established to address the many medical and policy issues that WorkSafeBC officers deal with on a regular basis. Members apply established techniques of critical appraisal and evidence-based review of topics solicited from both WorkSafeBC staff and other interested parties such as surgeons, medical specialists, and rehabilitation providers.

Suggested Citation

WorkSafeBC Evidence-Based Practice Group, Martin CW.
Blue Light from Digital Screens Used at Work
Richmond, BC: WorksafeBC Evidence-Based Practice Group; Sep 2018.

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Objective

This review aims to explore potential hazardous effects of blue light from digital screens (e.g., computer screens) used at workplaces

Background

Amongst all digital devices used in modern work life (e.g., tablets, laptops, netbooks, smart phones, digital sound/video conferencing and presentation systems) office desktop computers stand out as the essential ones.

According to a report from the US Department of Labor, computer use is higher (~80%) for managers and professionals, as well as for sales and office workers (67%) compared to other occupations.¹ A Canadian report states that computer use at work reaches 82% for clerical professions.² Since the first mainframe computers (1950s) and development of desktop computer (1970s) and word-processing systems, there has been major changes within work settings.³ Even if modern work life may offer flexible and remote work opportunities, Canada seems to have only a small percentage of employees (11%) working remotely through a full week.⁴ Hence, office computers are likely to remain as the primary digital interface for many Canadian workers for the immediate future.

After the introduction of desktop computers to office life, in 1980s studies on repetitive upper limb musculoskeletal injuries; as well as on visual signs, symptoms and discomfort related to computer usage began to appear in the literature.⁵⁻¹⁰ For example, one of the earlier observational studies (1996) reported a significantly greater number of VDU users with fundal, vitreal, or macular disturbances compared to non-VDU users.⁵ Computers were viewed as a key component of visual/video display units (VDUs).⁸ Over time electric and magnetic fields, nonionizing radiation, and in particular, blue light from digital screens were questioned as being potentially harmful.^{5, 11, 12}

The International Commission on Non-Ionizing Radiation Protection (ICNIRP) published guidelines for optical radiation to set exposure limits.¹³ These guidelines do not distinguish between working or the general population and have set their threshold for onset of damage in up to 48 hours of exposure. Blue light retinal injury (photochemically induced photoretinopathy) can develop when exposed to either to an 'extremely bright light for a short duration' (type II, short/sudden exposure) or to a 'less bright light for a longer duration' (type I, chronic exposure). Photochemical exposure limits

can be used to evaluate the risk for photochemically induced photoretinopathy. Action spectrum of optical radiation takes into account the tempering of radiation before reaching the tissue, as well as its relative sensitivity. For a phakic eye (with an intact crystalline lens), the sensitivity peaks at approximately 440 nm.

Blue light is a visible light (440 to 500 nm wavelength) at the short-wavelength side of the full visible light spectrum (380 to 760 nm).¹⁴ In the office environment blue light exposure is acquired from different sources. Not only computer monitors, but also other digital screen devices,¹⁵ as well as indoor illumination fluorescent lamps and light-emitting diode (LED) bulbs emit blue light.¹⁴ In addition, there is blue light exposure from sunlight and from personal digital devices used outside of work.¹⁶ In general, there is an increased tendency of visual discomfort during computer use amongst workers with existing refractory problems (already using eyeglasses or contact lenses).¹⁷⁻²¹ Some other preexisting health conditions and medications in use are also implied (e.g., allergies, diabetes, eye surgeries, irritable bowel syndrome, migraines, osteoarthritis, Sjogren's syndrome, cigarette smoking; antidepressants, antihistamines, beta blockers, corticosteroids, diuretics, hormone replacement therapies).¹⁵ Hence, it is difficult to disentangle the major source of exposure and confounding factors when an individual has visual complaints potentially linked to blue light exposure.

