



The prevalence of latex sensitisation and allergy and associated risk factors amongst health care workers using hypoallergenic latex gloves at King Edward VIII hospital, KwaZulu-Natal South Africa: A cross sectional study

Journal:	<i>BMJ Open</i>
Manuscript ID:	bmjopen-2013-002900
Article Type:	Research
Date Submitted by the Author:	18-Mar-2013
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Primary Subject Heading:	Occupational and environmental medicine
Secondary Subject Heading:	Immunology (including allergy), Occupational and environmental medicine, Epidemiology
Keywords:	Latex, Hypoallergenic, Healthcare workers, South Africa

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3 1 **The prevalence of latex sensitisation and allergy and associated risk factors among healthcare**
4 **workers using hypoallergenic latex gloves at King Edward VIII Hospital, KwaZulu-Natal South**
5 **Africa: A cross sectional study**
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40 20 Keywords: Latex, hypoallergenic, healthcare workers, South Africa

41
42 21 Word Count:

43
44 22 Abstract: 299

45
46 23 Body: 4,359

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ARTICLE SUMMARY**ARTICLE FOCUS**

- The use of hypoallergenic latex gloves has been adopted as policy in different healthcare settings globally.
- However, information with regard to their use and the development of latex sensitisation and allergy among exposed healthcare workers is limited.
- We hypothesised that there is latex sensitization and allergy in healthcare workers using hypoallergenic latex gloves in a South African hospital.

KEY MESSAGE

- In the presence of powder free hypoallergenic gloves, latex sensitisation and latex allergy is still an important occupational health effect in healthcare workers.
- Healthcare workers should be continuously monitored for the development of latex sensitisation and allergy.
- There is a need for a national policy accompanied by clear implementation plans as well as sustainable education and training programmes to address latex sensitisation and allergy among HCWs.

STRENGTH AND LIMITATIONS

- Strength of the study included the presence of a control group providing a background prevalence of latex sensitisation in this population and random selection of participants which minimised the potential of participant bias that arises with a volunteer approach.
- This study was limited by the cross sectional study design as it only allowed for the determination of the prevalence of latex sensitisation; recall bias with regard to the number of gloves used in the past 7 working days and the self-reporting of personal and family atopic disorders may have resulted in the misclassification of exposure and atopy respectively.

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12 34 **What this paper adds**
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15 35 In the presence of powder free hypoallergenic gloves, latex sensitisation and latex allergy is still an
16 36 important occupational health effects in healthcare workers
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19 37 Healthcare workers should be continuously monitored for the development of latex sensitisation and
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23 39 There is a need for a national policy accompanied by clear implementation plans as well as sustainable
24 40 education and training programmes to address latex sensitisation and allergy among HCWs
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30 42 **ABSTRACT**
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33 43 **Objectives**
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36 44 The present study describes latex sensitisation and allergy prevalences and associated factors among
37 45 healthcare workers using hypoallergenic latex gloves at King Edward VIII Hospital in KwaZulu-Natal
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40 46 South Africa.
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43 47 **Design**
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46 48 Cross sectional study
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52 50 A tertiary hospital in eThekweni municipality, KwaZulu Natal, South Africa
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55 51 **Participants**
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600 healthcare workers were randomly selected and 501(337 exposed and 164 unexposed) participated. Participants who were pregnant, less than one year of work as healthcare worker and history of anaphylactic reaction were excluded from the study.

Primary and secondary outcome measures

Latex sensitisation and latex allergy were the outcome of interest and they were successfully measured

Results

Prevalence of latex sensitisation and allergy was observed among exposed workers (7.1% and 5.9%) and unexposed workers (3.1% and 1.8%). Work related allergy symptoms were significantly higher in exposed workers (40.9%, $p < 0.05$). Duration of employment was inversely associated with latex allergy (OR: 0.9; 95% CI: 0.8-0.9). The risk of latex sensitisation (OR: 4.2; 95% CI: 1.2-14.1) and allergy (OR: 5.1; 95% CI: 1.2-21.2) increased with exclusive use of powder-free latex gloves. A dose-response relationship was observed for powdered latex gloves (OR: 1.1; 95% CI: 1.0-1.2). Atopy (OR: 1.5; 95% CI: 0.7-3.3 and OR: 1.4; 95% CI: 0.6-3.2) and fruit allergy (OR: 2.3; 95% CI: 0.8-6.7 and OR: 3.1; 95% CI: 1.1-9.2) also increased the risk of latex sensitisation and allergy.

Conclusion

This study adds to previous findings that healthcare workers exposed to hypoallergenic latex gloves are at risk for developing latex sensitisation highlighting its importance as an occupational hazard in healthcare. More research is needed to identify the most cost effective way of implementing a latex free environment in resource limited countries, such as South Africa. In addition more cohort analysis is required to better understand the chronicity of illness and disability associated with latex allergy.

73 INTRODUCTION

74 Latex allergy (LA) as an occupational disease among healthcare workers (HCWs) gained
75 recognition after Nutter published a case report of contact urticaria in a HCW in 1979.¹ The
76 increase in prevalence coincided with the emergence of the Human Immunodeficiency Virus/
77 Acquired immunodeficiency syndrome (HIV/AIDS) epidemic and the introduction of “universal
78 precautions” in the healthcare industry which had resulted in the increased use of latex gloves
79 among HCWs.²

80 Latex gloves are preferred due to their superior barrier and physical properties as compared to
81 the non-latex gloves.³ International epidemiological studies have reported the prevalence of latex
82 allergy among HCWs to range between 2-22% depending on the population and diagnostic
83 methods used.⁴⁻¹¹ The prevalence in the general population has been reported to range between
84 1-6%.^{12 13}

85 In South Africa studies amongst HCWs reported a latex sensitisation prevalence of between 2.7
86 to 20.8%.¹⁴⁻¹⁶ Latex allergy in HCWs is a compensable disease in South Africa in terms of the
87 Compensation of Occupational Injuries and Diseases Act No. 130 of 1993.¹⁷ Latex allergy
88 comprised an estimated 1.4 % of all occupational diseases reported by the Surveillance of Work
89 Related and Occupational Respiratory Diseases of South Africa programme (SORDSA) between
90 1996 and 1998.¹⁸ In 2000 De Beers and De Villiers documented a high prevalence (20.8%) of
91 latex sensitisation among theatre and laboratory staff (n=277) employed at Tygerberg hospital in
92 the Western Cape Province.¹⁵ Potter and colleagues conducted a latex allergy screening survey
93 among Groote Schuur hospital employees. They reported latex sensitisation of 11.9% among 969
94 respondents with the majority of sensitised HCWs being nursing staff (64%) followed by doctors
95 (10%), technologists (8%), paramedics (7%) and cleaners (6%).¹⁶ A 2001 survey at the Red

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3 96 Cross childrens hospital in Cape Town reported a latex sensitisation prevalence of 7% amongst
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5 97 the HCWs working in clinical and laboratory areas of the hospital.¹⁴
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9 98 Powdered latex gloves were identified as an important risk factor for latex sensitisation and
10
11 99 allergy in HCWs as they were found to contain a high allergenic protein content.¹⁹ Following
12
13 100 these findings, hypoallergenic gloves with low allergen content namely, low powdered and
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15 101 powder free latex gloves were introduced. The European definition of powder free gloves is
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17 102 gloves with powder content not exceeding 2 mg per glove and leachable latex protein which is as
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19 103 low as is reasonably practical.²⁰
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24 104 Hypoallergenic gloves have been associated with reduced latex aeroallergen concentrations,
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26 105 reduced conversion rates and a subsequent decrease in clinic visits, and compensation claims for
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28 106 latex induced occupational asthma and allergic contact dermatitis among HCWs.^{19, 21} As much as
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30 107 the use of low or powder free gloves has been shown to reduce latex related symptoms, other
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32 108 studies have shown that exposed HCWs still exhibit symptoms at very low levels of measureable
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34 109 airborne latex allergens.²² Most studies have reported on the airborne levels and inhalational
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36 110 route of exposure hence the recommendation on low powdered or powder free latex gloves.
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38 111 There is little consideration given to the dermal route of exposure despite the fact that exposure
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40 112 is as a result of direct contact in these instances.²³ Eliminating the cornstarch powder only
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42 113 removed the carrier and not the source of allergen which is in the latex itself. Therefore workers
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44 114 using powder free gloves are still exposed to the allergenic content of latex gloves. It has been
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46 115 shown that different brands from different suppliers contain differing levels of protein due to a
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48 116 lack of standards in latex glove manufacture.²⁴ A South African study reported that some powder
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50 117 free latex gloves were found to have high allergenic protein content.²⁴ HCWs using these gloves
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3 118 are exposed via direct dermal contact and are at risk for developing latex sensitisation and if
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6 119 exposure continues they can later develop latex allergy.
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9 120 In South Africa the health and safety of workers is regulated by the Occupational Health and
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11 121 Safety Act No 85 of 1993 (OHSA).²⁵ The accompanying Hazardous Chemical Substances
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13 122 Regulations No?? (HCS) of OHSA has tasked the employer with ensuring health and safety in
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15 123 the workplace by applying the hierarchy of hygiene controls in addressing workplace hazardous
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17 124 chemicals.²⁵ In South African hospitals the procurement of latex gloves is based on the cost of
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19 125 gloves and the stock is obtained from various providers who meet the South African Bureau of
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21 126 Standards (SABS) specifications for latex gloves.
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27 127 While it is important to diagnose and manage an individual worker with latex allergy, complete
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29 128 control of hazardous substance in the workplace is equally important. While a latex free work
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31 129 environment would be a preferred control strategy, substitution of powdered latex gloves with
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33 130 powder free gloves was shown to be cost effective and associated with improved clinical
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35 131 outcome.²¹ As a result this was adopted as the most reasonable and practical approach in
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37 132 addressing the problem of latex allergy among HCWs both internationally and to some extent
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39 133 nationally.²⁶⁻²⁸ This has proven to reduce latex induced clinical outcomes. Even with this
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41 134 intervention, studies in Western countries such as Germany and the UK have shown that the risk
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43 135 of latex sensitisation still exists and more needs to be done to protect HCWs.^{29, 30}
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49 136 The current study described the prevalence of latex sensitisation and allergy among healthcare
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51 137 workers who use hypoallergenic powder free and lightly powdered latex gloves.
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138 METHODS

139 Study design and population

140 This was a cross sectional study conducted between July 2011 and January 2012. The study
141 location was King Edward VIII hospital, the second largest hospital in the Southern hemisphere,
142 providing regional and tertiary services to the whole of KwaZulu-Natal (KZN) and the Eastern
143 Cape Province in South Africa. It has a bed status of 1300 and has a workforce of 2400. The
144 hospital was chosen due to the large workforce with different departments, and the policy of
145 using both powder free and low powdered latex gloves for approximately 10 years.

146 The study population was limited to HCWs currently employed at King Edward VIII Hospital
147 for more than 12 months. HCWs were defined as all personnel employed in the hospital.

148 The prevalence of latex sensitization in HCWs using powdered latex gloves in the Western Cape
149 Province was 11.9% in 2001.¹⁶ We expected the prevalence at King Edward VIII hospital to be
150 less than the 11.9% observed in the Western Cape Province due to the adoption of a
151 hypoallergenic latex glove policy. Using EPI Info calculator version 3.04.04., it was assumed
152 that 50% of sensitised workers have remained sensitive despite the introduction of
153 hypoallergenic latex gloves 10 years prior. Using an expected latex sensitization prevalence of
154 6% for the exposed group and the prevalence among the general population being reported as
155 less than 1% the required sample size was calculated to be 585 participants 2 exposed
156 participants for every 1 non-exposed participant (exposed =390; unexposed =195). HCWs were
157 considered to be exposed if they were likely to use gloves. Unexposed HCWs were drawn from
158 the administrative staff of the hospital.

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3 159 **Questionnaire**
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7 160 We used an adaptation of the questionnaire used in an epidemiological study conducted at
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9 161 Groote Schuur in 2001¹⁶ with permission from Professor Paul Potter, Allergology Unit, Medical
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11 162 School, University of Cape Town. The questionnaire containing open and closed ended questions
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14 163 was adapted to include items on exposure assessment. The questionnaire was administered by a
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16 164 trained research assistant (Honours degree in medical science) immediately prior to the skin
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18 165 prick test. The questionnaire collected data on the participants' demographics, personal risk
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21 166 factors, latex exposure assessment, clinical manifestations of latex sensitization (dermal and
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23 167 respiratory) and history of previous reactions suggestive of latex allergy.
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27 168 **Exposure Assessment**
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30 169 *Individual Exposure*
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33 170 Individual latex exposure was determined by the type of gloves used, number of gloves used per
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36 171 day, and duration of glove use. The information was limited to 7 working shifts/days prior to the
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41 173 *Departmental Exposure*
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45 174 Departmental exposure was defined as glove usage in the past 12 months (01 January 2011-31
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47 175 December 2011). The overall departmental exposure was obtained by reviewing monthly glove
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50 176 usage by each department from the stock room register. This was used to estimate the annual
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52 177 exposure for employees who had rotated through different departments in the past 12 months.
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54 178 Non sterile latex gloves are distributed throughout the clinical departments while a high
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57 179 proportion of sterile gloves are distributed to labour ward, theatre, surgical wards and outpatient
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3 180 departments. Glove type was defined as powdered and powder-free and latex free based on the
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5 181 previous literature.^{24, 32}
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8 9 182 **Skin prick test (SPT)**

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12 183 The SPT was conducted using the Stallergenes kit.³² It was performed in a room with access to
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14 184 emergency resuscitation services by a trained research assistant. The research assistant and
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17 185 principal investigator were trained by the Chief Pulmonary Technician at Inkosi Albert Luthuli
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19 186 Central hospital (A Quaternary Hospital in KwaZulu-Natal) on 2 separate occasions. The test
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22 187 was performed on the inner aspect of the participants' forearms, between the wrist and the elbow
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24 188 on normal skin. A positive and negative control were performed using histamine and buffered
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27 189 normal saline solution respectively on the same arm and they were 3 cm apart to prevent cross
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29 190 contamination. The protein concentration of the latex extract was 500µg/ml and the solution was
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32 191 applied as it was with no further dilutions. After 15-20 minutes subsequent to puncturing the
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34 192 skin, the SPT reaction wheal and flare was outlined by a black ink and clear tape was used to
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36 193 transfer the outline from skin to the results sheet by the trained research assistant or principal
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38 194 investigator.³³ A positive result was indicated by a mean wheal diameter measuring 3 mm or
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41 195 greater than the negative control. Results were recorded on a standardized result sheet. The
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43 196 research assistant's test performance was audited by the principal investigator at regular intervals
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46 197 to ensure correctness of technique and interpretation of the results.
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49 198 Informed signed consent was obtained from all the participants prior to participation. They had
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51 199 the option of participating in the questionnaire interview and the SPT or refusing the SPT. The
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54 200 study protocol was approved by the Biomedical Research Ethics Committee of the University of
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3 201 KwaZulu-Natal (BE048/11). Permission to conduct the study was also obtained from the KZN
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6 202 Provincial Department of Health and King Edward VIII hospital management.
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9 **203 Statistical analysis**

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12 204 Data was captured in Excel and analysed in Stata Version 11. Frequencies and medians with
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14 205 ranges were presented for categorical and continuous variables respectively. The Chi-square and
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17 206 the Kruskal-Wallis test was used to test for significant associations between categorical an
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19 207 continuous variables and the dependent variables under study on bivariate analysis respectively.
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23 208 Binary logistic regression was used to test for significant associations between independent and
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25 209 dependent variables on multivariate analysis. The dependent variables used in the regression
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28 210 analysis were: Latex sensitisation, which was defined as having a SPT wheal of ≥ 3 mm to latex
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30 211 extract; Latex allergy (LA) was defined as being SPT positive and a report of having any one or
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32 212 more of the listed work related clinical symptoms namely itchy eyes, red eyes, runny eyes, runny
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35 213 nose, itchy nose, sneezing, coughing, tight chest, wheezing, itchy skin, skin rash or dizziness.
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37 214 Independent variables that were considered for analysis were as follows: Age (yrs) and sex,
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39 215 duration of employment, job title, current department employed in, type of gloves used, number
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41 216 of pairs of gloves used per day, self reported and family history of atopy, food allergy and
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44 217 previous history of open surgery and number of surgical procedures. In the multivariate analysis,
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46 218 age was omitted due to collinearity with duration of employment. Departmental glove
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49 219 consumption was omitted and number of pair of gloves was used as an indicator of individual
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51 220 latex glove exposure. The variable number of pairs of gloves used and duration of employment
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54 221 were retained as continuous variables in the multivariate model.
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222 RESULTS

223 Participant Demographics

224 Sixty five HCWs refused to participate in the study. Among the 520 HCWs who responded to
225 the invitation there was an overall participation rate of 85.5 % (n=501) with 3.6% (n=19)
226 refusing SPT. There was no significant difference between those refusing SPT and those who
227 had the SPT with respect to latex exposure status, age, sex and duration of employment.

228 The median age of participants was 42.2 years (range: 22 years-65 years) with the greater
229 proportion of them being females. The median duration of employment was 10.9 years (range: 1
230 year-42 years) with the majority of exposed participants having worked as a HCW for < 10
231 years. Most unexposed healthcare workers had been employed for > 20 years . Personal and
232 family history of allergy were more prevalent among unexposed HCWs while exposed HCWS
233 reported a higher prevalence of a fruit allergy and history of previous surgery (Table 1).

234 Prevalence of Latex Sensitisation and Allergy

235 The overall prevalence of latex sensitisation and latex allergy were 5.9% (n=29) and 4.6%
236 (n=23) respectively. Although the difference was not significant, the prevalence of latex
237 sensitisation was higher among the exposed group (7.1%) as compared to the unexposed group
238 (3.1%). Latex allergy was significantly higher in the exposed group than unexposed group (5.9%
239 vs 1.8%, p=0.04). There was a significant difference in the work related allergy symptoms
240 between exposed and unexposed workers (40.9% vs. 31.7%, p=0.04) (Table 1). Symptoms that
241 were significantly associated with latex sensitisation were skin rash (p< 0.000), itchy skin
242 (p=0.001), runny nose (p=0.004), red eyes (p=0.01) and itchy eyes (p=0.01).

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3 243 The prevalence of latex sensitization was higher among those who were exposed and those with
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5 244 employment duration of < 10yrs. Although the prevalence of latex sensitisation was lower
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8 245 among participants < 30 years of age, there was no significant variation with age or sex. There
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10 246 was a significant difference (p=0.04) in the prevalence of fruit allergy between those participants
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12 247 with latex sensitisation (17.2%) and unsensitised participants (6.9%) The exclusive use of
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14 248 powder free latex gloves was found to be significantly (p=0.003) higher among the participants
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16 249 who had latex sensitisation. There was equal distribution of powdered and powder free latex
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18 250 gloves among those who reported the use of mixed gloves. The prevalence of reporting previous
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20 251 open surgery and use of other non- occupational exposure latex containing material did not vary
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22 252 significantly between those who had latex sensitisation and those who were unsensitised. There
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24 253 was a significantly higher prevalence of reporting allergic reactions when handling other latex
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26 254 containing medical equipment among participants with latex allergy as compared to unsensitised
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28 255 participants (10.3% vs 1.7%, p=0.002) (Table 2).

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35 256 **Crude association of demographics, exposure status, medical and personal history and latex**
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37 257 **sensitisation, latex allergy**

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41 258 Latex exposure was significantly associated with latex allergy (OR: 3.4; 95% CI: 1.1-10.8).
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43 259 Working as a HCW for 5-9 yrs was significantly associated with latex sensitisation (OR: 2.6;
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45 260 95% CI: 1.2-5.5) and latex allergy (OR: 3.3; 95% CI: 1.4-7.6), respectively. Employment
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47 261 duration as a HCW for >20 years was protective against latex allergy (OR: 0.2; 95% CI: 0.0-0.8).
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49 262 Working as an enrolled nurse was significantly associated with both latex sensitisation (OR: 2.5;
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51 263 95% CI: 1.2-5.3) and latex allergy (OR: 2.4; 95% CI: 1.1-5.6). The exclusive use of powder free
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53 264 latex gloves was significantly associated with latex sensitisation (OR: 3.1; 95% CI: 1.4-6.8) and
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55 265 latex allergy (OR: 3.1; 95% CI: 1.7-9.1). Powdered and powder free latex gloves were equally
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3 266 distributed among those who reported the use of mixed gloves. The annual consumption of pairs
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5 267 of gloves per HCW by department was ranked and grouped into tertiles. Although medical and
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8 268 surgical wards had low and moderate pairs of gloves consumption per HCW, these wards had the
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10 269 highest proportion of workers with latex sensitisation (n=6, 20.0% each). However the relation
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12 270 was only significant for those who reported the medical ward as being the current department in
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14 271 which they worked (p=0.01). The proportions for powdered latex glove use were 71% and 69%
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16 272 in medical and surgical wards, respectively and this was not statistically significant. Exposure to
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18 273 other latex containing medical devices was not significantly different from what was reported in
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20 274 other wards. There was no significant association between personal history, latex sensitisation
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22 275 and latex allergy. Fruit allergy was significantly associated with latex allergy (OR: 3.7; 95%:
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24 276 1.4-10.4) (Table 3). Listed fruits were evaluated for their independent association with latex
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26 277 sensitisation. Avocado (p=0.01) and others (p=0.003) which included pineapple and orange
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28 278 showed significant associations with latex sensitisation (data not shown).

279 **Multivariate analysis**

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38 280 While latex exposure had estimates above 2, there was no significant association with latex
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40 281 sensitisation and latex allergy. Duration of employment was found to be inversely associated
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42 282 with latex allergy in models I and II. The exclusive use of powder free latex gloves was
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44 283 significantly associated with latex sensitisation (OR: 4.2; 95% CI: 1.2-14.1) and latex allergy
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46 284 (OR: 5.1; 95%CI: 1.2-21.2) on multivariate analysis. This significant association disappeared
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48 285 when examining the number of pairs of powder free gloves used in the last 7 days. A weak
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50 286 association was observed for the number of pairs of powdered latex gloves used in the last 7 days
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53 287 with both latex sensitisation and latex allergy (model III and IV). There was a significant
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3 288 association between fruit allergy and latex allergy in model I (OR: 3.1: 95% CI: 1.1-9.2) (Table
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9 **DISCUSSION**

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11 291 This is an important study for South African HCWs as it examined the risk of latex sensitisation
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13 292 in a group of workers exposed to hypoallergenic latex gloves. As previously mentioned there has
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15 293 been no literature documenting the prevalence of latex sensitisation among South African HCWs
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17 294 using hypoallergenic lightly powdered or powder-free latex gloves. The prevalence of latex
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19 295 sensitisation among exposed HCWs (7.1%) in this study is comparable to findings among HCWs
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21 296 in another South African hospital.¹⁴ However it was considerably lower than the 11.9%
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23 297 prevalence reported by Potter in the same year.¹⁶ While a substantial number of participants
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25 298 (37%) reported work related allergy symptoms, only 4.6% met our definition of latex allergy.
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27 299 The important symptoms associated with latex sensitisation were skin rash, itchy skin, runny
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29 300 nose, red and itchy eyes in keeping with previous studies.^{4, 5} Elimination of powdered latex
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31 301 gloves has shown a reduction in the concentration of aeroallergens in the operating room with
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33 302 the low prevalence of latex allergy in our study population.
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41 303 Although the relationship was weak, this study showed that the risk of latex sensitisation
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43 304 decreases with duration of employment. The explanation of our finding may be that new
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45 305 employees are only sensitised and have not yet manifested clinical symptoms and they continue
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47 306 using latex gloves. On the other hand senior HCWs may have been sensitised during their earlier
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49 307 years of employment and as a result they either moved to departments with less exposure to latex
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51 308 gloves or deliberately avoid latex containing products and therefore exhibit less latex related
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53 309 symptoms. Furthermore the introduction of hypoallergenic gloves 10 years prior to the study
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55 310 may explain the reduced sensitisation in senior HCWs as demonstrated in the study by smith et al
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3 311 in 2007.²¹ The published literature has been inconsistent in reporting the association between
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5 312 duration of employment and latex sensitisation. Jones and co-workers observed a high
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8 313 prevalence of latex sensitisation among junior dental students exposed to exclusive powder free
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10 314 latex gloves compared to dental staff and senior students.³⁴ Among Singaporean HCWs no
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12 315 significant difference was reported between duration of employment and latex sensitisation,³⁵
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14 316 while among Italian nurses latex sensitisation was associated with an increasing duration of
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17 317 employment.³⁶

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20 318 In our study HCWs who exclusively used powdered free latex gloves had a 4 times greater odds
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22 319 of developing latex sensitisation. A possible explanation for this is that those who are sensitised
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24 320 and manifesting glove related symptoms preferentially used exclusive powder free latex gloves.
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27 321 Moreover the background prevalence of latex sensitisation in this study was relatively higher
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29 322 (3.5%) than previously reported prevalence in the general population by Bousquet et al.¹³ Studies
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31 323 have shown that some of these “hypoallergenic” latex gloves actually contain high levels of
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33 324 allergens which can be release into the environment with aggressive manipulation.²⁴ Some of the
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35 325 sensitised HCWs may have been sensitised before the hospital implemented a hypoallergenic
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37 326 latex glove policy. Also Smith et al showed that complete avoidance of powdered latex glove can
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39 327 result in the reduction or no change in measurable IgE antibodies .³⁷ A study in Germany
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41 328 reported a high prevalence of 8% among 226 dental students who had only been exposed to
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43 329 exclusive powder free latex gloves.²⁹ Similarly in the UK despite a total ban on powdered latex
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45 330 gloves Clayton found a 10% prevalence of latex sensitisation in HCWs.³⁰ It is also not clear to
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47 331 what extent the aeroallergens released by colleagues using powdered latex gloves influence this
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49 332 finding. Furthermore the role of other latex containing medical devices during sensitisation
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51 333 period cannot be entirely ruled out.
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3 334 In our study, frequency of exposure as measured by the number of gloves used in the last 7
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6 335 working days showed a weak association between powdered latex gloves and latex sensitisation
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8 336 but no association could be demonstrated with powder free latex gloves. Airborne latex
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11 337 aeroallergens have been shown to increase with the number of powdered gloves used which
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13 338 subsequently increases the risk of latex sensitisation and clinical latex glove related allergy
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15 339 symptoms.¹⁹

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19 340 The positive association between department with low glove consumption per HCW and latex
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21 341 sensitisation is in contrast with previous finding by Liss and co-workers.⁹ They reported positive
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23 342 association with departments that had high glove consumption per HCWs. A possible reason for
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26 343 our observation is that HCWs with latex sensitisation may have been relocated to wards with low
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29 344 glove consumptions to minimise the exposure. In addition, the annual pair of gloves
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31 345 consumption per HCW by department does not provide an accurate indication of individual
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33 346 exposure; rather it gives us the annual distribution of gloves to different departments.

