Health effects of exposure to chlorination by-products in swimming pools: Position Paper

Article *in* Allergy · July 2021

DOI: 10.1111/all.15014

11 authors, including:

Mariana Couto
University of Porto
105 PUBLICATIONS **760** CITATIONS
SEE PROFILE

Luís Delgado
University of Porto
377 PUBLICATIONS **6,096** CITATIONS
SEE PROFILE

Franchek Drobnic
Shanghai Shenhua FC
160 PUBLICATIONS **2,044** CITATIONS
SEE PROFILE

Marcin Kurowski
Medical University of Łódź
51 PUBLICATIONS **795** CITATIONS
SEE PROFILE

Received: 21 February 2021 | Revised: 14 June 2021 | Accepted: 13 July 2021

DOI: 10.1111/all.15014

Allergy EUROPEAN JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY EAACI WILEY

EAACI POSITION PAPER

Health effects of exposure to chlorination by-products in swimming pools

Mariana Couto[1] | Alfred Bernard[2] | Luís Delgado[3,4,5] | Franchek Drobnic[6] | Marcin Kurowski[7] | André Moreira[3,4,8] | Rodrigo Rodrigues-Alves[9] | Maia Rukhadze[10] | Sven Seys[11] | Marta Wiszniewska[12] | Santiago Quirce[13]

[1]Centro de Alergia, Hospital CUF Descobertas, Lisboa, Portugal

[2]Louvain Centre for Toxicology and Applied Pharmacology, Institute of Experimental and Clinical Research (IREC), Catholic University of Louvain, Brussels, Belgium

[3]Basic and Clinical Immunology, Department of Pathology, Faculty of Medicine, University of Porto, Porto, Portugal

[4]Serviço de Imunoalergologia, Centro Hospitalar de São João E.P.E., Porto, Portugal

[5]Center for Health Technology and Services Research (CINTESIS@RISE), Faculty of Medicine, University of Porto, Porto, Portugal

[6]Head of Medical Services - Shenhua Greenland FC, Shanghai, China

[7]Department of Immunology and Allergy, Medical University of Łódź, Łódź, Poland

[8]Epidemiology Research Unit- Instituto de Saúde Pública, Universidade do Porto, Porto, Portugal

[9]Unidade de Imunoalergologia, Hospital do Divino Espírito Santo, Ponta Delgada, Portugal

[10]Center of Allergy & Immunology, Teaching University Geomedi LLC, Tbilisi, Georgia

[11]Laboratory of Clinical Immunology, Department of Clinical Immunology, KU Leuven, Leuven, Belgium

[12]Department of Occupational Diseases and Environmental Health, Nofer Institute of Occupational Medicine, Lodz, Poland

[13]Department of Allergy, La Paz University Hospital, IdiPAZ, and Universidad Autónoma de Madrid, Madrid, Spain

Correspondence
Mariana Couto, Centro de Alergia, Hospital CUF Descobertas, Lisboa, Portugal.
Email: marianafercouto@gmail.com

Funding information
EAACI provided funding for the group meetings.

Abstract

Concerns have been raised regarding the potential negative effects on human health of water disinfectants used in swimming pools. Among the disinfection options, the approaches using chlorine-based products have been typically preferred. Chlorine readily reacts with natural organic matter that are introduced in the water mainly through the bathers, leading to the formation of potentially harmful chlorination by-products (CBPs). The formation of CBPs is of particular concern since some have been epidemiologically associated with the development of various clinical manifestations. The higher the concentration of volatile CBPs in the water, the higher their concentration in the air above the pool, and different routes of exposure to chemicals in swimming pools (water ingestion, skin absorption, and inhalation) contribute to the individual exposome. Some CBPs may affect the respiratory and skin health of those who stay indoor for long periods, such as swimming instructors, pool staff, and competitive swimmers. Whether those who use chlorinated pools as customers, particularly children, may also be affected has been a matter of debate. In this article, we discuss the current evidence regarding the health effects of both acute and chronic

EAACI Joint Task Force of the WG Allergy, Asthma & Sports and the IG Environmental & Occupational Allergy

exposures in different populations (work-related exposures, intensive sports, and recreational attendance) and identify the main recommendations and unmet needs for research in this area.

KEYWORDS
chlorination by-products, disinfection by-products, occupational exposure, recreational exposure, sports

1 | INTRODUCTION

The quality of the water and the air of swimming pools is currently a topic of interest in occupational and environmental health. Even though the beneficial effects of swimming on increasing physical activity, cardiopulmonary fitness, and improving lung function are undeniable,[1] concerns have been raised regarding the potential negative effects on human health of water disinfectants used in swimming pools.

The World Health Organization (WHO) highlights the need of adequate water disinfection of swimming pools to prevent microbial proliferation.[2] Disinfectants are the principal management-derived chemicals added to minimize the risk of microbial contaminants; chlorine-based products are the most commonly used in indoor pools,[2] typically preferred due to their effectiveness and lower overall relative cost, in spite of possibly leading to unwanted effects. Although several disinfection options are available such as bromine, ozone, copper-silver, UV irradiation, electrochemically generated mixed oxidants, and UV/hydrogen peroxide, some of these kill or inactivate microorganisms as the water undergoes treatment, but there is no lasting disinfectant effect or "residual" that reaches the pool and continues to act upon chemicals and microorganisms in the water. Thus, where these types of disinfection are used, a chlorine- or bromine-type disinfectant is also employed to provide continued disinfection.[2] Swimming pools treated exclusively with chlorine were found to be more toxic than those treated in combination with ozone[3] or UV,[4,5] due to the lower chlorination by-product (CBPs) formation when these secondary treatments were employed, compared to that when chlorination was used alone.

The addition of chlorine-based disinfectants (chlorine gas, sodium or calcium hypochlorite, di- or trichloroisocyanurates) to the swimming pools water releases hypochlorous acid (HClO), which is the active biocide. HClO is a weak acid with a pKa of 7.5 at 25°C that reversely dissociates into hypochlorite (ClO^-) and hydrogen ion. The sum of HClO and ClO^- is referred to as free chlorine. HClO is a non-specific biocide that inactivates most waterborne pathogens but also reacts with organic matter to produce a wide range of CBPs.[6] Compared to tap water, CBP formation in pools is much more important due to the higher input of organic matter and the constant addition of disinfectants.[7] In chlorinated pools, major groups of CBPs include chloramines, trihalomethanes (THMs), haloacetics acids (HAAs), haloacetaldehydes (HALs), and haloacetonitriles (HANs) (Figure 1).

Indoor swimming pools are of particular concern since they are used regularly all year round, and volatile CBPs can accumulate in the indoor environment over time in swimming facilities where the fresh air supply is insufficient,[8] even if some air movement above the swimming pools occurs. The higher the concentration of these volatile CBPs in the water, the higher their concentration in the air above the pool.[9] Besides inhalation of volatile or aerosolized solutes, there are two other main routes of exposure to chemicals in swimming pools: water ingestion and skin absorption (which may represent a source of muco-cutaneous symptoms). These several routes add to the individual "exposome," which comprises all environmental exposures that a person experiences from conception throughout the lifespan.[10]

Some CBPs may affect the respiratory and skin health of those who stay indoor for long periods, such as swimming instructors, pool staff,[11] and the competitive swimmers.[12,13] Whether those who use chlorinated pools as customers, particularly children, may also be affected has been a matter of debate. We aimed to review this topic, by describing the chemical nature and toxicity of these compounds given the types of exposure and reviewing health effects of such exposures in different populations considering also personal and environmental risk factors, in order to propose recommendations and to identify unmet needs in this area.

2 | THE SWIMMING POOL ENVIRONMENT

Swimming pool environment is a complex and dynamic ecosystem that can be affected by the type of swimming pool (indoor, outdoor) and by other factors, including water temperature, ventilation, climate, location, purpose of use (competition, relaxation, recreational activities), and swimming habits, particularly swimmer's hygiene.[14–16] In the case of an indoor swimming pool, the environment consists of the water in the pool, the air above the pool within the building, and the people in the pool.[9]

Both organic and inorganic compounds are continuously entering this ecosystem via filling waters (eg, tap water, seawater, thermal water), disinfectant addition (eg, chlorine, bromine, ozone, UV), pharmaceuticals and personal care products (eg, analgesics, antibiotics, sunscreens, lotions, cosmetics, soaps), and human body excretions

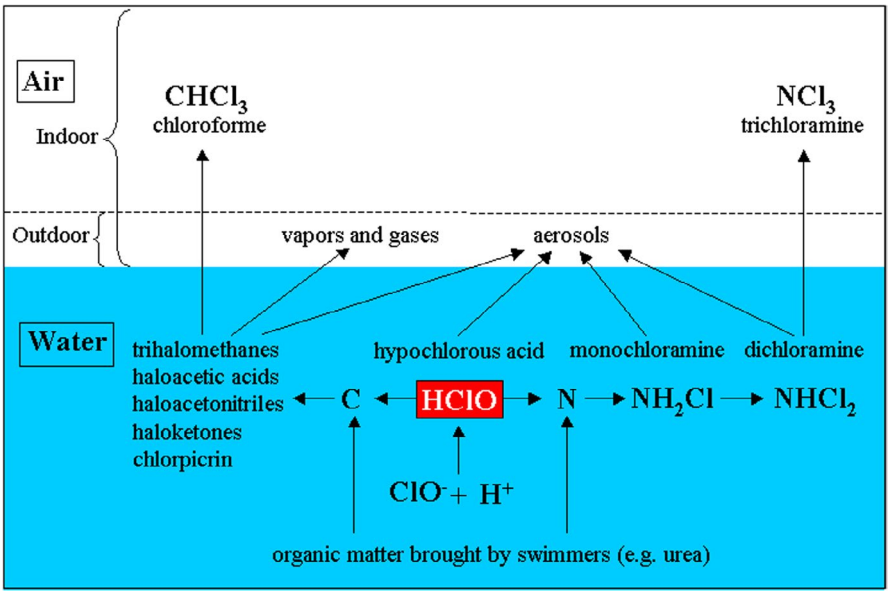

FIGURE 1 Chlorination by-products presented at the water and the air of chlorinated swimming pools—adapted from Bernard A[37]

(eg, urine, sweat, saliva). Interactions between all these compounds generate CBPs, some of which are of health concern.[8]

Chloramines are formed as a result of the reaction of HClO with urea and other nitrogenous compounds brought by swimmers. This group comprises monochloramine (chloramide, NH_2Cl), dichloramine (chlorimide, $NHCl_2$), and trichloramine (nitrogen trichloride, NCl_3). Monochloramine and dichloramine (the sum of which is referred to as combined chlorine) are mainly found in water. Trichloramine, which is 400 times more volatile than its two congeners, is mainly found in the air at levels that are inversely proportional to the ventilation rate of indoor swimming pools.[17,18] The odor and taste of water are mainly affected by the monochloramine/dichloramine ratio and the trichloramine concentration. This last compound is also responsible for the distinctive odor of indoor pools, wrongly attributed to chlorine.[7] Chloramines are typically controlled in chlorinated swimming pools and regulations guidelines for chloramines (measured as combined chlorine) are encouraged to be no greater than half of the free chlorine equivalent concentrations in pool water, although lower ideal concentrations (<0.2–0.4 mg/L) have been suggested.[2,19] NCl_3 in the swimming pool air has also been regulated, with WHO recommending maximum concentrations of 0.5 mg/m^3.[2] In 2019, the Nordic Expert Group published a Criteria Document of health risks from exposure to inorganic chloramines in which a limit value for exposure to NCl_3 of 0.2 mg/m^3 (stationary samples) was proposed.[20]

Trihalomethanes represent between 5 and 10% of total organohalogens in swimming pool water and air, with chloroform ($CHCl_3$) being the dominant species or bromoform (CHBr3) when bromide is present in high concentrations or used as disinfectant.[6] THMs also include dichlorobromomethane and bromodichloromethane. For the purposes of testing and regulation, the concentrations of these four compounds are often added to form a parameter commonly referred to as total THMs (TTHMs). THMs are generated from the complex reaction between active chlorine and carbonaceous organic matter naturally present or imported. Parameters influencing the formation of THMs include organic matter concentration, chlorine concentration, contact time, water pH, temperature, and bromine ion concentrations.[21] THMs are regulated in swimming pool waters. For the TTHM concentrations (sum of trichloro-, bromodichloro-, dibromochloro-, and tribromo-methane), the German standard DIN 19643 issued by the German Institute for Standardization in 2012 suggests a guideline value of 20 µg/L, while Denmark's Statutory in 2012 recommended TTHM concentrations not to exceed 25 µg/L. THMs are generally well absorbed by inhalation, ingestion, and skin contact. People working in swimming pools (lifeguards, instructors, and technical staff) are largely exposed to THMs by inhalation, while the main source of THM exposure for swimmers is expected to be the pool water. In agreement, some studies identified the dermal exposure route to be dominant.[22,23] It turns out that THMs are highly volatile, and some reports claim that THMs are absorbed via the respiratory route.[24–26] Erdinger et al[27] demonstrated that the content of THMs in swimmers' blood is correlated with their content in the ambient air of swimming pools and not with the content in the water, and with a direct impact of swimming intensity on THM accumulation in the organism of swimmers.