The effects of shortwave length/high energy blue light on the retina depends on exposure duration, intensity, wavelength, time (in a day), and repetitiveness (cumulative effect); hence, it is important to take into account the overall output from these effects.^{16, 22} Potentially, the host and environmental factors (e.g., genetic factors, concurrent diseases, preexisting ocular conditions, baseline sun exposure, nutrition/supplements, indoor lighting, properties of the digital screen (including glare amount, font size) play a role. As mentioned above¹³, Class I photochemical damage (i.e., blue-green toxicity), which involves intermediate molecules, develops by low light levels and long exposures. Class II photochemical damage (i.e., blue-light hazard) occurs after shorter exposure with high intensity.²³

The macula lutea of the retina provides the sharp and high resolution central vision.²⁴ Discussions on the macular pigment's protective role against blue light and harmful short wavelength radiation began as early as the late 1800s.²⁵ Clinical research on the health effects of blue light is ongoing and remains inconclusive. Many invitro²⁶⁻²⁸ and animal²⁹⁻³¹ studies explored the effects of blue light on ocular structures. They generally focused on phototoxicity from blue light which plays a role in retinal degeneration.^{19, 30,}

³¹ Connections between blue light and oxidative stress was identified. For example, a murine study by Kuse et al. ³⁰ found that the blue light increased the reactive oxygen species (ROS) generation and was found to damage the retinal cone photoreceptor cells severely. They concluded that genetic “antioxidants could potentially be used to improve the retinal photoreceptor”. A study by Marie et al. ¹⁹ reported that “blue-light exposure affected oxidative defense mechanisms by reducing mRNA expression levels of the three main proteins (SOD2, catalase, and GPX1) involved in defensive mechanisms against oxidative stress” and “RPE [retinal pigment epithelium] cells can actively neutralize ROS under oxidative conditions by generating glutathione only if the oxidative stress remains below a certain oxidative threshold.” Lin et al. ³¹ studied phototoxicity using a rat model and found that “fundus damage, decreased total retinal thickness, caused atrophy of photoreceptors, and injured neuron transduction in the retina”. Other studies highlighted some intermediate molecules, photosensitizers (e.g., rhodopsin, lipofuscin, mitochondrial respiratory chain enzymes) that play a role in the cascade of reactions towards cellular damage after absorption of light. ²³ Nonetheless, the basic message by Ham et al. ²⁹ in 1976 still holds: “The sensitivity of the retina to blue light may have more profound effects for man-made optical sources than for sunlight”.

A number of studies focused on lutein and zeaxanthin which are found in high concentrations in macula lutea of the retina (as components of the macular pigment), and are known for their antioxidant and potentially anti-inflammatory properties. ^{24, 25, 32} Hence, a number of studies advocate for supplementation with lutein and zeaxanthin to avoid or help with ocular disorders such as age-related macular degeneration (AMD), potentially associated with blue light exposure. ³³⁻³⁵

Prolonged computer use has been linked to eye symptoms (e.g., strain and ache, dryness, irritation, burning, blur, double vision). ^{17, 36, 37} The American Optometric Association (AOA) defines computer vision syndrome (CVS) as “a group of eye and vision-related problems that result from prolonged computer, tablet, e-reader and cell phone use.” ³⁸ Sometimes, the terms ‘digital eye strain’ and ‘visual fatigue’ are also used. ¹⁶ Common symptoms are transient loss of vision, blurred vision, dry eyes, headache, eye fatigue, and neck pain. The patients can sometimes present with headaches and visual symptoms similar to the ones seen with transient ischemic attack (TIA). ³⁹ To help quantify visual fatigue there are questionnaires (e.g., Six-item Visual Fatigue Scale, Computer Vision Syndrome Questionnaire) and other indicators (e.g., critical flicker–fusion frequency(CFF), blink rate and completeness, accommodative function and pupil characteristics) that can be used. ¹⁶ In general, vision screening is suggested for computer workers. ⁶

