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REVIEW

Effectiveness of N95 respirators for nanoparticle exposure control (2000–2016): a systematic review and meta-analysis

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Abstract Workers are increasingly exposed to nanoparticles, mostly via inhalation. Respiratory protection is recommended as an additional control measure. Particulate respirators are certified for protection against micro-sized particles, where a most penetrating particle size (MPPS) of 100–400 nm is assumed. Commonly used N95 respirators are certified by the National Institute for Occupational Safety and Health after passing a 95% collection efficiency test. Electret media used in respirators have been demonstrated to be shifting the MPPS to a nanosized region. Experimental studies have therefore been conducted to assess N95 respirator penetration specifically by nanoparticles. This systematic review and meta-analysis was aimed at systematically reviewing these studies and meta-analysing the mean penetration percentage (PP). The review was conducted following a Preferred Reporting Items for Systematic Reviews and Meta-Analyses guideline. Fourteen studies were selected to be reviewed qualitatively, while 13 of these with 29 data points were included in the meta-analysis. Sensitivity analysis was performed based on a respirator mounting protocol, while subgroup analysis was done for aerosol dispersity and repeated for the respirator mounting protocol. The size range of particles used across the reviewed studies was 1 nm–10 μm. The MPPS for all studies was in the nanosized particle range, with the lowest at approximately 39 nm. The estimated mean PP was between 1 and 6%, exceeding the 5% guideline threshold for four of the studies. All the meta-analysed mean PPs were however below the 5% guideline. This means that the N95 respirators may be effective for nanoparticles in workplaces, but subject to factors including respirator characteristics and particle dispersity.

Keywords Nanoparticles · N95 respirator · Effectiveness · Penetration · Exposure control · Protection · Environmental · Health and safety issues

Introduction

Engineered nanoparticles are synthesised with specific properties including shape, size and surface properties, with the aim of exploiting their functionalities such as improved strength and enhanced thermal and electrical conductivity (Eninger et al. 2008a; Matsoukas et al. 2015). Incidental nanoparticles exist as by-products of human activities. This could be emissions from chemical processing, exhaust fumes, welding, grinding,

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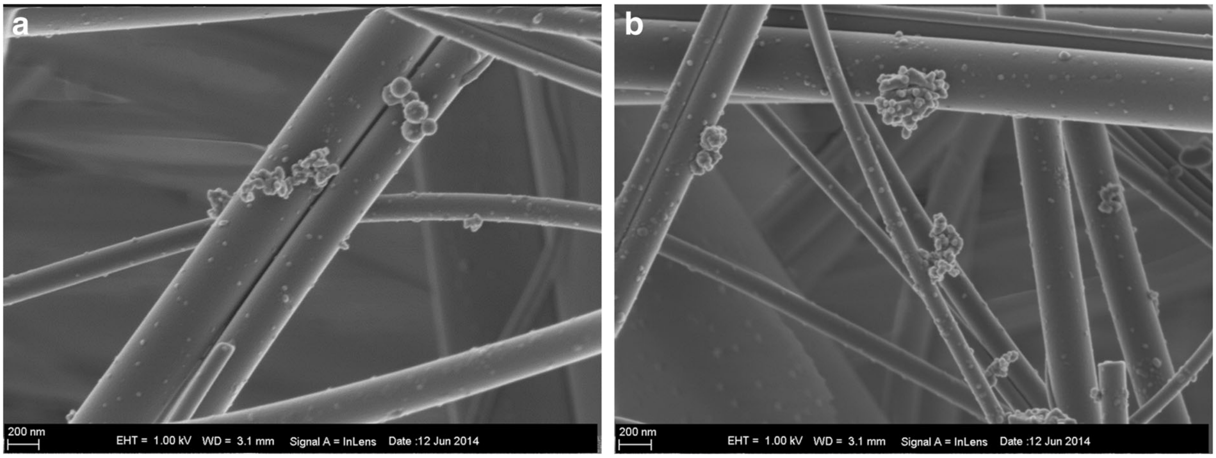

Fig. 1 Images of incidental nanoparticles collected on a glass fibre filter, analysed by a Jeol 200-kV FEGTEM Model 2100F transmission electron microscope (TEM) (NIOH, Occupational hygiene survey and risk assessment at a smelter, unpublished)

smelting and spray painting (Buzea et al. 2007; NIOSH 2009). Figure 1 shows different types of particles between 21.8 and 140.6 nm in size, collected in a converter section of a smelter (NIOH, Occupational hygiene survey and risk assessment at a smelter, unpublished).

There have been reports on harmful health effects elicited by nanoparticles, including death (Phillips et al. 2010). While conclusions about the health effects of nanoparticles are still pending, it is recommended that the principle of precaution be applied to limit exposure during the synthesis and application. This includes the use of engineering controls and personal protective equipment (PPE). According to the hierarchy of exposure controls, PPE should be the last resort after source elimination, substitution, engineering and administration measures, to bring the exposure levels to below their respective occupational exposure limit (OEL) (NIOSH 2015). Since OELs have not yet been established for most engineered nanoparticles and are under proposal in the case of others, precaution to limit potential exposure by the use of PPE in addition to other control measures is advised (EASHW n.d.).