Haloacetics acids (HAAs), haloacetaldehydes (HALs), and haloacetonitriles (HANs) are less frequent CBPs and therefore described in the Appendix S1.

Respiratory risks of CBPs are not limited to indoor pools. A Belgian study shows that regular attendance at an outdoor chlorinated pool, at home or during holidays, is associated with an exposure-dependent increase in the risk of asthma.[28] Adolescents having regularly attended a residential pool were also more likely to have a positive result in the exhaled nitric oxide test result and, when attendance was during infancy, to be sensitized against cat or house dust mite allergens. According to the authors, the cause of these respiratory effects has to be sought among the chlorination products that are present in pool water or that build up at the surface of the pool. Trichloramine is indeed unlikely to be responsible for these effects as this highly volatile gas is very quickly dispersed into the atmosphere.

For similar pool attendance, health risks are likely to be more important in seawater swimming pools as in addition of reacting with organic matter from swimmers, chlorine also reacts with organic matter natural present in sea water, releasing thus more CBPs. Furthermore, the bromide and iodine ions present in great concentrations in seawater are known to increase the cytotoxicity and genotoxicity of CBPs.[29]

3 | EFFECTS OF ACUTE EXPOSURES

Pool chemical–associated health events resulted in >4.500 emergency department visits annually during 2008–2017 in the United States, as reported by the Centers for Disease Control and Prevention (CDC), and over one-third were children or teenagers.[30] Irritated eye, nose, throat, and respiratory complaints are the most frequent symptoms in swimmers and workers of indoor swimming pools caused by CBPs; NCl_3 causes the most irritative symptoms.[11,31] A significant concentration-response relation was found between NCl_3 exposure concentrations and irritant eye, nasal, and throat symptoms.[32]

3.1 | Respiratory symptoms

Fantuzzi et al identified cold and sneezing as the most frequent self-reported complaints (65.4% and 52.6%, respectively) among indoor swimming pool workers, while only 7.5% described an asthmatic condition.[11] It is discussed whether recreational swimming or working in indoor swimming pools may aggravate asthma or actually cause it.[33] Irritant-induced asthma (IIA) is defined as development of asthma, non-specific bronchial hyperresponsiveness (BHR), and airway inflammation induced by irritant mechanisms, as opposed to occupational asthma (OA) caused by immunologic mechanisms.[34] Reactive airway dysfunction syndrome and acute-onset irritant-induced asthma are associated with a single, most often accidental, high-level exposure to irritant substances in subjects without pre-existing asthma and can be induced by ammonia, chlorine, and chloramine present in the swimming pools.[34] Three cases of OA in swimming pool workers have been documented,[35] two of them had a positive bronchial provocation test to chloramine. Another study with a large sample of swimming pool workers ($n = 624$) also showed increased risk of respiratory symptoms indicative of asthma upon NCl_3 exposure.[31]

3.2 | Short-term changes in respiratory biomarkers

Chlorination by-products have a strong oxidizing potential and may contribute to airway damage through opening tight junctions, causing barrier disruption.[36,37] A summary of the studies describing short-term changes in respiratory biomarkers is presented in Table 1. It is important to note that some of these studies did not measure NCl_3 and/or did not compare with a nonchlorinated pool, which precludes drawing clear conclusions. Biomarkers measured included biomarkers of airway inflammation, oxidative stress, lung permeability and immunologic response and lung damage. FeNO is the most commonly used in clinical practice. In a recent study, Karetsi et al suggested that the presence of chlorine in the indoor swimming pool could be responsible for the elevated FeNO levels before and after swimming in asthmatic swimmers compared to adolescents practicing a different exercise field.[38] This, however, is inconsistent with previous literature. Carbonelle et al found an increase in FeNO after the exercise session performed in the nonchlorinated pool, whereas in the chlorinated one FeNO remained unchanged, suggesting that chlorination might inhibit NO-induced vasodilation observed during exercise.[39] Consistently, Font-Ribera evaluated short-term changes in several respiratory biomarkers in healthy nonsmoking adults before and after they swam for 40 minutes in a chlorinated indoor swimming pool and FeNO was unchanged overall but tended to decrease among atopics.[40] Bonetto et al reported a decreased FeNO in the acute phase after accidental exposure of children to high chlorine concentrations and suggested it may occur as a consequence of massive epithelial destruction with subsequent damage of NO-producing epithelial, endothelial, and nervous cells, an hypothesis supported by the increased values of serum CC16 observed in the intoxicated children, interpreted as a sign of injury to the lung epithelial permeability barrier.[41] On the contrary, other studies reported an increased FeNO after similar incident[42] or after long-term exposure to chlorine,[43] while Bonsignore et al reported a decreased FeNO after swimming in a chlorinated pool, whereas FeNO remained unchanged in seawater,[44] suggesting that chlorinated sanitation of swimming pools can interfere with the ability of the lung to produce NO. This is also supported by a study demonstrating that L-arginine chlorination results in the formation of a nonselective nitric oxide synthase inhibitor.[45]

The role of physical activity should not be neglected in this type of studies measuring biomarkers before and after swimming. Actually, swimming in pools entails two kinds of exposures with an impact on the respiratory health: chemical (or biological) exposure and physical activity. The mechanical stress on the epithelial barrier caused by overinflation and/or hyperventilation during intense exercise may acutely increase airway permeability, as shown in the study by Carbonnelle et al[46] where serum levels of CC16 peaked immediately after the swimming session, both in the copper/silver pool and in the chlorinated pool. In a different study, the increase in serum CC16 concentration was significantly correlated with energy expenditure, an indicator of physical activity.[40] A physiological role of NO during exercise has been suggested,[47] but studies focused on changes in FeNO during exercise provided inconsistent results with increases, decreases, or even no changes of FeNO depending on the health status of the subjects, the nature, the duration, and the intensity of exercise.[44,48–51]

TABLE 1 Studies describing short-term changes in respiratory biomarkers

Authors	Conditions	Biomarkers	Main findings
Carbonnelle et al. 2002[46]	Chlorinated pool (NCl_3 mean concentration: 490 μg/m^3) for recreational swimmers. Chlorinated pool (NCl_3 mean concentration: 355 μg/m^3) vs. copper/silver pool for trained swimmers	Serum SP-A, SP-B and CC16	• CC16 was not increased in recreational swimmers • In trained swimmers CC16 peaked immediately after strenuous exercise, both in the copper/silver and in the chlorinated pools • SP-A and SP-B were unaffected by strenuous exercise in the copper/silver pool • SP-A and SP-B were significantly increased in a time-dependent manner in recreational and trained swimmers attending the chlorinated pool
Carbonnelle et al. 2008[39]	Chlorinated pool (NCl_3 concentration: 160–280 μg/m^3) vs. copper/silver pool (NCl_3 <20 μg/m^3)	FeNO; serum SP-A, SP-B, CC16, KL-6	• FeNO increased in the copper/silver pool, whereas it did not change in the chlorinated pool, suggesting that chlorination might inhibit NO-induced vasodilation in exercise • Serum pneumoproteins were unchanged excepted SP-A which decreased after exercise in the chlorinated pool ($p < .05$)
Font-Ribera et al. 2010[40]	Chlorinated indoor pool	FeNO; serum SP-D and CC16; 8-isoprostane, several cytokines[a] and VEGF in EBC	• CC16 slightly increased after a swimming session • No significant changes in lung function, SP-D, 8-isoprostane, cytokines, or VEGF.
Fernández-Luna et al. 2013[142]	Chlorinated pool vs. ozone-treated pool	Serum SP-D and CC16	• No change was observed in lung function and SP-D in swimmers attending both pools • CC16 was significantly increased in subjects attending the chlorinated pool but not in those using the ozone-treated pool
Font-Ribera et al. 2019[143]	Chlorinated pool (NCl_3 mean concentration: 473 μg/m^3)	Serum CC16; exhaled breath THMs; urinary TCAA; genotoxicity biomarkers[b]	• Creatinine-adjusted urinary TCAA increased by 3.1 μmol/mol • Urine mutagenicity, MN-PBL, MN-Ret and serum CC16 levels remained unchanged after swimming • No correlation between CBP exposure and MN-PBL, urine mutagenicity and CC16 • Moderate associations observed for MN-Ret and CBP exposure

Abbreviations: CBPs, chlorination by-products; CC, Clara cell protein; EBC, exhaled breath condensate; FeNO, fractional exhaled nitric oxide; KL-6, Krebs von den Lungen-6 protein; SP, surfactant-associated protein; TCAA, trichloroacetic acid; THMs, trihalomethanes; VEGF, vascular endothelial growth factor.

[a]RANTES, Ip10, TNF, IL-12p70, IL-10, IL-8, IFN-γ, and IL-4.

[b]Urine mutagenicity, micronuclei in peripheral blood lymphocytes (MN-PBL), and micronuclei in reticulocytes (MN-Ret).

3.3 | Non-respiratory symptoms

Concerning self-reported ocular symptoms, in the study by Fantuzzi et al indoor swimming pool employees declared frequently having red (48.9%) and itchy (44.4%) eyes, mostly lifeguards and trainers.[11]

Regarding the skin, both water itself and CBPs have negative effects due to a dilution or flushing out of the natural moisturizing. An increasing risk of irritative skin symptoms was demonstrated dependent on the NCl_3 concentrations.[52] Recreational swimming leads to transient but significant changes in skin surface properties of women with healthy skin[53]; skin dryness, itch and erythema are non-specific complains in swimming pool attendants.[54,55] Additionally, both allergic contact dermatitis and contact urticaria due to chlorinated pool water have been identified.[37,54,56,57] Swimming in public pools/spas in the current or previous week has been associated with dermal symptoms (rash, generalized itching, dermal infection).[58]

Besides, more verrucas, mycosis, eczema, and rash have been identified in lifeguards and trainers compared to other workers at swimming pools.[11]

Three different disinfection systems (chlorine, chlorine/ozone, and bromine/ozone) were investigated to assess adverse skin and eye effects[59]: Compared with the bromine/ozone pool, the odds ratio (OR) of having a rash <24 h after pool use was 1.91 (CI 0.71–5.10) for the chlorine pool and 1.88 (CI 0.61–5.81) for the chlorine/ozone pool. Gomà et al[60] reported the efficacy of a new disinfection method (based upon on replacement of the strong hydrochloric acid (HCl) by CO_2, inclusion of a low concentration salt electrolysis system, and ultraviolet radiation phase) to markedly reduce the irritant substances levels in the pool atmosphere and significantly reduce eye, nose, skin, and cough complaints, in both recreational and competitive swimmers.

4 | EFFECTS OF CHRONIC EXPOSURES

Studies based on serum pneumoproteins show that not only acute but also chronic exposure to NCl_3 can increase the lung epithelium permeability and thereby perhaps facilitate the transepithelial delivery of allergens to dendritic cells[46] and contribute to a T2-dependent immune response.[61,62] Recent experimental evidence in mice has shown that chronic chlorine inhalation contributes to exacerbate airways inflammation in asthma by mobilizing pro-inflammatory macrophages into the lung as well as stimulating group 2 and 3 ILCs.[63]

The barrier disruption effect may occur also on the dermal layer. The high temperature of the water, the hydration of the skin, and the disrupting effects of CBPs on the skin barrier are all factors that in combination decrease the water-holding capacity of the skin stratum corneum[64] and greatly facilitate the permeation of CBPs across the skin, especially thin areas such as the scrotum.