A number of narrative reviews further explain computer vision syndrome (CVS).^{8, 17, 40, 41} It is regarded as an “ocular repetitive strain disorder relating to the use of computer screens”.⁸ The symptoms are categorized as asthenopic (eyestrain, tired/sore eyes), ocular–surface related (dry/watery/irritated eyes and contact lens problems), visual (blurred vision, slowed focus change, double vision, or presbyopia), and extraocular problems (neck, back, and shoulder pain).⁸ Often, poor lighting, glare on a digital screen, improper viewing distances, small font, uncorrected vision problems, poor seating posture are listed as associated factors, with no mention of blue light exposure. The reason for this may be the fact that the majority of the CVS publications are from earlier years when the ‘blue light’ from computers was not under the research spotlight.⁴¹ Nonetheless, some recent CVS studies also have not referred to blue light. For example, the Ranasinghe study²⁰ found associations between computer office workers’ gender, longer duration of occupation, higher daily computer usage, pre-existing eye disease, not using a visual display terminal (VDT) filter [antiglare screen], use of contact lenses, weaker ergonomic practices and CVS knowledge, and presence of pre-existing eye diseases and CVS. Hasanah et al. (2017)⁴² studied the prevalence of CVS in VDT operators. They found that viewing distance (less than 50 cm from the screen), break time (shorter than 4 minutes), and non-ergonomic work posture were significantly associated with CVS occurrence with Odds ratios (OR) of 8.33, 7.28, and 5, respectively. A 2018 study³⁶ reported on the ‘tear’ content of the VDT workers, focusing on the effects of nerve growth factor (NGF) and nitric oxide synthase (iNOS), again with no reference to a blue light effect.

There are a limited number of publications bridging computer vision syndrome (CVS) with the adverse effects of blue light.^{6, 15, 16, 43} In her workplace health focused article on CVS Lurati¹⁵ states that “The use of computers has increased exposure to short-wavelength (450 nm to 495 nm on the high-energy visible light spectrum) light, which is mostly blue light, and can damage the retina and contribute to eye fatigue.”

When reviewing digital eye strain, Sheppard and Wolffsohn described the effects of blue light emitted from digital screens and in their conclusion called for consideration of this condition by eye care practitioners, and for research to provide evidence to develop treatment options.¹⁶ Isono et al.⁴³ questioned the true effect of blue light from LCD display devices. They used both subjective (questionnaires) and objective (Critical Flicker Frequency-CFF) for their assessments and found that higher blue light emissions from devices posed higher strain on eyes. They suggested using blue light blocking filters, and working in sepia mode and reducing screen

luminance. In their narrative review Coles-Brennan et al.⁶ advised prescription of colour filters (especially blue light-absorbing ones) during vision corrections as part of strategies to manage eye strain.

To help with the visual symptoms that may follow computer use and to protect the retina/macula from potential phototoxicity (i.e., light-induced retinal damage) intraocular lenses (IOLs) that filter/block blue light and eye glasses to reduce shortwave-length light in general were introduced.^{14, 44, 45} A recent industry supported randomized controlled trial found that critical flicker fusion frequency (CFF), a measure of eye fatigue, was significantly better with short wavelength–blocking eyeglasses versus non-blocking ones.⁴⁵ Intraocular lenses (IOLs) are synthetic lenses surgically implanted within the eye after removal of the natural crystalline lens during cataract operations.¹⁴ In fact, the aged lens which progressively becomes less transparent is known to lower the transmission of short-wavelength visible light (including blue light) to retina, hence protects it.¹⁴ Therefore, IOL replacements (without blue-block), as well as young/natural lenses of children which are more transparent are hypothesized to put retinal macula at an increased risk for blue light-induced degeneration. There are also opposing studies showing no significant difference in macular changes between blue light filtering and non-filtering IOLs.^{14, 46, 47} While potentially protecting macula from blue light-induced degeneration; blue light blocking IOLs are also blamed for potentially impairing colour detection, reducing scotopic sensitivity, and disturbing circadian cycle.⁴⁸ Nonetheless, with conflicting results from studies, the debate on blue-blocking IOLs continues and future studies are required.^{14, 23, 48}

With this report we aim to highlight studies that focused on blue light exposure from office computers and other digital screens used at work, and their potential hazardous effects on visual health.

Methods

- I. The **first** systematic literature search was conducted on July 20, 2018.
 - Selected commercial medical databases included Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, Health Technology Assessment, Embase, MEDLINE and MEDLINE Epub Ahead of Print, In-Process & Other Non-Indexed Citations, and Daily were searched under the

OvidSP platform.