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37 347 Several studies have reported atopy as a significant risk factor for latex sensitisation.^{9, 10, 36}

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39 348 Similarly, the prevalence of reporting a history of personal atopy in this study was higher among
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42 349 latex sensitised participants although the association was not statistically significant. Watts and
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44 350 colleagues reported that the risk of latex sensitisation was increased by 14 times in the presence
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46 351 of personal atopy and 4 times in the presence of a family history atopy among 122 American
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49 352 HCWs studied.¹⁰ Contrary to Watts and co-workers findings, the risk of latex sensitisation did
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51 353 not increase with a reporting of family history of atopy in our study population.¹⁰

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54 354 Fruit latex allergy syndrome is a phenomenon seen where latex sensitised individuals
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57 355 demonstrate a cross reactivity with specific foods; particularly fruit. Studies have identified this

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3 356 phenomenon among sensitised HCWs and the general population. This has been attributed to the
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5 357 similarity between fruit proteins and latex allergens.³⁸ Fruit allergy was significantly associated
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8 358 with latex sensitisation and latex allergy in our study. Our study was dependent on the self-
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10 359 reporting of fruit allergy and no objective tests were carried out. It is therefore possible that
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12 360 participants have independent simultaneous allergies to both fruit and latex without cross
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14 361 reactivity. Also, we were unable to determine whether latex sensitisation preceded the
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16 362 development of fruit allergy or vice versa.
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21 363 Latex sensitised participants reported a high prevalence of a history of previous open surgery in
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23 364 our study. This has been reported to occur as a result of direct intraoperative exposure to latex
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25 365 containing medical devices such as catheters or tubes. Studies in children with congenital
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27 366 abnormalities have demonstrated that the risk for latex allergy increases with the number of open
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29 367 surgical procedures that they undergo.³⁹ Frequency of invasive procedures among adults was
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31 368 shown to increase the risk of latex sensitisation reporting while more than 10 procedures
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33 369 increased the risk of developing latex allergy.⁴⁰
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38 370 Strengths of this study include the high response rate (85.5%) and comparability to other
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40 371 studies.^{8, 16} Access to the hospital employee database allowed us to better assess the
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42 372 representativeness of this study population by comparing demographic data of the non-
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44 373 participants and the participants. The participants were randomly selected minimising the
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46 374 potential of participant's bias that comes with a volunteer approach.
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51 375 The presence of a control group provided a background prevalence of latex sensitisation in this
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53 376 population which allowed for a better estimation of associations attributable to work related
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55 377 factors. The use of Stallergenes latex specific SPT further strengthens the study. The SPT test is
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3 378 regarded as the gold standard for the diagnosis of latex allergy and Stallergenes has been shown
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5 379 to have a diagnostic sensitivity and specificity of 93% and 100%, respectively.³² The research
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8 380 assistant employed on this study was trained and initially shadowed and periodically supervised
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10 381 by the principal investigator to ensure appropriate administration of the questionnaire and the
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12 382 SPT thereby improving the reliability and validity of the study.

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15 383 This study was limited by the cross sectional study design which was relatively low in cost and
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17 384 quick to conduct. It only allowed for the determination of prevalence of latex sensitisation at one
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19 385 point in time. Consequently the prevalence of latex sensitisation may have been underestimated
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21 386 as it is possible that HCWs who had already developed latex sensitisation have left the hospital
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23 387 before the study was conducted. Recall bias is another potential limitation in this study as
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25 388 workers were asked to recall the number of gloves used in the past 7 working days. HCWs may
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27 389 have overestimated or underestimated their individual exposures. Our study depended on self-
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29 390 reporting of personal and family atopic disorders and this may have resulted in the
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31 391 misclassification of atopy.

32 33 34 35 36 37 38 392 **CONCLUSION**

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40 393 This study shows that even in the presence of powder free hypoallergenic glove use there is latex
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42 394 sensitisation and latex allergy, adding to previous findings that HCWs exposed to hypoallergenic
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44 395 latex gloves are still at risk for developing latex sensitisation and latex allergy. This indicates that
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46 396 latex sensitisation and allergy are still an important occupational hazard for HCWs. While it may
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48 397 be economically impractical to replace the latex gloves in our setting, reduction of allergen
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50 398 content in latex products is another strategy that can be implemented to address the problem and
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52 399 protect HCWs. A policy accompanied by clear implementation plans as well as sustainable
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54 400 education and training programmes to address latex sensitisation and allergy among HCWs

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3 401 should be implemented.⁴¹ In addition HCWs must be continuously monitored for the
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6 402 development of latex sensitisation and alternate latex free glove must be made available for
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8 403 them. More research is needed to identify the most cost effective way of implementing a latex
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10 404 free environment in resource limited countries, such as South Africa. In addition the current
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12 405 studies in South Africa have largely been cross-sectional in nature. More cohort analysis is
13
14 406 required to better understand the chronicity of illness and disability associated with latex allergy.
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18 407 **ACKNOWLEDGEMENT**

19
20
21 408 I would like to thank the hospital employees participating in this study and their management for
22
23 409 allowing me access to the human resource database. I would like to thank Professor Mohamed
24
25 410 Jeebhay (Centre of Occupational and Environmental Health, University of Cape Town, SA) and
26
27 411 Professor David L Nordstrom (Occupational and Environmental Safety and Health, University of
28
29 412 Wisconsin-Whitewater, USA) for their comments on my initial proposal. I would like to thank
30
31 413 Professor Rajen Naidoo (Discipline of Occupational and Environmental Health, UKZN, SA) for
32
33 414 his statistical advice during the data analysis. In addition thank you to Mr. Nhlanhla Jwara for
34
35 415 conducting the field work.
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3 416 **Contributorship**
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6 417 Dr Shumani Phaswana is the principal investigator who was involved from the conception of the idea,
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9 418 proposal writing, data collection, data management and interpretation of the results.
10

11 419 Dr Saloshni Naidoo contributed to the conception and design of the study, analysis and interpretation of
12
13 420 the data, critical review of the intellectual content of the article and final approval of the article.
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17 421 **Data sharing**
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20 422 No additional unpublished data
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23
24 423 **Funding**
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27 424 None
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30 425 **Competing interests**
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Characteristic	Exposed N (%)	Unexposed N (%)
Number of participants	337 (67.3)	164 (32.7)
Demographics		

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48 **520 TABLES**

49
50 **521 Table 1: Demographics and associated risk factors amongst latex exposed and unexposed**
51 **522 healthcare workers at King Edward VIII Hospital, KwaZulu-Natal South Africa, (n=501)**
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Age (years)		
≤30	30(8.9)	19(11.6)
>30-40	121(35.9)	40(24.4)
>40-50	101(29.9)	59(35.9)
>50	85(25.2)	46(28.1)
Duration of employment (years)		
Characteristics	Latex SPT +ve† (29)	Latex SPT -ve†† (472)
≤5	135(401.0%)	N (%)32(19.5)
>5-10**	49(14.5)	17(10.4)
Demographics		
>15-20	24(7.1)	20(12.2)
>20*	90(26.7)	67(40.9)
Sex **		
Female	309(91.7)	95(57.9)
Male	28(8.3)	69(42.1)
Job Title (yes)		
Administrative		164(100.0)
Professional nurses	123(36.5)	
Enrolled nurses	141(41.8)	
Enrolled nursing assistants	73 (21.7)	
Medical and Personal History		
Personal history of Allergy Disease (yes)	147(43.6)	83(50.6)
Family history of Allergy Disease (yes)	197(58.5)	102(62.2)
Fruit allergy (yes)	29(8.6)	9(5.5)
Previous open surgery (yes)*	168(49.8)	61(37.2)
Work-related allergy symptoms(yes)*	138(40.9)	52(31.7)
Non-occupational latex exposure (yes)	161(47.8)	76(46.3)
Latex sensitisation (yes)	24(7.1)	5(3.1)
Current latex allergy (yes)*	20(5.9)	3(1.8)
Chi square, *p<0.05, **p<0.001		

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Table 2: Comparison of risk factors between latex sensitised (skin prick test positive) and non-sensitised (skin prick test negative) healthcare workers at King Edward VIII Hospital, KwaZulu-Natal South Africa (n=501)

Age (years.)				538
≤30	1 (3.5)		48(10.2)	539
>30-40	13 (44.8)		148(31.4)	540
>40-50	8 (27.6)		152(32.2)	541
>50	7 (24.1)		124(26.3)	542
Duration of employment				543
Characteristics	N=2	Latex Sensitisation	N=23	544
≤5	3(10.3)	OR (95%CI)	64(13.6)	545
>5-10	16(55.2)		151(31.9)	546
10-15	3(10.3)		63(13.4)	547
15-20	1(3.5)		43(9.1)	548
≥20	1	0.2(0.0-1.9)	1151(31.9)	549
Sex (yes)				550
Male	5(17.2)		118(25.0)	551
Female	24(82.8)		354(75.0)	552
Job Title (yes)				553
Administrative	5(17.2)		159(33.7)	554
Professional nurses	5(17.2)		118(25.0)	555
Enrolled nurses	14(48.3)		127(26.9)	556
Enrolled nursing assistants	5(17.2)		68(14.4)	557
Latex Exposure				558
Exposure status(yes)	24 (82.8)		313(66.3)	559
Type of gloves				560
None	5(17.2)		165(34.6)	561
Exclusive powdered latex glove (yes)	2(6.9)		36(7.6)	562
Exclusive powder free latex glove (yes)*	11(37.9)		77(16.3)	563
Mixed (yes)	11(37.9)		198(41.9)	564
Medical and Personal History				565
Personal history of Allergy Disease (yes)	16(55.2)		214(45.3)	566
Family history of Allergy Disease (yes)	18(62.1)		281(59.5)	567
Fruit allergy (yes) *	5(17.2)		33(6.9)	568
Previous open surgery (yes)	18(62.1)		211(44.7)	569
Non-occupational latex exposure (yes)	12(41.4)		225(47.7)	570
Reaction to other latex medical devices (yes)*	3(10.3)		8(1.7)	571
Chi Square, *p<0.05				572
†Latex Skin Prick Test Positive				573
#Latex Skin Prick Test Negative				574

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579 **Table 3: Crude Odds Ratios (OR) (95%CI) of demographics, exposure status, medical and personal**
580 **history and latex sensitisation and latex allergy amongst healthcare workers at King Edward VIII**
581 **Hospital, KwaZulu-Natal South Africa, (n=501)**

>30-40	13	1.8(0.8-3.7)	11	2.0(0.9-4.6) ⁵⁸²
>40-50	8	0.8(0.4-1.8)	7	0.9(0.4-2.2)
>50	7	0.8(0.4-2.1)	4	0.6(0.2-1.7) ⁵⁸³
Duration of employment (years)				
<5	3	0.7(0.2-2.4)	3	0.9(0.3-3.2) ⁵⁸⁴
5-10	16	2.6(1.2-5.5)*	14	3.3(1.4-7.6) ⁵⁸⁵
>10-15	3	0.7(0.2-2.4)	3	0.9(0.3-3.2)
>15-20	1	0.4(0.0-2.1)	1	0.5(0.0-2.8) ⁵⁸⁶
>20	6	0.5(0.2-1.4)	2	0.2(0.0-0.8)*
Sex (yes)				
Female	24	1.6(0.6-4.1)	20	2.2(0.7-7.2) ⁵⁸⁷
Job Title (yes)				
Administrative	5	0.4(0.2-1.1)	3	0.3(0.1-0.9)* ⁵⁸⁹
Professional nurses	5	0.6(0.2-1.6)	4	0.6(0.2-1.8)
Enrolled nurses	14	2.5(1.2-5.3)*	11	2.4(1.1-5.6) ⁵⁹⁰
Enrolled nursing assistants	5	1.2(0.5-3.3)	5	1.7(0.6-4.5) ⁵⁹¹
Latex Exposure				
Exposure status (yes)	24	2.4(0.9-6.3)	20	3.4(1.1-10.8)* ⁵⁹²
Type of gloves				
None	5	0.4(0.2-1.0)	3	0.3(0.1-0.9)* ⁵⁹³
Exclusive Powdered latex glove (yes)	2	0.9(0.0-3.6)	2	1.2(0.0-1.7) ⁵⁹⁴
Exclusive Powder free latex glove (yes)	11	3.1(1.4-6.8)*	10	3.1(1.7-9.1)* ⁵⁹⁵
Mixed gloves(yes)	11	0.8(0.4-1.8)	8	0.7(0.3-1.7) ⁵⁹⁶
Medical and Personal History				
Personal history of Allergy Disease (yes)	16	1.4(0.7-3.1)	12	1.3(0.5-2.9) ⁵⁹⁷
Family history of Allergy Disease (yes)	18	1.1(0.5-2.4)	14	1.1(0.5-2.4) ⁵⁹⁸
Fruit allergy (yes)	5	2.8(1.0-7.5)	5	3.7(1.4-10.5) ⁵⁹⁹
Previous open surgery (yes)	18	1.1(0.5-2.4)	14	1.5(0.7-3.1) ⁶⁰⁰
Chi square, *p<0.05				
†Latex Skin Prick Test Positive				599
‡Latex Skin Prick Test Positive and work related clinical symptoms of allergy				600

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Table 4: Multivariate analysis of demographics, medical and personal history, exposure history and latex sensitisation (LS)[†] and latex allergy (LA)[#] amongst healthcare workers at King Edward III Hospital, KwaZulu-Natal South Africa, (n=501)

Characteristics	MODEL I* (n=501)		MODEL II** (n=501)		MODEL III***(n=202)		MODEL IV****(n=252)	
	LS OR (95%CI)	LA OR (95%CI)	LS OR (95%CI)	LA OR (95%CI)	LS OR (95%CI)	LA OR (95%CI)	LS OR (95%CI)	LA OR (95%CI)
Demographics								
Sex (female)	0.9(0.2-2.7)	1.1(0.3-4.4)	0.9(0.3-2.7)	1.1(0.3-4.5)	0.3(0.0-1.8)	0.3(0.0-3.1)	2.5(0.5-12.2)	2.5(0.5-12.2)
Duration of employment (years)	0.9(0.9-1.0)	0.9(0.8-0.9)	0.9(0.9-1.0)	0.9(0.8-0.8)	0.9(0.9-1.8)	0.7(0.5-1.0)	0.9(0.9-1.0)	0.9(0.9-1.0)
Latex Exposure								
Exposure status(yes)	2.2(0.7-6.7)	2.6(0.7-9.8)						
Type of gloves								
None			1	1				
Exclusive lightly powdered latex glove (yes)			1.6(0.3-9.8)	2.6(0.4-17.7)				
Exclusive Powder free latex glove (yes)			4.2(1.2-14.1)	5.1(1.2-21.2)				
Mixed gloves (yes)			1.7(0.5-5.6)	1.7(0.4-7.1)				

Pairs of Powdered latex Gloves in the last 7 days					1.1(1.0-1.2)	1.2(1.0-1.4)		
Pairs of Powder Free Latex Gloves in the last 7 days							1.0(0.9-1.1)	1.0(0.9-1.1)
Personal and Medical History								
Personal history of allergy disease (yes)	1.5(0.7-3.3)	1.4(0.6-3.2)	1.5(0.7-3.3)	1.3(0.6-3.2)	1.4(0.3-6.8)	1.6(0.2-11.6)	1.0(0.4-2.9)	0.9(0.3-2.8)
Family history of allergy disease (yes)	1.0(0.45-2.2)	0.9(0.4-2.2)	1.1(0.5-2.3)	0.9(0.4-2.3)	0.4(0.1-1.9)	0.5(0.1-3.6)	0.7(0.2-2.0)	0.8(0.3-2.7)
Fruit allergy (yes)	2.3(0.8-6.7)	3.1(1.1-9.2)	2.2(0.8-6.5)	3.0(0.9-9.1)	5.0(0.4-56.9)	9.7(0.6-163.0)	1.7(0.3-8.5)	2.0(0.4-10.4)
Previous open surgery (yes)	2.0(0.9-4.4)	1.9(0.8-4.6)	2.1(0.9-4.6)	1.9(0.8-4.7)	1.4(0.3-7.4)	1.2(0.1-11.1)	1.1(0.4-3.2)	1.2(0.4-3.8)

†Latex Skin Prick Test Positive

‡Latex Skin Prick Test Positive and work related clinical symptoms of allergy

*Model included latex glove exposure status

**Model included type of gloves

***Model included number of pairs of powdered latex gloves

****Model included number of pairs of powder free latex gloves



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60STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest
Outcome data	15*	Report numbers of outcome events or summary measures
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses

Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.



The prevalence of latex sensitisation and allergy and associated risk factors amongst health care workers using hypoallergenic latex gloves at King Edward VIII hospital, KwaZulu-Natal South Africa: A cross sectional study

Journal:	<i>BMJ Open</i>
Manuscript ID:	bmjopen-2013-002900.R1
Article Type:	Research
Date Submitted by the Author:	12-Aug-2013
Complete List of Authors:	Phaswana, Shumani; University of KwaZulu Natal, Occupational and Environmental Health Naidoo, Saloshni; University of KwaZulu Natal, Occupational and Environmental Health
Primary Subject Heading:	Occupational and environmental medicine
Secondary Subject Heading:	Immunology (including allergy), Occupational and environmental medicine, Epidemiology
Keywords:	Latex, Hypoallergenic, Healthcare workers, South Africa

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3 1 **The prevalence of latex sensitisation and allergy and associated risk factors among healthcare**
4 **workers using hypoallergenic latex gloves at King Edward VIII Hospital, KwaZulu-Natal South**
5 **Africa: A cross sectional study**
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10 4
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38 19
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40 20 Keywords: Latex, hypoallergenic, healthcare workers, South Africa

41
42 21 Word Count:

43
44 22 Abstract: 299

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46 23 Body: 4,359

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ARTICLE SUMMARY**ARTICLE FOCUS**

- The use of hypoallergenic latex gloves has been adopted as policy in different healthcare settings globally.
- However, information with regard to their use and the development of latex sensitisation and allergy among exposed healthcare workers is limited.
- We hypothesised that there is latex sensitization and allergy in healthcare workers using hypoallergenic latex gloves in a South African hospital.

KEY MESSAGE

- In the presence of powder free hypoallergenic gloves, latex sensitisation and latex allergy is still an important occupational health effect in healthcare workers.
- Healthcare workers should be continuously monitored for the development of latex sensitisation and allergy.
- There is a need for a national policy accompanied by clear implementation plans as well as sustainable education and training programmes to address latex sensitisation and allergy among HCWs.

STRENGTH AND LIMITATIONS

- Strength of the study included the presence of a control group providing a background prevalence of latex sensitisation in this population and random selection of participants which minimised the potential of participant bias that arises with a volunteer approach.
- This study was limited by the cross sectional study design as it only allowed for the determination of the prevalence of latex sensitisation; recall bias with regard to the number of gloves used in the past 7 working days and the self-reporting of personal and family atopic disorders may have resulted in the misclassification of exposure and atopy respectively.

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31 **What this paper adds**

32 In the presence of powder free hypoallergenic gloves, latex sensitisation and latex allergy is still an
33 important occupational health hazard in healthcare workers

34 Healthcare workers should be continuously monitored for the development of latex sensitisation and
35 allergy

36 There is a need for a national policy accompanied by clear implementation plans as well as sustainable
37 education and training programmes to address latex sensitisation and allergy among HCWs

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For peer review only

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7 40 **ABSTRACT**
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10 41 **Objectives**
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12 42 The present study describes latex sensitisation and allergy prevalence and associated factors among
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14 43 healthcare workers using hypoallergenic latex gloves at King Edward VIII Hospital in KwaZulu-Natal
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16 44 South Africa.
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20 45 **Design**
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22 46 Cross sectional study
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26 47 **Setting**
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29 48 A tertiary hospital in eThekweni municipality, KwaZulu Natal, South Africa
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32 49 **Participants**
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35 50 600 healthcare workers were randomly selected and 501(337 exposed and 164 unexposed) participated.
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37 51 Participants who were pregnant, less than one year of work as healthcare worker and history of
38
39 52 anaphylactic reaction were excluded from the study.
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42 53 **Primary and secondary outcome measures**
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44
45 54 Latex sensitisation and latex allergy were the outcome of interest and they were successfully measured
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48 55 **Results**
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50
51 56 Prevalence of latex sensitisation and allergy was observed among exposed workers (7.1% and 5.9%) and
52
53 57 unexposed workers (3.1% and 1.8%). Work related allergy symptoms were significantly higher in
54
55 58 exposed workers (40.9%, p<0.05). Duration of employment was inversely associated with latex allergy
56
57 59 (OR: 0.9; 95% CI: 0.8-0.9). The risk of latex sensitisation (OR: 4.2; 95% CI: 1.2-14.1) and allergy (OR:
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3 60 5.1; 95% CI: 1.2-21.2) increased with exclusive use of powder-free latex gloves. A dose –response
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5 61 relationship was observed for powdered latex gloves (OR: 1.1; 95% CI: 1.0-1.2). Atopy (OR: 1.5; 95%
6
7 62 CI: 0.7-3.3 and OR: 1.4; 95% CI: 0.6-3.2) and fruit allergy (OR: 2.3; 95% CI: 0.8-6.7 and OR: 3.1; 95%
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9 63 CI: 1.1-9.2) also increased the risk of latex sensitisation and allergy.
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12 13 64 **Conclusion**

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16 65 This study adds to previous findings that healthcare workers exposed to hypoallergenic latex gloves are at
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18 66 risk for developing latex sensitisation highlighting its importance as an occupational hazard in healthcare.
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20 67 More research is needed to identify the most cost effective way of implementing a latex free environment
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22 68 in resource limited countries, such as South Africa. In addition more cohort analysis is required to better
23
24 69 understand the chronicity of illness and disability associated with latex allergy.
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71 INTRODUCTION

72 Latex allergy (LA) as an occupational disease among healthcare workers (HCWs) gained
73 recognition after Nutter published a case report of contact urticaria in a HCW in 1979.¹ The
74 increase in prevalence coincided with the emergence of the Human Immunodeficiency Virus/
75 Acquired immunodeficiency syndrome (HIV/AIDS) epidemic and the introduction of “universal
76 precautions” in the healthcare industry which had resulted in the increased use of latex gloves
77 among HCWs.²

78 Latex gloves are preferred due to their superior barrier and physical properties as compared to
79 the non-latex gloves.³ International epidemiological studies have reported the prevalence of latex
80 allergy among HCWs to range between 2-22% depending on the population and diagnostic
81 methods used.⁴⁻¹¹ The prevalence in the general population has been reported to range between
82 1-6%.^{12, 13} In South Africa studies amongst HCWs reported a latex sensitisation prevalence of
83 between 2.7 to 20.8%.¹⁴⁻¹⁶ Latex allergy in HCWs is a compensable disease in South Africa in
84 terms of the Compensation of Occupational Injuries and Diseases Act No. 130 of 1993.¹⁷

85 Powdered latex gloves were identified as an important risk factor for latex sensitisation and
86 allergy in HCWs as they were found to contain high allergenic protein content.¹⁸ Following these
87 findings, hypoallergenic gloves with low allergen content namely, low powdered and powder
88 free latex gloves were introduced. The European definition of powder free gloves is gloves with
89 powder content not exceeding 2 mg per glove and leachable latex protein which is as low as is
90 reasonably practical.¹⁹

91 Hypoallergenic gloves have been associated with reduced latex aeroallergen concentrations,
92 reduced conversion rates and a subsequent decrease in clinic visits, and compensation claims for

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3 93 latex induced occupational asthma and allergic contact dermatitis among HCWs.^{18, 20} As much as
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6 94 the use of low or powder free gloves has been shown to reduce latex related symptoms, other
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8 95 studies have shown that exposed HCWs still exhibit symptoms at very low levels of measureable
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10 96 airborne latex allergens.²¹ Most studies have reported on the airborne levels and inhalational
11
12 97 route of exposure hence the recommendation on low powdered or powder free latex gloves.
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15 98 There is little consideration given to the dermal route of exposure despite the fact that exposure
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17 99 is as a result of direct contact in these instances.²² Eliminating the cornstarch powder only
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20 100 removed the carrier and not the source of allergen which is in the latex itself. Therefore workers
21
22 101 using powder free gloves are still exposed to the allergenic content of latex gloves. It has been
23
24 102 shown that different brands from different suppliers contain differing levels of protein due to a
25
26 103 lack of standards in latex glove manufacture.²³ A South African study reported that some powder
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28 104 free latex gloves were found to have high allergenic protein content.²³ HCWs using these gloves
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30 105 are exposed via direct dermal contact and are at risk for developing latex sensitization which
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32 106 maybe asymptomatic and if exposure continues they can later develop latex allergy which
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34 107 presents with clinical manifestations.
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40 108 While it is important to diagnose and manage an individual worker with latex allergy in the early
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42 109 stages of the disease, complete control of hazardous substance in the workplace is equally if not
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44 110 more important. While a latex free work environment would be a preferred control strategy,
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46 111 substitution of powdered latex gloves with powder free gloves was shown to be cost effective
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48 112 and associated with improved clinical outcome.^{20, 24-26} As a result this was adopted as the most
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50 113 reasonable and practical approach in addressing the problem of latex allergy among HCWs both
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52 114 internationally and to some extent nationally.²⁷⁻²⁹ This has proven to reduce latex induced
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54 115 clinical outcomes. Even with this intervention, studies in Western countries such as Germany
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3 116 and the UK have shown that the risk of latex sensitisation still exists and more needs to be done
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5 117 to protect HCWs.^{30, 31}
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9 118 The current study described the prevalence of latex sensitisation and allergy among healthcare
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11 119 workers who use hypoallergenic powder free and lightly powdered latex gloves.
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14 120 **METHODS**

15 121 **Study design and population**

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18 122 This was a cross sectional study conducted between July 2011 and January 2012. The study
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21 123 location was King Edward VIII hospital, the second largest hospital in the Southern hemisphere,
22
23 124 providing regional and tertiary services to the whole of KwaZulu-Natal (KZN) and the Eastern
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25 125 Cape Province in South Africa. It has a bed status of 1300 and has a workforce of 2400. The
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27 126 hospital was chosen due to the large workforce with different departments, and the policy of
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29 127 using both powder free and low powdered latex gloves for approximately 10 years.
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37 128 The study population was limited to HCWs currently employed at King Edward VIII Hospital
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39 129 for more than 12 months. HCWs were defined as all personnel employed in the hospital.
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43 130 The prevalence of latex sensitization in HCWs using powdered latex gloves in the Western Cape
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45 131 Province was 11.9% in 2001.¹⁶ We expected the prevalence at King Edward VIII hospital to be
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47 132 less than the 11.9% observed in the Western Cape Province due to the adoption of a
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49 133 hypoallergenic latex glove policy in 2001. Using EPI Info calculator version 3.04.04., it was
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51 134 assumed that 50% of sensitised workers have remained sensitised despite the introduction of
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53 135 hypoallergenic latex gloves 10 years prior. Using an expected latex sensitization prevalence of
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55 136 6% for the exposed group and the prevalence among the general population being reported as
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3 137 less than 1% the required sample size was calculated to be 585 participants 2 exposed
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6 138 participants for every 1 non-exposed participant (exposed =390; unexposed =195). HCWs were
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8 139 considered to be exposed if they were likely to use gloves. Unexposed HCWs were drawn from
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11 140 the administrative staff of the hospital.