4.1 | Work-related exposure

Parrat et al identified lifeguards, swim teachers, and physiotherapists as having the highest CBP cumulative exposure when compared to other swimming pool workers.[52] Although WHO has imposed a reference value for NCl_3 of 0.5 mg/m^3, airborne NCl_3 is not regularly monitored in most European countries and dose-response relationships between NCl_3 levels and different respiratory (runny nose, blocked nose, voice loss) and ocular (red or itchy eyes) symptoms have been reported from a level of 0.5 mg/m^3 onwards.[65] Interestingly, another study demonstrated increasing risk of respiratory symptoms at a level of 0.2–0.3 mg/m^3 of NCl_3, urging to revisit the WHO occupational exposure limit.[52] More recently, in France, the "Agence française de sécurité sanitaire de l'environnement et du travail" (AFSSET) issued a reference limit of 0.3 mg/m^3 mainly for young children and workers. This is also in line with other study, where very low levels of NCl_3 in indoor swimming pools (0.017–0.15 mg/m^3) were detected with increased risk for sore throat (OR: 11.28; 95% CI: 1.44–88.33) and phlegm (OR: 4.22; 95% CI: 1.16–15.4).[66] In a recent study aiming to investigate exposure to trichloramine and THMs (chloroform, bromodichloromethane, dibromochloromethane, and bromoform) and its adverse health effects on the personnel at swimming pools, a slightly higher, but not significant, prevalence of reported eye- and throat-related symptoms occurred among the exposed workers compared to unexposed office workers.[67] A significantly increased risk of at least one ocular symptom was attributed to NCl_3 exposure above the median (20 μg/m^3).[67]

Bureau et al reported that upper and lower respiratory symptoms while on duty were related to duration of lifetime exposure. Lifeguards exposed >500 h in the previous 12 months experienced more cough, throat, and eye irritation than non- or less-exposed lifeguards, and those with prior asthma had a significantly higher risk of suffering from asthma attack(s) than non-exposed asthmatic subjects.[68] Physician-diagnosed asthma was high among lifeguards (23%).[68]

Conversely, the Swedish study found no significant change in lung function before and after shift, and hourly registered PEF values during the day of the investigation did not show any unusual individual variability, but an increase in the difference in FeNO during the work shift of the exposed workers.[67]

4.2 | Intensive sports

4.2.1 | Respiratory symptoms

Competitive and synchronized swimming ranked second among sport disciplines associated with increased prevalence of asthma symptoms.[69] The long-term exposure to CBPs in a sport setting underlines some aspects: 1) the role in inducing and sustaining airway inflammation; 2) the contribution to airway remodeling; and 3) possible promotion of allergic sensitization in regularly exposed competitive swimmers.

A significantly higher rate of BHR with increased inflammatory parameters has been observed in elite swimmers. Long-term swimming pool exposure effects included increase in both eosinophilic and neutrophilic inflammation, as reflected not only in sputum cell counts but also in higher concentration of sputum eosinophil peroxidase and human neutrophil lipocalin, respectively.[70] Inflammatory and remodeling changes reported in bronchial biopsies of competitive swimmers were similar to non-exercising mild asthmatics and were present also during off-training period. Discontinuation of a swimming career decreases eosinophilic and neutrophilic inflammation and reduces BHR, although these findings should be interpreted with caution given the small sample sizes.[71,72] These inflammatory changes did not seem, however, to correlate with BHR. A study carried out in a mixed population of competitive athletes including mostly non-asthmatic swimmers and speed skaters indicated that the baseline pattern of pro-inflammatory cytokine TNF-α and anti-inflammatory IL-1ra concentrations in the lower airways appears to

be similar in top level athletes and asthmatic patients, but different in healthy controls.[73]

Increased airway edema due to CBP-induced vascular leakage has been also hypothesized for airway inflammation in swimmers. A significant association of vascular permeability index (quotient of albumin levels in sputum and in serum) with increased sputum eosinophil and neutrophil counts was found,[74] although vascular leakage did not correlate with lung function and BHR. In synchronized swimmers, no evidence was found for negative influence of CBPs on the pulmonary function.[75]

A study assessing rhinitis in swimmers showed 44% presented baseline allergic rhinitis and 35% had inflammation with neutrophilic predominance.[76] Neutrophilic influx is mainly attributed to irritation through CBP exposure and is possibly reversed—contrarily to eosinophil infiltration—after nose clip introduction.[76] Mucociliary transport impairment and reduced ciliary beats frequency have been described in swimmers and also attributed to irritation by CBPs. Nasal lavage fluid (NLF) collected immediately after competitive swimming contains more neutrophils with decreased phagocytic activity. However, NLF changes tend to subside in swimmers shortly after training cessation or introduction of protective measures, such as nose clip.[77] In the study[73] involving swimmers and speed skaters, TNF-α concentrations in nasal secretions were similar between athletes, asthmatics, and healthy controls. However, IL-1ra levels in upper airways were higher in athletes and asthmatics than healthy subjects. Seemingly paradoxical, this fact may reflect a local anti-inflammatory response of the nasal mucosa.

4.2.2 | Non-respiratory symptoms

A wide spectrum of dermatoses of various etiologies (infectious, traumatic, irritant, allergic, neoplastic, etc.) are listed in the context of regular swimming pools use or aquatic sports performance.[78] Xerosis is one of the most frequent condition experienced by swimmers[79] and especially among those with sensitive and eczematous skin.[80] The dryness effect is particularly pronounced in atopic skin, since the threshold residual chlorine concentration required for considerable drop in water-holding properties is significantly lower than in healthy subjects (0.5 mg/l vs. 2.0 mg/l, respectively),[64] possibly explaining the higher probability of skin symptoms compared to other disinfection methods (bromine, ozone, UV lamps, and salt electrolysis).[80] Also eye symptoms are more significantly associated with chlorine-disinfected pools, comparing with other disinfection methods[80] and often listed as a common problem in competitive swimmers. The risk of otitis externa in swimmers and water-polo players was higher than in soccer players.[81]

4.3 | Recreational attendance

Table 2 summarizes studies that have investigated the respiratory effects of NCl_3 and other inhalable CBPs among recreational swimmers. The first study was conducted among schoolchildren in Belgium.[82] While assessing the effects of ambient air pollution, the authors unexpectedly found that indoor chlorinated pools attendance correlated with lung epithelium hyperpermeability and asthma prevalence. Further studies in Belgium revealed that the asthma risk among adolescents and children using chlorinated pools stemmed from an interaction with atopic status.[43,83] The odds of developing asthma increased with the cumulative chlorinated pool attendance only among swimmers with elevated total serum IgE or among those sensitized to aeroallergens. Important to note also that the risk of allergic asthma was more strongly linked to pool attendance during early childhood.[43] Two studies in Sweden confirmed these observations while showing that the risk of allergic asthma correlated with the cumulative inhalation exposure to NCl_3.[84,85]

Associations between asthma and recreational swimming in chlorinated pools were also reported in Ireland,[86] Italy,[87] and Portugal.[88] Several other studies, however, provided no evidence of an increased asthma risk in recreational swimmers.[89–92] Of these, one of the most contradictory but also the most influential owing to its large size is the UK prospective birth cohort study (ALSPAC study),[91] which was suggestive, if anything, of a protective effect of swimming toward asthma risk. There are several possible explanations for these contrasting observations. A first explanation is that children examined in these negative studies[89–92] were too young to detect associations with allergic asthma. Another possible explanation is an underestimation of the exposure with consequently a risk of miss-classifying some categories of swimmers.[93,94] For instance, data in the ALSPAC study were collected in the 1990s at a time when there was no suspicion of respiratory risks in chlorinated pools. Therefore, the ALSPAC questionnaire was not designed for an accurate assessment of the lifetime attendance of indoor chlorinated pools.[93,94] The need for an accurate exposure assessment is especially important as during infancy and early childhood the first steps of the allergic march (eg, eczema or allergic sensitization) leading to asthma can be triggered after only a few tens hours spent in chlorinated pools (see below).

The pattern of exposure and effects implicating chlorinated pools might, however, be much broader than initially thought. First, disorders caused by chlorination products in swimming are probably not limited to atopic asthma. Swimming in indoor chlorinated pools during infancy has also been associated with a higher risk of bronchiolitis or recurrent respiratory infection mainly in children with family antecedents of atopic diseases.[7,95,96] Associations have also been reported between indoor chlorinated pool attendance and the risks of allergic rhinitis,[83,97] autonomic changes,[88] and airway inflammation assessed by FeNO.[43] Further complicating the issue, some studies suggest that early swimming in chlorinated pools may increase the risks of allergic sensitization in particular to perennial allergens.[61,92,98] In other terms, airway irritation by chlorination products might exert a promoting effect not only on the clinical expression of respiratory allergies but even on the process of allergic sensitization itself, that is, on the development of atopy.

Last, respiratory risks when swimming in chlorinated pools are probably not limited to the exposure to NCl_3. Risks of bronchiolitis and

TABLE 2 Risks of respiratory diseases, aeroallergen sensitization, and airway epithelial defects associated with recreational swimming in indoor and/or outdoor chlorinated pools

Authors	Country	Type of study	*N* (age, yrs)	NCl_3 mg/m^3	Main findings
Bernard et al. 2003[82]	Belgium	Cross-sectional	226 (8–12) 1,881 (7–14)	-	Dose-effect relation between CCPA and serum SP-A and SP-B ($n = 226$). Correlations between the prevalence of asthma and the CCPA ($n = 1,881$).
Nystad et al. 2003[95]	Norway	Cross-sectional	2,862 children	-	Increased risk of recurrent respiratory tract infections in baby swimmers from atopic parents (aOR, 2.08, 95% CI: 1.08–4.031).
Lagerkvist et al. 2004[99]	Sweden	Cross-sectional	57 (10–11)	-	Significant decrease of serum CC16 in children ($n = 20$) regularly visiting indoor chlorinated pools
Kohlhammer et al. 2006[97]	Germany	Cross-sectional	2,606 (35–74)	-	Dose-related associations between the risk of hay fever and the current and school-age pool attendance.
Bernard et al. 2006[43]	Belgium	Cross-sectional	341 (10–13)	0.25–0.54	Increased risk of asthma (doctor-diagnosed or EIB) with CCPA in children with serum IgE >100 kIU/L (aOR for each 100-hr increase in CCPA = 1.79; 95% CI, 1.07–2.72).
Nickmilder and Bernard, 2007[144]	Belgium	Ecological	(13–14) (6–7)	_	In both age groups, the prevalence of ever asthma across Europe correlated with the availability of indoor chlorinated pools.
Bernard et al. 2007[7]	Belgium	Cross-sectional	341 (10–13)	-	Decrease of serum CC16 and higher risks of asthma and bronchitis in 43 children who swam in indoor chlorinated pools during infancy
Bernard et al. 2008[28]	Belgium	Cross-sectional	847 (13–18)	-	Use of outdoor pools was associated with higher risks of elevated FeNO, cat or HDM sensitization and asthma in subjects with serum IgE>25 kIU/L
Nystad et al. 2008[95]	Norway	Prospective	30,870 (0.5–1.5)	-	Increased risk of wheeze (aOR, 1.24, 95% CI 1.11, 1.39) in baby swimmers from atopic mothers.
Schoefer et al. 2008[145]	Germany	Prospective	2,196 (6)	-	Baby swimmers had higher risk of asthma (aOR 2.15 95% CI 1.16–3.99) due potentially to reverse causation and respiratory infections in the 1st yr
Cotter and Ryan 2009[86]	Ireland	Cross-sectional	97 (6–12)	-	Associations between CCPA and the risk of diagnosed asthma and wheezing in the last 12 months
Bernard et al. 2009[83]	Belgium	Cross-sectional	847 (13–18)	0.30–0.50	Among atopic adolescents, aOR for asthma, hay fever or allergic rhinitis increased with CCPA but not with the Cu/Ag pool attendance.
Voisin et al. 2010[96]	Belgium	Cross-sectional	430 (5–7)	-	Infant swimming in indoor or outdoor chlorinated pools is associated with increased risks of bronchiolitis and later of allergic sensitization
Font-Ribera et al. 2011[91]	UK	Prospective	5,738 (7 and 10)	-	Swimming was associated with increased lung function and lower risk of asthma symptoms.