- Relevant keywords identified through scoping searches were used and combined with appropriate Boolean Operators (i.e., 'OR', 'AND')
- Search strategy was as follows:
[(visual display unit) OR (visual display terminal) OR (video display terminal) OR (computer terminal) OR (VDU) OR (VDT) OR (blue light) OR (blue-light) OR (digital light) OR (screen light)] **AND** [(macular health) OR (macular degeneration) OR (retinal degeneration) OR (maculopathy) OR (digital eye strain) OR (blue-light-induced oxidative stress) OR (computer vision syndrome) OR (eye strain) OR (ocular discomfort) OR (blurred vision)]
- There were 833 citations identified with this search strategy. We limited the search to include citations from studies on humans, adult populations (ages 19 and up), written in English, published in the last 10 years. The number of citations were down to 271, and with removal of duplicates, was 209. We limited publications to meta-analysis, systematic reviews, randomized clinical trials, and controlled clinical trials. Abstracts for the remaining 145 citations were scanned for relevance employing the inclusion/exclusion criteria outlined below. In total, eight articles were collected in full text, and one of them was included in this review.

I. The **second** systematic literature search was conducted on August 15, 2018 using the same commercial medical databases, employing a different set of keywords

- [(blue light) **AND** (computer) **AND** (eye)]
- There were 76 citations identified with this search strategy. We limited the language to English and the number of citations was down to 70. Duplicates were removed.
- Abstracts for the remaining 51 citations were scanned for relevance employing the inclusion/exclusion criteria outlined below.
- In total, three articles which studied adult populations and were published in the last 10 years were collected in full text. One was already identified by the previous search strategy. All three

articles were included in this review.

- Additionally, by reviewing the references of the collected articles, we identified one more article to be included.

Include articles

- on blue light exposure from
 - computers/laptops/tablets
 - settings including work/offices
- focused on potential hazardous effects of blue light on ocular health
- studied adult populations
- published in English
- published in the last 10 years

Exclude articles

- on blue light blocking/filtering intraocular lenses (IOLs)
- on technical aspects of shortwave-length light-reducing eye glasses
- on blue light exposure from only LED and fluorescent light fixtures
- on blue light exposure from solely out of office use of digital screens (tablets, cell-phones, home computers, etc.)
- on exclusively night-time blue light exposure from digital screens (tablets, cell-phones, home computers, etc.)
- on nutritional studies (lutein, zeaxanthin, etc.)
- in the publication formats of single case reports, conference abstracts, narrative reviews, study protocols, letters to editors
- published prior to the last 10 years
- published in languages other than English

Results

The four selected articles (three ^{12, 24, 49} from the Ovid SP searches and one ⁴³ from the hand searches) were focused on the outcomes of blue light hazard, visual performance, visual fatigue, and macular health. The only systematic review ⁴⁹ amongst selected articles was on the effects of blue light blocking spectacle lenses on visual performance, macular health and the sleep-wake cycle. Except for the Tudosescu study ²⁴ which explicitly focused on computers; the three remaining studies explored blue light effects from various digital screens, including computers, laptops, tablets, smartphones.

Selected articles (OvidSP search)

The effect of blue-light blocking spectacle lenses on visual performance, macular health and the sleep-wake cycle: a systematic review of the literature (Lawrenson JG, 2017) ⁴⁹

Since there are claims that blue-blocking eye spectacle lenses “can alleviate eyestrain and discomfort (particularly when using computers and other digital devices), improve sleep quality and possibly confer protection from retinal phototoxicity”, Lawrence et al. aimed to study the best available research evidence on relative benefits and potential harms of these lenses in general spectacle wearing population and conducted a systematic review. Their outcome of interest was the effects of these lenses primarily, on visual performance/fatigue and secondarily, on macular health and sleep-wake cycle. They included three randomized controlled- and pseudo-randomized controlled trials (RCTs), with 136 participants in total. Because of the limited number and quality of the studies (e.g., selection, selective reporting biases, and small sample sizes) the authors were not able to undertake a meta-analysis. They used Grades of Recommendation, Assessment and Evaluation (GRADE) approach to assess the certainty of the evidence and stated that they had ‘very little’ to ‘no confidence’ in the effect estimates from the studies, as the overall certainty of the evidence using the GRADE method was ‘low’ or ‘very low’. The authors mentioned that the proxy-measure used by one of the studies (i.e., critical fusion frequency (CFF) to explore eye fatigue) may have not been the appropriate measure as it had been shown that CFF declined after reading either from paper or from e-reader. With the available evidence, the authors concluded with low certainty, that “there was no significant difference in relation to the proportion of subjects showing an improvement in symptoms of eyestrain or eye fatigue between the intervention (blue-blocking) and control spectacle lenses”. They also concluded that the current evidence was not sufficient to demonstrate

improvement of sleep by blue blocking spectacle lenses, and there were no studies that explored the effects of these lenses on macular structure or function.