The most common route of occupational exposure to humans is through inhalation. A respirator is a device used to prevent the inhalation of harmful airborne substances and/or also used in an oxygen-deficient atmosphere. It works by either purifying the air by removing contaminants before they reach the breathing zone of the worker, or providing clean air from an uncontaminated source in cases of oxygen-deficient atmosphere (OSHA n.d.).

Disposable half-piece air-purifying respirators are widely used because they are low-cost, easily accessible, lightweight with minimal deterrent during task operations; offer a variety of sizes; and are easy to maintain (Han et al. 1997; Popendorf et al. 1995; Rengasamy et al. 2007). Advanced technology has allowed for development of respirators that are much more effective for a range of chemicals, are lightweight and can be used in conjunction with other personal protective equipment (OSHA n.d.).

As part of the respiratory protection standard of the Occupational Safety and Health Act (OSHA), USA, respirators are certified by the National Institute for Safety and Health (NIOSH). The certification test for N95 respirators is performed following 'worst case' scenarios including storage at 85% relative humidity and 25 °C temperature conditions for 25 h prior and charge neutralisation of the challenge aerosol. The sodium chloride (NaCl) test aerosol has a mass median diameter (MMD) of 238 nm, a mass median aerodynamic diameter (MMAD) of 347 nm and a count median diameter of 0.075 ± 0.020 μm and tested at a flow rate of 85 l/min. The respirator's efficiency is assessed as either initial penetration or maximum penetration, depending on a loading curve obtained after it is challenged with 200 mg of the NaCl for the first 3 sample filters. This test is performed with a photometer. Once approved, a respirator is marked 'NIOSH' and the filter classification indicated i.e. N95 in this case (NIOSH 2016).

Electret filters, which are composed of charged fibres, are used in particulate respirators as they have been found to be more effective than solely mechanical ones, and have the added advantage of low airflow resistance (Mostofi 2010; Löffler 1974). Earlier studies however demonstrated a shift of the most penetrating particle size (MPPS), a region in filtration where particle penetration is at its maximum and filter efficiency is at its minimum, from the traditional 100–400 nm to a more nanosized region, with the addition of the electret mechanism on a filter (Huang et al. 2007; Balazy et al. 2006). A number of organisations such as NIOSH and the Organization for Economic Co-operation and Development and the European Commission have advocated for the testing of the current control measures for nanoparticle filtration (OECD 2009; NIOSH 2012; EC 2015).

This has prompted a number of experimental studies on the penetration of nanoparticles through certified respirators. The studies have used nanosized particles and analysing techniques that are more sensitive to this size range.

It should be noted that there are no standard tests for nanoparticle penetration on respirators. If no automated filter testers for nanosized particles were available, researchers adopted the conventional filter testing protocols and customised them to allow for nanoparticle characterisation (see Fig. 2 for a typical experiment set-up). This included the use of particle counters in the place of photometers as the latter has been reported to be ineffective in measuring particles in the ultrafine/nanoregion (Eninger et al. 2008b; Rengasamy et al. 2011; Gebhart 2001). To evaluate the MPPS, the penetration is assessed as a function of particle size. Penetration percentage (PP) is determined as follows:

$$\mathrm{PP} = \left(\frac{C\{\mathrm{down}\}}{C\{\mathrm{up}\}}\right) \times 100\%$$

where

$C\{\mathrm{down}\}$ particle number concentration downstream of the filter
$C\{\mathrm{up}\}$ particle number concentration upstream of the filter

Eninger et al. (2008a) presented a data summary of studies that assessed the shift of MPPS. The studies tested respirators such as N95, N99, R95 and P100 as well as filters used in these respirators. All the studies noted an MPPS below 100 nm, except in 2 studies, where one reported an MPPS of 120 nm for a high-efficiency filter used in NIOSH-certified N100 and P100 respirators. The other MPPS at ≤ 120 nm was for filters challenged with latex spheres. A systematic review by Shaffer and Rengasamy (2009) on respirator filter penetration, face seal leakage and protection factors against nanoparticles also reported on studies that assessed performance of respirator filters and a range of respirator types, including those previously certified under the EN protocol. Similarly to Eninger et al. (2008a), the review also noted a shift on an MPPS, with a range of 30–200 nm. The highest 200 nm MPPS was for a P100 cartridge used as part of a non-disposable respirators. The review also reported penetration percentage corresponding to the MPPS. The highest penetrations were 8.8% for the previously described P100 cartridge and 10% on a filter media used in N95 respirators. None of the 2 reviews however have performed quantitative analysis of the reviewed data but Shaffer and Rengasamy (2009) have highlighted the reasons that could potentially contribute to the variations in the individual studies.