(Continues)

TABLE 2 (Continued)

Authors	Country	Type of study	*N* (age, yrs)	NCl_3 mg/m^3	Main findings
Ferrari et al. 2011[87]	Italy	Prospective	1,136 (18–55)	-	Higher risk of new-onset asthma associated with CCPA.
Jacobs et al. 2012[92]	Netherlands	Cross-sectional	2,359 (6–13)	0.21	Association of HDM sensitization with frequent baby swimming and lower serum CC16 ($n = 419$). No association with asthma.
Font-Ribera et al. 2013[90]	Spain	Prospective	2,205 (0–1.17)	-	No association between indoor or outdoor swimming pool attendance during the 1st year of life and LRTI, wheezing, atopic eczema or otitis
Voisin et al. 2013, 2014[61,98]	Belgium	Prospective	196 (5.7 and 7.7)	-	Swimming at indoor or outdoor chlorinated pools before the age of 3 years was associated with higher risks of HDM sensitization and increased FeNO
Schuez-Havupalo et al. 2014[146]	Finland	Prospective	1,827 (0–1.42)	-	Association between infant swimming and rhinovirus-associated wheezing among children with atopic eczema ($n = 635$, $p = .006$).
Font-Ribera et al. 2014[89]	Spain	Cross-sectional	2,758 (6–12)	-	No associations between regular indoor pool attendance before 2 years and asthma, wheezing, eczema.
Bernard et al. 2015[100]	Belgium	Cross-sectional	835 (13–18)	-	Associations of serum CC16/SP-D with CCPA, allergic sensitization (especially to HDM) and allergic diseases among sensitized adolescents
Andersson et al. 2015[85]	Sweden	Cross-sectional	1,866 (11–12)	-	Asthma associated with indoor pool attendance (≥1 week) only among sensitized subjects ($n = 1,652$, aOR1.9, 95% CI 1.09–3.32).
Bernard et al. 2017[147]	Belgium	Prospective	121 (5.8, 7.8)	-	Low CC16 in NALF associated with CCPA predicts persistent sensitization to aeroallergens, especially to HDM
Cavaleiro-Rufo et al. 2018[88]	Portugal	Cross-sectional	858 (7–12)	-	Indoor pool attendance associated with autonomic changes and baseline bronchoconstriction and before 3 years with functional asthma
Andersson et al. 2018[84]	Sweden	Prospective	970 (16–17)	0.15	Early indoor pool attendance (< 3 years) associated with asthma onset. Risks are particularly high for atopics. Dose-response relationships with NCl_3.

Note: Cu/Ag pool, swimming pool disinfected by copper/silver electrofiltration. Age and NCl_3 values are reported as mean or range.

Abbreviations: CC16, club cell protein; CCPA, cumulative chlorinated pool attendance; EIB, exercise-induced bronchoconstriction; FeNO: fractional exhaled nitric oxide; HDM, house dust mite; LRTI, lower respiratory tract infection; NCl_3, nitrogen trichloride or trichloramine in pool air; SP-A, surfactant-associated protein A; SP-D, surfactant-associated protein D.

of atopic asthma were also found to increase exposure-dependently with the attendance of outdoor chlorinated pools.[96] This suggests that airways can also be affected by the chlorine-based oxidants at the surface of water that swimmers actively inhale as aerosols or gases.

Biomarkers studies have revealed that the attendance of chlorinated pools correlates with a disruption of airway epithelial barrier as reflected by altered serum levels of lung epithelium-specific proteins (pneumoproteins). Several studies have shown that early swimming in chlorinated pools is associated with decreased serum levels of CC16.[7,92,99,100] This finding is of particular interest as CC16 is capable of down-regulating the airway inflammation as well as the Th2 differentiation both in vitro and in vivo.[101–104] Supporting this important protective role of CC16 in the respiratory tract, recent research shows that lower levels of circulating CC16 in children are associated with subsequent decreased lung function and increased risks of developing asthma and other respiratory diseases.[100,105–107] There is also evidence from studies based on serum pneumoproteins that both chronic and acute exposure to NCl_3 can increase the lung epithelium permeability and thereby perhaps facilitate the transepithelial delivery of allergens to dendritic cells.[46]

4.4 | Other health effects

Many *in vitro* and *in vivo* toxicological studies have provided evidence about genotoxic and cytotoxic effects induced by some CBPs, and the WHO International Agency for Research on Cancer acknowledges sufficient evidence for the carcinogenicity of chloroform and some other widespread CBPs in animals.[108]

In humans, however, the epidemiologic evidence overall has generally been considered insufficient to declare CBPs to be carcinogenic. It is worth noting that the majority of the studies evaluate the risk of cancer related to drinking water and not exposure in swimming pools, so this lack of evidence should be considered with concern and not extrapolated. In fact, a recent study showed that for elite swimmers and their coaches, the levels of THMs in a Portuguese swimming pool exceeded the limits for cancer risk.[109]

Regarding bladder cancer, epidemiologic evidence indicates that exposure to THMs increases its risk.[110,111] While the majority of the studies were related to drinking water, there are also studies finding increased risk of bladder cancer related to exposures to THMs through showering, bathing, or swimming.[23,112,113]

Associations with other types of cancer have been suggested, but evidence remains inconclusive. A prior history of swimming during the summer months in swimming pools and in open waters such as rivers and seas before the age of 15 years was associated with odds ratios of 2.20 (95% confidence interval (CI), 1.05–4.62) and 2.41 (95% CI, 1.04–5.58), of melanoma, respectively, compared with no swimming at all or swimming in relatively unpolluted waters, such as lakes and fens.[114] A meta-analysis using the search terms 'chlorination by-products', 'trichloromethane', 'chloroform' and 'bromoform' pointed to an association between exposure to these CBPs in drinking water and an increase in the risk of colorectal cancer.[115]

Regarding reproductive effects, there is no clear evidence linking CBP exposure to poor pregnancy outcomes, except for a slight association of THM exposure with fetal growth-related outcomes. A meta-analysis found little or no evidence for associations between third-trimester trihalomethane exposure and low birthweight, term low birthweight, preterm delivery, but some evidence for small for gestational age.[116] Meta-analyses of all currently available studies demonstrate little evidence of an association between congenital anomalies and exposure to water chlorination or TTHMs.[117]

Potential impact of CBPs on male fertility has been much less studied and is of great concern given the remarkable permeability of the scrotal skin. Most studies have addressed mainly the risks related to drinking water, while one study addressed the exposure through swimming pool water and found that adolescents having attended indoor chlorinated pools for >250 h before the age of 10 years or >125 h before the age of 7 years were three times more likely to have an abnormally low serum inhibin B and/or total testosterone than their peers who never visited these pools and those who attended outdoor chlorinated pools or a copper-silver pool.[118] To which specific CBP adolescents were exposed in the indoor chlorinated pools was not determined.

5 | RISK FACTORS

There is a complex interaction between the building environment, infectious agents, allergens, occupational exposures, school environment, and recreational exposures, which contribute to shape the exposome.[10]

The amount and impact of CBP exposure may be influenced by the dose of disinfectant, the resultant concentration of CBPs in the water and the air, the number of attending swimmers, temperature of water and air, ventilation rates in the building, duration of swimming, and the water turbulence.[9,119] In a recent study, the distribution of TTHM 0.05 m and 0.60 m above the water surface at six different locations in the poolroom and the covariation between the water and air quality parameters were investigated in 93 air samples collected via stationary sampling.[120] Based on a linear mixed effects model, the most important determinants in terms of predicting the air concentration of $CHCl_3$ were height above water surface, air changes of fresh air per hour, concentration of combined chlorine in the water, relative humidity, and day of the week; approximately 36% of the total variability could be attributed to these variables.[120] In a different study, targeting NCl_3,[121] it was shown that time of day, occupancy, and pool management affect the concentration of NCl_3. Furthermore, using the concentration of CO_2 to evaluate whether this contaminant could be used to predict the number of pool occupants as well as the concentration of NCl_3 in the air, became evident that CO_2 was significantly correlated with occupancy level ($\rho = .82$, $p = .01$) and NCl_3 concentration ($r = .80$, $p = .01$); moreover, the

concentration of CO_2 explained 52% of the variation observed in the air concentration of NCl_3.[121]

The three routes of exposure (inhalation, ingestion, and dermal absorption) vary for different age groups and are affected by several factors (Figure 2).

5.1 | Inhalation

Inhalation exposure will be largely associated with volatile substances that are lost from the water surface. Volatile CBPs include THMs and trichloramine, which are the most investigated, among many others such as cyanogen chloride (CNCl), cyanogen chloride (CNCl), dichloroacetonitrile ($CNCHCl_2$), and dichloromethylamine (CH_3NCl_2).[122,123] Although HAAs are non-volatile and have little skin permeability, swimmers may be exposed through inhalation of aerosol.[124] Swimming pool attendants inhale from the atmosphere just above the water's surface, and the volume of air inhaled is a function of the effort intensity and time. In indoor swimming pools, individuals also breathe air in the wider area of the building housing the pool. The normal assumption is that an adult will inhale approximately 10 m^3 of air during an 8-h working day.[125] However, this will also depend on the physical effort involved. Therefore, significant individual variation will be depending upon the type of activity and level of effort. A recent study using metabolomics identified a high correlation between physical activity, measured by kcal, and THM concentrations,[126] notably due to the fact that the internal dose increases significantly with intensity of physical activity.[127] The content of THMs in swimmers' blood is correlated with their content in the ambient air of swimming pools and not with the content in the water, suggesting a direct impact of swimming intensity on THM accumulation in the organism of swimmers.[128] It must be also noted that experienced swimmers present a peculiar breathing patter, and they inhale water droplets also through their mouth, besides the nose.

5.2 | Ingestion

Inadvertent water intake in the swimming pool varies according to age and sex. The amount of water ingested by swimmers and pool users will depend upon a range of factors, including experience, age, skill, and type of activity. The duration of exposure will vary significantly in different circumstances, but for adults, extended exposure would be expected to be associated with greater skill (eg, competitive swimmers), and so there would be a lower rate of ingestion in a comparable time than for less skilled users.[2] A pilot study conducted by Evans et al[129] found that the average water intake by children (37 ml) was higher than the intake by adults (16 ml). In addition, the intake by adult men (22 ml) was higher than that by women (12 ml); the intake by boys (45 ml) was higher than the intake by girls (30 ml). The upper 95th percentile intake was for children and was approximately 90 ml.[129]

5.3 | Dermal/mucosal absorption

Exposure to chlorinated bathing water has shown to change the dermal barrier function, especially of atopic skin,[64] the same being expected for exposure to the chlorinated swimming pool water. Infant swimming practice combined with atopy has been shown to increase the prevalence of eczema.[130] The skin permeability of some CBPs has been studied. Xu et al investigated THMs, haloketones (HKs), and HAAs, reporting that THMs had the highest skin permeability, with brominated THMs being more permeable than chlorinated THMs.[131] HKs were reported to be less permeable to human skin than THMs, but more permeable than HAAs, which showed almost no permeability.[131] HANs were investigated by Trabaris et al, with dibromoacetonitrile being found to have the highest permeability to human skin, while chloroacetonitrile had the least. HANs were shown to be less permeable to human skin than chloral hydrate.[132] Both studies correlated an increase in temperature to increased human skin permeability.[131,132]

Some conditions related to competitive swimmers are highlighted in Table 3.

Age seems to be the most relevant personal risk factor for respiratory and reproductive health effects of CBP exposure in swimming pools.[9] The first years of life may be seen as a "window of vulnerability" given the progressive increase in maturation of respiratory tract and reproductive system.[133] In acute outbreaks, children were predominantly affected.[134] As previously mentioned, the use of indoor chlorinated pools especially by young children interacts with atopic status to promote the development of childhood asthma,[43] and a synergistic action of exposure to pets and environmental tobacco smoke in chlorinated pools attendants predisposes to the development of asthma.[82]

Age also directly impacts the other risk factors, including the surface areas of both the head and the body, the breathing rate and body weight.[9] The contribution from each exposure route changes dramatically for each age group, and the time spent swimming must also be taken into consideration. Adjusted for body weight, the uptake of CBPs by all routes is clearly higher in infants or children and decreases with age.[133] A schematic representation is presented in Figure 3.