141 **Questionnaire**

142 We used an adaptation of the questionnaire used in an epidemiological study conducted at
143 Groote Schuur in 2001¹⁶ with permission from Professor Paul Potter, Allergy Unit, Medical
144 School, University of Cape Town. The questionnaire containing open and closed ended questions
145 was adapted to include items on exposure assessment. The questionnaire was administered by a
146 trained research assistant immediately prior to the skin prick test. The questionnaire collected
147 data on the participants' demographics, personal risk factors, latex exposure assessment, clinical
148 manifestations of latex sensitization (dermal and respiratory) and history of previous reactions
149 suggestive of latex allergy.

150 **Exposure Assessment**

151 *Individual Exposure*

152 Individual latex exposure was determined by the type of gloves used, number of gloves used per
153 day, and duration of glove use. The information was limited to 7 working shifts/days prior to the
154 interview.

155 *Departmental Exposure*

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3 156 Departmental exposure was defined as glove usage in the past 12 months (01 January 2011-31
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6 157 December 2011). The overall departmental exposure was obtained by reviewing monthly glove
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8 158 usage by each department from the stock room register. This was used to estimate the annual
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10 159 exposure for employees who had rotated through different departments in the past 12 months.
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12 160 Non sterile latex gloves are distributed throughout the clinical departments while a high
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14 161 proportion of sterile gloves are distributed to labour ward, theatre, surgical wards and outpatient
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16 162 departments. Glove type was defined as powdered and powder-free and latex free based on the
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18 163 previous literature.^{23, 32}
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23 164 **Skin prick test (SPT)**

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26 165 The SPT was conducted using the Stallergenes kit.³² It was performed in a room with access to
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28 166 emergency resuscitation services by a trained research assistant. The research assistant and
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30 167 principal investigator were trained on 2 separate occasions. The test was performed on the inner
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32 168 aspect of the participants' forearms, between the wrist and the elbow on normal skin. A positive
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34 169 and negative control were performed using histamine (0.61% concentration of phenol) and
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36 170 buffered normal saline solution respectively on the same arm and they were 3 cm apart to
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38 171 prevent cross contamination. The protein concentration of the latex extract was 500µg/ml and the
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40 172 solution was applied as it was with no further dilutions. After 15-20 minutes subsequent to
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42 173 puncturing the skin, the SPT reaction wheal and flare was outlined by a black ink and clear tape
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44 174 was used to transfer the outline from skin to the results sheet by the trained research assistant or
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46 175 principal investigator.³³ A positive result was indicated by a mean wheal diameter measuring 3
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48 176 mm or greater than the negative control. Results were recorded on a standardized result sheet.
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50 177 The research assistant's test performance was audited by the principal investigator at regular
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52 178 intervals to ensure correctness of technique and interpretation of the results.
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3 179 Informed signed consent was obtained from all the participants prior to participation. They had
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6 180 the option of participating in the questionnaire interview and the SPT or refusing the SPT. The
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8 181 study protocol was approved by the Biomedical Research Ethics Committee of the University of
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10 182 KwaZulu-Natal (BE048/11). Permission to conduct the study was also obtained from the KZN
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13 183 Provincial Department of Health and King Edward VIII hospital management.

14 15 16 184 **Statistical analysis**

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20 185 Data was captured in Excel and analysed in Stata Version 11. Frequencies and medians with
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22 186 ranges were presented for categorical and continuous variables respectively. The Chi-square and
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24 187 the Kruskal-Wallis test were used to test for significant associations between categorical and
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26 188 continuous variables and the dependent variables under study on bivariate analysis, respectively.

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30 189 Binary logistic regression was used to test for significant associations between independent and
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32 190 dependent variables on multivariate analysis. The dependent variables used in the regression
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34 191 analysis were: Latex sensitisation, which was defined as having a SPT wheal of ≥ 3 mm to latex
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36 192 extract; Latex allergy (LA) was defined as being SPT positive and a report of having any one or
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38 193 more of the listed work related clinical symptoms namely itchy eyes, red eyes, runny eyes, runny
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40 194 nose, itchy nose, sneezing, coughing, tight chest, wheezing, itchy skin, skin rash or dizziness.

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42 195 Independent variables that were considered for analysis were as follows: Age (yrs.) and sex,
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44 196 duration of employment, job title, current department employed in, type of gloves used, number
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46 197 of pairs of gloves used per day, self reported and family history of atopy, food allergy and
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48 198 previous history of open surgery and number of surgical procedures. In the multivariate analysis,
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50 199 age was omitted due to collinearity with duration of employment. Departmental glove
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52 200 consumption was omitted as this only indicated annual distribution of gloves per department and
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3 201 not necessarily employees' exposure since enrolled nursing assistants and enrolled nurses are
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5 202 rotated through different departments in any given year. The number of pair of gloves was used
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8 203 as an indicator of individual latex glove exposure. The variable number of pairs of gloves used
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10 204 and duration of employment were retained as continuous variables in the multivariate model.
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12 205 Fractional polynomial and a fractional plot was used to visualise the dose-response relationship
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14 206 of these continuous exposure variables.
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19 207 **RESULTS**

20 21 22 208 **Participant Demographics**

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25 209 Sixty five HCWs refused to participate in the study. Among the 520 HCWs who responded to
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27 210 the invitation there was an overall participation rate of 85.5 % (n=501) with 3.6% (n=19)
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29 211 refusing SPT. There was no significant difference between those refusing SPT and those who
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31 212 had the SPT with respect to latex exposure status, age, sex and duration of employment.
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36 213 The median age of participants was 42.2 years (range: 22 years-65 years) with the greater
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38 214 proportion of them being females. The median duration of employment was 10.9 years (range: 1
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40 215 year-42 years) with the majority of exposed participants having worked as a HCW for < 10
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42 216 years. Most unexposed healthcare workers had been employed for > 20 years. Personal and
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44 217 family history of allergy was more prevalent among unexposed HCWs while exposed HCWS
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46 218 reported a higher prevalence of a fruit allergy and history of previous surgery (Table 1).
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51 219 **Prevalence of Latex Sensitisation and Allergy**

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54 220 The overall prevalence of latex sensitisation and latex allergy were 5.9% (n=29) and 4.6%
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56 221 (n=23) respectively. Although the difference was not significant, the prevalence of latex
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3 222 sensitisation was higher among the exposed group (7.1%) as compared to the unexposed group
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6 223 (3.1%). Latex allergy was significantly higher in the exposed group than unexposed group (5.9%
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8 224 vs 1.8%, $p=0.04$). There was a significant difference in the work related allergy symptoms
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10 225 between exposed and unexposed workers (40.9% vs. 31.7%, $p=0.04$) (Table 1). Symptoms that
11
12 226 were significantly associated with latex sensitisation were skin rash ($p< 0.000$), itchy skin
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14 227 ($p=0.001$), runny nose ($p=0.004$), red eyes ($p=0.01$) and itchy eyes ($p=0.01$).
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18 228 The prevalence of latex sensitization was higher among those who were exposed and those with
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20 229 employment duration of < 10 yrs. Although the prevalence of latex sensitisation was lower
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22 230 among participants < 30 years of age, there was no significant variation with age or sex. There
23
24 231 was a significant difference ($p=0.04$) in the prevalence of fruit allergy between those participants
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26 232 with latex sensitisation (17.2%) and unsensitised participants (6.9%) The exclusive use of
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28 233 powder free latex gloves was found to be significantly ($p=0.003$) higher among the participants
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30 234 who had latex sensitisation. There was equal distribution of powdered and powder free latex
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32 235 gloves among those who reported the use of mixed gloves. The prevalence of reporting previous
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34 236 open surgery and use of other non- occupational exposure latex containing material did not vary
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36 237 significantly between those who had latex sensitisation and those who were unsensitised. There
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38 238 was a significantly higher prevalence of reporting allergic reactions when handling other latex
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40 239 containing medical equipment among participants with latex allergy as compared to unsensitised
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42 240 participants (10.3% vs 1.7%, $p=0.002$) (Table 2).
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50 241 **Crude association of demographics, exposure status, medical and personal history and latex**
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52 242 **sensitisation, latex allergy**
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3 243 Latex exposure was significantly associated with latex allergy (OR: 3.4; 95% CI: 1.1-10.8).
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5 244 Working as a HCW for 5-9 years was significantly associated with latex sensitisation (OR: 2.6;
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7 245 95% CI: 1.2-5.5) and latex allergy (OR: 3.3; 95% CI: 1.4-7.6), respectively. Employment
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9 246 duration as a HCW for >20 years was protective against latex allergy (OR: 0.2; 95% CI: 0.0-0.8).
10
11 247 In comparison with unexposed workers, working as an enrolled nurse was significantly
12
13 248 associated with both latex sensitisation (OR: 2.5; 95% CI: 1.2-5.3) and latex allergy (OR: 2.4;
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15 249 95% CI: 1.1-5.6). The exclusive use of powder free latex gloves was significantly associated
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17 250 with latex sensitisation (OR: 3.1; 95% CI: 1.4-6.8) and latex allergy (OR: 3.1; 95% CI: 1.7-9.1).
18
19 251 Powdered and powder free latex gloves were equally distributed among those who reported the
20
21 252 use of mixed gloves. The annual consumption of pairs of gloves per HCW by department was
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23 253 ranked and grouped into tertiles. Although medical and surgical wards had low and moderate
24
25 254 pairs of gloves consumption per HCW, these wards had the highest proportion of workers with
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27 255 latex sensitisation (n=6, 20.0% each). However the relation was only significant for those who
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29 256 reported the medical ward as being the current department in which they worked (p=0.01). The
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31 257 proportions for powdered latex glove use were 71% and 69% in medical and surgical wards,
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33 258 respectively and this was not statistically significant. Exposure to other latex containing medical
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35 259 devices was not significantly different from what was reported in other wards. There was no
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37 260 significant association between reported personal history of allergy disease, latex sensitisation
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39 261 and latex allergy. Fruit allergy was significantly associated with latex allergy (OR: 3.7; 95%:
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41 262 1.4-10.4) (Table 3). Listed fruits were evaluated for their independent association with latex
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43 263 sensitisation. Avocado (OR: 12.3; 95% CI: 5.1-29.6) and others (OR: 5.1; 95% CI: 2.1-11.8)
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45 264 which included pineapple and orange showed significant associations with latex sensitisation
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47 265 (data not shown).
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266 **Multivariate analysis**

267 While latex exposure had estimates of the OR above 2, there was no significant association with
268 latex sensitisation and latex allergy. Duration of employment was found to be inversely
269 associated with latex allergy in models I and II. The exclusive use of powder free latex gloves
270 was significantly associated with latex sensitisation (OR: 4.2; 95% CI: 1.2-14.1) and latex
271 allergy (OR: 5.1; 95%CI: 1.2-21.2) on multivariate analysis. This significant association
272 disappeared when examining the number of pairs of powder free gloves used in the last 7 days. A
273 weak association was observed for the number of pairs of powdered latex gloves used in the last
274 7 days with both latex sensitisation and latex allergy (model III and IV). Further analysis of
275 duration of employment and number of pairs of gloves using fractional polynomial failed to
276 demonstrate a dose-response relationship with either latex sensitisation or latex allergy. There
277 was a significant association between fruit allergy and latex allergy in model I (OR: 3.1; 95% CI:
278 1.1-9.2) (Table 4).

279 **DISCUSSION**

280 This is an important study for South African HCWs as it examined the risk of latex sensitisation
281 in a group of workers exposed to hypoallergenic latex gloves. As previously mentioned there has
282 been no literature documenting the prevalence of latex sensitisation among South African HCWs
283 using hypoallergenic lightly powdered or powder-free latex gloves. The prevalence of latex
284 sensitisation among exposed HCWs (7.1%) in this study is comparable to findings among HCWs
285 in another South African hospital.¹⁴ However it was considerably lower than the 11.9%
286 prevalence reported by Potter in the same year.¹⁶ While a substantial number of participants
287 (37%) reported work related allergy symptoms, only 4.6% met our definition of latex allergy.
288 The important symptoms associated with latex sensitisation were skin rash, itchy skin, runny

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3 289 nose, red and itchy eyes in keeping with previous studies. Elimination of powdered latex gloves
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6 290 has shown a reduction in the concentration of aeroallergens in the operating room with the low
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8 291 prevalence of latex allergy in our study population.
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11 292 Although the relationship was weak, this study showed that the risk of latex sensitisation
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14 293 decreases with duration of employment. The healthy worker effect is a possible explanation of
15
16 294 this finding. Prior to availability of hypoallergenic latex gloves, workers who had developed
17
18 295 latex allergy may have left employment or they may have changed their career path and moved
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20 296 into a more administrative or managerial role with no contact with latex gloves. Furthermore
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23 297 new employees are only sensitised and have not yet manifested clinical symptoms and they
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25 298 continue using latex gloves. On the other hand senior HCWs may have been sensitised during
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28 299 their earlier years of employment and as a result they either moved to departments with less
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30 300 exposure to latex gloves or deliberately avoid latex containing products and therefore exhibit less
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33 301 latex related symptoms. Moreover, the introduction of hypoallergenic gloves 10 years prior to
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35 302 the study may explain the reduced sensitisation in senior HCWs as demonstrated in the study by
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37 303 Smith et al in 2007. The published literature has been inconsistent in reporting the association
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39 304 between duration of employment and latex sensitisation. Although latex is one of the best studied
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41 305 allergens, no exposure response studies have been published with measured latex allergen levels.
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43 306 In addition, studies have demonstrated variation in allergen content of different gloves. These
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45 307 may lead to discrepancies in the literature with regard to the role of duration of employment as a
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47 308 surrogate measure of exposure.
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53 309 In our study HCWs who exclusively used powdered free latex gloves had a 4 times greater odds
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55 310 of developing latex sensitisation. The fact that HCWs with latex sensitisation or allergy work
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57 311 more often with powder free latex gloves is indicative of reverse causality because of symptoms.
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3 312 Moreover the background prevalence of latex sensitisation in this study was relatively higher
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5 313 (3.5%) than previously reported prevalence in the general population by Bousquet et al.¹³ Studies
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8 314 have shown that some of these “hypoallergenic” latex gloves actually contain high levels of
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10 315 allergens which can be release into the environment with aggressive manipulation.²³ Some of the
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12 316 sensitised HCWs may have been sensitised before the hospital implemented a hypoallergenic
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14 317 latex glove policy. Also Smith et al showed that complete avoidance of powdered latex glove can
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16 318 result in the reduction or no change in measurable IgE antibodies.³⁴ A study in Germany reported
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18 319 a high prevalence of 8% among 226 dental students who had only been exposed to exclusive
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20 320 powder free latex gloves.³⁰ Similarly in the UK despite a total ban on powdered latex gloves
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22 321 Clayton found a 10% prevalence of latex sensitisation in HCWs.³¹ It is also not clear to what
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24 322 extent the aeroallergens released by colleagues using powdered latex gloves influence this
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26 323 finding. Furthermore the role of other latex containing medical devices during sensitisation
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28 324 period cannot be entirely ruled out.

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35 325 In our study, frequency of exposure as measured by the number of gloves used in the last 7
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37 326 working days showed a weak association between powdered latex gloves and latex sensitisation
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39 327 but no association could be demonstrated with powder free latex gloves. Airborne latex
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41 328 aeroallergens have been shown to increase with the number of powdered gloves used which
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43 329 subsequently increases the risk of latex sensitisation and clinical latex glove related allergy
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45 330 symptoms.¹⁸

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50 331 The positive association between department with low glove consumption per HCW and latex
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52 332 sensitisation is in contrast with previous finding by Liss and co-workers.⁹ They reported positive
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54 333 association with departments that had high glove consumption per HCWs. Again, this could be
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56 334 as a result of reverse causality where HCWs with latex sensitisation may have been relocated to

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3 335 wards with low glove consumption to minimise the exposure. In addition, the annual pair of
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5 336 gloves consumption per HCW by department does not provide an accurate indication of
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8 337 individual exposure; rather it gives us the annual distribution of gloves to different departments.
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11 338 Several studies have reported atopy as a significant risk factor for latex sensitisation.^{9, 10, 35}

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13 339 Similarly, the prevalence of reporting a history of personal atopy in this study was higher among
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15 340 latex sensitised participants although the association was not statistically significant. The role of
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17 341 atopy is complex because some individuals might also have become atopic after having been
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19 342 latex sensitised and cross sectional study is not suitable in establishing this association.
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24 343 Fruit latex allergy syndrome is a phenomenon seen where latex sensitised individuals
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26 344 demonstrate a cross reactivity with specific foods; particularly fruit. Studies have identified this
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28 345 phenomenon among sensitised HCWs and the general population. This has been attributed to the
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30 346 similarity between fruit proteins and latex allergens.³⁶ Fruit allergy was significantly associated
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32 347 with latex sensitisation and latex allergy in our study. Our study was dependent on the self-
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34 348 reporting of fruit allergy and no objective tests were carried out. It is therefore possible that
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36 349 participants have independent simultaneous allergies to both fruit and latex without cross
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38 350 reactivity. Also, we were unable to determine whether latex sensitisation preceded the
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40 351 development of fruit allergy or vice versa. Fruit allergy prior to latex exposure could have
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42 352 contributed to the association observed in our study.
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49 353 Latex sensitised participants reported a high prevalence of a history of previous open surgery in
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51 354 our study. This has been reported to occur as a result of direct intraoperative exposure to latex
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53 355 containing medical devices such as catheters or tubes. Studies in children with congenital
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55 356 abnormalities have demonstrated that the risk for latex allergy increases with the number of open
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3 357 surgical procedures that they undergo.³⁷ Frequency of invasive procedures among adults was
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6 358 shown to increase the risk of latex sensitisation reporting while more than 10 procedures
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8 359 increased the risk of developing latex allergy.³⁸
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11 360 Strengths of this study include the high response rate (85.5%) and comparability to other
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13 361 studies.^{8, 16} Access to the hospital employee database allowed us to better assess the
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15 362 representativeness of this study population by comparing demographic data of the non-
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17 363 participants and the participants. The participants were randomly selected minimising the
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19 364 potential of participant's bias that comes with a volunteer approach.
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24 365 The presence of a control group provided a background prevalence of latex sensitisation in this
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26 366 population which allowed for a better estimation of associations attributable to work related
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28 367 factors. The use of Stallergenes latex specific SPT further strengthens the study. The SPT test is
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30 368 regarded as the gold standard for the diagnosis of latex allergy and Stallergenes has been shown
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32 369 to have a diagnostic sensitivity and specificity of 93% and 100%, respectively.³² The research
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34 370 assistant employed on this study was trained and initially shadowed and periodically supervised
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36 371 by the principal investigator to ensure appropriate administration of the questionnaire and the
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38 372 SPT thereby improving the reliability and validity of the study.
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44 373 This study was limited by the cross sectional study design which was relatively low in cost and
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46 374 quick to conduct. It only allowed for the determination of prevalence of latex sensitisation at one
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48 375 point in time. Consequently the prevalence of latex sensitisation may have been underestimated
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50 376 as it is possible that HCWs who had already developed latex sensitisation have left the hospital
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52 377 before the study was conducted. Some of the observed associations in the study may be as a
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54 378 result of a complex interplay between the healthy worker effect, reverse causality and exposure
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3 379 reduction by the introduction of powder free latex gloves. These interactions can be better
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6 380 explored and understood in a longitudinal study. Recall bias is another potential limitation in this
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8 381 study as workers were asked to recall the number of gloves used in the past 7 working days.
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10 382 HCWs may have overestimated or underestimated their individual exposures. Our study
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12 383 depended on self-reporting of personal and family atopic disorders and this may have resulted in
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14 384 the misclassification of atopy. The role of atopy and cross-reactivity between allergens is a
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16 385 complex phenomenon which cannot be investigated in cross sectional study. Therefore, cohort
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18 386 studies are necessary to disentangle this phenomenon.
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23 387 **CONCLUSION**

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26 388 This study shows that even in the presence of powder free hypoallergenic glove use there is latex
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28 389 sensitisation and latex allergy, adding to previous findings that HCWs exposed to hypoallergenic
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30 390 latex gloves are still at risk for developing latex sensitisation and latex allergy. This indicates that
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32 391 latex sensitisation and allergy are still an important occupational hazard for HCWs. While it may
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34 392 be economically impractical to replace the latex gloves in our setting, reduction of allergen
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36 393 content in latex products is another strategy that can be implemented to address the problem and
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38 394 protect HCWs. A policy accompanied by clear implementation plans as well as sustainable
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40 395 education and training programmes to address latex sensitisation and allergy among HCWs
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42 396 should be implemented.³⁹ In addition HCWs must be continuously monitored for the
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44 397 development of latex sensitisation and alternate latex free glove must be made available for
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46 398 them. More research is needed to identify the most cost effective way of implementing a latex
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48 399 free environment in resource limited countries, such as South Africa. In addition the current
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50 400 studies in South Africa have largely been cross-sectional in nature. More cohort analysis is
51
52 401 required to better understand the chronicity of illness and disability associated with latex allergy.
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402 ACKNOWLEDGEMENT

403 I would like to thank the hospital employees participating in this study and their management for
404 allowing me access to the human resource database. I would like to thank Professor Mohamed
405 Jeebhay (Centre of Occupational and Environmental Health, University of Cape Town, SA) and
406 Professor David L Nordstrom (Occupational and Environmental Safety and Health, University of
407 Wisconsin-Whitewater, USA) for their comments on my initial proposal. I would like to thank
408 Professor Rajen Naidoo (Discipline of Occupational and Environmental Health, UKZN, SA) for
409 his statistical advice during the data analysis. In addition thank you to Mr. Nhlanhla Jwara for
410 conducting the field work.

411 Contributorship

412 Dr Shumani Phaswana is the principal investigator who was involved from the conception of the idea,
413 proposal writing, data collection, data management and interpretation of the results.

414 Dr Saloshni Naidoo contributed to the conception and design of the study, analysis and interpretation of
415 the data, critical review of the intellectual content of the article and final approval of the article.