While NaCl is commonly used as a standard aerosol for filter testing, penetration through a filter may be different for particles encountered in a workplace. Zhou and Cheng (2016) tested N95 respirators with titanium dioxide (TiO_2), carbon nanotube (CNT) and fullerene engineered nanomaterials at 85 l/min. The results showed that although higher than that for the NaCl used in the study, the mean PP for all the 3 nanomaterials never exceeded the 5% threshold, with an MPPS of about 91–154 nm. The authors did not mention if the aerosols were charge-neutralised, and this method may have increased penetration; however, workplace aerosols are expected to be charged. Cho et al. (2011) however observed lower penetrations of welding fumes when compared to NaCl.

The aim of this study was to determine if N95 respirators are effective against nanoparticle exposure by systematically reviewing the studies that tested this effectiveness and providing a summary estimate of the outcomes by means of a meta-analysis.

In absence of standardised tests for nanoparticle filtration on respirators and regulated thresholds for efficiency, the estimated PP was compared to the NIOSH 5% for N95 respirators, as a guideline.

Overall, respirator performance is also dependant on a face fit and how it is used by the wearer. Respirator fit testing is done to assess any particulate leakage around the seal of a respirator when worn by the user. This fit testing does not form part of the certification tests. The leakage assessment of nanoparticles around a face seal and exhalation valve and how a respirator is used on site were outside the scope of this study.

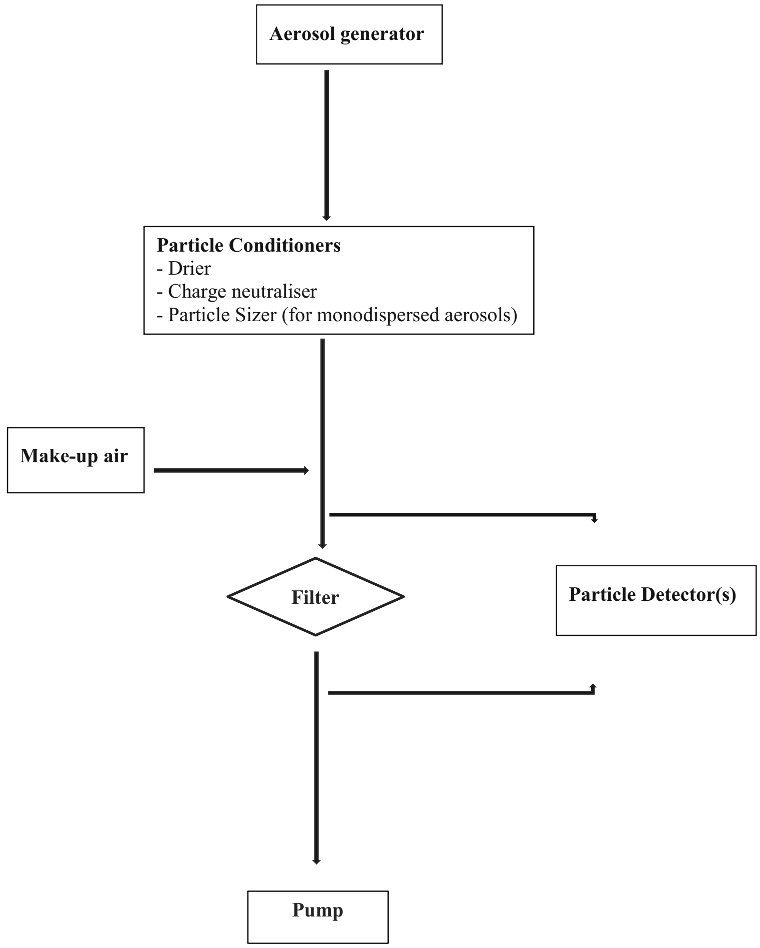

Fig. 2 Typical set-up respirator filtration tests for nanoparticles

Methodology

Study selection

Studies published between 2000 and 2016 met the selection criteria if

- they were laboratory-based experiments
- the challenge aerosol was NaCl at an ultrafine or nanoparticle range
- the test was carried out on N95 respirators
- the constant flow rate used was 85 l/min
- measuring techniques suitable for nanoparticles were used (product description of the equipment was obtained, to assess if it uses particle counting techniques and at detection ranges for nano/ultrafine sizes)
- the estimated mean PP was reported as a function of particle size

Studies published in languages other than English where translation was not feasible were omitted.

Information sources

The following data sources were searched:

- CISILO
- NIOSHTIC
- MEDLINE
- Google scholar
- Occupational Health and Nanotechnology related conference proceedings
- Reference list of the studies included in this review
- Relevant systematic reviews

Experts in the field were consulted via e-mails for related literature that was not present in the available sources.

Literature search

The following keywords were used on the aforementioned sources:

- "nanoparticles/ultrafine particles" and "respirators"
- "nanoparticles/ultrafine particles" and "respirators" and "penetration"
- "nanoparticles/ultrafine particles" and "face-piece respirators" and "effectiveness"
- "N95 respirators" and "nanoparticles/ultrafine particles" and "effectiveness"
- "nanoparticles/ultrafine particles" and "NIOSH-certified" and "respirators" and "performance"
- "aerosols" and "nanoparticles nanoparticles/ultrafine particles" and "respirator" and "penetration"
- "aerosols" and "nanoparticles nanoparticles/ultrafine particles" and "respirator" and "filtration"
- "aerosols" and "nanoparticles nanoparticles/ultrafine particles" and "respirator" and "performance"

Study selection

The title and abstract of the studies were first screened for relevance to the review and then accepted if they met the selection criteria described above.