6 | RECOGNIZING CBP EXPOSURE-ASSOCIATED HEALTH EFFECTS

Depending on the exposed epithelium, the level of exposure, the past medical history, and/or certain individual characteristics, different signs and symptoms associated with CBP exposure will be observed. These symptoms will be exacerbated in those patients with an underlying chronic inflammatory disease (asthma, eczema, allergy, dermatosis, etc.).

The diversity of tissues exposed to CBPs in swimming pool attendants offers a wide variety of clinical conditions (summarized in Table 4), which require a differential diagnosis with other disorders

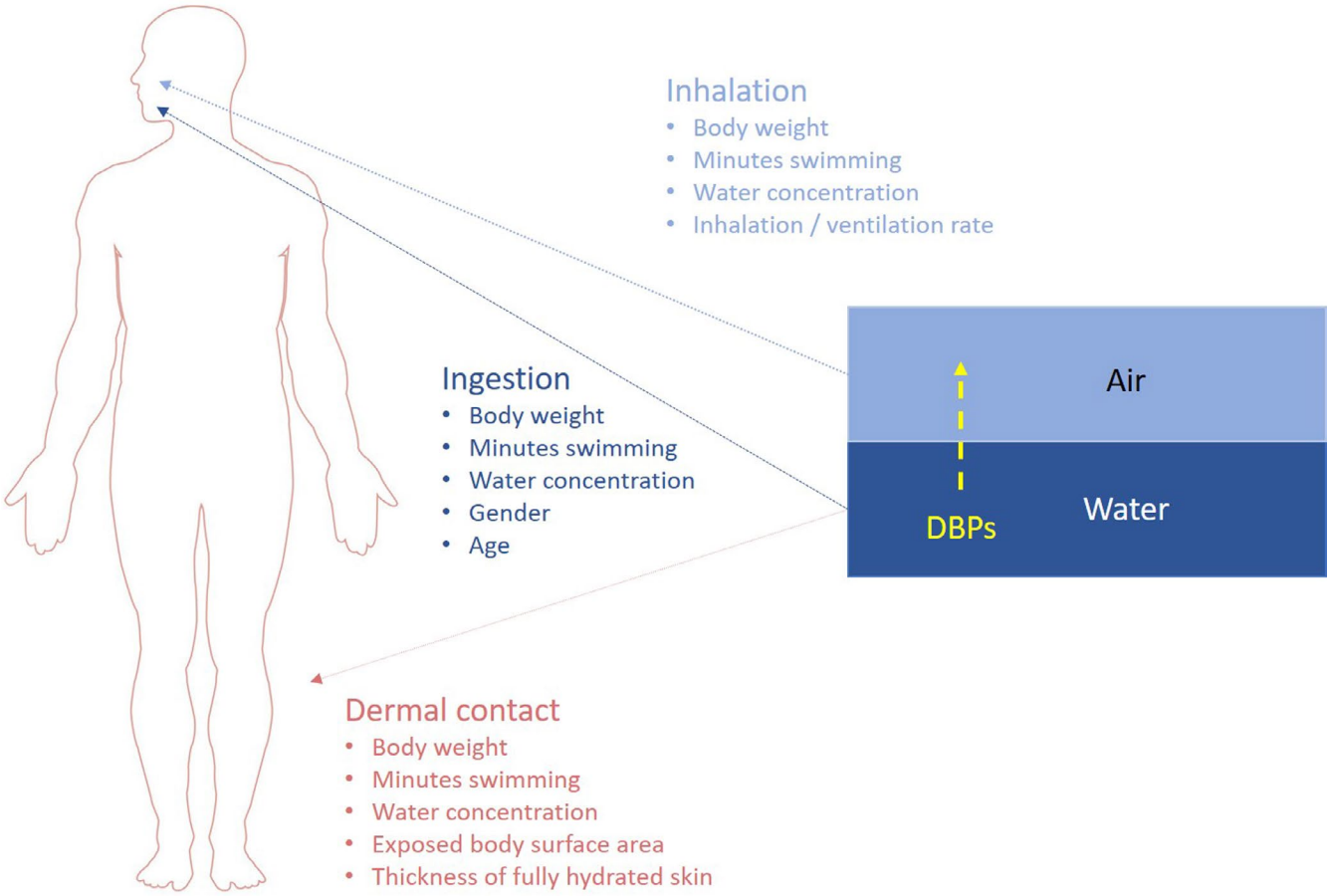

FIGURE 2 The routes of exposure to disinfection by-products in swimming pools and the factors affecting each route—adapted from Dyck et al[9]

TABLE 3 Conditions inherent to the competitive swimmers and the respective consequences on their exposure to disinfection by-products

Condition	Consequence
High physical effort	The internal dose of THMs increases significantly with intensity of physical activity.[127] The content of THMs in swimmers' blood is correlated with their content in the ambient air, and not in the water, of swimming pools[128]
	Stronger impact of the inhalation route compared to ingestion or dermal absorption
Oral inhalation of water droplets	Increases the amount of exposure and may also alter the lung microbiome
Greater swimming skills	Lower rate of ingestion in a comparable time than for less skilled users

that present similar symptoms and signs, although their history is different. More detailed information on this topic is provided as Appendix S1.

7 | MANAGEMENT

Although evidence is lacking, there is consensus on the recommendation to assure that water treatment processes prevent CBP formation in order to minimize the chance of an increased risk of cancer from its long-term exposure. Current standards for the assessment of THM exposure are mostly defined for the THM content in swimming pool water, although THMs are quite volatile and likely to be present in appreciable concentrations also in the air of indoor swimming pool facilities. Though it has been progressively acknowledged that airborne THM levels have a central role in inducing CBP-related adverse health effects, there are presently no standards or guidelines for controlling THM levels in indoor air of swimming pool amenities. There is currently no international standard for the treatment of swimming pools, with different regulations often provided by state or local governing bodies.

Inhalation of airborne THM and other CBPs is generally considered to be the predominant route of exposure for competitive swimmers, who have an increased breathing rate throughout their

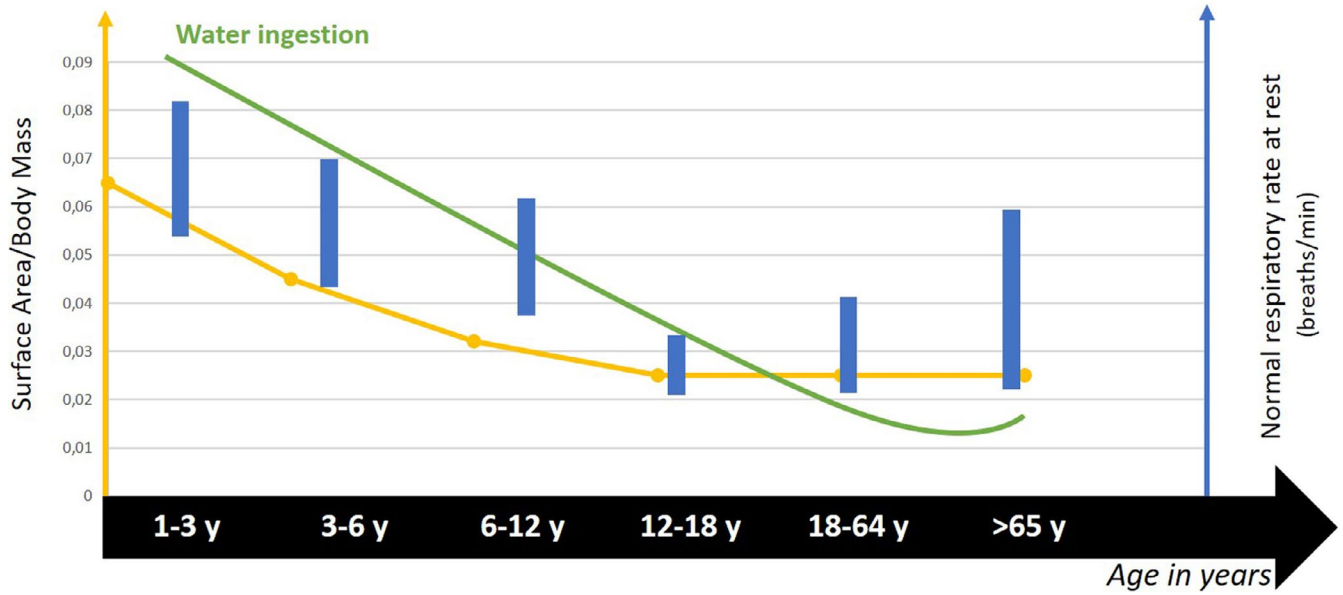

FIGURE 3 Schematic representation of the relation between water ingestion and surface area/body mass and respiratory rates throughout different ages (based on data from WHO Training package for the Health sector—Children's health and the environment)

TABLE 4 Differential diagnosis of the chlorine exposure-related clinical conditions in pool attendants

Organ or system	Pathology (signs & symptoms)	Diagnosis	Differential diagnosis
Hair	Hair coloration/ discoloration, fragile and/or dry	Clinical history Medical examination	Other abrasive agents
Eyes	Corneal epithelial erosions or dysfunction	Clinical history Medical examination	Corneal abrasion Recurrent corneal erosion
	Conjunctivitis	Clinical history Medical examination	Allergic conjunctivitis Irritative conjunctivitis
Ear	External Otitis "Swimmer's Ear"	Clinical history Medical examination	Skin injuries, foreign bodies, chronic inflammation
Nails	Surface damage of the nail plates	Clinical history Medical examination	Fungal infection Nail polish effects
Teeth	Enamel erosion	Clinical history Medical examination	Attrition and abrasion of the enamel
Skin	Dry, itching, fragile skin Eczema	Clinical history Medical examination	"Primary" eczema Dermatoses and systemic illnesses with dry skin
Respiratory system	Nose itching	Clinical history Medical examination Skin prick tests	Allergic rhinitis
	Anosmia	Clinical history Medical examination Olfactive tests Imaging	Allergic rhinitis Obstructive/traumatic nasal diseases Sensorineural diseases of the olfactive tract
	Dyspnea, respiratory fatigue, cough, wheezing, chest tightness, muscular fatigue	Clinical history Medical examination Complementary test: Spirometry pre/ post-exposure, Monitored exercise test, pre/post- exercise DLCO, Skin prick tests	Dyspneic pathologies: • Cardiovascular • Respiratory • Hematology • Oncology • Rheumatology/Immunology • Environmental stress • ...

regular and prolonged sports and training actions, and for coaches and other pool workers and staff, who experience an intense occupational exposure to the THM-rich environment that surrounds the pool. In studies using scuba tanks to eliminate inhalation exposure, Erdinger et al[135] and Levesque et al[136] estimated the contribution from dermal contact to be less than inhalation, 1/3 and 24% respectively, for THMs exposure. However, Lindstrom et al actually found the dermal exposure route to trihalomethanes to be dominant in competitive swimmers under prolonged, high-effort training.[22] Limited information about the importance of proper ventilation in preventing the accumulation of DBPs above the water surface exists. In a recently published study of one indoor swimming pool in Canada, results showed that some zones have appropriate air-renewal, while others are poorly ventilated or even over-ventilated.[137] It is also known that parameters such as water temperature, water turbulence, water surface, relative humidity, and air temperature can impact air quality.[138] A recent study also showed that the breathing zones of users and occupants of an indoor swimming pool, including elite swimmers their coaches and maintenance staff, presented significantly different concentrations of airborne THMs, predictably carrying different environment-related health risks. Ventilation conditions, occupancy rates, and some water-related parameters were factors that partially explained these observations.[139]

Traditionally, ventilation strategies in indoor swimming pools have been based on reducing condensation on the windows rather than ensuring proper air quality in the users' breathing zone.[120] Proper maintenance schedules and ventilation conditions are needed to guarantee a stable indoor environment—temperature and relative humidity—in the areas of water activities. Water-related factors—air/water temperature ratio and pH, the number of swimmers within the pool—also explain variations of the volatile organic compound (VOC) levels found in the water-surface air, the air zone that is regularly inhaled by swimmers. Thus, maintaining water pH between 6.9 and 8.0 and air temperature 2°C above the pool water are recommended to avoid level fluctuations and the undesired volatilization of CBP, particularly during periods of high attendance.[139] Considering the results of recent studies, the supplied air should be balanced with respect to the water quality, and not just the relative humidity and air temperature, as well as the bather load by the use of CO_2 sensors to control the air supply that can help reduce the air concentrations of NCl_3 and balance the air supply based on occupancy level.[120,121] Checking declared indoor sources of VOC emissions, and the heating, ventilation and air conditioning (HVAC) systems (particulate matter filtration capacity and efficient removal of indoor pollutants), should also be considered,[140] as well as the HVAC system design, in order to guarantee that fresh air supply and exhaust airflows do not mix by proximity.