416 Data sharing

417 No additional unpublished data

418 Funding

419 None

420 Competing interests

421 None

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506 **TABLES**507 **Table 1: Demographics and associated risk factors amongst latex exposed and unexposed**
508 **healthcare workers at King Edward VIII Hospital, KwaZulu-Natal South Africa, (n=501)**509
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Characteristic	Exposed N (%)	Unexposed N (%)
Number of participants	337 (67.3)	164 (32.7)
Demographics		
Age (years)		
≤30	30(8.9)	19(11.6)
>30-40	121(35.9)	40(24.4)
>40-50	101(29.9)	59(35.9)
>50	85(25.2)	46(28.1)
Duration of employment (years)		
≤5	39(11.6)	28(17.1)
>5-10**	135(40.1)	32(19.5)
>10-15	49(14.5)	17(10.4)
>15-20	24(7.1)	20(12.2)
>20*	90(26.7)	67(40.9)
Sex**		
Female	309(91.7)	95(57.9)
Male	28(8.3)	69(42.1)
Job Title (yes)		
Administrative		164(100.0)
Professional nurses	123(36.5)	
Enrolled nurses	141(41.8)	
Enrolled nursing assistants	73 (21.7)	
Medical and Personal History		
Personal history of Allergy Disease (yes)	147(43.6)	83(50.6)
Family history of Allergy Disease (yes)	197(58.5)	102(62.2)
Fruit allergy (yes)	29(8.6)	9(5.5)
Previous open surgery (yes)*	168(49.8)	61(37.2)
Work-related allergy symptoms(yes)*	138(40.9)	52(31.7)
Non-occupational latex exposure (yes)	161(47.8)	76(46.3)
Latex sensitisation (yes)	24(7.1)	5(3.1)
Current latex allergy (yes)*	20(5.9)	3(1.8)
Chi square, *p<0.05, **p<0.001		

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Table 2: Comparison of risk factors between latex sensitised (skin prick test positive) and non-sensitised (skin prick test negative) healthcare workers at King Edward VIII Hospital, KwaZulu-Natal South Africa (n=501)

Characteristics	Latex SPT +ve† (29) N (%)	Latex SPT -ve† ‡ (472) N (%)	520 521 522
Demographics			523
Age (years.)			524
≤30	1 (3.5)	48(10.2)	525
>30-40	13 (44.8)	148(31.4)	526
>40-50	8 (27.6)	152(32.2)	527
>50	7 (24.1)	124(26.3)	528
Duration of employment			529
≤5	3(10.3)	64(13.6)	530
>5-10	16(55.2)	151(31.9)	531
>10-15	3(10.3)	63(13.4)	532
>15-20	1(3.5)	43(9.1)	533
>20	6(20.7)	151(31.9)	534
Sex (yes)			535
Male	5(17.2)	118(25.0)	536
Female	24(82.8)	354(75.0)	537
Job Title (yes)			538
Administrative	5(17.2)	159(33.7)	539
Professional nurses	5(17.2)	118(25.0)	540
Enrolled nurses	14(48.3)	127(26.9)	541
Enrolled nursing assistants	5(17.2)	68(14.4)	542
Latex Exposure			543
Exposure status(yes)	24 (82.8)	313(66.3)	544
Type of gloves			545
None	5(17.2)	165(34.6)	546
Exclusive powdered latex glove (yes)	2(6.9)	36(7.6)	547
Exclusive powder free latex glove (yes)*	11(37.9)	77(16.3)	548
Mixed (yes)	11(37.9)	198(41.9)	549
Medical and Personal History			550
Personal history of Allergy Disease (yes)	16(55.2)	214(45.3)	551
Family history of Allergy Disease (yes)	18(62.1)	281(59.5)	552
Fruit allergy (yes) *	5(17.2)	33(6.9)	553
Previous open surgery (yes)	18(62.1)	211(44.7)	554
Non-occupational latex exposure (yes)	12(41.4)	225(47.7)	555
Reaction to other latex medical devices (yes)*	3(10.3)	8(1.7)	556
Chi Square, *p<0.05			557
†Latex Skin Prick Test Positive			558
‡Latex Skin Prick Test Negative			559
			560

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565 **Table 3: Crude Odds Ratios (OR) (95%CI) of demographics, exposure status, medical and personal**
 566 **history and latex sensitisation and latex allergy amongst healthcare workers at King Edward VIII**
 567 **Hospital, KwaZulu-Natal South Africa, (n=501)**

Characteristics	N=2 9	Latex Sensitisation OR (95%CI)	N=23	LA# OR (95%CI)	568 569 570
Demographics					
Age (years)					571
≤30	1	0.3(0.0-1.9)	1	0.4(0.0-2.4)	572
>30-40	13	1.8(0.8-3.7)	11	2.0(0.9-4.6)	573
>40-50	8	0.8(0.4-1.8)	7	0.9(0.4-2.2)	574
>50	7	0.8(0.4-2.1)	4	0.6(0.2-1.7)	575
Duration of employment (years)					576
<5	3	0.7(0.2-2.4)	3	0.9(0.3-3.2)	577
5-10	16	2.6(1.2-5.5)*	14	3.3(1.4-7.6)*	578
>10-15	3	0.7(0.2-2.4)	3	0.9(0.3-3.2)	579
>15-20	1	0.4(0.0-2.1)	1	0.5(0.0-2.8)	580
>20	6	0.5(0.2-1.4)	2	0.2(0.0-0.8)	581
Sex (yes)					582
Female	24	1.6(0.6-4.1)	20	2.2(0.7-7.2)	583
Job Title (yes)					584
Administrative	5	0.4(0.2-1.1)	3	0.3(0.1-0.9)*	585
Professional nurses	5	0.6(0.2-1.6)	4	0.6(0.2-1.8)	586
Enrolled nurses	14	2.5(1.2-5.3)*	11	2.4(1.1-5.6)*	587
Enrolled nursing assistants	5	1.2(0.5-3.3)	5	1.7(0.6-4.5)	588
Latex Exposure					
Exposure status (yes)	24	2.4(0.9-6.3)	20	3.4(1.1-10.8)	589
Type of gloves					590
None	5	0.4(0.2-1.0)	3	0.3(0.1-0.9)*	591
Exclusive Powdered latex glove (yes)	2	0.9(0.0-3.6)	2	1.2(0.0-1.7)	592
Exclusive Powder free latex glove (yes)	11	3.1(1.4-6.8)*	10	3.1(1.7-9.1)*	593
Mixed gloves(yes)	11	0.8(0.4-1.8)	8	0.7(0.3-1.7)	
Medical and Personal History					
Personal history of Allergy Disease (yes)	16	1.4(0.7-3.1)	12	1.3(0.5-2.9)	
Family history of Allergy Disease (yes)	18	1.1(0.5-2.4)	14	1.1(0.5-2.4)	
Fruit allergy (yes)	5	2.8(1.0-7.5)	5	3.7(1.4-10.5)*	
Previous open surgery (yes)	18	1.1(0.5-2.4)	14	1.5(0.7-3.1)	
Chi square, *p<0.05					
†Latex Skin Prick Test Positive					
‡Latex Skin Prick Test Positive and work related clinical symptoms of allergy					

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Table 4: Multivariate analysis of demographics, medical and personal history, exposure history and latex sensitisation (LS)[†] and latex allergy (LA)[#] amongst healthcare workers at King Edward III Hospital, KwaZulu-Natal South Africa, (n=501)

Characteristics	MODEL I* (n=501)		MODEL II** (n=501)		MODEL III***(n=202)		MODEL IV****(n=252)	
	LS OR (95%CI)	LA OR (95%CI)	LS OR (95%CI)	LA OR (95%CI)	LS OR (95%CI)	LA OR (95%CI)	LS OR (95%CI)	LA OR (95%CI)
Demographics								
Sex (female)	0.9(0.2-2.7)	1.1(0.3-4.4)	0.9(0.3-2.7)	1.1(0.3-4.5)	0.3(0.0-1.8)	0.3(0.0-3.1)	2.5(0.5-12.2)	2.5(0.5-12.2)
Duration of employment (years)	0.9(0.9-1.0)	0.9(0.8-0.9)	0.9(0.9-1.0)	0.9(0.8-0.8)	0.9(0.9-1.8)	0.7(0.5-1.0)	0.9(0.9-1.0)	0.9(0.9-1.0)
Latex Exposure								
Exposure status(yes)	2.2(0.7-6.7)	2.6(0.7-9.8)						
Type of gloves								
None			1	1				
Exclusive lightly powdered latex glove (yes)			1.6(0.3-9.8)	2.6(0.4-17.7)				
Exclusive Powder free latex glove (yes)			4.2(1.2-14.1)	5.1(1.2-21.2)				
Mixed gloves (yes)			1.7(0.5-5.6)	1.7(0.4-7.1)				

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Pairs of Powdered latex Gloves in the last 7 days					1.1(1.0-1.2)	1.2(1.0-1.4)		
Pairs of Powder Free Latex Gloves in the last 7 days							1.0(0.9-1.1)	1.0(0.9-1.1)
Personal and Medical History								
Personal history of allergy disease (yes)	1.5(0.7-3.3)	1.4(0.6-3.2)	1.5(0.7-3.3)	1.3(0.6-3.2)	1.4(0.3-6.8)	1.6(0.2-11.6)	1.0(0.4-2.9)	0.9(0.3-2.8)
Family history of allergy disease (yes)	1.0(0.45-2.2)	0.9(0.4-2.2)	1.1(0.5-2.3)	0.9(0.4-2.3)	0.4(0.1-1.9)	0.5(0.1-3.6)	0.7(0.2-2.0)	0.8(0.3-2.7)
Fruit allergy (yes)	2.3(0.8-6.7)	3.1(1.1-9.2)	2.2(0.8-6.5)	3.0(0.9-9.1)	5.0(0.4-56.9)	9.7(0.6-163.0)	1.7(0.3-8.5)	2.0(0.4-10.4)
Previous open surgery (yes)	2.0(0.9-4.4)	1.9(0.8-4.6)	2.1(0.9-4.6)	1.9(0.8-4.7)	1.4(0.3-7.4)	1.2(0.1-11.1)	1.1(0.4-3.2)	1.2(0.4-3.8)

†Latex Skin Prick Test Positive
 ‡Latex Skin Prick Test Positive and work related clinical symptoms of allergy
 *Model included latex glove exposure status
 **Model included type of gloves
 ***Model included number of pairs of powdered latex gloves
 ****Model included number of pairs of powder free latex gloves



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60STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest
Outcome data	15*	Report numbers of outcome events or summary measures
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses

Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

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3 1 **The prevalence of latex sensitisation and allergy and associated risk factors among healthcare**
4 **workers using hypoallergenic latex gloves at King Edward VIII Hospital, KwaZulu-Natal South**
5 **Africa: A cross sectional study**
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10 4
11 5 S M Phaswana¹, S Naidoo¹

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38 19
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40 20 Keywords: Latex, hypoallergenic, healthcare workers, South Africa

41
42 21 Word Count:

43
44 22 Abstract: 299

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46 23 Body: 4,359

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ARTICLE SUMMARY**ARTICLE FOCUS**

- The use of hypoallergenic latex gloves has been adopted as policy in different healthcare settings globally.
- However, information with regard to their use and the development of latex sensitisation and allergy among exposed healthcare workers is limited.
- We hypothesised that there is latex sensitization and allergy in healthcare workers using hypoallergenic latex gloves in a South African hospital.

KEY MESSAGE

- In the presence of powder free hypoallergenic gloves, latex sensitisation and latex allergy is still an important occupational health effect in healthcare workers.
- Healthcare workers should be continuously monitored for the development of latex sensitisation and allergy.
- There is a need for a national policy accompanied by clear implementation plans as well as sustainable education and training programmes to address latex sensitisation and allergy among HCWs.

STRENGTH AND LIMITATIONS

- Strength of the study included the presence of a control group providing a background prevalence of latex sensitisation in this population and random selection of participants which minimised the potential of participant bias that arises with a volunteer approach.
- This study was limited by the cross sectional study design as it only allowed for the determination of the prevalence of latex sensitisation; recall bias with regard to the number of gloves used in the past 7 working days and the self-reporting of personal and family atopic disorders may have resulted in the misclassification of exposure and atopy respectively.

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3 31 **What this paper adds**
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6 32 In the presence of powder free hypoallergenic gloves, latex sensitisation and latex allergy is still an
7 33 important occupational health hazard in healthcare workers
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10 34 Healthcare workers should be continuously monitored for the development of latex sensitisation and
11 35 allergy
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14 36 There is a need for a national policy accompanied by clear implementation plans as well as sustainable
15 37 education and training programmes to address latex sensitisation and allergy among HCWs
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7 40 **ABSTRACT**
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10 41 **Objectives**
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12 42 The present study describes latex sensitisation and allergy prevalence and associated factors among
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14 43 healthcare workers using hypoallergenic latex gloves at King Edward VIII Hospital in KwaZulu-Natal
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16 44 South Africa.
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19 45 **Design**
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22 46 Cross sectional study
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25 47 **Setting**
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28 48 A tertiary hospital in eThekweni municipality, KwaZulu Natal, South Africa
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31 49 **Participants**
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34 50 600 healthcare workers were randomly selected and 501(337 exposed and 164 unexposed) participated.
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36 51 Participants who were pregnant, less than one year of work as healthcare worker and history of
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38 52 anaphylactic reaction were excluded from the study.
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41 53 **Primary and secondary outcome measures**
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44 54 Latex sensitisation and latex allergy were the outcome of interest and they were successfully measured
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47 55 **Results**
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49
50 56 Prevalence of latex sensitisation and allergy was observed among exposed workers (7.1% and 5.9%) and
51
52 57 unexposed workers (3.1% and 1.8%). Work related allergy symptoms were significantly higher in
53
54 58 exposed workers (40.9%, p<0.05). Duration of employment was inversely associated with latex allergy
55
56 59 (OR: 0.9; 95% CI: 0.8-0.9). The risk of latex sensitisation (OR: 4.2; 95% CI: 1.2-14.1) and allergy (OR:
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3 60 5.1; 95% CI: 1.2-21.2) increased with exclusive use of powder-free latex gloves. A dose –response
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5 61 relationship was observed for powdered latex gloves (OR: 1.1; 95% CI: 1.0-1.2). Atopy (OR: 1.5; 95%
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7 62 CI: 0.7-3.3 and OR: 1.4; 95% CI: 0.6-3.2) and fruit allergy (OR: 2.3; 95% CI: 0.8-6.7 and OR: 3.1; 95%
8
9 63 CI: 1.1-9.2) also increased the risk of latex sensitisation and allergy.
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11

12 13 **Conclusion**

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16 65 This study adds to previous findings that healthcare workers exposed to hypoallergenic latex gloves are at
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18 66 risk for developing latex sensitisation highlighting its importance as an occupational hazard in healthcare.
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20 67 More research is needed to identify the most cost effective way of implementing a latex free environment
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22 68 in resource limited countries, such as South Africa. In addition more cohort analysis is required to better
23
24 69 understand the chronicity of illness and disability associated with latex allergy.
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71 INTRODUCTION

72 Latex allergy (LA) as an occupational disease among healthcare workers (HCWs) gained
73 recognition after Nutter published a case report of contact urticaria in a HCW in 1979.¹ The
74 increase in prevalence coincided with the emergence of the Human Immunodeficiency Virus/
75 Acquired immunodeficiency syndrome (HIV/AIDS) epidemic and the introduction of “universal
76 precautions” in the healthcare industry which had resulted in the increased use of latex gloves
77 among HCWs.²

78 Latex gloves are preferred due to their superior barrier and physical properties as compared to
79 the non-latex gloves.³ International epidemiological studies have reported the prevalence of latex
80 allergy among HCWs to range between 2-22% depending on the population and diagnostic
81 methods used.⁴⁻¹¹ The prevalence in the general population has been reported to range between
82 1-6%.^{12, 13} In South Africa studies amongst HCWs reported a latex sensitisation prevalence of
83 between 2.7 to 20.8%.¹⁴⁻¹⁶ Latex allergy in HCWs is a compensable disease in South Africa in
84 terms of the Compensation of Occupational Injuries and Diseases Act No. 130 of 1993.¹⁷

85 Powdered latex gloves were identified as an important risk factor for latex sensitisation and
86 allergy in HCWs as they were found to contain high allergenic protein content.¹⁸ Following these
87 findings, hypoallergenic gloves with low allergen content namely, low powdered and powder
88 free latex gloves were introduced. The European definition of powder free gloves is gloves with
89 powder content not exceeding 2 mg per glove and leachable latex protein which is as low as is
90 reasonably practical.¹⁹

91 Hypoallergenic gloves have been associated with reduced latex aeroallergen concentrations,
92 reduced conversion rates and a subsequent decrease in clinic visits, and compensation claims for

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3 93 latex induced occupational asthma and allergic contact dermatitis among HCWs.^{18, 20} As much as
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5 94 the use of low or powder free gloves has been shown to reduce latex related symptoms, other
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8 95 studies have shown that exposed HCWs still exhibit symptoms at very low levels of measureable
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10 96 airborne latex allergens.²¹ Most studies have reported on the airborne levels and inhalational
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12 97 route of exposure hence the recommendation on low powdered or powder free latex gloves.
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14 98 There is little consideration given to the dermal route of exposure despite the fact that exposure
15
16 99 is as a result of direct contact in these instances.²² Eliminating the cornstarch powder only
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18 100 removed the carrier and not the source of allergen which is in the latex itself. Therefore workers
19
20 101 using powder free gloves are still exposed to the allergenic content of latex gloves. It has been
21
22 102 shown that different brands from different suppliers contain differing levels of protein due to a
23
24 103 lack of standards in latex glove manufacture.²³ A South African study reported that some powder
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26 104 free latex gloves were found to have high allergenic protein content.²³ **HCWs using these gloves**
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28 105 **are exposed via direct dermal contact and are at risk for developing latex sensitization which**
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30 106 **maybe asymptomatic and if exposure continues they can later develop latex allergy which**
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32 107 **presents with clinical manifestations.**
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39 108 While it is important to diagnose and manage an individual worker with latex allergy **in the early**
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41 109 **stages of the disease**, complete control of hazardous substance in the workplace is equally if not
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43 110 more important. While a latex free work environment would be a preferred control strategy,
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45 111 substitution of powdered latex gloves with powder free gloves was shown to be cost effective
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47 112 and associated with improved clinical outcome.^{20, 24-26} As a result this was adopted as the most
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49 113 reasonable and practical approach in addressing the problem of latex allergy among HCWs both
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51 114 internationally and to some extent nationally.²⁷⁻²⁹ This has proven to reduce latex induced
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53 115 clinical outcomes. Even with this intervention, studies in Western countries such as Germany
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3 116 and the UK have shown that the risk of latex sensitisation still exists and more needs to be done
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5 117 to protect HCWs.^{30, 31}
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9 118 The current study described the prevalence of latex sensitisation and allergy among healthcare
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11 119 workers who use hypoallergenic powder free and lightly powdered latex gloves.
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14 120 **METHODS**

15 121 **Study design and population**

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18 122 This was a cross sectional study conducted between July 2011 and January 2012. The study
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21 123 location was King Edward VIII hospital, the second largest hospital in the Southern hemisphere,
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23 124 providing regional and tertiary services to the whole of KwaZulu-Natal (KZN) and the Eastern
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25 125 Cape Province in South Africa. It has a bed status of 1300 and has a workforce of 2400. The
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27 126 hospital was chosen due to the large workforce with different departments, and the policy of
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29 127 using both powder free and low powdered latex gloves for approximately 10 years.
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37 128 The study population was limited to HCWs currently employed at King Edward VIII Hospital
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39 129 for more than 12 months. HCWs were defined as all personnel employed in the hospital.
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43 130 The prevalence of latex sensitization in HCWs using powdered latex gloves in the Western Cape
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45 131 Province was 11.9% in 2001.¹⁶ We expected the prevalence at King Edward VIII hospital to be
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47 132 less than the 11.9% observed in the Western Cape Province due to the adoption of a
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49 133 hypoallergenic latex glove policy in 2001. Using EPI Info calculator version 3.04.04., it was
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51 134 assumed that 50% of sensitised workers have remained sensitised despite the introduction of
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53 135 hypoallergenic latex gloves 10 years prior. Using an expected latex sensitization prevalence of
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55 136 6% for the exposed group and the prevalence among the general population being reported as
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3 137 less than 1% the required sample size was calculated to be 585 participants 2 exposed
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6 138 participants for every 1 non-exposed participant (exposed =390; unexposed =195). HCWs were
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8 139 considered to be exposed if they were likely to use gloves. Unexposed HCWs were drawn from
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11 140 the administrative staff of the hospital.

141 **Questionnaire**

142 We used an adaptation of the questionnaire used in an epidemiological study conducted at
143 Groote Schuur in 2001¹⁶ with permission from Professor Paul Potter, Allergology Unit, Medical
144 School, University of Cape Town. The questionnaire containing open and closed ended questions
145 was adapted to include items on exposure assessment. The questionnaire was administered by a
146 trained research assistant immediately prior to the skin prick test. The questionnaire collected
147 data on the participants' demographics, personal risk factors, latex exposure assessment, clinical
148 manifestations of latex sensitization (dermal and respiratory) and history of previous reactions
149 suggestive of latex allergy.

150 **Exposure Assessment**

151 *Individual Exposure*

152 Individual latex exposure was determined by the type of gloves used, number of gloves used per
153 day, and duration of glove use. The information was limited to 7 working shifts/days prior to the
154 interview.

155 *Departmental Exposure*

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3 156 Departmental exposure was defined as glove usage in the past 12 months (01 January 2011-31
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6 157 December 2011). The overall departmental exposure was obtained by reviewing monthly glove
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8 158 usage by each department from the stock room register. This was used to estimate the annual
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10 159 exposure for employees who had rotated through different departments in the past 12 months.
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12 160 Non sterile latex gloves are distributed throughout the clinical departments while a high
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14 161 proportion of sterile gloves are distributed to labour ward, theatre, surgical wards and outpatient
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16 162 departments. Glove type was defined as powdered and powder-free and latex free based on the
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18 163 previous literature.^{23, 32}

164 **Skin prick test (SPT)**

165 The SPT was conducted using the Stallergenes kit.³² It was performed in a room with access to
166 emergency resuscitation services by a trained research assistant. The research assistant and
167 principal investigator were trained on 2 separate occasions. The test was performed on the inner
168 aspect of the participants' forearms, between the wrist and the elbow on normal skin. A positive
169 and negative control were performed using histamine (0.61% concentration of phenol) and
170 buffered normal saline solution respectively on the same arm and they were 3 cm apart to
171 prevent cross contamination. The protein concentration of the latex extract was 500µg/ml and the
172 solution was applied as it was with no further dilutions. After 15-20 minutes subsequent to
173 puncturing the skin, the SPT reaction wheal and flare was outlined by a black ink and clear tape
174 was used to transfer the outline from skin to the results sheet by the trained research assistant or
175 principal investigator.³³ A positive result was indicated by a mean wheal diameter measuring 3
176 mm or greater than the negative control. Results were recorded on a standardized result sheet.
177 The research assistant's test performance was audited by the principal investigator at regular
178 intervals to ensure correctness of technique and interpretation of the results.

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3 179 Informed signed consent was obtained from all the participants prior to participation. They had
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6 180 the option of participating in the questionnaire interview and the SPT or refusing the SPT. The
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8 181 study protocol was approved by the Biomedical Research Ethics Committee of the University of
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10 182 KwaZulu-Natal (BE048/11). Permission to conduct the study was also obtained from the KZN
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13 183 Provincial Department of Health and King Edward VIII hospital management.