Full texts of eligible papers determined by the primary screening, as well as those whose eligibility during screening was unclear, were obtained. These were then further assessed and accepted for the systematic review and subsequent meta-analysis if they had met the selection criteria (see Fig. 3). The reasons for exclusion of studies were noted (see Appendix, Table 5).

Data collection process

A standardised form adopted from the Cochrane Public Health Group (Cochrane 2011) was used to extract the data.

Data

The following variables were extracted from the selected studies:

- Study reference
- Challenge aerosol dispersity and size range
- MPPS
- Estimated mean PP
- Nanoparticle measuring technique
- Filter mounting protocol

In addition, to generate variables for the meta-analysis (see below), the test sample number was also extracted.

Summary measures

The summary measures from the studies were the estimated mean PP and the corresponding particle size, regarded as the MPPS. For studies that did not explicitly state the highest mean PP, these were estimated manually from the penetration curves using a ruler, and the associated MPPS determined.

Standard error (SE) was estimated using the following formula for proportions:

$$SE = \left(p \text{ X } \frac{1-p}{n}\right)^{0.5}$$

where

p penetration proportion
n sample size

The estimated mean PP and SE were used as variables for the meta-analysis. The analysis was done using StataCorp STATA version 12 with a 'metan' option. For an I^2 of > 90%, a random-effects model assuming great variation between studies was used. The model allowed the studies to be weighted by the inverse of their variances where the mean was pulled more towards the outcome of smaller studies (StataCorp 2011; Sterne et al. 2011).

Heterogeneity

The I^2 test for heterogeneity was used to assess variation between the studies and the degree thereof. The following rules were applied (Ryan 2016):

- 0 to 40%: might not be important
- 30 to 60%: may represent moderate heterogeneity
- 50 to 90%: may represent substantial heterogeneity
- 75 to 100%: considerable heterogeneity

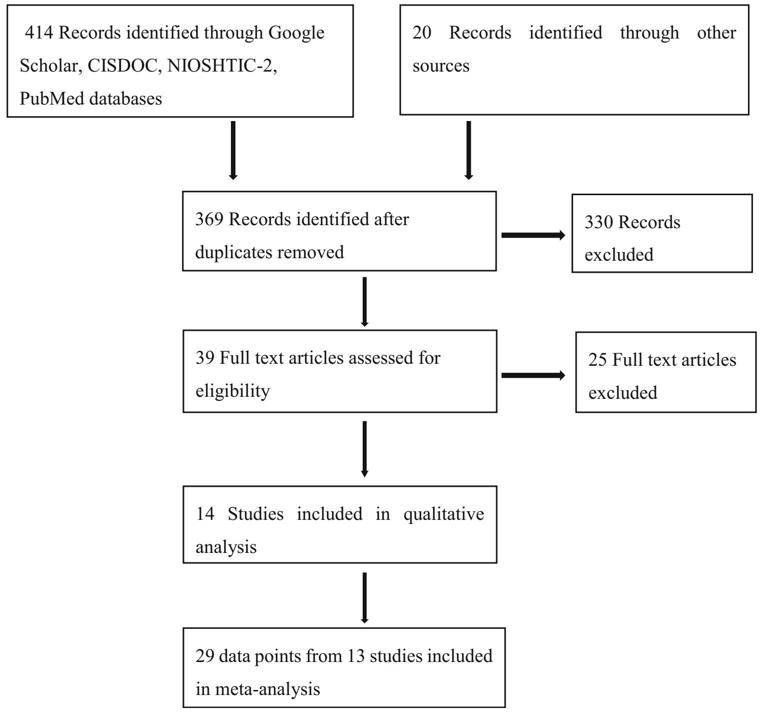

Fig. 3 Study selection flow diagram

Publication bias was limited by also searching for unpublished studies.

Additional analyses

The respirator certification test uses a respirator filter holder for mounting. The use of a manikin when using constant flow in studies is regarded as arbitrary, as the purpose of these is for mostly studying other parameters such as cyclic flows. However, some researchers used manikins to simulate a real-life scenario or to address other study objectives. Sensitivity analysis was therefore performed for studies that followed this manikin-based protocol. These studies were excluded from the meta-analysis to assess whether they influence the aggregated mean PP.

Subgroup analysis was performed for studies that used polydispersed NaCl aerosols as well as those that used monodispersed aerosols, excluding studies that did not indicate the dispersity of the challenge aerosols. As some studies used manikins as described above, subgroup analysis was also repeated for these study protocols vs those without manikins.

The I^2 test for degree of heterogeneity was repeated for each additional analysis.

As a result of the nature of the study i.e. the small sample size, statistical significant tests could not be performed for the analyses.