Data on the real long-term exposure to CBPs and the risks that this exposure may represent for the health of competitive swimmers and coaches over the course of their careers are currently lacking. The United States Environmental Protection Agency (US EPA) developed a screening level model, SWIMODEL, to assess swimmers' exposures to chemicals by inhalation, ingestion, and dermal contact routes, as well as buccal/sublingual, nasal/orbital, and aural routes.[141] The model allows selection of swimmer age, gender, and activity level (competitive or non-competitive swimming) and could be of benefit when assessing relevant management strategies. Nevertheless, a few easy and effective steps that all can take to maintain water and air quality are presented as a checklist in Table 5.

8 | RECOMMENDATIONS AND UNMET NEEDS

The expansion of indoor aquatic activities resulted in a major focus of public authorities and local legislators on the prevention of waterborne infectious diseases, through the implementation and inspection of water disinfection practices. Comparatively, much less attention has been dedicated from health authorities to the indoor air quality (IAQ) of aquatic facilities, and there are still unmet needs

TABLE 5 Healthy swimming water and air quality checklist, based on the recommendations of the Centers for Disease Control and Prevention and the guidelines from the World Health Organization

Swimmers checklist	Stay out of the water if you have: • Diarrhea (for patients with cryptosporidiosis, don't swim for an additional 2 weeks after diarrhea has resolved) • A gastrointestinal (stomach) upset or skin or respiratory infection • An open wound (eg, from surgery or a piercing) that is not covered with a waterproof bandage
	Keep ears as dry as possible and dry ears thoroughly after swimming
	Shower before you get into the water, rinsing off in the shower for just 1 minute removes most of the dirt or anything else on your body
	Remove make-up
	Don't pee or poop in the water
	Don't swallow the water
Swimming pool checklist	Check the pool's latest inspection results
	Check the free chlorine level and pH before getting into the water: proper free chlorine level (1–3 mg/L or parts per million) and pH (7.2–7.8) maximize germ-killing power.

to guarantee a generally safe and healthy indoor sport environment for both recreational and professional swimmers, and to those involved in their instruction, training, safety vigilance and pool maintenance. While chloramines are typically controlled in chlorinated swimming pools with guidelines regulating their maximum concentrations, THM exposure assessment is mostly defined for the TTHM content in swimming pool water, although inhalation is a relevant exposure route. Except for occupational chloroform exposure, there is currently no international standard or specific regulation for THM in swimming pools indoor air, and regulations in Europe should be provided.

Due to the presence of both indoor THM and non-THM VOC, effective ventilation and acclimatization systems are a particular need for indoor swimming facilities to prevent the accumulation and promote the effective elimination of these harmful chlorine-derived volatile compounds.[120,141]

Among the available options for water disinfection, other than chlorine-derived solutions should be considered in the planning and development of new public indoor swimming pools. For existing facilities, avoiding any factors that promote the development, introduction and retention of air pollutants, that is, controlling pollutant sources and ventilation levels, constitute the major action plans proposed for IAQ improvements of swimming pools.[120,121,139,141]

Recommendations concerning prophylactic procedures during occupational exposure are lacking but given the fluctuations of indoor pollutants concentrations found throughout a working day,[139] it is advisable that pool maintenance staff minimize occupational exposure by carrying in the early morning activities that require a prolonged stay in the swimming pool surrounding area.

Findings suggest that early and chronic exposure to swimming pool CBP may have a promoting effect not only on airway inflammation and hyperreactivity, but also on the process of allergic sensitization itself.[86,93] Other health outcomes, namely male fertility and bladder cancer, are of particular concern, as the majority of published studies evaluate these risks in relation to drinking water and not swimming pool exposure.[110,113,118] Early age exposure (baby and pre-school swimming) may turn to be a relevant personal risk factor for respiratory and reproductive health effects of CBP exposure in swimming pools, given the progressive increase in maturation of respiratory tract and reproductive system.[95,133]

There is still need of more environmental and epidemiological research data, to ascertain the health risk associated with the exposure of different swimming pool users, namely babies, infants and children, lifeguards and swimming pool maintenance staff, coaches and elite swimmers. Additional prospective and intervention studies are also needed to confirm the relationship between exposure to pollutants in swimming pool environments and the risk of certain health effects, to support the development of evidence-based guidelines for preventive measures and indoor swimming pools' air quality.

ACKNOWLEDGEMENTS

The authors thank EAACI for providing the support and funding to the present work.

CONFLICT OF INTEREST

Dr. Couto, Dr. Bernard, Dr. Delgado, Dr. Drobnic, Dr. Kurowski, Dr. Moreira, Dr. Rodrigues-Alves, Dr. Rukhadze, Dr. Seys, and Dr. Wiszniewska have nothing to disclose. Dr. Quirce reports personal fees and non-financial support from GSK, personal fees and non-financial support from AstraZeneca, personal fees and non-financial support from Sanofi, personal fees and non-financial support from Novartis, personal fees and non-financial support from Mundipharma, personal fees and non-financial support from Teva, and personal fees and non-financial support from Allergy Therapeutics, all outside the submitted work.

ORCID

Mariana Couto https://orcid.org/0000-0003-4987-9346
Luís Delgado https://orcid.org/0000-0003-2375-9071
Marcin Kurowski https://orcid.org/0000-0002-0653-7533
André Moreira https://orcid.org/0000-0002-7294-9296

REFERENCES

1. Geiger KR, Henschke N. Swimming for children and adolescents with asthma. *Br J Sports Med*. 2015;49(12):835-836.
2. World Health Organization. *Guidelines for safe recreational water environments. Swimming pools and similar environments*. World Health Organization; 2006;2.
3. Fernández-Luna Á, Gallardo L, Plaza-Carmona M, et al. Respiratory function and changes in lung epithelium biomarkers after a short-training intervention in chlorinated vs. ozone indoor pools. *PLoS One*. 2013;8(7):e68447.
4. Liviac D, Wagner ED, Mitch WA, Altonji MJ, Plewa MJ. Genotoxicity of water concentrates from recreational pools after various disinfection methods. *Environ Sci Technol*. 2010;44(9):3527-3532.
5. Plewa MJ, Wagner ED, Mitch WA. Comparative mammalian cell cytotoxicity of water concentrates from disinfected recreational pools. *Environ Sci Technol*. 2011;45(9):4159-4165.
6. Manasfi T, Coulomb B, Boudenne JL. Occurrence, origin, and toxicity of disinfection byproducts in chlorinated swimming pools: an overview. *Int J Hyg Environ Health*. 2017;220(3):591-603.
7. Bernard A, Carbonnelle S, Dumont X, Nickmilder M. Infant swimming practice, pulmonary epithelium integrity, and the risk of allergic and respiratory diseases later in childhood. *Pediatrics*. 2007;119(6):1095-1103.
8. Carter RAA, Joll CA. Occurrence and formation of disinfection by-products in the swimming pool environment: a critical review. *J Environ Sci (China)*. 2017;58:19-50.
9. Dyck R, Sadiq R, Rodriguez MJ, Simard S, Tardif R. Trihalomethane exposures in indoor swimming pools: a level III fugacity model. *Water Res*. 2011;45(16):5084-5098.
10. Agache I, Miller R, Gern JE, et al. Emerging concepts and challenges in implementing the exposome paradigm in allergic diseases and asthma. *Allergy*. 2019;74(3):449-463.
11. Fantuzzi G, Righi E, Predieri G, Giacobazzi P, Mastroianni K, Aggazzotti G. Prevalence of ocular, respiratory and cutaneous symptoms in indoor swimming pool workers and exposure to disinfection by-products (DBPs). *Int J Environ Res Public Health*. 2010;7(4):1379-1391.
12. Nemery B, Hoet PH, Nowak D. Indoor swimming pools, water chlorination and respiratory health. *Eur Respir J*. 2002;19(5):790-793.
13. Levesque B, Duchesne JF, Gingras S, et al. The determinants of prevalence of health complaints among young competitive swimmers. *Int Arch Occup Environ Health*. 2006;80(1):32-39.