14 15 16 184 **Statistical analysis**

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20 185 Data was captured in Excel and analysed in Stata Version 11. Frequencies and medians with
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22 186 ranges were presented for categorical and continuous variables respectively. **The Chi-square and**
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24 187 **the Kruskal-Wallis test were used to test for significant associations between categorical and**
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26 188 **continuous variables and the dependent variables under study on bivariate analysis, respectively.**

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30 189 Binary logistic regression was used to test for significant associations between independent and
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32 190 dependent variables on multivariate analysis. The dependent variables used in the regression
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34 191 analysis were: Latex sensitisation, which was defined as having a SPT wheal of ≥ 3 mm to latex
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36 192 extract; Latex allergy (LA) was defined as being SPT positive and a report of having any one or
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38 193 more of the listed work related clinical symptoms namely itchy eyes, red eyes, runny eyes, runny
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40 194 nose, itchy nose, sneezing, coughing, tight chest, wheezing, itchy skin, skin rash or dizziness.
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42 195 Independent variables that were considered for analysis were as follows: Age (yrs.) and sex,
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44 196 duration of employment, job title, current department employed in, type of gloves used, number
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46 197 of pairs of gloves used per day, self reported and family history of atopy, food allergy and
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48 198 previous history of open surgery and number of surgical procedures. In the multivariate analysis,
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50 199 age was omitted due to collinearity with duration of employment. **Departmental glove**
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52 200 **consumption was omitted as this only indicated annual distribution of gloves per department and**
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3 201 not necessarily employees' exposure since enrolled nursing assistants and enrolled nurses are
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6 202 rotated through different departments in any given year. The number of pair of gloves was used
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8 203 as an indicator of individual latex glove exposure. The variable number of pairs of gloves used
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10 204 and duration of employment were retained as continuous variables in the multivariate model.
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12 205 Fractional polynomial and a fractional plot was used to visualise the dose-response relationship
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14 206 of these continuous exposure variables.
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19 207 RESULTS

20 21 22 208 Participant Demographics

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25 209 Sixty five HCWs refused to participate in the study. Among the 520 HCWs who responded to
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27 210 the invitation there was an overall participation rate of 85.5 % (n=501) with 3.6% (n=19)
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29 211 refusing SPT. There was no significant difference between those refusing SPT and those who
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31 212 had the SPT with respect to latex exposure status, age, sex and duration of employment.
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36 213 The median age of participants was 42.2 years (range: 22 years-65 years) with the greater
37
38 214 proportion of them being females. The median duration of employment was 10.9 years (range: 1
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40 215 year-42 years) with the majority of exposed participants having worked as a HCW for < 10
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42 216 years. Most unexposed healthcare workers had been employed for > 20 years. Personal and
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44 217 family history of allergy was more prevalent among unexposed HCWs while exposed HCWS
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46 218 reported a higher prevalence of a fruit allergy and history of previous surgery (Table 1).
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51 219 Prevalence of Latex Sensitisation and Allergy

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54 220 The overall prevalence of latex sensitisation and latex allergy were 5.9% (n=29) and 4.6%
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56 221 (n=23) respectively. Although the difference was not significant, the prevalence of latex
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3 222 sensitisation was higher among the exposed group (7.1%) as compared to the unexposed group
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5 223 (3.1%). Latex allergy was significantly higher in the exposed group than unexposed group (5.9%
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7
8 224 vs 1.8%, $p=0.04$). There was a significant difference in the work related allergy symptoms
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10 225 between exposed and unexposed workers (40.9% vs. 31.7%, $p=0.04$) (Table 1). Symptoms that
11
12 226 were significantly associated with latex sensitisation were skin rash ($p < 0.000$), itchy skin
13
14 227 ($p=0.001$), runny nose ($p=0.004$), red eyes ($p=0.01$) and itchy eyes ($p=0.01$).
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18 228 The prevalence of latex sensitization was higher among those who were exposed and those with
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20 229 employment duration of < 10 yrs. Although the prevalence of latex sensitisation was lower
21
22 230 among participants < 30 years of age, there was no significant variation with age or sex. There
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24 231 was a significant difference ($p=0.04$) in the prevalence of fruit allergy between those participants
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26 232 with latex sensitisation (17.2%) and unsensitised participants (6.9%) The exclusive use of
27
28 233 powder free latex gloves was found to be significantly ($p=0.003$) higher among the participants
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30 234 who had latex sensitisation. There was equal distribution of powdered and powder free latex
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32 235 gloves among those who reported the use of mixed gloves. The prevalence of reporting previous
33
34 236 open surgery and use of other non- occupational exposure latex containing material did not vary
35
36 237 significantly between those who had latex sensitisation and those who were unsensitised. There
37
38 238 was a significantly higher prevalence of reporting allergic reactions when handling other latex
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40 239 containing medical equipment among participants with latex allergy as compared to unsensitised
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42 240 participants (10.3% vs 1.7%, $p=0.002$) (Table 2).
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50 241 **Crude association of demographics, exposure status, medical and personal history and latex**
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52 242 **sensitisation, latex allergy**
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3 243 Latex exposure was significantly associated with latex allergy (OR: 3.4; 95% CI: 1.1-10.8).
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5 244 Working as a HCW for 5-9 years was significantly associated with latex sensitisation (OR: 2.6;
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7 245 95% CI: 1.2-5.5) and latex allergy (OR: 3.3; 95% CI: 1.4-7.6), respectively. Employment
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9 246 duration as a HCW for >20 years was protective against latex allergy (OR: 0.2; 95% CI: 0.0-0.8).
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11 247 **In comparison with unexposed workers**, working as an enrolled nurse was significantly
12
13 248 associated with both latex sensitisation (OR: 2.5; 95% CI: 1.2-5.3) and latex allergy (OR: 2.4;
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15 249 95% CI: 1.1-5.6). The exclusive use of powder free latex gloves was significantly associated
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17 250 with latex sensitisation (OR: 3.1; 95% CI: 1.4-6.8) and latex allergy (OR: 3.1; 95% CI: 1.7-9.1).
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19 251 Powdered and powder free latex gloves were equally distributed among those who reported the
20
21 252 use of mixed gloves. The annual consumption of pairs of gloves per HCW by department was
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23 253 ranked and grouped into tertiles. Although medical and surgical wards had low and moderate
24
25 254 pairs of gloves consumption per HCW, these wards had the highest proportion of workers with
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27 255 latex sensitisation (n=6, 20.0% each). However the relation was only significant for those who
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29 256 reported the medical ward as being the current department in which they worked (p=0.01). The
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31 257 proportions for powdered latex glove use were 71% and 69% in medical and surgical wards,
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33 258 respectively and this was not statistically significant. Exposure to other latex containing medical
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35 259 devices was not significantly different from what was reported in other wards. There was no
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37 260 significant association between **reported personal history of allergy disease**, latex sensitisation
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39 261 and latex allergy. Fruit allergy was significantly associated with latex allergy (OR: 3.7; 95%:
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41 262 1.4-10.4) (Table 3). Listed fruits were evaluated for their independent association with latex
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43 263 sensitisation. Avocado (**OR: 12.3; 95% CI: 5.1-29.6**) and others (**OR: 5.1; 95% CI: 2.1-11.8**)
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45 264 which included pineapple and orange showed significant associations with latex sensitisation
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47 265 (data not shown).
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266 **Multivariate analysis**

267 While latex exposure had estimates of the OR above 2, there was no significant association with
268 latex sensitisation and latex allergy. Duration of employment was found to be inversely
269 associated with latex allergy in models I and II. The exclusive use of powder free latex gloves
270 was significantly associated with latex sensitisation (OR: 4.2; 95% CI: 1.2-14.1) and latex
271 allergy (OR: 5.1; 95%CI: 1.2-21.2) on multivariate analysis. This significant association
272 disappeared when examining the number of pairs of powder free gloves used in the last 7 days. A
273 weak association was observed for the number of pairs of powdered latex gloves used in the last
274 7 days with both latex sensitisation and latex allergy (model III and IV). Further analysis of
275 duration of employment and number of pairs of gloves using fractional polynomial failed to
276 demonstrate a dose-response relationship with either latex sensitisation or latex allergy. There
277 was a significant association between fruit allergy and latex allergy in model I (OR: 3.1; 95% CI:
278 1.1-9.2) (Table 4).

279 **DISCUSSION**

280 This is an important study for South African HCWs as it examined the risk of latex sensitisation
281 in a group of workers exposed to hypoallergenic latex gloves. As previously mentioned there has
282 been no literature documenting the prevalence of latex sensitisation among South African HCWs
283 using hypoallergenic lightly powdered or powder-free latex gloves. The prevalence of latex
284 sensitisation among exposed HCWs (7.1%) in this study is comparable to findings among HCWs
285 in another South African hospital.¹⁴ However it was considerably lower than the 11.9%
286 prevalence reported by Potter in the same year.¹⁶ While a substantial number of participants
287 (37%) reported work related allergy symptoms, only 4.6% met our definition of latex allergy.
288 The important symptoms associated with latex sensitisation were skin rash, itchy skin, runny

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3 289 nose, red and itchy eyes in keeping with previous studies. Elimination of powdered latex gloves
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5 290 has shown a reduction in the concentration of aeroallergens in the operating room with the low
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8 291 prevalence of latex allergy in our study population.
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11 292 Although the relationship was weak, this study showed that the risk of latex sensitisation
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13 293 decreases with duration of employment. The healthy worker effect is a possible explanation of
14
15 294 this finding. Prior to availability of hypoallergenic latex gloves, workers who had developed
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17 295 latex allergy may have left employment or they may have changed their career path and moved
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19 296 into a more administrative or managerial role with no contact with latex gloves. Furthermore
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21 297 new employees are only sensitised and have not yet manifested clinical symptoms and they
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23 298 continue using latex gloves. On the other hand senior HCWs may have been sensitised during
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25 299 their earlier years of employment and as a result they either moved to departments with less
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27 300 exposure to latex gloves or deliberately avoid latex containing products and therefore exhibit less
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29 301 latex related symptoms. Moreover, the introduction of hypoallergenic gloves 10 years prior to
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31 302 the study may explain the reduced sensitisation in senior HCWs as demonstrated in the study by
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33 303 Smith et al in 2007. The published literature has been inconsistent in reporting the association
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35 304 between duration of employment and latex sensitisation. Although latex is one of the best studied
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37 305 allergens, no exposure response studies have been published with measured latex allergen levels.
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39 306 In addition, studies have demonstrated variation in allergen content of different gloves. These
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41 307 may lead to discrepancies in the literature with regard to the role of duration of employment as a
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43 308 surrogate measure of exposure.
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53 309 In our study HCWs who exclusively used powdered free latex gloves had a 4 times greater odds
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55 310 of developing latex sensitisation. The fact that HCWs with latex sensitisation or allergy work
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57 311 more often with powder free latex gloves is indicative of reverse causality because of symptoms.
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3 312 Moreover the background prevalence of latex sensitisation in this study was relatively higher
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5 313 (3.5%) than previously reported prevalence in the general population by Bousquet et al.¹³ Studies
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8 314 have shown that some of these “hypoallergenic” latex gloves actually contain high levels of
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10 315 allergens which can be release into the environment with aggressive manipulation.²³ Some of the
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12 316 sensitised HCWs may have been sensitised before the hospital implemented a hypoallergenic
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14 317 latex glove policy. Also Smith et al showed that complete avoidance of powdered latex glove can
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16 318 result in the reduction or no change in measurable IgE antibodies.³⁴ A study in Germany reported
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18 319 a high prevalence of 8% among 226 dental students who had only been exposed to exclusive
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20 320 powder free latex gloves.³⁰ Similarly in the UK despite a total ban on powdered latex gloves
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22 321 Clayton found a 10% prevalence of latex sensitisation in HCWs.³¹ It is also not clear to what
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24 322 extent the aeroallergens released by colleagues using powdered latex gloves influence this
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26 323 finding. Furthermore the role of other latex containing medical devices during sensitisation
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28 324 period cannot be entirely ruled out.

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35 325 In our study, frequency of exposure as measured by the number of gloves used in the last 7
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37 326 working days showed a weak association between powdered latex gloves and latex sensitisation
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39 327 but no association could be demonstrated with powder free latex gloves. Airborne latex
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41 328 aeroallergens have been shown to increase with the number of powdered gloves used which
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43 329 subsequently increases the risk of latex sensitisation and clinical latex glove related allergy
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45 330 symptoms.¹⁸

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50 331 The positive association between department with low glove consumption per HCW and latex
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52 332 sensitisation is in contrast with previous finding by Liss and co-workers.⁹ They reported positive
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54 333 association with departments that had high glove consumption per HCWs. **Again, this could be**
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56 334 **as a result of reverse causality where HCWs with latex sensitisation may have been relocated to**

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3 335 wards with low glove consumption to minimise the exposure. In addition, the annual pair of
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6 336 gloves consumption per HCW by department does not provide an accurate indication of
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8 337 individual exposure; rather it gives us the annual distribution of gloves to different departments.

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11 338 Several studies have reported atopy as a significant risk factor for latex sensitisation.^{9, 10, 35}

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14 339 Similarly, the prevalence of reporting a history of personal atopy in this study was higher among
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16 340 latex sensitised participants although the association was not statistically significant. The role of
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18 341 atopy is complex because some individuals might also have become atopic after having been
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21 342 latex sensitised and cross sectional study is not suitable in establishing this association.

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24 343 Fruit latex allergy syndrome is a phenomenon seen where latex sensitised individuals
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26 344 demonstrate a cross reactivity with specific foods; particularly fruit. Studies have identified this
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28 345 phenomenon among sensitised HCWs and the general population. This has been attributed to the
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30 346 similarity between fruit proteins and latex allergens.³⁶ Fruit allergy was significantly associated
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32 347 with latex sensitisation and latex allergy in our study. Our study was dependent on the self-
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34 348 reporting of fruit allergy and no objective tests were carried out. It is therefore possible that
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36 349 participants have independent simultaneous allergies to both fruit and latex without cross
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38 350 reactivity. Also, we were unable to determine whether latex sensitisation preceded the
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40 351 development of fruit allergy or vice versa. Fruit allergy prior to latex exposure could have
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43 352 contributed to the association observed in our study.

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49 353 Latex sensitised participants reported a high prevalence of a history of previous open surgery in
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51 354 our study. This has been reported to occur as a result of direct intraoperative exposure to latex
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53 355 containing medical devices such as catheters or tubes. Studies in children with congenital
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56 356 abnormalities have demonstrated that the risk for latex allergy increases with the number of open
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3 357 surgical procedures that they undergo.³⁷ Frequency of invasive procedures among adults was
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6 358 shown to increase the risk of latex sensitisation reporting while more than 10 procedures
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8 359 increased the risk of developing latex allergy.³⁸
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11 360 Strengths of this study include the high response rate (85.5%) and comparability to other
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13 361 studies.^{8, 16} Access to the hospital employee database allowed us to better assess the
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15 362 representativeness of this study population by comparing demographic data of the non-
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17 363 participants and the participants. The participants were randomly selected minimising the
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19 364 potential of participant's bias that comes with a volunteer approach.
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24 365 The presence of a control group provided a background prevalence of latex sensitisation in this
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26 366 population which allowed for a better estimation of associations attributable to work related
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28 367 factors. The use of Stallergenes latex specific SPT further strengthens the study. The SPT test is
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30 368 regarded as the gold standard for the diagnosis of latex allergy and Stallergenes has been shown
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32 369 to have a diagnostic sensitivity and specificity of 93% and 100%, respectively.³² The research
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34 370 assistant employed on this study was trained and initially shadowed and periodically supervised
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36 371 by the principal investigator to ensure appropriate administration of the questionnaire and the
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38 372 SPT thereby improving the reliability and validity of the study.
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44 373 This study was limited by the cross sectional study design which was relatively low in cost and
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46 374 quick to conduct. It only allowed for the determination of prevalence of latex sensitisation at one
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48 375 point in time. Consequently the prevalence of latex sensitisation may have been underestimated
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50 376 as it is possible that HCWs who had already developed latex sensitisation have left the hospital
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52 377 before the study was conducted. **Some of the observed associations in the study may be as a**
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54 378 **result of a complex interplay between the healthy worker effect, reverse causality and exposure**
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3 379 reduction by the introduction of powder free latex gloves. These interactions can be better
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6 380 explored and understood in a longitudinal study. Recall bias is another potential limitation in this
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8 381 study as workers were asked to recall the number of gloves used in the past 7 working days.
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10 382 HCWs may have overestimated or underestimated their individual exposures. Our study
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12 383 depended on self-reporting of personal and family atopic disorders and this may have resulted in
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14 384 the misclassification of atopy. The role of atopy and cross-reactivity between allergens is a
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16 385 complex phenomenon which cannot be investigated in cross sectional study. Therefore, cohort
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18 386 studies are necessary to disentangle this phenomenon.
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23 387 CONCLUSION

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26 388 This study shows that even in the presence of powder free hypoallergenic glove use there is latex
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28 389 sensitisation and latex allergy, adding to previous findings that HCWs exposed to hypoallergenic
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30 390 latex gloves are still at risk for developing latex sensitisation and latex allergy. This indicates that
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32 391 latex sensitisation and allergy are still an important occupational hazard for HCWs. While it may
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34 392 be economically impractical to replace the latex gloves in our setting, reduction of allergen
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36 393 content in latex products is another strategy that can be implemented to address the problem and
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38 394 protect HCWs. A policy accompanied by clear implementation plans as well as sustainable
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40 395 education and training programmes to address latex sensitisation and allergy among HCWs
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42 396 should be implemented.³⁹ In addition HCWs must be continuously monitored for the
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44 397 development of latex sensitisation and alternate latex free glove must be made available for
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46 398 them. More research is needed to identify the most cost effective way of implementing a latex
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48 399 free environment in resource limited countries, such as South Africa. In addition the current
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50 400 studies in South Africa have largely been cross-sectional in nature. More cohort analysis is
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52 401 required to better understand the chronicity of illness and disability associated with latex allergy.
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3 402 **ACKNOWLEDGEMENT**
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5

6 403 I would like to thank the hospital employees participating in this study and their management for
7
8 404 allowing me access to the human resource database. I would like to thank Professor Mohamed
9
10 405 Jeebhay (Centre of Occupational and Environmental Health, University of Cape Town, SA) and
11
12 406 Professor David L Nordstrom (Occupational and Environmental Safety and Health, University of
13
14 407 Wisconsin-Whitewater, USA) for their comments on my initial proposal. I would like to thank
15
16 408 Professor Rajen Naidoo (Discipline of Occupational and Environmental Health, UKZN, SA) for
17
18 409 his statistical advice during the data analysis. In addition thank you to Mr. Nhlanhla Jwara for
19
20 410 conducting the field work.
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25
26 411 **Contributorship**
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29 412 Dr Shumani Phaswana is the principal investigator who was involved from the conception of the idea,
30
31 413 proposal writing, data collection, data management and interpretation of the results.
32
33

34 414 Dr Saloshni Naidoo contributed to the conception and design of the study, analysis and interpretation of
35
36 415 the data, critical review of the intellectual content of the article and final approval of the article.
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38

39 416 **Data sharing**
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42 417 No additional unpublished data
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45
46 418 **Funding**
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48

49 419 None
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53 420 **Competing interests**
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56 421 None
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506 **TABLES**507 **Table 1: Demographics and associated risk factors amongst latex exposed and unexposed**
508 **healthcare workers at King Edward VIII Hospital, KwaZulu-Natal South Africa, (n=501)**509
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Characteristic	Exposed N (%)	Unexposed N (%)
Number of participants	337 (67.3)	164 (32.7)
Demographics		
Age (years)		
≤30	30(8.9)	19(11.6)
>30-40	121(35.9)	40(24.4)
>40-50	101(29.9)	59(35.9)
>50	85(25.2)	46(28.1)
Duration of employment (years)		
≤5	39(11.6)	28(17.1)
>5-10**	135(40.1)	32(19.5)
>10-15	49(14.5)	17(10.4)
>15-20	24(7.1)	20(12.2)
>20*	90(26.7)	67(40.9)
Sex**		
Female	309(91.7)	95(57.9)
Male	28(8.3)	69(42.1)
Job Title (yes)		
Administrative		164(100.0)
Professional nurses	123(36.5)	
Enrolled nurses	141(41.8)	
Enrolled nursing assistants	73 (21.7)	
Medical and Personal History		
Personal history of Allergy Disease (yes)	147(43.6)	83(50.6)
Family history of Allergy Disease (yes)	197(58.5)	102(62.2)
Fruit allergy (yes)	29(8.6)	9(5.5)
Previous open surgery (yes)*	168(49.8)	61(37.2)
Work-related allergy symptoms(yes)*	138(40.9)	52(31.7)
Non-occupational latex exposure (yes)	161(47.8)	76(46.3)
Latex sensitisation (yes)	24(7.1)	5(3.1)
Current latex allergy (yes)*	20(5.9)	3(1.8)
Chi square, *p<0.05, **p<0.001		

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Table 2: Comparison of risk factors between latex sensitised (skin prick test positive) and non-sensitised (skin prick test negative) healthcare workers at King Edward VIII Hospital, KwaZulu-Natal South Africa (n=501)

Characteristics	Latex SPT +ve [†] (29) N (%)	Latex SPT -ve ^{††} (472) N (%)	520 521 522
Demographics			523
Age (years.)			524
≤30	1 (3.5)	48(10.2)	525
>30-40	13 (44.8)	148(31.4)	526
>40-50	8 (27.6)	152(32.2)	527
>50	7 (24.1)	124(26.3)	528
Duration of employment			529
≤5	3(10.3)	64(13.6)	530
>5-10	16(55.2)	151(31.9)	531
>10-15	3(10.3)	63(13.4)	532
>15-20	1(3.5)	43(9.1)	533
>20	6(20.7)	151(31.9)	534
Sex (yes)			535
Male	5(17.2)	118(25.0)	536
Female	24(82.8)	354(75.0)	537
Job Title (yes)			538
Administrative	5(17.2)	159(33.7)	539
Professional nurses	5(17.2)	118(25.0)	540
Enrolled nurses	14(48.3)	127(26.9)	541
Enrolled nursing assistants	5(17.2)	68(14.4)	542
Latex Exposure			543
Exposure status(yes)	24 (82.8)	313(66.3)	544
Type of gloves			545
None	5(17.2)	165(34.6)	546
Exclusive powdered latex glove (yes)	2(6.9)	36(7.6)	547
Exclusive powder free latex glove (yes)*	11(37.9)	77(16.3)	548
Mixed (yes)	11(37.9)	198(41.9)	549
Medical and Personal History			550
Personal history of Allergy Disease (yes)	16(55.2)	214(45.3)	551
Family history of Allergy Disease (yes)	18(62.1)	281(59.5)	552
Fruit allergy (yes)*	5(17.2)	33(6.9)	553
Previous open surgery (yes)	18(62.1)	211(44.7)	554
Non-occupational latex exposure (yes)	12(41.4)	225(47.7)	555
Reaction to other latex medical devices (yes)*	3(10.3)	8(1.7)	556
Chi Square, *p<0.05			557
†Latex Skin Prick Test Positive			558
††Latex Skin Prick Test Negative			559
			560

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565 **Table 3: Crude Odds Ratios (OR) (95% CI) of demographics, exposure status, medical and personal**
 566 **history and latex sensitisation and latex allergy amongst healthcare workers at King Edward VIII**
 567 **Hospital, KwaZulu-Natal South Africa, (n=501)**

Characteristics	N=2 9	Latex Sensitisation OR (95%CI)	N=23	LA# OR (95%CI)	569 570
Demographics					
Age (years)					571
≤30	1	0.3(0.0-1.9)	1	0.4(0.0-2.4)	572
>30-40	13	1.8(0.8-3.7)	11	2.0(0.9-4.6)	573
>40-50	8	0.8(0.4-1.8)	7	0.9(0.4-2.2)	574
>50	7	0.8(0.4-2.1)	4	0.6(0.2-1.7)	575
Duration of employment (years)					576
<5	3	0.7(0.2-2.4)	3	0.9(0.3-3.2)	577
5-10	16	2.6(1.2-5.5)*	14	3.3(1.4-7.6)*	578
>10-15	3	0.7(0.2-2.4)	3	0.9(0.3-3.2)	579
>15-20	1	0.4(0.0-2.1)	1	0.5(0.0-2.8)	580
>20	6	0.5(0.2-1.4)	2	0.2(0.0-0.8)	581
Sex (yes)					582
Female	24	1.6(0.6-4.1)	20	2.2(0.7-7.2)	583
Job Title (yes)					584
Administrative	5	0.4(0.2-1.1)	3	0.3(0.1-0.9)*	585
Professional nurses	5	0.6(0.2-1.6)	4	0.6(0.2-1.8)	586
Enrolled nurses	14	2.5(1.2-5.3)*	11	2.4(1.1-5.6)*	587
Enrolled nursing assistants	5	1.2(0.5-3.3)	5	1.7(0.6-4.5)	588
Latex Exposure					
Exposure status (yes)	24	2.4(0.9-6.3)	20	3.4(1.1-10.8)	589
Type of gloves					590
None	5	0.4(0.2-1.0)	3	0.3(0.1-0.9)*	591
Exclusive Powdered latex glove (yes)	2	0.9(0.0-3.6)	2	1.2(0.0-1.7)	592
Exclusive Powder free latex glove (yes)	11	3.1(1.4-6.8)*	10	3.1(1.7-9.1)*	593
Mixed gloves(yes)	11	0.8(0.4-1.8)	8	0.7(0.3-1.7)	
Medical and Personal History					
Personal history of Allergy Disease (yes)	16	1.4(0.7-3.1)	12	1.3(0.5-2.9)	594
Family history of Allergy Disease (yes)	18	1.1(0.5-2.4)	14	1.1(0.5-2.4)	595
Fruit allergy (yes)	5	2.8(1.0-7.5)	5	3.7(1.4-10.5)*	596
Previous open surgery (yes)	18	1.1(0.5-2.4)	14	1.5(0.7-3.1)	597
Chi square, *p<0.05					
†Latex Skin Prick Test Positive					
‡Latex Skin Prick Test Positive and work related clinical symptoms of allergy					

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Table 4: Multivariate analysis of demographics, medical and personal history, exposure history and latex sensitisation (LS)[†] and latex allergy (LA)[#] amongst healthcare workers at King Edward III Hospital, KwaZulu-Natal South Africa, (n=501)

Characteristics	MODEL I* (n=501)		MODEL II** (n=501)		MODEL III***(n=202)		MODEL IV****(n=252)	
	LS OR (95%CI)	LA OR (95%CI)	LS OR (95%CI)	LA OR (95%CI)	LS OR (95%CI)	LA OR (95%CI)	LS OR (95%CI)	LA OR (95%CI)
Demographics								
Sex (female)	0.9(0.2-2.7)	1.1(0.3-4.4)	0.9(0.3-2.7)	1.1(0.3-4.5)	0.3(0.0-1.8)	0.3(0.0-3.1)	2.5(0.5-12.2)	2.5(0.5-12.2)
Duration of employment (years)	0.9(0.9-1.0)	0.9(0.8-0.9)	0.9(0.9-1.0)	0.9(0.8-0.8)	0.9(0.9-1.8)	0.7(0.5-1.0)	0.9(0.9-1.0)	0.9(0.9-1.0)
Latex Exposure								
Exposure status(yes)	2.2(0.7-6.7)	2.6(0.7-9.8)						
Type of gloves								
None			1	1				
Exclusive lightly powdered latex glove (yes)			1.6(0.3-9.8)	2.6(0.4-17.7)				
Exclusive Powder free latex glove (yes)			4.2(1.2-14.1)	5.1(1.2-21.2)				
Mixed gloves (yes)			1.7(0.5-5.6)	1.7(0.4-7.1)				

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Pairs of Powdered latex Gloves in the last 7 days					1.1(1.0-1.2)	1.2(1.0-1.4)		
Pairs of Powder Free Latex Gloves in the last 7 days							1.0(0.9-1.1)	1.0(0.9-1.1)
Personal and Medical History								
Personal history of allergy disease (yes)	1.5(0.7-3.3)	1.4(0.6-3.2)	1.5(0.7-3.3)	1.3(0.6-3.2)	1.4(0.3-6.8)	1.6(0.2-11.6)	1.0(0.4-2.9)	0.9(0.3-2.8)
Family history of allergy disease (yes)	1.0(0.45-2.2)	0.9(0.4-2.2)	1.1(0.5-2.3)	0.9(0.4-2.3)	0.4(0.1-1.9)	0.5(0.1-3.6)	0.7(0.2-2.0)	0.8(0.3-2.7)
Fruit allergy (yes)	2.3(0.8-6.7)	3.1(1.1-9.2)	2.2(0.8-6.5)	3.0(0.9-9.1)	5.0(0.4-56.9)	9.7(0.6-163.0)	1.7(0.3-8.5)	2.0(0.4-10.4)
Previous open surgery (yes)	2.0(0.9-4.4)	1.9(0.8-4.6)	2.1(0.9-4.6)	1.9(0.8-4.7)	1.4(0.3-7.4)	1.2(0.1-11.1)	1.1(0.4-3.2)	1.2(0.4-3.8)

†Latex Skin Prick Test Positive
 ‡Latex Skin Prick Test Positive and work related clinical symptoms of allergy
 *Model included latex glove exposure status
 **Model included type of gloves
 ***Model included number of pairs of powdered latex gloves
 ****Model included number of pairs of powder free latex gloves





The prevalence of latex sensitisation and allergy and associated risk factors amongst health care workers using hypoallergenic latex gloves at King Edward VIII hospital, KwaZulu-Natal South Africa: A cross sectional study

Journal:	<i>BMJ Open</i>
Manuscript ID:	bmjopen-2013-002900.R2
Article Type:	Research
Date Submitted by the Author:	18-Oct-2013
Complete List of Authors:	Phaswana, Shumani; University of KwaZulu Natal, Occupational and Environmental Health Naidoo, Saloshni; University of KwaZulu Natal, Occupational and Environmental Health
Primary Subject Heading:	Occupational and environmental medicine
Secondary Subject Heading:	Immunology (including allergy), Occupational and environmental medicine, Epidemiology
Keywords:	Latex, Hypoallergenic, Healthcare workers, South Africa

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3 1 **The prevalence of latex sensitisation and allergy and associated risk factors among healthcare**
4 2 **workers using hypoallergenic latex gloves at King Edward VIII Hospital, KwaZulu-Natal South**
5 3 **Africa: A cross sectional study**
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41
42 20 Keywords: Latex, hypoallergenic, healthcare workers, South Africa

43
44 21 Word Count:

45
46 22 Abstract: 299

47
48 23 Body: 4,359
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27 ABSTRACT

28 Objectives

29 The present study describes latex sensitisation and allergy prevalence and associated factors among
30 healthcare workers using hypoallergenic latex gloves at King Edward VIII Hospital in KwaZulu-Natal
31 South Africa.