Low-energy light bulbs, computers, tablets and the blue light hazard (O'Hagan JB, 2016) ¹²

The authors compared blue light emissions from lamps (CFL and LED), computer screens, tablet computers, laptops, and smartphones with the blue light hazard exposure limits from the International Commission on Non-ionizing Radiation Protection (ICNIRP). They assessed the worst case exposure conditions (e.g., staring at a visual screen for extended periods of time) and measured the spectral irradiance incident using different screen colours. All digital screens (n=25) were set to maximum brightness and the highest luminance and the blue light spectral irradiance was observed using a white screen. The authors used relevant factors (e.g., luminance to obtain the weighted values for specific blue light wavelengths) and compared them with the guideline exposure limits. Blue light hazard, determined as the ratio of blue light weighted irradiance to luminance, was accepted staying nearly constant for any given type of light source. The authors also studied the LED light sources and found that the blue light weighted radiance limit for long-term viewing was exceeded by a factor of up to three by the LED sources (the worst being the three indicator LEDs). The authors concluded that "under even extreme long-term viewing conditions, none of the assessed sources suggested cause for concern for public health" and the percentage of blue light transmitted to the retina from corneal surface was age related and children were at a higher risk.

Correlations between internal and external ocular factors and macular pigment optical density (Tudosescu R, 2018) ²⁴

The authors conducted a prospective observational study in a hospital based ophthalmology clinic. Their objective was to explore whether there was a relationship between macular pigment optical density (MPOD) and blue light from computer screens, and secondly, if there were any correlations between MPOD and glare and contrast sensibility, iris color, age, sex or refractive errors. The authors highlighted the protective role of retinal macula/macular pigment in age related macular degeneration, light induced oxidative stress, and improvement of visual performance with regards to glare and contrast. They also listed the factors that may affect the concentrations of macular pigment (e.g., smoking, exposure to blue light at 499-530 nm wavelength, the low intake of lutein and zeaxanthin; and obesity, lifestyle, the color of the iris, refractive errors like myopia, low carotenoid levels in the serum and possibly ageing). They included 83

patients (166 eyes) in total; 43 patients in study group (i.e., people working in informatics, spending time in front of the computer for a minimum of 8 hours per day, 5 days per week, for 2 years) and 40 patients in a control group (working in a medical field). They used the Heterochromatic Flicker Photometry (HFP) technique to measure absorbance of the blue light by the macular pigment, pointing to the value of MPOD (e.g., lower the value, higher the level of blue light reaching the macula). The authors categorized patients based on their MPOD levels (i.e., 0-0.25 - very low, 0.25-0.5 - low, 0.5-0.75 - good, 0.75-1 - very good). They found no significant difference between the left or right eye in terms of MPOD levels; no statistically significant correlation between the MPOD and glare of each eye, between MPOD and colour of the iris (i.e., light coloured vs. dark coloured), between the time spent working with computer, or refraction error type (hypermetropia vs myopia). The authors acknowledged the small sample size of their study and concluded that even if their findings were negative ("failed to illustrate a significant correlation between MPOD and blue-light issued by computers"); they were important for future studies on the distribution of macular pigment and the effects of blue- light on MPOD.

Additional articles (Hand search)

The effect of blue light on visual fatigue when reading on LED-backlit tablet LCDs (Isono H, 2013) ⁴³

The authors' aim was to identify factors leading to visual fatigue after viewing digital screens (on computers, tablets, mobiles, etc) constantly. They explored the relationship between visual fatigue and blue light emitted from LED-backlit tablet liquid crystal displays (LCDs). The authors hypothesized that the LED backlighting with significantly higher intensity blue light (~450 nm) was the reason for visual fatigue during reading from tablets. They used Apple iPad3 for testing and their concern was that the spectrum of blue light from iPad3 and the blue light hazard action function (regarding safety limit) were very close. When switched from white to sepia background colour the blue light emission (i.e., blue light effective radiance) decreased. The outcome of interest (visual fatigue) was measured by the Critical Flicker Frequency (CFF) at regular intervals and by subjective questionnaire responses from the five study subjects. They found that for majority of subjects the CFF variation and subjective responses on symptoms such as eye strain, blurry vision and tiredness were worse with the white background colour. The authors concluded that blue light had an effect on visual fatigue, as higher blue light emissions caused more eye strain. They suggested working in sepia mode, decreasing screen luminescence, and/or using blue light blocking filters to reduce the blue light effective radiance.