Results

Figure 3 demonstrates a flow diagram of how the studies were selected for the systematic review and subsequent meta-analysis. From the 39 full studies assessed for eligibility, only 14 met the selection criteria (see Appendix, Table 5 for reasons of exclusion). Huang et al. (2007) was excluded from the meta-analysis component as there were no sample numbers reported, to estimate the SE.

For studies with multiple data points, each observation, such as respirator model or a different type of a particle counter, was regarded as a separate observation (estimated mean PP). There were a total of 29 observations from the 13 studies aggregated for the meta-analysis. Mean PP was manually estimated for the following 6 studies; (Balazy et al. 2006; Gao et al. 2015; Mostofi et al. 2011; Rengasamy et al. 2007, 2009, 2011).

Table 1 presents the parameters used in the systematic review of the 14 studies. The oldest study was published in 2006 while the most recent was in 2016. All studies used particle sizes that consisted of nanoparticles (1–100 nm) and NaCl as a challenge aerosol and reported the mean PP as a function of particle number concentration using particle counting measurement techniques, as per the selection criteria. The estimated mean PP marked in bold were above the 5% acceptable criteria for N95 NIOSH–certified respirators, used as a guideline.

Figure 4 is a forest plot of the studies plotted using the estimated mean PP and SE, with pseudo confidence limits produced by the 'metan' command in STATA. Each observation from the 13 studies was regarded as an individual study. The figure also shows how each study weighted to the overall mean, due to the random-effects model chosen. This model was specifically chosen as it assumes heterogeneity in the overall mean (Ryan 2016).

The overall estimated mean PP for the 29 observations was estimated to be 2.79%, but with a heterogeneity of 99.8%.

To simulate more real-life scenarios or to address certain study objectives, 7 of the studies, Bahloul et al. (2014), Balazy et al. (2006), Eninger et al. (2008b), Mahdavi et al. (2015), Mostofi et al. (2011), Mostofi et al. (2012) and Zhou and Cheng (2016), mounted the respirators on manikins. The rest of the studies used filter boxes to mount the respirator, as per the NIOSH protocol. To assess if the manikin-based protocol greatly influenced the overall mean PP, a separate meta-analysis was conducted without these 6 studies. Table 2 contains the two aggregated means, with corresponding confidence intervals as well as the heterogeneity levels.

Table 1 Characteristics of selected studies for systematic review

Study	Challenge aerosol dispersity and size (nm)	MPPS (nm)	Estimated mean PP (%)	NP measuring technique
Bahloul et al. (2014)	Polydispersed; 10–205.4	40	2.66	TSI Scanning Mobility Particle Sizer (SMPS) 3080
Balazy et al. (2006)	10–600	40–50	4.9–*6*#	MSP Corp Wide-Range Particle Spectrophotometer (WPS) 1000 XP
Eninger et al. (2008b)	20–500	< 100	4.8	MSP Corp WPS 1000 XP
Eshbaugh et al. (2008)	Monodispersed; 20–2900	50	2.8–4.2	TSI Fractional Efficiency Tester (FET) 3160
Gao et al. (2015)	20–500	70	1.3#	Grimm Technologies Nanoparticle Aerosol Monitor 1320
Huang et al. (2007)*	4.5–10 000	50	*5.8*	TSI SMPS 3936
Mahdavi et al. (2015)	Polydispersed; 10–205.4	39	2.7	TSI SMPS 3080
Mostofi et al. (2011)	Polydispersed; 15–200 Monodispersed; 20–200	41–46 60	2.66–2.73 4.2#	TSI SMPS 3936 TSI CPC 3775
Mostofi et al. (2012)	Polydispersed; 1–100	40–70	3.08–3.37	SMPS and Electrical Low Pressure Impactor
Rengasamy et al. (2007)	Monodispersed; 20–400	40	1.4–*5.2*#	TSI FET 3160 with a Differential Mobility Analyser (DMA)
Rengasamy et al. (2009)	Monodispersed; 20–400	< 40–40	2.3–4.3#	TSI FET 3160
Rengasamy et al. (2011)	Monodispersed; 20–1000	40	1.4–*5.23*#	TSI FET 3160
Rengasamy et al. (2013)	Monodispersed; 20–100; 200–400	40	1.48	TSI FET 3160
Zhou and Cheng (2016)	5.5–308.7	43	1–2.4	Grimm Technologies SMPS

Estimated mean PP in italics are at or above the 5% acceptance criteria for N95 respirators