32 Design

33 Cross sectional study

34 Setting

35 A tertiary hospital in eThekweni municipality, KwaZulu Natal, South Africa

36 Participants

37 600 healthcare workers were randomly selected and 501(337 exposed and 164 unexposed) participated.

38 Participants who were pregnant, less than one year of work as healthcare worker and history of
39 anaphylactic reaction were excluded from the study.

40 Primary and secondary outcome measures

41 Latex sensitisation and latex allergy were the outcome of interest and they were successfully measured

42 Results

43 Prevalence of latex sensitisation and allergy was observed among exposed workers (7.1% and 5.9%) and
44 unexposed workers (3.1% and 1.8%). Work related allergy symptoms were significantly higher in
45 exposed workers (40.9%, $p < 0.05$). Duration of employment was inversely associated with latex allergy
46 (OR: 0.9; 95% CI: 0.8-0.9). The risk of latex sensitisation (OR: 4.2; 95% CI: 1.2-14.1) and allergy (OR:
47 5.1; 95% CI: 1.2-21.2) increased with exclusive use of powder-free latex gloves. A dose –response

48 relationship was observed for powdered latex gloves (OR: 1.1; 95% CI: 1.0-1.2). Atopy (OR: 1.5; 95%
 49 CI: 0.7-3.3 and OR: 1.4; 95% CI: 0.6-3.2) and fruit allergy (OR: 2.3; 95% CI: 0.8-6.7 and OR: 3.1; 95%
 50 CI: 1.1-9.2) also increased the risk of latex sensitisation and allergy.

51 Conclusion

52 This study adds to previous findings that healthcare workers exposed to hypoallergenic latex gloves are at
 53 risk for developing latex sensitisation highlighting its importance as an occupational hazard in healthcare.
 54 More research is needed to identify the most cost effective way of implementing a latex free environment
 55 in resource limited countries, such as South Africa. In addition more cohort analysis is required to better
 56 understand the chronicity of illness and disability associated with latex allergy.

57

ARTICLE SUMMARY

ARTICLE FOCUS

- The use of hypoallergenic latex gloves has been adopted as policy in different healthcare settings globally.
- However, information with regard to their use and the development of latex sensitisation and allergy among exposed healthcare workers is limited.
- We hypothesised that there is latex sensitization and allergy in healthcare workers using hypoallergenic latex gloves in a South African hospital.

KEY MESSAGE

- In the presence of powder free hypoallergenic gloves, latex sensitisation and latex allergy is still an important occupational health effect in healthcare workers.
- Healthcare workers should be continuously monitored for the development of latex sensitisation and allergy.
- There is a need for a national policy accompanied by clear implementation plans as well as sustainable education and training programmes to address latex sensitisation and allergy among HCWs.

STRENGTH AND LIMITATIONS

- Strength of the study included the presence of a control group providing a background prevalence of latex sensitisation in this population and random selection of participants which minimised the potential of participant bias that arises with a volunteer approach.
- This study was limited by the cross sectional study design as it only allowed for the determination of the prevalence of latex sensitisation; recall bias with regard to the number of gloves used in the past 7 working days and the self-reporting of personal and family atopic disorders may have resulted in the misclassification of exposure and atopy respectively.

What this paper adds

- In the presence of powder free hypoallergenic gloves, latex sensitisation and latex allergy is still an important occupational health hazard in healthcare workers
- Healthcare workers should be continuously monitored for the development of latex sensitisation and allergy
- There is a need for a national policy accompanied by clear implementation plans as well as sustainable education and training programmes to address latex sensitisation and allergy among HCWs

74 INTRODUCTION

75 Latex allergy (LA) as an occupational disease among healthcare workers (HCWs) gained
76 recognition after Nutter published a case report of contact urticaria in a HCW in 1979.¹ The
77 increase in prevalence coincided with the emergence of the Human Immunodeficiency Virus/
78 Acquired immunodeficiency syndrome (HIV/AIDS) epidemic and the introduction of “universal
79 precautions” in the healthcare industry which had resulted in the increased use of latex gloves
80 among HCWs.²

81 Latex gloves are preferred due to their superior barrier and physical properties as compared to
82 the non-latex gloves.³ International epidemiological studies have reported the prevalence of latex
83 allergy among HCWs to range between 2-22% depending on the population and diagnostic
84 methods used.⁴⁻¹¹ The prevalence in the general population has been reported to range between
85 1-6%.^{12, 13} In South Africa studies amongst HCWs reported a latex sensitisation prevalence of
86 between 2.7 to 20.8%.¹⁴⁻¹⁶ Latex allergy in HCWs is a compensable disease in South Africa in
87 terms of the Compensation of Occupational Injuries and Diseases Act No. 130 of 1993.¹⁷

88 Powdered latex gloves were identified as an important risk factor for latex sensitisation and
89 allergy in HCWs as they were found to contain high allergenic protein content.¹⁸ Following these
90 findings, hypoallergenic gloves with low allergen content namely, low powdered and powder
91 free latex gloves were introduced. The European definition of powder free gloves is gloves with
92 powder content not exceeding 2 mg per glove and leachable latex protein which is as low as is
93 reasonably practical.¹⁹

94 Hypoallergenic gloves have been associated with reduced latex aeroallergen concentrations,
95 reduced conversion rates and a subsequent decrease in clinic visits, and compensation claims for

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3 96 latex induced occupational asthma and allergic contact dermatitis among HCWs.^{18, 20} As much as
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6 97 the use of low or powder free gloves has been shown to reduce latex related symptoms, other
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8 98 studies have shown that exposed HCWs still exhibit symptoms at very low levels of measureable
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10 99 airborne latex allergens.²¹ Most studies have reported on the airborne levels and inhalational
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13 100 route of exposure hence the recommendation on low powdered or powder free latex gloves.

14
15 101 There is little consideration given to the dermal route of exposure despite the fact that exposure
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17 102 is as a result of direct contact in these instances.²² Eliminating the cornstarch powder only
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20 103 removed the carrier and not the source of allergen which is in the latex itself. Therefore workers
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22 104 using powder free gloves are still exposed to the allergenic content of latex gloves. It has been
23
24 105 shown that different brands from different suppliers contain differing levels of protein due to a
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27 106 lack of standards in latex glove manufacture.²³ A South African study reported that some powder
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29 107 free latex gloves were found to have high allergenic protein content.²³ HCWs using these gloves
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31 108 are exposed via direct dermal contact and are at risk for developing latex sensitization which
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34 109 maybe asymptomatic and if exposure continues they can later develop latex allergy which
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36 110 presents with clinical manifestations.

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39 111 While it is important to diagnose and manage an individual worker with latex allergy in the early
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41 112 stages of the disease, complete control of hazardous substance in the workplace is equally if not
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44 113 more important. While a latex free work environment would be a preferred control strategy,
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47 114 substitution of powdered latex gloves with powder free gloves was shown to be cost effective
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49 115 and associated with improved clinical outcome.^{20, 24-26} As a result this was adopted as the most
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51 116 reasonable and practical approach in addressing the problem of latex allergy among HCWs both
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54 117 internationally and to some extent nationally.²⁷⁻²⁹ This has proven to reduce latex induced
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56 118 clinical outcomes. Even with this intervention, studies in Western countries such as Germany
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3 119 and the UK have shown that the risk of latex sensitisation still exists and more needs to be done
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6 120 to protect HCWs.^{30, 31}
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9 121 The current study described the prevalence of latex sensitisation and allergy among healthcare
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11 122 workers who use hypoallergenic powder free and lightly powdered latex gloves.
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14 123 **METHODS**

15 124 **Study design and population**

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18 125 This was a cross sectional study conducted between July 2011 and January 2012. The study
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22 126 location was King Edward VIII hospital, the second largest hospital in the Southern hemisphere,
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24 127 providing regional and tertiary services to the whole of KwaZulu-Natal (KZN) and the Eastern
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26 128 Cape Province in South Africa. It has a bed status of 1300 and has a workforce of 2400. The
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29 129 hospital was chosen due to the large workforce with different departments, and the policy of
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32 130 using both powder free and low powdered latex gloves for approximately 10 years.
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37 131 The study population was limited to HCWs currently employed at King Edward VIII Hospital
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39 132 for more than 12 months. HCWs were defined as all personnel employed in the hospital.
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43 133 The prevalence of latex sensitization in HCWs using powdered latex gloves in the Western Cape
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45 134 Province was 11.9% in 2001.¹⁶ We expected the prevalence at King Edward VIII hospital to be
46
47 135 less than the 11.9% observed in the Western Cape Province due to the adoption of a
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50 136 hypoallergenic latex glove policy in 2001. Using EPI Info calculator version 3.04.04., it was
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52 137 assumed that 50% of sensitised workers have remained sensitised despite the introduction of
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54 138 hypoallergenic latex gloves 10 years prior. Using an expected latex sensitization prevalence of
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56 139 6% for the exposed group and the prevalence among the general population being reported as
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3 140 less than 1% the required sample size was calculated to be 585 participants 2 exposed
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5 141 participants for every 1 non-exposed participant (exposed =390; unexposed =195). HCWs were
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8 142 considered to be exposed if they were likely to use gloves. Unexposed HCWs were drawn from
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11 143 the administrative staff of the hospital.
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14 144 **Questionnaire**

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17 145 We used an adaptation of the questionnaire used in an epidemiological study conducted at
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19 146 Groote Schuur in 2001¹⁶ with permission from Professor Paul Potter, Allergy Unit, Medical
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21 147 School, University of Cape Town. The questionnaire containing open and closed ended questions
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24 148 was adapted to include items on exposure assessment. The questionnaire was administered by a
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26 149 trained research assistant immediately prior to the skin prick test. The questionnaire collected
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29 150 data on the participants' demographics, personal risk factors, latex exposure assessment, clinical
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31 151 manifestations of latex sensitization (dermal and respiratory) and history of previous reactions
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34 152 suggestive of latex allergy.
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37 153 **Exposure Assessment**

40 154 *Individual Exposure*

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44 155 Individual latex exposure was determined by the type of gloves used, number of gloves used per
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46 156 day, and duration of glove use. The information was limited to 7 working shifts/days prior to the
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49 157 interview.
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52 158 *Departmental Exposure*

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3 159 Departmental exposure was defined as glove usage in the past 12 months (01 January 2011-31
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6 160 December 2011). The overall departmental exposure was obtained by reviewing monthly glove
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8 161 usage by each department from the stock room register. This was used to estimate the annual
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10 162 exposure for employees who had rotated through different departments in the past 12 months.
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12 163 Non sterile latex gloves are distributed throughout the clinical departments while a high
13
14 164 proportion of sterile gloves are distributed to labour ward, theatre, surgical wards and outpatient
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16 165 departments. Glove type was defined as powdered and powder-free and latex free based on the
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18 166 previous literature.^{23, 32}
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23 167 **Skin prick test (SPT)**

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26 168 The SPT was conducted using the Stallergenes kit.³² It was performed in a room with access to
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28 169 emergency resuscitation services by a trained research assistant. The research assistant and
29
30 170 principal investigator were trained on 2 separate occasions. The test was performed on the inner
31
32 171 aspect of the participants' forearms, between the wrist and the elbow on normal skin. A positive
33
34 172 and negative control were performed using histamine (0.61% concentration of phenol) and
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36 173 buffered normal saline solution respectively on the same arm and they were 3 cm apart to
37
38 174 prevent cross contamination. The protein concentration of the latex extract was 500µg/ml and the
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40 175 solution was applied as it was with no further dilutions. After 15-20 minutes subsequent to
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42 176 puncturing the skin, the SPT reaction wheal and flare was outlined by a black ink and clear tape
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44 177 was used to transfer the outline from skin to the results sheet by the trained research assistant or
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46 178 principal investigator.³³ A positive result was indicated by a mean wheal diameter measuring 3
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48 179 mm or greater than the negative control. Results were recorded on a standardized result sheet.
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51 180 The research assistant's test performance was audited by the principal investigator at regular
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53 181 intervals to ensure correctness of technique and interpretation of the results.
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3 182 Informed signed consent was obtained from all the participants prior to participation. They had
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5 183 the option of participating in the questionnaire interview and the SPT or refusing the SPT. The
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8 184 study protocol was approved by the Biomedical Research Ethics Committee of the University of
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10 185 KwaZulu-Natal (BE048/11). Permission to conduct the study was also obtained from the KZN
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13 186 Provincial Department of Health and King Edward VIII hospital management.

16 187 **Statistical analysis**

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19 188 Data was captured in Excel and analysed in Stata Version 11. Frequencies and medians with
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22 189 ranges were presented for categorical and continuous variables respectively. The Chi-square and
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24 190 the Kruskal-Wallis test were used to test for significant associations between categorical and
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26 191 continuous variables and the dependent variables under study on bivariate analysis, respectively.

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30 192 Logistic regression was used to test for significant associations between independent and
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32 193 dependent variables on multivariate analysis. The dependent variables used in the regression
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34 194 analysis were: Latex sensitisation, which was defined as having a SPT wheal of ≥ 3 mm to latex
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36 195 extract; Latex allergy (LA) was defined as being SPT positive and a report of having any one or
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38 196 more of the listed work related clinical symptoms namely itchy eyes, red eyes, runny eyes, runny
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40 197 nose, itchy nose, sneezing, coughing, tight chest, wheezing, itchy skin, skin rash or dizziness.
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42 198 Independent variables that were considered for analysis were as follows: Age (yrs.) and sex,
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44 199 duration of employment, job title, current department employed in, type of gloves used, number
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46 200 of pairs of gloves used per day, self reported and family history of atopy, food allergy and
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48 201 previous history of open surgery and number of surgical procedures. In the multivariate analysis,
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50 202 age was omitted due to collinearity with duration of employment. Departmental glove
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54 203 consumption was omitted as this only indicated annual distribution of gloves per department and
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204 not necessarily employees' exposure since enrolled nursing assistants and enrolled nurses are
205 rotated through different departments in any given year. The number of pair of gloves was used
206 as an indicator of individual latex glove exposure. The variable number of pairs of gloves used
207 and duration of employment were retained as continuous variables in the multivariate model.
208 Fractional polynomial and a fractional plot was used to visualise the dose-response relationship
209 of these continuous exposure variables.

210 **RESULTS**

211 **Participant Demographics**

212 Sixty five HCWs refused to participate in the study. Among the 520 HCWs who responded to
213 the invitation there was an overall participation rate of 85.5 % (n=501) with 3.6% (n=19)
214 refusing SPT. There was no significant difference between those refusing SPT and those who
215 had the SPT with respect to latex exposure status, age, sex and duration of employment.

216 The median age of participants was 42.2 years (range: 22 years-65 years) with the greater
217 proportion of them being females. The median duration of employment was 10.9 years (range: 1
218 year-42 years) with the majority of exposed participants having worked as a HCW for < 10
219 years. Most unexposed healthcare workers had been employed for > 20 years. Personal and
220 family history of allergy was more prevalent among unexposed HCWs while exposed HCWS
221 reported a higher prevalence of a fruit allergy and history of previous surgery (Table 1).

222 **Prevalence of Latex Sensitisation and Allergy**

223 The overall prevalence of latex sensitisation and latex allergy were 5.9% (n=29) and 4.6%
224 (n=23) respectively. Although the difference was not significant, the prevalence of latex

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3 225 sensitisation was higher among the exposed group (7.1%) as compared to the unexposed group
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5 226 (3.1%). Latex allergy was significantly higher in the exposed group than unexposed group (5.9%
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8 227 vs 1.8%, $p=0.04$). There was a significant difference in the work related allergy symptoms
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10 228 between exposed and unexposed workers (40.9% vs. 31.7%, $p=0.04$) (Table 1). Symptoms that
11
12 229 were significantly associated with latex sensitisation were skin rash ($p < 0.000$), itchy skin
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14 230 ($p=0.001$), runny nose ($p=0.004$), red eyes ($p=0.01$) and itchy eyes ($p=0.01$).
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19 231 The prevalence of latex sensitization was higher among those who were exposed and those with
20
21 232 employment duration of < 10 yrs. Although the prevalence of latex sensitisation was lower
22
23 233 among participants < 30 years of age, there was no significant variation with age or sex. There
24
25 234 was a significant difference ($p=0.04$) in the prevalence of fruit allergy between those participants
26
27 235 with latex sensitisation (17.2%) and unsensitised participants (6.9%) The exclusive use of
28
29 236 powder free latex gloves was found to be significantly ($p=0.003$) higher among the participants
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31 237 who had latex sensitisation. There was equal distribution of powdered and powder free latex
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33 238 gloves among those who reported the use of mixed gloves. The prevalence of reporting previous
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35 239 open surgery and use of other non- occupational exposure latex containing material did not vary
36
37 240 significantly between those who had latex sensitisation and those who were unsensitised. There
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39 241 was a significantly higher prevalence of reporting allergic reactions when handling other latex
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41 242 containing medical equipment among participants with latex allergy as compared to unsensitised
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43 243 participants (10.3% vs 1.7%, $p=0.002$) (Table 2).
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50 244 **Crude association of demographics, exposure status, medical and personal history and latex**
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52 245 **sensitisation, latex allergy**
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3 246 Latex exposure was significantly associated with latex allergy (OR: 3.4; 95% CI: 1.1-10.8).
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6 247 Working as a HCW for 5-9 years was significantly associated with latex sensitisation (OR: 2.6;
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8 248 95% CI: 1.2-5.5) and latex allergy (OR: 3.3; 95% CI: 1.4-7.6), respectively. Employment
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10 249 duration as a HCW for >20 years was protective against latex allergy (OR: 0.2; 95% CI: 0.0-0.8).
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12 250 In comparison with unexposed workers, working as an enrolled nurse was significantly
13
14 251 associated with both latex sensitisation (OR: 2.5; 95% CI: 1.2-5.3) and latex allergy (OR: 2.4;
15
16 252 95% CI: 1.1-5.6). The exclusive use of powder free latex gloves was significantly associated
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18 253 with latex sensitisation (OR: 3.1; 95% CI: 1.4-6.8) and latex allergy (OR: 3.1; 95% CI: 1.7-9.1).
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20 254 Powdered and powder free latex gloves were equally distributed among those who reported the
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22 255 use of mixed gloves. The annual consumption of pairs of gloves per HCW by department was
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24 256 ranked and grouped into tertiles. Although medical and surgical wards had low and moderate
25
26 257 pairs of gloves consumption per HCW, these wards had the highest proportion of workers with
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28 258 latex sensitisation (n=6, 20.0% each). However the relation was only significant for those who
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30 259 reported the medical ward as being the current department in which they worked (p=0.01). The
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32 260 proportions for powdered latex glove use were 71% and 69% in medical and surgical wards,
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34 261 respectively and this was not statistically significant. Exposure to other latex containing medical
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36 262 devices was not significantly different from what was reported in other wards. There was no
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38 263 significant association between reported personal history of allergy disease, latex sensitisation
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40 264 and latex allergy. Fruit allergy was significantly associated with latex allergy (OR: 3.7; 95%:
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42 265 1.4-10.4) (Table 3). Listed fruits were evaluated for their independent association with latex
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44 266 sensitisation. Avocado (OR: 12.3; 95% CI: 5.1-29.6) and others (OR: 5.1; 95% CI: 2.1-11.8)
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46 267 which included pineapple and orange showed significant associations with latex sensitisation
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48 268 (data not shown).
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269 **Multivariate analysis**

270 While latex exposure had estimates of the OR above 2, there was no significant association with
271 latex sensitisation and latex allergy. Duration of employment was found to be inversely
272 associated with latex allergy in models I and II. The exclusive use of powder free latex gloves
273 was significantly associated with latex sensitisation (OR: 4.2; 95% CI: 1.2-14.1) and latex
274 allergy (OR: 5.1; 95%CI: 1.2-21.2) on multivariate analysis. This significant association
275 disappeared when examining the number of pairs of powder free gloves used in the last 7 days. A
276 weak association was observed for the number of pairs of powdered latex gloves used in the last
277 7 days with both latex sensitisation and latex allergy (model III and IV). Further analysis of
278 duration of employment and number of pairs of gloves using fractional polynomial failed to
279 demonstrate significant dose-response relationship with either latex sensitisation or latex allergy.
280 Duration of employment showed significant ($p=0.000$) dose-response relationship when
281 analysed using using penalised spline with degree of freedom =2 (Figure1). There was a
282 significant association between fruit allergy and latex allergy in model I (OR: 3.1; 95% CI: 1.1-
283 9.2) (Table 4).

284 **DISCUSSION**

285 This is an important study for South African HCWs as it examined the risk of latex sensitisation
286 in a group of workers exposed to hypoallergenic latex gloves. As previously mentioned there has
287 been no literature documenting the prevalence of latex sensitisation among South African HCWs
288 using hypoallergenic lightly powdered or powder-free latex gloves. The prevalence of latex
289 sensitisation among exposed HCWs (7.1%) in this study is comparable to findings among HCWs
290 in another South African hospital.¹⁴ However it was considerably lower than the 11.9%
291 prevalence reported by Potter in the same year.¹⁶ While a substantial number of participants

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3 292 (37%) reported work related allergy symptoms, only 4.6% met our definition of latex allergy.
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5 293 The important symptoms associated with latex sensitisation were skin rash, itchy skin, runny
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8 294 nose, red and itchy eyes in keeping with previous studies. Elimination of powdered latex gloves
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10 295 has shown a reduction in the concentration of aeroallergens in the operating room with the low
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12 296 prevalence of latex allergy in our study population.
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16 297 Although the relationship was weak, this study showed that the risk of latex sensitisation
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18 298 decreases with duration of employment. The healthy worker effect is a likely explanation of this
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20 299 finding. Prior to availability of hypoallergenic latex gloves, workers who had developed latex
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22 300 allergy may have left employment or they may have changed their career path and moved into a
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24 301 more administrative or managerial role with no contact with latex gloves. Furthermore new
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26 302 employees are only sensitised and have not yet manifested clinical symptoms and they continue
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28 303 using latex gloves. On the other hand senior HCWs may have been sensitised during their earlier
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30 304 years of employment and as a result they either moved to departments with less exposure to latex
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32 305 gloves or deliberately avoid latex containing products and therefore exhibit less latex related
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34 306 symptoms. Moreover, the introduction of hypoallergenic gloves 10 years prior to the study may
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36 307 explain the reduced sensitisation in senior HCWs as demonstrated in the study by Smith et al in
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38 308 2007. The published literature has been inconsistent in reporting the association between
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40 309 duration of employment and latex sensitisation. Although latex is one of the best studied
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42 310 allergens, no exposure response studies have been published with measured latex allergen levels.
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44 311 In addition, studies have demonstrated variation in allergen content of different gloves. These
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46 312 may lead to discrepancies in the literature with regard to the role of duration of employment as a
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48 313 surrogate measure of exposure.
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3 314 In our study HCWs who exclusively used powdered free latex gloves had a 4 times greater odds
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5 315 of developing latex sensitisation. The fact that HCWs with latex sensitisation or allergy work
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7 316 more often with powder free latex gloves is indicative of reverse causality because of symptoms.
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10 317 Moreover the background prevalence of latex sensitisation in this study was relatively higher
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12 318 (3.5%) than previously reported prevalence in the general population by Bousquet et al.¹³ Studies
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14 319 have shown that some of these “hypoallergenic” latex gloves actually contain high levels of
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16 320 allergens which can be release into the environment with aggressive manipulation.²³ Some of the
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18 321 sensitised HCWs may have been sensitised before the hospital implemented a hypoallergenic
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20 322 latex glove policy. Also Smith et al showed that complete avoidance of powdered latex glove can
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22 323 result in the reduction or no change in measurable IgE antibodies.³⁴ A study in Germany reported
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24 324 a high prevalence of 8% among 226 dental students who had only been exposed to exclusive
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26 325 powder free latex gloves.³⁰ Similarly in the UK despite a total ban on powdered latex gloves
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28 326 Clayton found a 10% prevalence of latex sensitisation in HCWs.³¹ It is also not clear to what
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30 327 extent the aeroallergens released by colleagues using powdered latex gloves influence this
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32 328 finding. Furthermore the role of other latex containing medical devices during sensitisation
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34 329 period cannot be entirely ruled out.
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42 330 In our study, frequency of exposure as measured by the number of gloves used in the last 7
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44 331 working days showed a weak association between powdered latex gloves and latex sensitisation
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46 332 but no association could be demonstrated with powder free latex gloves. Airborne latex
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48 333 aeroallergens have been shown to increase with the number of powdered gloves used which
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50 334 subsequently increases the risk of latex sensitisation and clinical latex glove related allergy
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52 335 symptoms.¹⁸
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3 336 The positive association between department with low glove consumption per HCW and latex
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6 337 sensitisation is in contrast with previous finding by Liss and co-workers.⁹ They reported positive
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8 338 association with departments that had high glove consumption per HCWs. Again, this could be
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10 339 as a result of reverse causality where HCWs with latex sensitisation may have been relocated to
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12 340 wards with low glove consumption to minimise the exposure. In addition, the annual pair of
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14 341 gloves consumption per HCW by department does not provide an accurate indication of
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16 342 individual exposure; rather it gives us the annual distribution of gloves to different departments.
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18 343 Several studies have reported atopy as a significant risk factor for latex sensitisation.^{9, 10, 35}
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20 344 Similarly, the prevalence of reporting a history of personal atopy in this study was higher among
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22 345 latex sensitised participants although the association was not statistically significant. The role of
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24 346 atopy is complex because some individuals might also have become atopic after having been
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26 347 latex sensitised and cross sectional study is not suitable in establishing this association.
27
28 348 Fruit latex allergy syndrome is a phenomenon seen where latex sensitised individuals
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30 349 demonstrate a cross reactivity with specific foods; particularly fruit. Studies have identified this
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32 350 phenomenon among sensitised HCWs and the general population. This has been attributed to the
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34 351 similarity between fruit proteins and latex allergens.³⁶ Fruit allergy was significantly associated
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36 352 with latex sensitisation and latex allergy in our study. Our study was dependent on the self-
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38 353 reporting of fruit allergy and no objective tests were carried out. It is therefore possible that
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40 354 participants have independent simultaneous allergies to both fruit and latex without cross
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42 355 reactivity. Also, we were unable to determine whether latex sensitisation preceded the
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44 356 development of fruit allergy or vice versa. Fruit allergy prior to latex exposure could have
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46 357 contributed to the association observed in our study.
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3 358 Latex sensitised participants reported a high prevalence of a history of previous open surgery in
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6 359 our study. This has been reported to occur as a result of direct intraoperative exposure to latex
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8 360 containing medical devices such as catheters or tubes. Studies in children with congenital
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10 361 abnormalities have demonstrated that the risk for latex allergy increases with the number of open
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12 362 surgical procedures that they undergo.³⁷ Frequency of invasive procedures among adults was
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14 363 shown to increase the risk of latex sensitisation reporting while more than 10 procedures
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16 364 increased the risk of developing latex allergy.³⁸

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21 365 Strengths of this study include the high response rate (85.5%) and comparability to other
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23 366 studies.^{8, 16} Access to the hospital employee database allowed us to better assess the
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25 367 representativeness of this study population by comparing demographic data of the non-
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27 368 participants and the participants. The participants were randomly selected minimising the
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29 369 potential of participant's bias that comes with a volunteer approach.