14. Zwiener C, Richardson SD, DeMarini DM, Grummt T, Glauner T, Frimmel FH. Drowning in disinfection byproducts? Assessing swimming pool water. *Environ Sci Technol*. 2007;41(2):363-372.
15. Weng S, Blatchley ER 3rd. Disinfection by-product dynamics in a chlorinated, indoor swimming pool under conditions of heavy use: national swimming competition. *Water Res*. 2011;45(16):5241-5248.
16. Keuten MG, Peters MC, Daanen HA, de Kreuk MK, Rietveld LC, van Dijk JC. Quantification of continual anthropogenic pollutants released in swimming pools. *Water Res*. 2014;53:259-270.
17. Levesque B, Vezina L, Gauvin D, Leroux P. Investigation of air quality problems in an indoor swimming pool: a case study. *Ann Occup Hyg*. 2015;59(8):1085-1089.
18. Gérardin F, Cloteaux A, Midoux N. Modeling of variations in nitrogen trichloride concentration over time in swimming pool water. *Process Saf Environ Protect*. 2015;94:452-462.
19. CDC. 2016 Model Aquatic Health Code. In: Prevention CfDC, ed2016.
20. Wastensson G, Eriksson K. 152. Inorganic chloramines. In: Torén K, ed. *The Nordic Expert Group for Criteria Documentation of Health Risks from Chemicals*, Vol. 53, 2nd edn. 2019. https://gupea.ub.gu.se/bitstream/2077/61724/4/gupea_2077_61724_4.pdf
21. Florentin A, Hautemaniere A, Hartemann P. Health effects of disinfection by-products in chlorinated swimming pools. *Int J Hyg Environ Health*. 2011;214(6):461-469.
22. Lindstrom A, Pleil J, Berkoff D. Alveolar breath sampling and analysis to assess trihalomethane exposures during competitive swimming training. *Environ Health Perspect*. 1997;105(6):636-642.
23. Panyakapo M, Soontornchai S, Paopuree P. Cancer risk assessment from exposure to trihalomethanes in tap water and swimming pool water. *J Environ Sci (China)*. 2008;20(3):372-378.
24. Gomà A, Guisasola A, Tayà C, et al. Benefits of carbon dioxide as pH reducer in chlorinated indoor swimming pools. *Chemosphere*. 2010;80:428-432.
25. Lee J, Ha KT, Zoh KD. Characteristics of trihalomethane (THM) production and associated health risk assessment in swimming pool waters treated with different disinfection methods. *Sci Total Environ*. 2009;407:1990-1997.
26. Villanueva CM, Font-Ribera L. Health impact of disinfection by-products in swimming pools. *Ann Ist Super Sanita*. 2012;48(4):387-396.
27. Erdinger K, Kühn L, Gabrio T. Formation of trihalomethanes in swimming pool water – identification of precursors and kinetics of formation. Proceedings of the 1st International Conference of Health and Water Quality Aspects of the Man Made Recreational Water Environment; 10-11 March, 2005; Budapest.
28. Bernard A, Nickmilder M, Voisin C. Outdoor swimming pools and the risks of asthma and allergies during adolescence. *Eur Respir J*. 2008;32(4):979-988.
29. Yang Y, Komaki Y, Kimura S, et al. Toxic impact of bromide and iodide on drinking water disinfected with chlorine or chloramines. *Environ Sci Technol*. 2014;48(20):12362-12369.
30. Hlavsa M, Robinson T, Collier S, Beach M. Pool chemical-associated health events in public and residential settings – United States, 2003–2012, and Minnesota, 2013. *MMWR Morb Mortal Wkly Rep*. 2014;63(19):427-430.
31. Jacobs JH, Spaan S, van Rooy GB, et al. Exposure to trichloramine and respiratory symptoms in indoor swimming pool workers. *Eur Respir J*. 2007;29(4):690-698.
32. Massin N, Bohadana AB, Wild P, Hery M, Toamain JP, Hubert G. Respiratory symptoms and bronchial responsiveness in lifeguards exposed to nitrogen trichloride in indoor swimming pools. *Occup Environ Med*. 1998;55(4):258-263.
33. Rundell KW, Anderson SD, Sue-Chu M, Bougault V, Boulet LP. Air quality and temperature effects on exercise-induced bronchoconstriction. *Compr Physiol*. 2015;5(2):579-610.
34. Vandenplas O, Wiszniewska M, Raulf M, et al. EAACI position paper: irritant-induced asthma. *Allergy*. 2014;69(9):1141-1153.
35. Thickett KM, McCoach JS, Gerber JM, Sadhra S, Burge PS. Occupational asthma caused by chloramines in indoor swimming-pool air. *Eur Respir J*. 2002;19(5):827-832.
36. Musch MW, Walsh-Reitz MM, Chang EB. Roles of ZO-1, occludin, and actin in oxidant-induced barrier disruption. *Am J Physiol Gastrointest Liver Physiol*. 2006;290(2):G222-G231.
37. Bernard A. Chlorination products: emerging links with allergic diseases. *Curr Med Chem*. 2007;14(16):1771-1782.
38. Kotsiou O, Peletidou S, Vavougios G, et al. Exhaled nitric oxide as a marker of chlorine exposure in young asthmatic swimmers. *Ann Allergy Asthma Immunol*. 2019;123(3):249-255.
39. Carbonnelle S, Bernard A, Doyle IR, Grutters J, Francaux M. Fractional exhaled NO and serum pneumoproteins after swimming in a chlorinated pool. *Med Sci Sports Exerc*. 2008;40(8):1472-1476.
40. Font-Ribera L, Kogevinas M, Zock JP, et al. Short-term changes in respiratory biomarkers after swimming in a chlorinated pool. *Environ Health Perspect*. 2010;118(11):1538-1544.
41. Bonetto G, Corradi M, Carraro S, et al. Longitudinal monitoring of lung injury in children after acute chlorine exposure in a swimming pool. *Am J Respir Crit Care Med*. 2006;174(5):545-549.
42. Grasemann H, Tschiedel E, Groch M, Klepper J, Ratjen F. Exhaled nitric oxide in children after accidental exposure to chlorine gas. *Inhal Toxicol*. 2007;19(10):895-898.
43. Bernard A, Carbonnelle S, de Burbure C, Michel O, Nickmilder M. Chlorinated pool attendance, atopy, and the risk of asthma during childhood. *Environ Health Perspect*. 2006;114(10):1567-1573.
44. Bonsignore M, Morici G, Riccobono L, et al. Airway cells after swimming outdoors or in the sea in nonasthmatic athletes. *Med Sci Sports Exerc*. 2003;35(7):1146-1152.
45. Yang J, Ji R, Cheng Y, Sun J, Jennings L, Zhang C. L-Arginine chlorination results in the formation of a nonselective nitric-oxide synthase inhibitor. *J Pharmacol Exp Ther*. 2006;318:1044-1049.
46. Carbonnelle S, Francaux M, Doyle I, et al. Changes in serum pneumoproteins caused by short-term exposures to nitrogen trichloride in indoor chlorinated swimming pools. *Biomarkers*. 2002;7(6):464-478.
47. Bauer J, Wald J, Doran S, Soda D. Endogenous nitric oxide in expired air: effects of acute exercise in humans. *Life Sci*. 1994;55(24):1903-1909.
48. Chirpaz-Oddou M, Favre-Juvin A, Flore P, et al. Nitric oxide response in exhaled air during an incremental exhaustive exercise. *J Appl Physiol*. 1997;82(4):1311-1318.
49. De Gouw H, Marshall-Partridge S, Van Der Veen H, Van Den Aardweg J, Hiemstra P, Sterk P. Role of nitric oxide in the airway response to exercise in healthy and asthmatic subjects. *J Appl Physiol*. 2001;90(2):586-592.
50. Persson M, Wiklund N, Gustafsson L. Endogenous nitric oxide in single exhalations and the change during exercise. *Am Rev Respir Dis*. 1993;148(5):1210-1214.
51. Phillips C, Giraud G, Holden W. Exhaled nitric oxide during exercise: site of release and modulation by ventilation and blood flow. *J Appl Physiol*. 1996;80(6):1865-1871.
52. Parrat J, Donze G, Iseli C, Perret D, Tomicic C, Schenk O. Assessment of occupational and public exposure to trichloramine in Swiss indoor swimming pools: a proposal for an occupational exposure limit. *Ann Occup Hyg*. 2012;56(3):264-277.
53. Gardinier S, Guehenneux S, Latreille J, Guinot C, Tschachler E. Variations of skin biophysical properties after recreational swimming. *Skin Res Technol*. 2009;15(4):427-432.
54. Dalmau G, Martinez-Escala ME, Gazquez V, et al. Swimming pool contact dermatitis caused by 1-bromo-3-chloro-5,5-dimethyl hydantoin. *Contact Dermatitis*. 2012;66(6):335-339.
55. Fernandez-Luna A, Burillo P, Felipe JL, del Corral J, Garcia-Unanue J, Gallardo L. Perceived health problems in swimmers according to

the chemical treatment of water in swimming pools. *Eur J Sport Sci*. 2016;16(2):256-265.
56. Sasseville D, Geoffrion G, Lowry RN. Allergic contact dermatitis from chlorinated swimming pool water. *Contact Dermatitis*. 1999;41(6):347-348.
57. Neering H. Contact urticaria from chlorinated swimming pool water. *Contact Dermatitis*. 1977;3(5):279.
58. Najnin N, Forbes A, Sinclair M, Leder K. Risk factors for community-based reports of gastrointestinal, respiratory, and dermal symptoms: findings from a cohort study in Australia. *Journal Epidemiol*. 2014;24(1):39-46.
59. Kelsall HL, Sim MR. Skin irritation in users of brominated pools. *Int J Environ Health Res*. 2001;11(1):29-40.
60. Goma A, de Lluis R, Roca-Ferrer J, Lafuente J, Picado C. Respiratory, ocular and skin health in recreational and competitive swimmers: beneficial effect of a new method to reduce chlorine oxidant derivatives. *Environ Res*. 2017;152:315-321.
61. Voisin C, Sardella A, Bernard A. Risks of new-onset allergic sensitization and airway inflammation after early age swimming in chlorinated pools. *Int J Hyg Environ Health*. 2014;217(1):38-45.
62. Kanikowska A, Napiórkowska-Baran K, Graczyk M, Kucharski MA. Influence of chlorinated water on the development of allergic diseases – An overview. *Ann Agric Environ Med*. 2018;25(4):651-655.
63. Shim JS, Lee HS, Park DE, et al. Aggravation of asthmatic inflammation by chlorine exposure via innate lymphoid cells and $CD11c^{intermediate}$ macrophages. *Allergy*. 2020;75(2):381-391.
64. Seki T, Morimatsu S, Nagahori H, Morohashi M. Free residual chlorine in bathing water reduces the water-holding capacity of the stratum corneum in atopic skin. *J Dermatol*. 2003;30(3):196-202.
65. Fantuzzi G, Righi E, Predieri G, Giacobazzi P, Petra B, Aggazzotti G. Airborne trichloramine (NCl(3)) levels and self-reported health symptoms in indoor swimming pool workers: dose-response relationships. *J Expo Sci Environ Epidemiol*. 2013;23(1):88-93.
66. Chu TS, Cheng SF, Wang GS, Tsai SW. Occupational exposures of airborne trichloramine at indoor swimming pools in Taipei. *Sci Total Environ*. 2013;461–462:317-322.
67. Westerlund JBI, Löfstedt H, Eriksson K, Westberg H, Graff P. Occupational exposure to trichloramine and trihalomethanes: adverse health effects among personnel in habilitation and rehabilitation swimming pools. *J Occup Environ Hyg*. 2019;16(1):78-88.
68. Bureau G, Levesque B, Dube M, Gauvin D, Lepine F, Laliberte D. Indoor swimming pool environments and self-reported irritative and respiratory symptoms among lifeguards. *Int J Environ Health Res*. 2017;27(4):306-322.
69. Mountjoy M, Fitch K, Boulet L-P, Bougault V, van Mechelen W, Verhagen E. Prevalence and characteristics of asthma in the aquatic disciplines. *J Allergy Clin Immunol*. 2015;136(3):588-594.
70. Helenius I, Rytilä P, Metso P, Haahtela T, Venge P, Tikkanen H. Respiratory symptoms, bronchial responsiveness, and cellular characteristics of induced sputum in elite swimmers. *Allergy*. 1998;53(4):346-352.
71. Helenius I, Rytilä P, Sarna S, et al. Effect of continuing or finishing high-level sports on airway inflammation, bronchial hyperresponsiveness, and asthma: a 5-year prospective follow-up study of 42 highly trained swimmers. *J Allergy Clin Immunol*. 2002;109(6):962-968.
72. Bougault V, Odashiro P, Turmel J, et al. Changes in airway inflammation and remodelling in swimmers after quitting sport competition. *Clin Exp Allergy*. 2018;48(12):1748-1751.
73. Kurowski M, Jurczyk J, Olszewska-Ziąber A, Jarzębska M, Krysztofiak H, Kowalski ML. A similar pro/anti-inflammatory cytokine balance is present in the airways of competitive athletes and non-exercising asthmatics. *Adv Med Sci*. 2018;63(1):79-86.
74. Moreira A, Palmares C, Lopes C, Delgado L. Airway vascular damage in elite swimmers. *Respir Med*. 2011;105(11):1761-1765.
75. Gabrilo G, Peric M, Stipic M. Pulmonary function in pubertal synchronized swimmers: 1-year follow-up results and its relation to competitive achievement. *Med Probl Perform Art*. 2011;26(1):39-43.
76. Gelardi M, Ventura MT, Fiorella R, et al. Allergic and non-allergic rhinitis in swimmers: clinical and cytological aspects. *British J Sports Med*. 2012;46(1):54-58.
77. Surda P, Walker A, Limpens J, Fokkens W, Putala M. Nasal changes associated with exercise in athletes: systematic review. *J Laryngol Otol*. 2018;132(3):191-197.
78. Metelitsa A, Barankin B, Lin AN. Diagnosis of sports-related dermatoses. *Int J Dermatol*. 2004;43(2):113-119.
79. Basler RSW, Basler GC, Palmer AH, Garcia MA. Special skin symptoms seen in swimmers. *J Am Acad Dermatol*. 2000;43(2, Part 1):299-305.
80. Fernández-Luna Á, Burillo P, Felipe JL, del Corral J, García-Unanue J, Gallardo L. Perceived health problems in swimmers according to the chemical treatment of water in swimming pools. *Eur J Sport Sci*. 2016;16(2):256-265.
81. Kujundzić M, Braut T, Manestar D, et al. Water related otitis externa. *Coll Antropol*. 2012;36(3):893-897.
82. Bernard A, Carbonnelle S, Michel O, et al. Lung hyperpermeability and asthma prevalence in schoolchildren: unexpected associations with the attendance at indoor chlorinated swimming pools. *Occup Environ Med*. 2003;60(6):385-394.
83. Bernard A, Nickmilder M, Voisin C, Sardella A. Impact of chlorinated swimming pool attendance on the respiratory health of adolescents. *Pediatrics*. 2009;124(4):1110-1118.
84. Andersson M, Backman H, Nordberg G, et al. Early life swimming pool exposure and asthma onset in children - a case-control study. *Environ Health*. 2018;17(1):34.
85. Andersson M, Hedman L, Nordberg G, Forsberg B, Eriksson K, Ronmark E. Swimming pool attendance is related to asthma among atopic school children: a population-based study. *Environ Health*. 2015;14:37.
86. Cotter A, Ryan CA. The pool chlorine hypothesis and asthma among boys. *Ir Med J*. 2009;102(3):79-82.
87. Ferrari M, Schenk K, Mantovani W, et al. Attendance at chlorinated indoor pools and risk of asthma in adult recreational swimmers. *J Sci Med Sport*. 2011;14(3):184-189.
88. Cavaleiro Rufo J, Paciencia I, Silva D, et al. Swimming pool exposure is associated with autonomic changes and increased airway reactivity to a beta-2 agonist in school aged children: a cross-sectional survey. *PLoS One*. 2018;13(3):e0193848.
89. Font-Ribera L, Villanueva CM, Gracia-Lavedan E, Borras-Santos A, Kogevinas M, Zock JP. Indoor swimming pool attendance and respiratory and dermal health in schoolchildren–HITEA Catalonia. *Respir Med*. 2014;108(7):1056-1059.
90. Font-Ribera L, Villanueva CM, Ballester F, et al. Swimming pool attendance, respiratory symptoms and infections in the first year of life. *Eur J Pediatr*. 2013;172(7):977-985.
91. Font-Ribera L, Villanueva CM, Nieuwenhuijsen MJ, Zock JP, Kogevinas M, Henderson J. Swimming pool attendance, asthma, allergies, and lung function in the avon longitudinal study of parents and children cohort. *Am J Respir Crit Care Med*. 2011;183(5):582-588.
92. Jacobs JH, Fuertes E, Krop EJ, Spithoven J, Tromp P, Heederik DJ. Swimming pool attendance and respiratory symptoms and allergies among Dutch children. *Occup Environ Med*. 2012;69(11):823-830.
93. Bernard A, Voisin C, Sardella A. Con: respiratory risks associated with chlorinated swimming pools: a complex pattern of exposure and effects. *Am J Respir Crit Care Med*. 2011;183(5):570-572.
94. Klootwijk T, Krul M. Some concerns remain about the proposed association between swimming and asthma. *Am J Respir Crit Care Med*. 2011;184(12):1419. author reply 1419–1420.