Summary

- The literature on computer vision syndrome (CVS)/digital eye strain/visual fatigue which includes discomfort and symptoms of the eyes and musculoskeletal system is a few decades old
- The literature on the physiologic effects of blue light (invitro and animal studies) is rich (e.g., blue light effect on macular pigment, retinal cells, oxidative stress, macular degeneration; hence photoretinopathy)
- There is almost a disconnect between the literature on the physiologic effects of blue light from digital screens and potentially related clinical discomfort, symptoms and signs of eyes (e.g., computer visual syndrome/digital eye strain/visual fatigue)
- The existing guidelines focus on the effects of extremely bright light exposure for a short duration of time (blue light hazard); but not on long term exposure
- One area of research is focusing on intraocular (applied during cataract operations) and spectacle lenses that filter/block blue light to prevent macular degeneration in the long run. However, this research is generally funded by optical companies and the quality of research evidence is weak
- There is insufficient research questioning the visual health effects of prolonged blue light exposure from office computers and other digital screens used at work
- When this relationship is questioned; a strong research methodology is needed to delineate the effects from concurrent blue light exposure from the sun, office illumination sources, and the digital devices used during out of work time
- Besides blue light, there are other potential internal and external factors affecting development of CVS/digital eye strain/visual fatigue. For example, improvement of office ergonomics and treatment of dry eye, correction of refractive error and management of accommodation and vergence anomalies are strongly recommended
- The American Academy of Ophthalmology [AAO] recommends that

employees have annual ophthalmology examinations to assess both refractive status as well as binocular vision after the age of 40, because antioxidant mechanisms and protective enzymes begin to decrease at this age

- Even if still controversial, there are studies suggesting use of short-wavelength blocking eyeglasses to decrease visual fatigue and discomfort from digital screens; and it is claimed that certain blue light filtering glasses do not interfere with visual performance or sleep quality
- However, until more conclusive research findings from high quality studies is available, the usage of blue light blocking/filtering glasses is controversial (e.g., potential help in protecting macular degeneration and caveats such as impaired colour detection, reduced scotopic sensitivity, and disturbed circadian cycle)
- Management of digital eye strain (or CVS) requires a tailored approach for every individual; as underlying or accompanying conditions may be different for each

Conclusion

Visible light has a cumulative effect on eye tissues and there are also other factors that must be taken into account (e.g., wavelength, intensity, duration of the light; time of the day, sources of illumination, screen glare level, distance from the screen, ergonomic conditions, comorbid health issues, preexisting eye disorders, use of contact lenses). Therefore, it is important to consider the overall effect and the long term consequences from blue light exposure. Preventive approaches, especially those that alter the potential harmful effects of blue light from computer screens are important. For example, workplace best practices to improve ergonomics at visual display units, education/awareness programs on the effects of blue light exposure, and encouragement of periodic eye examinations may be of benefit. Also, increasing awareness amongst eye professionals about the effects of blue light on macular health and the potential relation between 'computer vision syndrome' and blue light exposure from digital screens might be useful. Better quality research studies are needed to help inform conclusive policies regarding blue light exposure from digital screens at work.