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34 370 The presence of a control group provided a background prevalence of latex sensitisation in this
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36 371 population which allowed for a better estimation of associations attributable to work related
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38 372 factors. The use of Stallergenes latex specific SPT further strengthens the study. The SPT test is
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40 373 regarded as the gold standard for the diagnosis of latex allergy and Stallergenes has been shown
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42 374 to have a diagnostic sensitivity and specificity of 93% and 100%, respectively.³² The research
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44 375 assistant employed on this study was trained and initially shadowed and periodically supervised
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46 376 by the principal investigator to ensure appropriate administration of the questionnaire and the
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48 377 SPT thereby improving the reliability and validity of the study.

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54 378 This study was limited by the cross sectional study design which was relatively low in cost and
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56 379 quick to conduct. It only allowed for the determination of prevalence of latex sensitisation at one
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3 380 point in time. Consequently the prevalence of latex sensitisation may have been underestimated
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6 381 as it is possible that HCWs who had already developed latex sensitisation have left the hospital
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8 382 before the study was conducted. Some of the observed associations in the study may be as a
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10 383 result of a complex interplay between the healthy worker effect, reverse causality and exposure
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12 384 reduction by the introduction of powder free latex gloves. These interactions can be better
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15 385 explored and understood in a longitudinal study. Recall bias is another potential limitation in this
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17 386 study as workers were asked to recall the number of gloves used in the past 7 working days.
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20 387 HCWs may have overestimated or underestimated their individual exposures. Our study
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22 388 depended on self-reporting of personal and family atopic disorders and this may have resulted in
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24 389 the misclassification of atopy. The role of atopy and cross-reactivity between allergens is a
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26 390 complex phenomenon which cannot be investigated in cross sectional study. Therefore, cohort
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29 391 studies are necessary to disentangle this phenomenon.
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32 392 **CONCLUSION**

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35 393 This study shows that even in the presence of powder free hypoallergenic glove use there is latex
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37 394 sensitisation and latex allergy, adding to previous findings that HCWs exposed to hypoallergenic
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39 395 latex gloves are still at risk for developing latex sensitisation and latex allergy. This indicates that
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41 396 latex sensitisation and allergy are still an important occupational hazard for HCWs. While it may
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43 397 be economically impractical to replace the latex gloves in our setting, reduction of allergen
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45 398 content in latex products is another strategy that can be implemented to address the problem and
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47 399 protect HCWs. A policy accompanied by clear implementation plans as well as sustainable
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49 400 education and training programmes to address latex sensitisation and allergy among HCWs
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51 401 should be implemented.³⁹ In addition HCWs must be continuously monitored for the
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53 402 development of latex sensitisation and alternate latex free glove must be made available for
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3 403 them. More research is needed to identify the most cost effective way of implementing a latex
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5 404 free environment in resource limited countries, such as South Africa. In addition the current
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8 405 studies in South Africa have largely been cross-sectional in nature. More cohort analysis is
9
10 406 required to better understand the chronicity of illness and disability associated with latex allergy.
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13 14 407 **ACKNOWLEDGEMENT**

15
16 408 I would like to thank the hospital employees participating in this study and their management for
17
18 409 allowing me access to the human resource database. I would like to thank Professor Mohamed
19
20 410 Jeebhay (Centre of Occupational and Environmental Health, University of Cape Town, SA) and
21
22 411 Professor David L Nordstrom (Occupational and Environmental Safety and Health, University of
23
24 412 Wisconsin-Whitewater, USA) for their comments on my initial proposal. I would like to thank
25
26 413 Professor Rajen Naidoo (Discipline of Occupational and Environmental Health, UKZN, SA) for
27
28 414 his statistical advice during the data analysis. In addition thank you to Mr. Nhlanhla Jwara for
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30
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32 415 conducting the field work.
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3 416 **Contributorship**
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6 417 Dr Shumani Phaswana is the principal investigator who was involved from the conception of the idea,
7
8 418 proposal writing, data collection, data management and interpretation of the results.
9

10 419 Dr Saloshni Naidoo contributed to the conception and design of the study, analysis and interpretation of
11
12 420 the data, critical review of the intellectual content of the article and final approval of the article.
13
14

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16 421 **Data sharing**
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20 422 No additional unpublished data
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22
23 423 **Funding**
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26 424 None
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30 425 **Competing interests**
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33 426 None declared
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40 428 **Figure legend**
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43 429 **Figure 1: Exposure-response relationship between duration of employment and latex sensitisation using**
44 430 **penalised splines including a.) All particioants and b) Spt positive only**
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515 **TABLES**516 **Table 1: Demographics and associated risk factors amongst latex exposed and unexposed**
517 **healthcare workers at King Edward VIII Hospital, KwaZulu-Natal South Africa, (n=501)**518
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Characteristic	Exposed N (%)	Unexposed N (%)
Number of participants	337 (67.3)	164 (32.7)
Demographics		
Age (years)		
≤30	30(8.9)	19(11.6)
>30-40	121(35.9)	40(24.4)
>40-50	101(29.9)	59(35.9)
>50	85(25.2)	46(28.1)
Duration of employment (years)		
≤5	39(11.6)	28(17.1)
>5-10**	135(40.1)	32(19.5)
>10-15	49(14.5)	17(10.4)
>15-20	24(7.1)	20(12.2)
>20*	90(26.7)	67(40.9)
Sex**		
Female	309(91.7)	95(57.9)
Male	28(8.3)	69(42.1)
Job Title (yes)		
Administrative		164(100.0)
Professional nurses	123(36.5)	
Enrolled nurses	141(41.8)	
Enrolled nursing assistants	73 (21.7)	
Medical and Personal History		
Personal history of Allergy Disease (yes)	147(43.6)	83(50.6)
Family history of Allergy Disease (yes)	197(58.5)	102(62.2)
Fruit allergy (yes)	29(8.6)	9(5.5)
Previous open surgery (yes)*	168(49.8)	61(37.2)
Work-related allergy symptoms(yes)*	138(40.9)	52(31.7)
Non-occupational latex exposure (yes)	161(47.8)	76(46.3)
Latex sensitisation (yes)	24(7.1)	5(3.1)
Current latex allergy (yes)*	20(5.9)	3(1.8)
Chi square, *p<0.05, **p<0.001		

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Table 2: Comparison of risk factors between latex sensitised (skin prick test positive) and non-sensitised (skin prick test negative) healthcare workers at King Edward VIII Hospital, KwaZulu-Natal South Africa (n=501)

Characteristics	Latex SPT +ve† (29) N (%)	Latex SPT -ve† ‡ (472) N (%)	529 530 531
Demographics			532
Age (years.)			533
≤30	1 (3.5)	48(10.2)	534
>30-40	13 (44.8)	148(31.4)	535
>40-50	8 (27.6)	152(32.2)	536
>50	7 (24.1)	124(26.3)	537
Duration of employment			538
≤5	3(10.3)	64(13.6)	539
>5-10	16(55.2)	151(31.9)	540
>10-15	3(10.3)	63(13.4)	541
>15-20	1(3.5)	43(9.1)	542
>20	6(20.7)	151(31.9)	543
Sex (yes)			544
Male	5(17.2)	118(25.0)	545
Female	24(82.8)	354(75.0)	546
Job Title (yes)			547
Administrative	5(17.2)	159(33.7)	548
Professional nurses	5(17.2)	118(25.0)	549
Enrolled nurses	14(48.3)	127(26.9)	550
Enrolled nursing assistants	5(17.2)	68(14.4)	551
Latex Exposure			552
Exposure status(yes)	24 (82.8)	313(66.3)	553
Type of gloves			554
None	5(17.2)	165(34.6)	555
Exclusive powdered latex glove (yes)	2(6.9)	36(7.6)	556
Exclusive powder free latex glove (yes)*	11(37.9)	77(16.3)	557
Mixed (yes)	11(37.9)	198(41.9)	558
Medical and Personal History			559
Personal history of Allergy Disease (yes)	16(55.2)	214(45.3)	560
Family history of Allergy Disease (yes)	18(62.1)	281(59.5)	561
Fruit allergy (yes) *	5(17.2)	33(6.9)	562
Previous open surgery (yes)	18(62.1)	211(44.7)	563
Non-occupational latex exposure (yes)	12(41.4)	225(47.7)	564
Reaction to other latex medical devices (yes)*	3(10.3)	8(1.7)	565
Chi Square, *p<0.05			566
†Latex Skin Prick Test Positive			567
‡Latex Skin Prick Test Negative			568
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574 **Table 3: Crude Odds Ratios (OR) (95%CI) of demographics, exposure status, medical and personal**
 575 **history and latex sensitisation and latex allergy amongst healthcare workers at King Edward VIII**
 576 **Hospital, KwaZulu-Natal South Africa, (n=501)**

Characteristics	N=2 9	Latex Sensitisation OR (95%CI)	N=23	LA# OR (95%CI)	578 579
Demographics					
Age (years)					580
≤30	1	0.3(0.0-1.9)	1	0.4(0.0-2.4)	581
>30-40	13	1.8(0.8-3.7)	11	2.0(0.9-4.6)	582
>40-50	8	0.8(0.4-1.8)	7	0.9(0.4-2.2)	583
>50	7	0.8(0.4-2.1)	4	0.6(0.2-1.7)	584
Duration of employment (years)					585
<5	3	0.7(0.2-2.4)	3	0.9(0.3-3.2)	586
5-10	16	2.6(1.2-5.5)*	14	3.3(1.4-7.6)*	587
>10-15	3	0.7(0.2-2.4)	3	0.9(0.3-3.2)	588
>15-20	1	0.4(0.0-2.1)	1	0.5(0.0-2.8)	589
>20	6	0.5(0.2-1.4)	2	0.2(0.0-0.8)	590
Sex (yes)					591
Female	24	1.6(0.6-4.1)	20	2.2(0.7-7.2)	592
Job Title (yes)					593
Administrative	5	0.4(0.2-1.1)	3	0.3(0.1-0.9)*	594
Professional nurses	5	0.6(0.2-1.6)	4	0.6(0.2-1.8)	595
Enrolled nurses	14	2.5(1.2-5.3)*	11	2.4(1.1-5.6)*	596
Enrolled nursing assistants	5	1.2(0.5-3.3)	5	1.7(0.6-4.5)	597
Latex Exposure					
Exposure status (yes)	24	2.4(0.9-6.3)	20	3.4(1.1-10.8)	598
Type of gloves					599
None	5	0.4(0.2-1.0)	3	0.3(0.1-0.9)*	600
Exclusive Powdered latex glove (yes)	2	0.9(0.0-3.6)	2	1.2(0.0-1.7)	601
Exclusive Powder free latex glove (yes)	11	3.1(1.4-6.8)*	10	3.1(1.7-9.1)*	602
Mixed gloves(yes)	11	0.8(0.4-1.8)	8	0.7(0.3-1.7)	
Medical and Personal History					
Personal history of Allergy Disease (yes)	16	1.4(0.7-3.1)	12	1.3(0.5-2.9)	
Family history of Allergy Disease (yes)	18	1.1(0.5-2.4)	14	1.1(0.5-2.4)	
Fruit allergy (yes)	5	2.8(1.0-7.5)	5	3.7(1.4-10.5)*	
Previous open surgery (yes)	18	1.1(0.5-2.4)	14	1.5(0.7-3.1)	
Chi square, *p<0.05					597
†Latex Skin Prick Test Positive					598
‡Latex Skin Prick Test Positive and work related clinical symptoms of allergy					599

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Table 4: Multivariate analysis of demographics, medical and personal history, exposure history and latex sensitisation (LS)[†] and latex allergy (LA)[#] amongst healthcare workers at King Edward III Hospital, KwaZulu-Natal South Africa, (n=501)

Characteristics	MODEL I* (n=501)		MODEL II** (n=501)		MODEL III***(n=202)		MODEL IV****(n=252)	
	LS OR (95%CI)	LA OR (95%CI)	LS OR (95%CI)	LA OR (95%CI)	LS OR (95%CI)	LA OR (95%CI)	LS OR (95%CI)	LA OR (95%CI)
Demographics								
Sex (female)	0.9(0.2-2.7)	1.1(0.3-4.4)	0.9(0.3-2.7)	1.1(0.3-4.5)	0.3(0.0-1.8)	0.3(0.0-3.1)	2.5(0.5-12.2)	2.5(0.5-12.2)
Duration of employment (years)	0.9(0.9-1.0)	0.9(0.8-0.9)	0.9(0.9-1.0)	0.9(0.8-0.9)	0.9(0.9-1.8)	0.7(0.5-1.0)	0.9(0.9-1.0)	0.9(0.9-1.0)
Latex Exposure								
Exposure status(yes)	2.2(0.7-6.7)	2.6(0.7-9.8)						
Type of gloves								
None			1	1				
Exclusive lightly powdered latex glove (yes)			1.6(0.3-9.8)	2.6(0.4-17.7)				
Exclusive Powder free latex glove (yes)			4.2(1.2-14.1)	5.1(1.2-21.2)				
Mixed gloves (yes)			1.7(0.5-5.6)	1.7(0.4-7.1)				

Pairs of Powdered latex Gloves in the last 7 days					1.1(1.0-1.2)	1.2(1.0-1.4)		
Pairs of Powder Free Latex Gloves in the last 7 days							1.0(0.9-1.1)	1.0(0.9-1.1)
Personal and Medical History								
Personal history of allergy disease (yes)	1.5(0.7-3.3)	1.4(0.6-3.2)	1.5(0.7-3.3)	1.3(0.6-3.2)	1.4(0.3-6.8)	1.6(0.2-11.6)	1.0(0.4-2.9)	0.9(0.3-2.8)
Family history of allergy disease (yes)	1.0(0.45-2.2)	0.9(0.4-2.2)	1.1(0.5-2.3)	0.9(0.4-2.3)	0.4(0.1-1.9)	0.5(0.1-3.6)	0.7(0.2-2.0)	0.8(0.3-2.7)
Fruit allergy (yes)	2.3(0.8-6.7)	3.1(1.1-9.2)	2.2(0.8-6.5)	3.0(0.9-9.1)	5.0(0.4-56.9)	9.7(0.6-163.0)	1.7(0.3-8.5)	2.0(0.4-10.4)
Previous open surgery (yes)	2.0(0.9-4.4)	1.9(0.8-4.6)	2.1(0.9-4.6)	1.9(0.8-4.7)	1.4(0.3-7.4)	1.2(0.1-11.1)	1.1(0.4-3.2)	1.2(0.4-3.8)

†Latex Skin Prick Test Positive

‡Latex Skin Prick Test Positive and work related clinical symptoms of allergy

*Model included latex glove exposure status

**Model included type of gloves

***Model included number of pairs of powdered latex gloves

****Model included number of pairs of powder free latex gloves



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1 **The prevalence of latex sensitisation and allergy and associated risk factors among healthcare**
2 **workers using hypoallergenic latex gloves at King Edward VIII Hospital, KwaZulu-Natal South**
3 **Africa: A cross sectional study**

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20 Keywords: Latex, hypoallergenic, healthcare workers, South Africa

21 Word Count:

22 Abstract: 299

23 Body: 4,359

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ARTICLE SUMMARY**ARTICLE FOCUS**

- The use of hypoallergenic latex gloves has been adopted as policy in different healthcare settings globally.
- However, information with regard to their use and the development of latex sensitisation and allergy among exposed healthcare workers is limited.
- We hypothesised that there is latex sensitization and allergy in healthcare workers using hypoallergenic latex gloves in a South African hospital.

KEY MESSAGE

- In the presence of powder free hypoallergenic gloves, latex sensitisation and latex allergy is still an important occupational health effect in healthcare workers.
- Healthcare workers should be continuously monitored for the development of latex sensitisation and allergy.
- There is a need for a national policy accompanied by clear implementation plans as well as sustainable education and training programmes to address latex sensitisation and allergy among HCWs.

STRENGTH AND LIMITATIONS

- Strength of the study included the presence of a control group providing a background prevalence of latex sensitisation in this population and random selection of participants which minimised the potential of participant bias that arises with a volunteer approach.
- This study was limited by the cross sectional study design as it only allowed for the determination of the prevalence of latex sensitisation; recall bias with regard to the number of gloves used in the past 7 working days and the self-reporting of personal and family atopic disorders may have resulted in the misclassification of exposure and atopy respectively.

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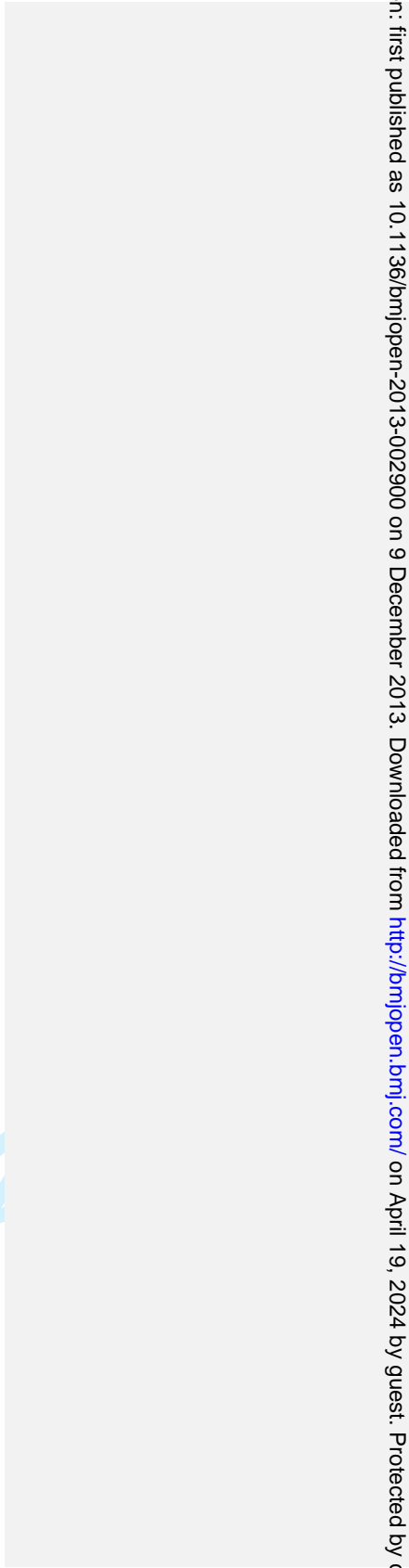
31 **What this paper adds**

- 32 In the presence of powder free hypoallergenic gloves, latex sensitisation and latex allergy is still an
- 33 important occupational health hazard in healthcare workers

- 34 Healthcare workers should be continuously monitored for the development of latex sensitisation and
- 35 allergy

- 36 There is a need for a national policy accompanied by clear implementation plans as well as sustainable
- 37 education and training programmes to address latex sensitisation and allergy among HCWs

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40 ABSTRACT**41 Objectives**

42 The present study describes latex sensitisation and allergy prevalence and associated factors among
43 healthcare workers using hypoallergenic latex gloves at King Edward VIII Hospital in KwaZulu-Natal
44 South Africa.

45 Design

46 Cross sectional study

47 Setting

48 A tertiary hospital in eThekweni municipality, KwaZulu Natal, South Africa

49 Participants

50 600 healthcare workers were randomly selected and 501(337 exposed and 164 unexposed) participated.
51 Participants who were pregnant, less than one year of work as healthcare worker and history of
52 anaphylactic reaction were excluded from the study.

53 Primary and secondary outcome measures

54 Latex sensitisation and latex allergy were the outcome of interest and they were successfully measured

55 Results

56 Prevalence of latex sensitisation and allergy was observed among exposed workers (7.1% and 5.9%) and
57 unexposed workers (3.1% and 1.8%). Work related allergy symptoms were significantly higher in
58 exposed workers (40.9%, $p<0.05$). Duration of employment was inversely associated with latex allergy
59 (OR: 0.9; 95% CI: 0.8-0.9). The risk of latex sensitisation (OR: 4.2; 95% CI: 1.2-14.1) and allergy (OR:

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9 60 5.1; 95% CI: 1.2-21.2) increased with exclusive use of powder-free latex gloves. A dose –response
10 61 relationship was observed for powdered latex gloves (OR: 1.1; 95% CI: 1.0-1.2). Atopy (OR: 1.5; 95%
11 62 CI: 0.7-3.3 and OR: 1.4; 95% CI: 0.6-3.2) and fruit allergy (OR: 2.3; 95% CI: 0.8-6.7 and OR: 3.1; 95%
13 63 CI: 1.1-9.2) also increased the risk of latex sensitisation and allergy.

16 64 **Conclusion**

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18 65 This study adds to previous findings that healthcare workers exposed to hypoallergenic latex gloves are at
19 66 risk for developing latex sensitisation highlighting its importance as an occupational hazard in healthcare.
20 67 More research is needed to identify the most cost effective way of implementing a latex free environment
21 68 in resource limited countries, such as South Africa. In addition more cohort analysis is required to better
22 69 understand the chronicity of illness and disability associated with latex allergy.
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71 INTRODUCTION

72 Latex allergy (LA) as an occupational disease among healthcare workers (HCWs) gained
73 recognition after Nutter published a case report of contact urticaria in a HCW in 1979.¹ The
74 increase in prevalence coincided with the emergence of the Human Immunodeficiency Virus/
75 Acquired immunodeficiency syndrome (HIV/AIDS) epidemic and the introduction of “universal
76 precautions” in the healthcare industry which had resulted in the increased use of latex gloves
77 among HCWs.²

78 Latex gloves are preferred due to their superior barrier and physical properties as compared to
79 the non-latex gloves.³ International epidemiological studies have reported the prevalence of latex
80 allergy among HCWs to range between 2-22% depending on the population and diagnostic
81 methods used.⁴⁻¹¹ The prevalence in the general population has been reported to range between
82 1-6%.^{12,13} In South Africa studies amongst HCWs reported a latex sensitisation prevalence of
83 between 2.7 to 20.8%.¹⁴⁻¹⁶ Latex allergy in HCWs is a compensable disease in South Africa in
84 terms of the Compensation of Occupational Injuries and Diseases Act No. 130 of 1993.¹⁷

85 Powdered latex gloves were identified as an important risk factor for latex sensitisation and
86 allergy in HCWs as they were found to contain high allergenic protein content.¹⁸ Following these
87 findings, hypoallergenic gloves with low allergen content namely, low powdered and powder
88 free latex gloves were introduced. The European definition of powder free gloves is gloves with
89 powder content not exceeding 2 mg per glove and leachable latex protein which is as low as is
90 reasonably practical.¹⁹

91 Hypoallergenic gloves have been associated with reduced latex aeroallergen concentrations,
92 reduced conversion rates and a subsequent decrease in clinic visits, and compensation claims for

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9 93 latex induced occupational asthma and allergic contact dermatitis among HCWs.^{18,20} As much as
10 94 the use of low or powder free gloves has been shown to reduce latex related symptoms, other
11 95 studies have shown that exposed HCWs still exhibit symptoms at very low levels of measureable
12 96 airborne latex allergens.²¹ Most studies have reported on the airborne levels and inhalational
13 97 route of exposure hence the recommendation on low powdered or powder free latex gloves.
14 98 There is little consideration given to the dermal route of exposure despite the fact that exposure
15 99 is as a result of direct contact in these instances.²² Eliminating the cornstarch powder only
16 100 removed the carrier and not the source of allergen which is in the latex itself. Therefore workers
17 101 using powder free gloves are still exposed to the allergenic content of latex gloves. It has been
18 102 shown that different brands from different suppliers contain differing levels of protein due to a
19 103 lack of standards in latex glove manufacture.²³ A South African study reported that some powder
20 104 free latex gloves were found to have high allergenic protein content.²³ HCWs using these gloves
21 105 are exposed via direct dermal contact and are at risk for developing latex sensitization which
22 106 maybe asymptomatic and if exposure continues they can later develop latex allergy which
23 107 presents with clinical manifestations.
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26 108 While it is important to diagnose and manage an individual worker with latex allergy in the early
27 109 stages of the disease, complete control of hazardous substance in the workplace is equally if not
28 110 more important. While a latex free work environment would be a preferred control strategy,
29 111 substitution of powdered latex gloves with powder free gloves was shown to be cost effective
30 112 and associated with improved clinical outcome.^{20, 24-26} As a result this was adopted as the most
31 113 reasonable and practical approach in addressing the problem of latex allergy among HCWs both
32 114 internationally and to some extent nationally.²⁷⁻²⁹ This has proven to reduce latex induced
33 115 clinical outcomes. Even with this intervention, studies in Western countries such as Germany

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9 116 and the UK have shown that the risk of latex sensitisation still exists and more needs to be done
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11 117 to protect HCWs.^{30, 31}

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13 118 The current study described the prevalence of latex sensitisation and allergy among healthcare
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15 119 workers who use hypoallergenic powder free and lightly powdered latex gloves.