95. Nystad W, Nja F, Magnus P, Nafstad P. Baby swimming increases the risk of recurrent respiratory tract infections and otitis media. *Acta Pediatr*. 2003;92(8):905-909.
96. Voisin C, Sardella A, Marcucci F, Bernard A. Infant swimming in chlorinated pools and the risks of bronchiolitis, asthma and allergy. *Eur Respir J*. 2010;36(1):41-47.
97. Kohlhammer Y, Doring A, Schafer T, Wichmann HE, Heinrich J. Swimming pool attendance and hay fever rates later in life. *Allergy*. 2006;61(11):1305-1309.
98. Voisin C, Sardella A, Bernard A. Allergic sensitization and airway inflammation after early swimming. *Am J Respir Crit Care Med*. 2013;187(12):1392-1394.
99. Lagerkvist BJ, Bernard A, Blomberg A, et al. Pulmonary epithelial integrity in children: relationship to ambient ozone exposure and swimming pool attendance. *Environ Health Perspect*. 2004;112(17):1768-1771.
100. Bernard A, Nickmilder M, Dumont X. Chlorinated pool attendance, airway epithelium defects and the risks of allergic diseases in adolescents: interrelationships revealed by circulating biomarkers. *Environ Res*. 2015;140:119-126.
101. Hung C, Chen L, Zhang Z, et al. Regulation of TH2 responses by the pulmonary clara cell secretory 10-kd protein. *J Allergy Clin Immunol*. 2004;114:664-670.
102. Johansson S, Wennergren G, Aberg N, Rudin A. Clara cell 16-kd protein downregulates T(H)2 differentiation of human naive neonatal T cells. *J Allergy Clin Immunol*. 2007;120:308-314.
103. Wang H, Long X, Cao P, et al. Clara cell 10-kD protein suppresses chitinase 3-like 1 expression associated with eosinophilic chronic rhinosinusitis. *Am J Respir Crit Care Med*. 2010;181:908-916.
104. Liu Y, Lu X, Yu H, et al. The expression of osteopontin and its association with clara cell 10 kDa protein in allergic rhinitis. *Clin Exp Allergy*. 2010;40:1632-1641.
105. Kurowski M, Jurczyk J, Jarzebska M, et al. Association of serum clara cell protein CC16 with respiratory infections and immune response to respiratory pathogens in elite athletes. *Respir Res*. 2014;15:45.
106. Zhu L, An L, Ran D, et al. The club cell marker SCGB1A1 downstream of FOXA2 is reduced in asthma. *Am J Respir Cell Mol Biol*. 2019;60(6):695-704.
107. Zhai J, Insel M, Addison KJ, et al. Club cell secretory protein deficiency leads to altered lung function. *Am J Respir Crit Care Med*. 2019;199(3):302-312.
108. IARC. International Agency for Research on Cancer Monographs on the evaluation of carcinogenic risks to humans. *Some chemicals that cause tumors of the kidney or urinary bladder in rodents and some other substances*. Lyon 1999.
109. Gouveia P, Felgueiras F, Mourao Z, Fernandes EO, Moreira A, Gabriel MF. Predicting health risk from exposure to trihalomethanes in an Olympic-size indoor swimming pool among elite swimmers and coaches. *J Toxicol Environ Health A*. 2019;82(9):577-590.
110. Costet N, Villanueva CM, Jaakkola JJ, et al. Water disinfection by-products and bladder cancer: is there a European specificity? A pooled and meta-analysis of European case-control studies. *Occup Environ Med*. 2011;68(5):379-385.
111. Villanueva CM, Cantor KP, Cordier S, et al. Disinfection by-products and bladder cancer: a pooled analysis. *Epidemiology*. 2004;15(3):357-367.
112. Villanueva CM, Cantor KP, Grimalt JO, et al. Bladder cancer and exposure to water disinfection by-products through ingestion, bathing, showering, and swimming in pools. *Am J Epidemiol*. 2007;165(2):148-156.
113. Beane Freeman LE, Cantor KP, Baris D, et al. Bladder cancer and water disinfection by-product exposures through multiple routes: a population-based case-control study (New England, USA). *Environ Health Perspect*. 2017;125(6):67010.
114. Nelemans PJ, Rampen FH, Groenendal H, Kiemeney LA, Ruiter DJ, Verbeek AL. Swimming and the risk of cutaneous melanoma. *Melanoma Res*. 1994;4(5):281-286.
115. Rahman MB, Driscoll T, Cowie C, Armstrong BK. Disinfection by-products in drinking water and colorectal cancer: a meta-analysis. *Int J Epidemiol*. 2010;39(3):733-745.
116. Grellier J, Bennett J, Patelarou E, et al. Exposure to disinfection by-products, fetal growth, and prematurity: a systematic review and meta-analysis. *Epidemiol*. 2010;21(3):300-313.
117. Nieuwenhuijsen M, Martinez D, Grellier J, et al. Chlorination disinfection by-products in drinking water and congenital anomalies: review and meta-analyses. *Environ Health Perspect*. 2009;117(10):1486-1493.
118. Nickmilder M, Bernard A. Associations between testicular hormones at adolescence and attendance at chlorinated swimming pools during childhood. *Int J Androl*. 2011;34(5 Pt 2). https://doi.org/10.1111/j.1365-2605.2011.01174.x
119. Chu H, Nieuwenhuijsen MJ. Distribution and determinants of trihalomethane concentrations in indoor swimming pools. *Occup Environ Med*. 2002;59(4):243-247.
120. Nitter T, Svendsen K. Modelling the concentration of chloroform in the air of a Norwegian swimming pool facility-A repeated measures study. *Sci Total Environ*. 2019;664:1039-1044.
121. Nitter T, Hirsch SK. Covariation amongst pool management, trichloramine exposure and asthma for swimmers in Norway. *Sci Total Environ*. 2020;723:138070.
122. Li J, Blatchley E. Volatile disinfection byproduct formation resulting from chlorination of organic-nitrogen precursors in swimming pools. *Environ Sci Technol*. 2007;41(19):6732-6739.
123. Weaver W, Li J, Wen Y, Johnston J, Blatchley M, Blatchley E. Volatile disinfection by-product analysis from chlorinated indoor swimming pools. *Water Res*. 2009;43(13):3308-3318.
124. Sa C, Boaventura R, Pereira I. Analysis of haloacetic acids in water and air (aerosols) from indoor swimming pools using HS-SPME/GC/ECD. *J Environ Sci Health A Tox Hazard Subst Environ Eng*. 2012;47(2):176-183.
125. World Health Organization. Guidelines for safe recreational-water environments. Vol 22000.
126. van Veldhoven K, Keski-Rahkonen P, Barupal DK, et al. Effects of exposure to water disinfection by-products in a swimming pool: a metabolome-wide association study. *Environ Int*. 2018;111:60-70.
127. Marco E, Lourencetti C, Grimalt JO, et al. Influence of physical activity in the intake of trihalomethanes in indoor swimming pools. *Environ Res*. 2015;140:292-299.
128. Bozym M, Wzorek M, Klosok-Bazan I. Health risk as a consequence of exposure to trihalomethanes in swimming pool water. *Rocz Panstw Zakl Hig*. 2017;68(4):331-337.
129. Evans O, Cantú R, Bahymer T, Kryak D, Dufour A. A pilot study to determine the water volume ingested by recreational swimmers. Annual Meeting of the Society for Risk Analysis; 2–5 December, 2001; Seattle, Washington.
130. Chaumont A, Voisin C, Sardella A, Bernard A. Interactions between domestic water hardness, infant swimming and atopy in the development of childhood eczema. *Environ Res*. 2012;116:52-57.
131. Xu X, Mariano T, Laskin J, Weisel C. Percutaneous absorption of trihalomethanes, haloacetic acids, and haloketones. *Toxicol Appl Pharmacol*. 2002;184(1):19-26.
132. Trabaris M, Laskin J, Weisel C. Percutaneous absorption of haloacetonitriles and chloral hydrate and simulated human exposures. *J Appl Toxicol*. 2012;32(6):387-394.
133. World Health Organization. Children are not little adults. *Children's Health and the Environment WHO Training Package for the Health Sector* 2008.
134. Bowen A, Kile J, Otto C, et al. Outbreaks of short-incubation ocular and respiratory illness following exposure to indoor swimming pools. *Environ Health Perspect*. 2007;115(2):267-271.

135. Erdinger L, Kühn KP, Kirsch F, et al. Pathways of trihalomethane uptake in swimming pools. *Int J Hyg Environ Health*. 2004;207:571-575.
136. Lévesque B, Ayotte P, LeBlanc A, et al. Evaluation of dermal and respiratory chloroform exposure in humans. *Environ Health Perspect*. 1994;102:1082-1087.
137. Lebon M, Fellouah H, Galanis N, Limane A, Guerfala N. Numerical analysis and field measurements of the airflow patterns and thermal comfort in an indoor swimming pool: a case study. *Energ Effic*. 2017;10(3):527-548.
138. Shah MM. Methods for calculation of evaporation fromswimming pools and other water surfaces. *ASHRAE Transactions*. 2014;120:3-17.
139. Felgueiras MZ, Morais C, Santos H, Gabriel M, de Oliveira FE. Comprehensive assessment of the indoor air quality in a chlorinated Olympic-size swimming pool. *Environ Health*. 2020;136:105401.
140. Gabriel M, Felgueiras F, Mourão Z, Fernandes EO. Assessment of the air quality in 20 public indoor swimming pools located in the Northern Region of Portugal. *Environ Int*. 2019;133(PT B):105274.
141. United States Environmental Protection Agency. *User's manual: swimmer exposure assessment model (SWIMODEL)*. Office of Pesticide Programs; 2003.
142. Fernandez-Luna A, Gallardo L, Plaza-Carmona M, et al. Respiratory function and changes in lung epithelium biomarkers after a short-training intervention in chlorinated vs. ozone indoor pools. *PLoS One*. 2013;8(7):e68447.
143. Font-Ribera L, Marco E, Grimalt JO, et al. Exposure to disinfection by-products in swimming pools and biomarkers of genotoxicity and respiratory damage - The PISCINA2 Study. *Environ Int*. 2019;131:104988.
144. Nickmilder M, Bernard A. Ecological association between childhood asthma and availability of indoor chlorinated swimming pools in Europe. *Occup Environ Med*. 2007;64(1):37-46.
145. Schoefer Y, Zutavern A, Brockow I, et al. Health risks of early swimming pool attendance. *Int J Hyg Environ Health*. 2008;211(3–4):367-373.
146. Schuez-Havupalo L, Karppinen S, Toivonen L, et al. Association between infant swimming and rhinovirus-induced wheezing. *Acta Pediatr*. 2014;103(11):1153-1158.
147. Bernard A, Sardella A, Voisin C, Dumont X. Nasal epithelium injury by chlorination products and other stressors predicts persistent sensitization to aeroallergens in young schoolchildren. *Environ Res*. 2017;158:145-152.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

How to cite this article: Couto M, Bernard A, Delgado L, et al. Health effects of exposure to chlorination by-products in swimming pools. *Allergy*. 2021;00:1–19. https://doi.org/10.1111/all.15014