* Excluded from meta-analysis

Manually extracted mean PP

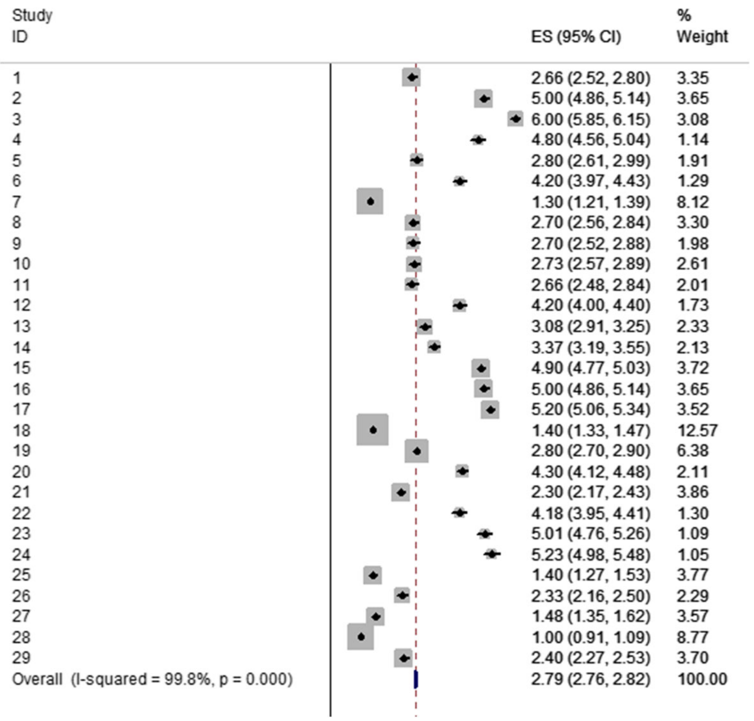

Fig. 4 Study estimates of mean NaCl penetration percentage of N95 respirators. The diamond shape represents a region where the calculated overall mean (2.79) lies

The analysis indicates that the use of manikin influenced penetration, as mean PP without these studies increased to 3.36%. The sample size for this analysis was however too small to assess statistical significance.

When analysed based on the dispersity of the aerosols, 16 of the data points were of monodispersed and 7 were of polydispersed aerosols, while the dispersity of 4 studies (6 data points) was not disclosed. Table 3 shows the separate meta-analysis results of studies that challenged the respirators with polydispersed aerosols and those that used monodispersed aerosols.

Mean PP was higher for monodispersed aerosols at 3.55% when compared to that for polydispersed aerosols at 2.82%. The sample size was also too small to assess statistical significance.

Table 4 demonstrates that when the analysis was grouped between the non-manikin-based vs manikin-based experimental set-up, the mean PP for the studies that did not use manikins was higher at 3.36% compared to those with PP at 2.94%.

Discussion

Nanoparticles in the workplace are a concern, particularly with the emergence of various nanotechnologies in industries. One case study demonstrated

Table 2 Sensitivity analysis of manikin-based studies

Included	Sample size (n)	Estimated mean PP	95% CI	Heterogeneity (%)
All studies	29	2.79	2.76–2.82	99.8 $p < 0.001$
Without manikin-based set-up studies	16	3.36	2.59–4.13	99.8 $p < 0.001$

n number of observations

Table 3 Subgroup analysis of monodispersed and polydispersed aerosols studies

Subgroup	Sample size (*n*)	Estimated mean PP	95% CI	Heterogeneity %
Monodispersed NaCl	16	3.55	2.78–4.32	99.8 $p < 0.001$
Polydispersed NaCl	7	2.82	2.76–2.88	90 $p < 0.001$

n number of observations

how nano nickel particles may have caused the death of a worker, by inhalation (Phillips et al. 2010). The most common route of occupational exposure is through inhalation, and while respirator protection should be the last resort for occupational exposure control, this method is widely used. Studies have been carried out to determine if these common respirators are effective for nanoparticle exposure. This systematic review and meta-analysis reports on studies that tested the efficiency of N95 respirator for NaCl nanoparticle penetration.

Systematic review

A total of 14 publications met the criteria for studies where NIOSH-certified N95 respirators were assessed for efficiency of filtering out nano/ultrafine sized NaCl aerosols at a constant flow rate of 85 l/min (see Table 1). The studies used nano/ultrafine particle counters to measure the particle number concentration (PNC) of the aerosols and reported particle penetration as a function of particle size. PNC is accepted as one of the most important metrics of nanoparticles rather than the traditional mass-interpreted method for micro-sized particles. The technique has allowed the studies to reliably observe a shift of the MPPS from the traditional 300 nm to a range of 39–< 100 nm, confirming an influence of electret filters, as demonstrated earlier by Balazy et al. (2006) and Huang et al. (2007).

All the studies reported MPPS of less than 300 nm, the lowest MPPS reported at approximately 39 nm was by Mostofi et al. 2011 while Rengasamy et al. (2007), Rengasamy et al. (2009), Rengasamy et al. (2011) and Rengasamy et al. (2013) mostly reported 40 nm. These MPPS fall within the size range that has been reported in exposure assessment studies (Phillips et al. 2010; Ham et al. 2012; NIOH, Occupational hygiene survey and risk assessment at a smelter, unpublished), indicating that a potential exposure risk to workers exists.