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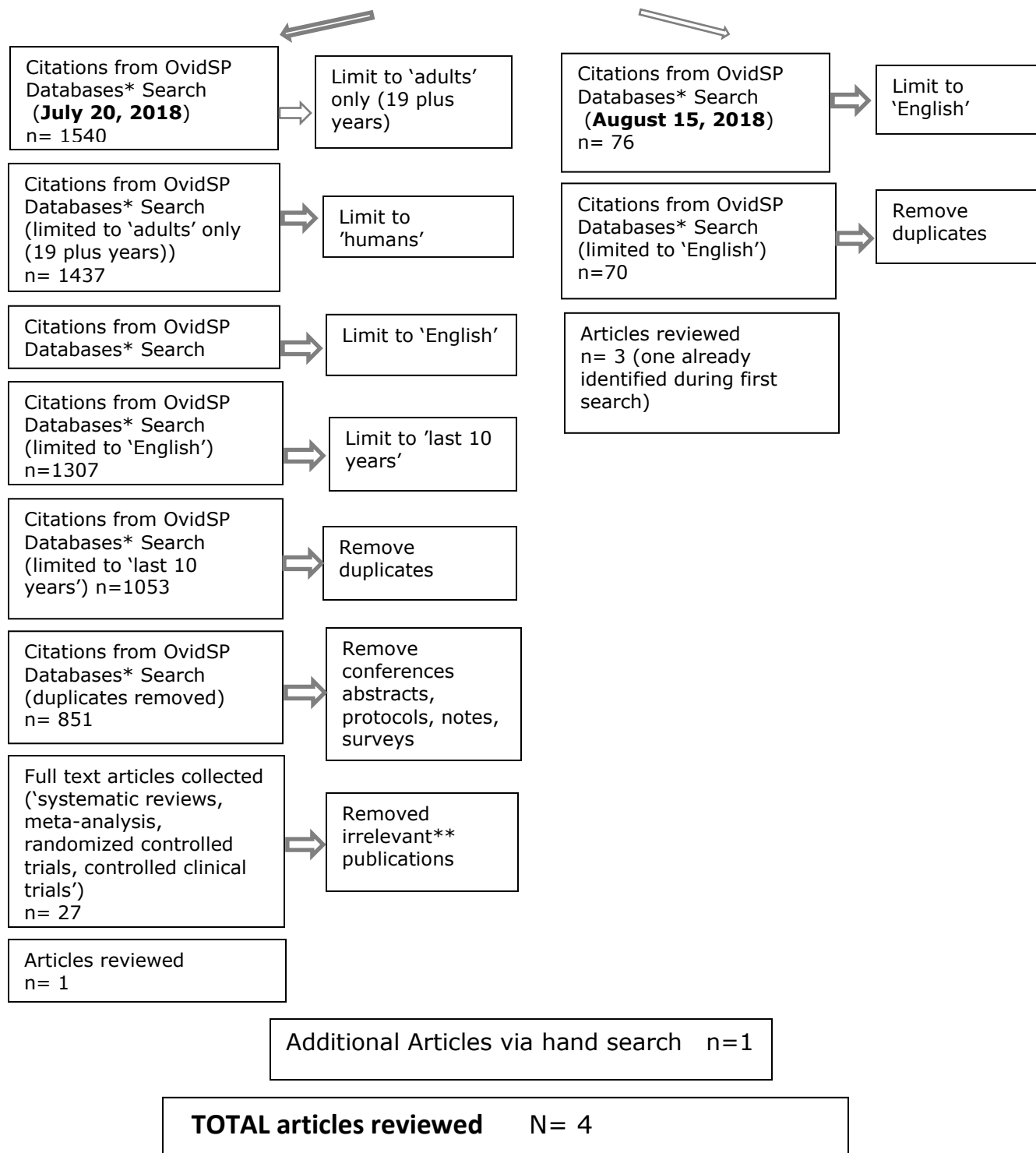
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Appendix 1

Flow Diagram (Study Selection)



* **OvidSP Databases searched:** Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, Health Technology Assessment, Embase, MEDLINE and MEDLINE Epub Ahead of Print, In-Process & Other Non-Indexed Citations, and Daily were searched under the OvidSP platform

Appendix 1

WorkSafeBC - Evidence-Based Practice Group Levels of Evidence

(adapted from 1,2,3,4)

1	Evidence from at least 1 properly randomized controlled trial (RCT) or systematic review of RCTs.
2	Evidence from well-designed controlled trials without randomization or systematic reviews of observational studies.
3	Evidence from well-designed cohort or case-control analytic studies, preferably from more than 1 centre or research group.
4	Evidence from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled
5	Opinions of respected authorities, based on clinical experience, descriptive studies or reports of expert committees.

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