The range of the estimated mean PP was 1–6%. Four of the studies (Balazy et al. 2006; Huang et al. 2007; Rengasamy et al. 2011) measured mean PP at or above the 5% threshold of the NIOSH testing protocol for N95 respirators, used as a guideline. While the size range of challenged particles differed across these studies whose mean PP was above 5%, these were of monodispersed distribution for 2 of the studies, whereas dispersity by Balazy et al. (2006) and Huang et al. (2007) was not disclosed. Only a TSI 3160 automated filter tester was common in 2 studies from the same author; the remaining measuring techniques were all different across the studies. MPPS was the same for Balazy et al. (2006) and Huang et al. (2007) at 50 nm as well as for both Rengasamy et al.'s (2007 and 2011) studies, at 40 nm. This variability of the parameters was also apparent in studies that measured PP of below 5%, indicating that other factors besides the dispersity of the aerosols, MPPS and measuring technique contributes to filter penetration. Assessment of other potential contributors to a shift in an MPPS, such as

Table 4 Subgroup analysis of manikin and without manikin-based protocol studies

Included	Sample size (*n*)	Estimated mean PP	95% CI	Heterogeneity (%)
Without manikin-based set-up studies	16	3.36	2.59–4.13	99.8 $p < 0.001$
With manikin-based set-up studies	13	2.94	2.90–2.98	99.8 $p < 0.001$

n number of observations

filtration mechanism, fibre charge density, aerosol particle charge distribution and filter property such as surface area, thickness and fibre diameter as detailed by Mostofi (2010) and Mostofi et al. (2010, 2011) was outside the scope of this study.

In addition to this, the experimental set-up, including the use of manikins, was also different among the studies. Furthermore, respirators are manufactured to be able pass certain test criteria e.g. filtering out 95% or more of particulates as in N95 respirator classes; however, these are manufactured by various manufactures, with various N95 models also available from the same manufacturer, which may differ in shape, whether they have an exhalation valve or not, etc. In addition, some models are manufactured to just meet the criteria while other are expected to exceed it (Shaffer and Rengasamy 2009) leading to a difference in penetration effectiveness and MPPS even from the same manufacturers. The studies assessed various N95 models, some of which were not disclosed, and comparison could therefore not be made. Knowledge of filtration within these N95 models may have subjected the individual studies to a selection bias.

Experimental studies are also subject to factors that can influence precision of the overall results, the most common one being a random error. This can occur by 'chance', caused by an instrument or any changes in the environment, and the results can go in any direction of the experiment (Joubert and Ehrlich 2007). The tests conducted in these studies were however done in repetition, reducing the risk of the random error. Only Huang et al. (2007) described the calibration of the measuring equipment.

Meta-analysis

With all these factors considered, 13 studies (29 observations) were included in the meta-analysis. The overall mean PP from the studies was estimated as 2.79% (2.76–2.82). This aggregated PP indicates that the N95 may be effective for nanoparticle protection, as it is below the 5% threshold as per NIOSH acceptable criteria for N95 respirator testing protocols, used herein as a guideline, however, subject to various testing and respirator parameters. The NIOSH criterion is based on penetration of particles with a MMAD of 347 nm, assuming a traditional MPPS at 100–400 nm for non-electret filters.

Heterogeneity test

Heterogeneity of the studies was illustrated by a statistically significant I^2 of 99.8%, with a $p < 0.001$, indicating that the heterogeneity is statistically significant. The reason for this significant heterogeneity could be as ascribed to the study-to-study parameter variations noted above.

While this indicates a great variation, the meta-analysis was still explored using a random effects model as it assumes variation within studies (Higgins and Green 2011).

Sensitivity and subgroup analysis

The use of manikin-based protocols influenced the outcome as the aggregated mean PP of 3.36% (95% CI 2.59–4.13) without studies that used manikins increased from the 2.79%. This indicates that the use of the manikin may be reducing penetration of aerosols, although the sample sizes were too small to assess for statistical significance.

The subgroup analysis of the studies that used either of the two aerosol types showed a mean PP of 3.55% (95% CI 2.78–4.32) for monodispersed aerosol studies and 2.82% (95% CI 2.76–2.88) for polydispersed. Fifteen of the 16 measurements were performed using a filter tester specifically designed for monodispersed aerosols, whereas the polydispersed aerosols in the studies were analysed by an SMPS, which has limitations when scanning particles at low concentrations (Wang and Tronville 2014). This may explain the higher PP observed for monodispersed aerosol studies. There is no relevant literature on whether filtration on a filter in a real-life scenario increases as a result of the particle dispersity.

A subgroup group analysis of manikin vs without manikin studies, indicated that the aerosols tend to penetrate less when mounted on manikins, demonstrated by a mean PP of 2.94% (95% CI 2.90–2.98) of 13 studies vs 3.36% (95% CI 2.59–4.13) of 16 studies. This demonstrates that although the use of manikins simulates a more real-life scenario, it may not represent a worst-case parameter. However, this can be explored more to investigate other contributing factors, particularly leaks around the respirator-manikin seal. Balazy et al. (2006) and Mostofi et al. (2011, 2012) highlighted the sealing of the respirator to the manikin during the experiment set-ups, with a leak test also performed around the seal.

Eninger et al. (2008b) however mention in their report that a leak check was not performed. When in use, a well-sealed respirator is needed to ensure that hazardous chemical substances will not leak into the respirator.

The heterogeneity tests for both the sensitivity and subgroup were also high, with all at a p value of < 0.001. This again shows that all the studies that were grouped were different.

Advantages of the study

- The study updates information available on penetrations of N95 respirators, as the last review was conducted in 2009 by Shaffer and Rengasamy (2009).
- The focus on specifically N95 respirators will benefit the industry using NIOSH-certified respirators, as these are the most common respirators used in workplaces. The respirator can be recommended as an additional control measure, in absence of engineering control measures or where these measures do not adequately contain the exposure. With the meta-analysis component, the uncertainty of filtration efficiency of N95 respirators can be reduced.

Limitations of the study

- The review was conducted by one person, and this may have been a source of selection bias.
- As translation was not feasible, studies published in languages other than English were omitted.
- It should be noted that the 5% threshold used as a criterion for effectiveness was set up for evaluation under certain conditions that are somewhat different to what was reported in the reviewed studies, direct comparison is therefore done with caution.
- The sample sizes used for the sensitivity and subgroup analysis were too small to assess for statistical significance.

Conclusion and recommendations

All of the studies indicated that the MPPS for the N95 face-piece respirators is in the nanosized particle range, the lowest at approximately 39 nm. The mean PP ranged from 1 to 6%, exceeding a NIOSH threshold of 5% for particularly N95 respirators used as a guideline, for 4 of the studies.

The aggregated mean PP of studies was 2.79% (95% CI 2.76–2.82), below the 5% threshold guideline. The mean PP for sensitivity and subgroup analysis were also below the NIOSH threshold reference. The significant heterogeneity test outcome however reflects a presence of bias and lack of a standardised approach to testing the respirators for nanoparticle penetration.

The results mean that the commonly used N95 respirators may be effective for nanoparticles in workplaces, but subject to factors including the dispersity of particles and characteristics of respirators. Recommendations to use the N95 respirators for nanoparticle exposure control should come after a comprehensive health risk assessment is conducted, in which the nature of the particles and exposure routes are noted. It should be reiterated that the use of these respirators will still be subject to fit testing and training of workers to ensure adequate protection.

Recommendations on further research

- With the available information, including a review by Wang and Tronville (2014), expert analysis needs to be performed and standard respirator testing protocols for nanoparticles be implemented or the current testing standard revised to include suitable assessment of these particles.
- The protocol testing should include the use of large enough sample sizes to be able to make conclusive findings with regards to the various tests parameters such as the use of manikins and aerosol dispersity.
- Future studies should clarify the use of polydispersed vs monodispersed aerosols during filter testing for nanoparticles as the latter are generated during the engineering and employees may be potentially exposed before agglomeration or aggregation.

Compliance with ethical standards Approval to conduct the review was granted by the Research Ethics Committee (REC) of the Faculty of Health Sciences, University of Pretoria, reference number 234/2016.

Conflict of interest The authors declare that they have no conflict of interest.

Appendix

Table 5 Studies excluded after full text review

Number	Study ID	Reason for exclusion
1	Brochot et al. (2012)	Did not test on N95 respirators
2	Cho et al. (2011)	Reported penetration as a function of mass load, used photometers for testing
3	Golanski et al. (2009)	Tested on filter materials/media of FFP3, using nanographites
4	Gao et al. (2016)	Only tested with cyclic flows
5	He et al. (2015)	Studied simulated workplace protection factors
6	He et al. (2013)	Used cyclic flows and did not use NaCl
7	Heim et al. (2005)	Tested on filter materials/media not respirators
8	Japuntich et al. (2007)	Tested on filter materials/media for extraction systems
9	Jung et al. (2014)	Did not report on penetration percentage as a function of particle size for N95 respirators
10	Kim et al. (2007)	Tested on filter materials/media not respirators
11	Lee et al. (2004)	Did not test at a 85 l/min flow rate
12	Lee et al. (2005a)	The use of NaCl as challenge aerosols was not stated
13	Lee et al. (2005b)	Assessed protection factors (all leakage paths), used human test subjects as well, did not use a constant flow rate of 85 l/min and did not present PP as a function of particle size
14	Lee et al. (2008)	Tested total inward leakage (TIL) (all leakage paths), used human test subjects and did not present penetration percentage as a function of particle size
15	Li et al. (2012)	Tested on filter materials/media not respirators
16	Martin and Moyer (2000)	Used photometers for testing
17	Penconek et al. (2013)	Did not test on N95 respirators
18	Qian et al. (1998)	Published year outside the criteria. Used measuring equipment with detection ranges outside the nano/ultrafine sizes
19	Rengasamy et al. (2008)	Presented data previously reported in Rengasamy et al. (2007)
20	Rengasamy and Eimer (2012a)	Presented data previously reported in Rengasamy et al. (2011)
21	Rengasamy and Eimer (2012b)	Studied respirator total inward leakage
22	Rengasamy et al. 2015)	Studied respirator total inward leakage on human test subjects
23	Richardson et al. (2006)	A report; results published by Eshbaugh et al. (2008)
24	Vo et al. (2015)	Studied simulated workplace protection factors on human test subjects
25	Vojtko et al. (2008)	Studied breathing resistance of a surgical mask worn over a N95 respirator

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