18 120 **METHODS**

21 121 **Study design and population**

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24 122 This was a cross sectional study conducted between July 2011 and January 2012. The study
25
26 123 location was King Edward VIII hospital, the second largest hospital in the Southern hemisphere,
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28 124 providing regional and tertiary services to the whole of KwaZulu-Natal (KZN) and the Eastern
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30 125 Cape Province in South Africa. It has a bed status of 1300 and has a workforce of 2400. The
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32 126 hospital was chosen due to the large workforce with different departments, and the policy of
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34 127 using both powder free and low powdered latex gloves for approximately 10 years.

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36 128 The study population was limited to HCWs currently employed at King Edward VIII Hospital
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38 129 for more than 12 months. HCWs were defined as all personnel employed in the hospital.

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40 130 The prevalence of latex sensitization in HCWs using powdered latex gloves in the Western Cape
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42 131 Province was 11.9% in 2001.¹⁶ We expected the prevalence at King Edward VIII hospital to be
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44 132 less than the 11.9% observed in the Western Cape Province due to the adoption of a
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46 133 hypoallergenic latex glove policy in 2001. Using EPI Info calculator version 3.04.04., it was
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48 134 assumed that 50% of sensitised workers have remained sensitised despite the introduction of
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50 135 hypoallergenic latex gloves 10 years prior. Using an expected latex sensitization prevalence of
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52 136 6% for the exposed group and the prevalence among the general population being reported as

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9 137 less than 1% the required sample size was calculated to be 585 participants 2 exposed
10 138 participants for every 1 non-exposed participant (exposed =390; unexposed =195). HCWs were
11 139 considered to be exposed if they were likely to use gloves. Unexposed HCWs were drawn from
12 140 the administrative staff of the hospital.

17 141 **Questionnaire**

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20 142 We used an adaptation of the questionnaire used in an epidemiological study conducted at
21 143 Groote Schuur in 2001¹⁶ with permission from Professor Paul Potter, Allergology Unit, Medical
22 144 School, University of Cape Town. The questionnaire containing open and closed ended questions
23 145 was adapted to include items on exposure assessment. The questionnaire was administered by a
24 146 trained research assistant immediately prior to the skin prick test. The questionnaire collected
25 147 data on the participants' demographics, personal risk factors, latex exposure assessment, clinical
26 148 manifestations of latex sensitization (dermal and respiratory) and history of previous reactions
27 149 suggestive of latex allergy.

36 150 **Exposure Assessment**

38 151 *Individual Exposure*

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41 152 Individual latex exposure was determined by the type of gloves used, number of gloves used per
42 153 day, and duration of glove use. The information was limited to 7 working shifts/days prior to the
43 154 interview.

48 155 *Departmental Exposure*

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9 156 Departmental exposure was defined as glove usage in the past 12 months (01 January 2011-31
10 157 December 2011). The overall departmental exposure was obtained by reviewing monthly glove
11 158 usage by each department from the stock room register. This was used to estimate the annual
12 159 exposure for employees who had rotated through different departments in the past 12 months.
13 160 Non sterile latex gloves are distributed throughout the clinical departments while a high
14 161 proportion of sterile gloves are distributed to labour ward, theatre, surgical wards and outpatient
15 162 departments. Glove type was defined as powdered and powder-free and latex free based on the
16 163 previous literature.^{23, 32}

164 **Skin prick test (SPT)**

165 The SPT was conducted using the Stallergenes kit.³² It was performed in a room with access to
166 emergency resuscitation services by a trained research assistant. The research assistant and
167 principal investigator were trained on 2 separate occasions. The test was performed on the inner
168 aspect of the participants' forearms, between the wrist and the elbow on normal skin. A positive
169 and negative control were performed using histamine (0.61% concentration of phenol) and
170 buffered normal saline solution respectively on the same arm and they were 3 cm apart to
171 prevent cross contamination. The protein concentration of the latex extract was 500µg/ml and the
172 solution was applied as it was with no further dilutions. After 15-20 minutes subsequent to
173 puncturing the skin, the SPT reaction wheal and flare was outlined by a black ink and clear tape
174 was used to transfer the outline from skin to the results sheet by the trained research assistant or
175 principal investigator.³³ A positive result was indicated by a mean wheal diameter measuring 3
176 mm or greater than the negative control. Results were recorded on a standardized result sheet.
177 The research assistant's test performance was audited by the principal investigator at regular
178 intervals to ensure correctness of technique and interpretation of the results.

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9 179 Informed signed consent was obtained from all the participants prior to participation. They had
10 180 the option of participating in the questionnaire interview and the SPT or refusing the SPT. The
11 181 study protocol was approved by the Biomedical Research Ethics Committee of the University of
12 182 KwaZulu-Natal (BE048/11). Permission to conduct the study was also obtained from the KZN
13 183 Provincial Department of Health and King Edward VIII hospital management.

184 **Statistical analysis**

185 Data was captured in Excel and analysed in Stata Version 11. Frequencies and medians with
186 ranges were presented for categorical and continuous variables respectively. The Chi-square and
187 the Kruskal-Wallis test were used to test for significant associations between categorical and
188 continuous variables and the dependent variables under study on bivariate analysis, respectively.

189 ~~Binary~~ Logistic regression was used to test for significant associations between independent and
190 dependent variables on multivariate analysis. The dependent variables used in the regression
191 analysis were: Latex sensitisation, which was defined as having a SPT wheal of ≥ 3 mm to latex
192 extract; Latex allergy (LA) was defined as being SPT positive and a report of having any one or
193 more of the listed work related clinical symptoms namely itchy eyes, red eyes, runny eyes, runny
194 nose, itchy nose, sneezing, coughing, tight chest, wheezing, itchy skin, skin rash or dizziness.
195 Independent variables that were considered for analysis were as follows: Age (yrs.) and sex,
196 duration of employment, job title, current department employed in, type of gloves used, number
197 of pairs of gloves used per day, self reported and family history of atopy, food allergy and
198 previous history of open surgery and number of surgical procedures. In the multivariate analysis,
199 age was omitted due to collinearity with duration of employment. Departmental glove
200 consumption was omitted as this only indicated annual distribution of gloves per department and

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9 201 not necessarily employees' exposure since enrolled nursing assistants and enrolled nurses are
10 202 rotated through different departments in any given year. The number of pair of gloves was used
11 203 as an indicator of individual latex glove exposure. The variable number of pairs of gloves used
12 204 and duration of employment were retained as continuous variables in the multivariate model.
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15 205 Fractional polynomial and a fractional plot was used to visualise the dose-response relationship
16 206 of these continuous exposure variables.
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207 RESULTS

208 Participant Demographics

209 Sixty five HCWs refused to participate in the study. Among the 520 HCWs who responded to
210 the invitation there was an overall participation rate of 85.5 % (n=501) with 3.6% (n=19)
211 refusing SPT. There was no significant difference between those refusing SPT and those who
212 had the SPT with respect to latex exposure status, age, sex and duration of employment.

213 The median age of participants was 42.2 years (range: 22 years-65 years) with the greater
214 proportion of them being females. The median duration of employment was 10.9 years (range: 1
215 year-42 years) with the majority of exposed participants having worked as a HCW for < 10
216 years. Most unexposed healthcare workers had been employed for > 20 years. Personal and
217 family history of allergy was more prevalent among unexposed HCWs while exposed HCWS
218 reported a higher prevalence of a fruit allergy and history of previous surgery (Table 1).

219 Prevalence of Latex Sensitisation and Allergy

220 The overall prevalence of latex sensitisation and latex allergy were 5.9% (n=29) and 4.6%
221 (n=23) respectively. Although the difference was not significant, the prevalence of latex

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9 222 sensitisation was higher among the exposed group (7.1%) as compared to the unexposed group
10 223 (3.1%). Latex allergy was significantly higher in the exposed group than unexposed group (5.9%
11 224 vs 1.8%, $p=0.04$). There was a significant difference in the work related allergy symptoms
12 225 between exposed and unexposed workers (40.9% vs. 31.7%, $p=0.04$) (Table 1). Symptoms that
13 226 were significantly associated with latex sensitisation were skin rash ($p< 0.000$), itchy skin
14 227 ($p=0.001$), runny nose ($p=0.004$), red eyes ($p=0.01$) and itchy eyes ($p=0.01$).

15 228 The prevalence of latex sensitization was higher among those who were exposed and those with
16 229 employment duration of < 10 yrs. Although the prevalence of latex sensitisation was lower
17 230 among participants < 30 years of age, there was no significant variation with age or sex. There
18 231 was a significant difference ($p=0.04$) in the prevalence of fruit allergy between those participants
19 232 with latex sensitisation (17.2%) and unsensitised participants (6.9%) The exclusive use of
20 233 powder free latex gloves was found to be significantly ($p=0.003$) higher among the participants
21 234 who had latex sensitisation. There was equal distribution of powdered and powder free latex
22 235 gloves among those who reported the use of mixed gloves. The prevalence of reporting previous
23 236 open surgery and use of other non- occupational exposure latex containing material did not vary
24 237 significantly between those who had latex sensitisation and those who were unsensitised. There
25 238 was a significantly higher prevalence of reporting allergic reactions when handling other latex
26 239 containing medical equipment among participants with latex allergy as compared to unsensitised
27 240 participants (10.3% vs 1.7%, $p=0.002$) (Table 2).

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46 241 **Crude association of demographics, exposure status, medical and personal history and latex**
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48 242 **sensitisation, latex allergy**
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9 243 Latex exposure was significantly associated with latex allergy (OR: 3.4; 95% CI: 1.1-10.8).
10 244 Working as a HCW for 5-9 years was significantly associated with latex sensitisation (OR: 2.6;
11 245 95% CI: 1.2-5.5) and latex allergy (OR: 3.3; 95% CI: 1.4-7.6), respectively. Employment
12 246 duration as a HCW for >20 years was protective against latex allergy (OR: 0.2; 95% CI: 0.0-0.8).
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14 247 In comparison with unexposed workers, working as an enrolled nurse was significantly
15 248 associated with both latex sensitisation (OR: 2.5; 95% CI: 1.2-5.3) and latex allergy (OR: 2.4;
16 249 95% CI: 1.1-5.6). The exclusive use of powder free latex gloves was significantly associated
17 250 with latex sensitisation (OR: 3.1; 95% CI: 1.4-6.8) and latex allergy (OR: 3.1; 95% CI: 1.7-9.1).
18 251 Powdered and powder free latex gloves were equally distributed among those who reported the
19 252 use of mixed gloves. The annual consumption of pairs of gloves per HCW by department was
20 253 ranked and grouped into tertiles. Although medical and surgical wards had low and moderate
21 254 pairs of gloves consumption per HCW, these wards had the highest proportion of workers with
22 255 latex sensitisation (n=6, 20.0% each). However the relation was only significant for those who
23 256 reported the medical ward as being the current department in which they worked (p=0.01). The
24 257 proportions for powdered latex glove use were 71% and 69% in medical and surgical wards,
25 258 respectively and this was not statistically significant. Exposure to other latex containing medical
26 259 devices was not significantly different from what was reported in other wards. There was no
27 260 significant association between reported personal history of allergy disease, latex sensitisation
28 261 and latex allergy. Fruit allergy was significantly associated with latex allergy (OR: 3.7; 95%:
29 262 1.4-10.4) (Table 3). Listed fruits were evaluated for their independent association with latex
30 263 sensitisation. Avocado (OR: 12.3; 95% CI: 5.1-29.6) and others (OR: 5.1; 95% CI: 2.1-11.8)
31 264 which included pineapple and orange showed significant associations with latex sensitisation
32 265 (data not shown).
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266 **Multivariate analysis**

267 While latex exposure had estimates of the OR above 2, there was no significant association with
268 latex sensitisation and latex allergy. Duration of employment was found to be inversely
269 associated with latex allergy in models I and II. The exclusive use of powder free latex gloves
270 was significantly associated with latex sensitisation (OR: 4.2; 95% CI: 1.2-14.1) and latex
271 allergy (OR: 5.1; 95%CI: 1.2-21.2) on multivariate analysis. This significant association
272 disappeared when examining the number of pairs of powder free gloves used in the last 7 days. A
273 weak association was observed for the number of pairs of powdered latex gloves used in the last
274 7 days with both latex sensitisation and latex allergy (model III and IV). Further analysis of
275 duration of employment and number of pairs of gloves using fractional polynomial failed to
276 demonstrate significant dose-response relationship with either latex sensitisation or latex allergy.
277 Duration of employment showed significant (p= 0.000) dose-response relationship when
278 analysed using using penalised spline with degree of freedom =2 (Figure1). There was a
279 significant association between fruit allergy and latex allergy in model I (OR: 3.1; 95% CI: 1.1-
280 9.2) (Table 4).

281 **DISCUSSION**

282 This is an important study for South African HCWs as it examined the risk of latex sensitisation
283 in a group of workers exposed to hypoallergenic latex gloves. As previously mentioned there has
284 been no literature documenting the prevalence of latex sensitisation among South African HCWs
285 using hypoallergenic lightly powered or powder-free latex gloves. The prevalence of latex
286 sensitisation among exposed HCWs (7.1%) in this study is comparable to findings among HCWs
287 in another South African hospital.¹⁴ However it was considerably lower than the 11.9%
288 prevalence reported by Potter in the same year.¹⁶ While a substantial number of participants

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9 289 (37%) reported work related allergy symptoms, only 4.6% met our definition of latex allergy.
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11 290 The important symptoms associated with latex sensitisation were skin rash, itchy skin, runny
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13 291 nose, red and itchy eyes in keeping with previous studies. Elimination of powdered latex gloves
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15 292 has shown a reduction in the concentration of aeroallergens in the operating room with the low
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17 293 prevalence of latex allergy in our study population.
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19 294 Although the relationship was weak, this study showed that the risk of latex sensitisation
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21 295 decreases with duration of employment. The healthy worker effect is a likely possible explanation
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23 296 of this finding. Prior to availability of hypoallergenic latex gloves, workers who had developed
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25 297 latex allergy may have left employment or they may have changed their career path and moved
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27 298 into a more administrative or managerial role with no contact with latex gloves. Furthermore
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29 299 new employees are only sensitised and have not yet manifested clinical symptoms and they
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31 300 continue using latex gloves. On the other hand senior HCWs may have been sensitised during
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33 301 their earlier years of employment and as a result they either moved to departments with less
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35 302 exposure to latex gloves or deliberately avoid latex containing products and therefore exhibit less
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37 303 latex related symptoms. Moreover, the introduction of hypoallergenic gloves 10 years prior to
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39 304 the study may explain the reduced sensitisation in senior HCWs as demonstrated in the study by
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41 305 Smith et al in 2007. The published literature has been inconsistent in reporting the association
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43 306 between duration of employment and latex sensitisation. Although latex is one of the best studied
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45 307 allergens, no exposure response studies have been published with measured latex allergen levels.
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47 308 In addition, studies have demonstrated variation in allergen content of different gloves. These
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49 309 may lead to discrepancies in the literature with regard to the role of duration of employment as a
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51 310 surrogate measure of exposure.
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9 311 In our study HCWs who exclusively used powdered free latex gloves had a 4 times greater odds
10 312 of developing latex sensitisation. The fact that HCWs with latex sensitisation or allergy work
11 313 more often with powder free latex gloves is indicative of reverse causality because of symptoms.
12 314 Moreover the background prevalence of latex sensitisation in this study was relatively higher
13 315 (3.5%) than previously reported prevalence in the general population by Bousquet et al.¹³ Studies
14 316 have shown that some of these “hypoallergenic” latex gloves actually contain high levels of
15 317 allergens which can be release into the environment with aggressive manipulation.²³ Some of the
16 318 sensitised HCWs may have been sensitised before the hospital implemented a hypoallergenic
17 319 latex glove policy. Also Smith et al showed that complete avoidance of powdered latex glove can
18 320 result in the reduction or no change in measurable IgE antibodies.³⁴ A study in Germany reported
19 321 a high prevalence of 8% among 226 dental students who had only been exposed to exclusive
20 322 powder free latex gloves.³⁰ Similarly in the UK despite a total ban on powdered latex gloves
21 323 Clayton found a 10% prevalence of latex sensitisation in HCWs.³¹ It is also not clear to what
22 324 extent the aeroallergens released by colleagues using powdered latex gloves influence this
23 325 finding. Furthermore the role of other latex containing medical devices during sensitisation
24 326 period cannot be entirely ruled out.

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40 327 In our study, frequency of exposure as measured by the number of gloves used in the last 7
41 328 working days showed a weak association between powdered latex gloves and latex sensitisation
42 329 but no association could be demonstrated with powder free latex gloves. Airborne latex
43 330 aeroallergens have been shown to increase with the number of powdered gloves used which
44 331 subsequently increases the risk of latex sensitisation and clinical latex glove related allergy
45 332 symptoms.¹⁸

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9 333 The positive association between department with low glove consumption per HCW and latex
10 334 sensitisation is in contrast with previous finding by Liss and co-workers.⁹ They reported positive
11 335 association with departments that had high glove consumption per HCWs. Again, this could be
12 336 as a result of reverse causality where HCWs with latex sensitisation may have been relocated to
13 337 wards with low glove consumption to minimise the exposure. In addition, the annual pair of
14 338 gloves consumption per HCW by department does not provide an accurate indication of
15 339 individual exposure; rather it gives us the annual distribution of gloves to different departments.
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17 340 Several studies have reported atopy as a significant risk factor for latex sensitisation.^{9, 10, 35}
18 341 Similarly, the prevalence of reporting a history of personal atopy in this study was higher among
19 342 latex sensitised participants although the association was not statistically significant. The role of
20 343 atopy is complex because some individuals might also have become atopic after having been
21 344 latex sensitised and cross sectional study is not suitable in establishing this association.
22
23 345 Fruit latex allergy syndrome is a phenomenon seen where latex sensitised individuals
24 346 demonstrate a cross reactivity with specific foods; particularly fruit. Studies have identified this
25 347 phenomenon among sensitised HCWs and the general population. This has been attributed to the
26 348 similarity between fruit proteins and latex allergens.³⁶ Fruit allergy was significantly associated
27 349 with latex sensitisation and latex allergy in our study. Our study was dependent on the self-
28 350 reporting of fruit allergy and no objective tests were carried out. It is therefore possible that
29 351 participants have independent simultaneous allergies to both fruit and latex without cross
30 352 reactivity. Also, we were unable to determine whether latex sensitisation preceded the
31 353 development of fruit allergy or vice versa. Fruit allergy prior to latex exposure could have
32 354 contributed to the association observed in our study.

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9 355 Latex sensitised participants reported a high prevalence of a history of previous open surgery in
10 356 our study. This has been reported to occur as a result of direct intraoperative exposure to latex
11 357 containing medical devices such as catheters or tubes. Studies in children with congenital
12 358 abnormalities have demonstrated that the risk for latex allergy increases with the number of open
13 359 surgical procedures that they undergo.³⁷ Frequency of invasive procedures among adults was
14 360 shown to increase the risk of latex sensitisation reporting while more than 10 procedures
15 361 increased the risk of developing latex allergy.³⁸

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18 362 Strengths of this study include the high response rate (85.5%) and comparability to other
19 363 studies.^{8, 16} Access to the hospital employee database allowed us to better assess the
20 364 representativeness of this study population by comparing demographic data of the non-
21 365 participants and the participants. The participants were randomly selected minimising the
22 366 potential of participant's bias that comes with a volunteer approach.

23 367 The presence of a control group provided a background prevalence of latex sensitisation in this
24 368 population which allowed for a better estimation of associations attributable to work related
25 369 factors. The use of Stallergenes latex specific SPT further strengthens the study. The SPT test is
26 370 regarded as the gold standard for the diagnosis of latex allergy and Stallergenes has been shown
27 371 to have a diagnostic sensitivity and specificity of 93% and 100%, respectively.³² The research
28 372 assistant employed on this study was trained and initially shadowed and periodically supervised
29 373 by the principal investigator to ensure appropriate administration of the questionnaire and the
30 374 SPT thereby improving the reliability and validity of the study.

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33 375 This study was limited by the cross sectional study design which was relatively low in cost and
34 376 quick to conduct. It only allowed for the determination of prevalence of latex sensitisation at one

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9 377 point in time. Consequently the prevalence of latex sensitisation may have been underestimated
10 378 as it is possible that HCWs who had already developed latex sensitisation have left the hospital
11 379 before the study was conducted. Some of the observed associations in the study may be as a
12 380 result of a complex interplay between the healthy worker effect, reverse causality and exposure
13 381 reduction by the introduction of powder free latex gloves. These interactions can be better
14 382 explored and understood in a longitudinal study. Recall bias is another potential limitation in this
15 383 study as workers were asked to recall the number of gloves used in the past 7 working days.
16 384 HCWs may have overestimated or underestimated their individual exposures. Our study
17 385 depended on self-reporting of personal and family atopic disorders and this may have resulted in
18 386 the misclassification of atopy. The role of atopy and cross-reactivity between allergens is a
19 387 complex phenomenon which cannot be investigated in cross sectional study. Therefore, cohort
20 388 studies are necessary to disentangle this phenomenon.

31 32 389 **CONCLUSION**

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34 390 This study shows that even in the presence of powder free hypoallergenic glove use there is latex
35 391 sensitisation and latex allergy, adding to previous findings that HCWs exposed to hypoallergenic
36 392 latex gloves are still at risk for developing latex sensitisation and latex allergy. This indicates that
37 393 latex sensitisation and allergy are still an important occupational hazard for HCWs. While it may
38 394 be economically impractical to replace the latex gloves in our setting, reduction of allergen
39 395 content in latex products is another strategy that can be implemented to address the problem and
40 396 protect HCWs. A policy accompanied by clear implementation plans as well as sustainable
41 397 education and training programmes to address latex sensitisation and allergy among HCWs
42 398 should be implemented.³⁹ In addition HCWs must be continuously monitored for the
43 399 development of latex sensitisation and alternate latex free glove must be made available for

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9 400 them. More research is needed to identify the most cost effective way of implementing a latex
10 401 free environment in resource limited countries, such as South Africa. In addition the current
11 402 studies in South Africa have largely been cross-sectional in nature. More cohort analysis is
12 403 required to better understand the chronicity of illness and disability associated with latex allergy.

17 404 **ACKNOWLEDGEMENT**

18
19 405 I would like to thank the hospital employees participating in this study and their management for
20 406 allowing me access to the human resource database. I would like to thank Professor Mohamed
21 407 Jeebhay (Centre of Occupational and Environmental Health, University of Cape Town, SA) and
22 408 Professor David L Nordstrom (Occupational and Environmental Safety and Health, University of
23 409 Wisconsin-Whitewater, USA) for their comments on my initial proposal. I would like to thank
24 410 Professor Rajen Naidoo (Discipline of Occupational and Environmental Health, UKZN, SA) for
25 411 his statistical advice during the data analysis. In addition thank you to Mr. Nhlanhla Jwara for
26 412 conducting the field work.
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9 413 **Contributorship**

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11 414 Dr Shumani Phaswana is the principal investigator who was involved from the conception of the idea,
12 415 proposal writing, data collection, data management and interpretation of the results.

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14 416 Dr Saloshni Naidoo contributed to the conception and design of the study, analysis and interpretation of
15 417 the data, critical review of the intellectual content of the article and final approval of the article.

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19 418 **Data sharing**

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22 419 No additional unpublished data

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24 420 **Funding**

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29 422 **Competing interests**

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32 423 None declared

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508 **TABLES**509 **Table 1: Demographics and associated risk factors amongst latex exposed and unexposed**
510 **healthcare workers at King Edward VIII Hospital, KwaZulu-Natal South Africa, (n=501)**511
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Characteristic	Exposed N (%)	Unexposed N (%)
Number of participants	337 (67.3)	164 (32.7)
Demographics		
Age (years)		
≤30	30(8.9)	19(11.6)
>30-40	121(35.9)	40(24.4)
>40-50	101(29.9)	59(35.9)
>50	85(25.2)	46(28.1)
Duration of employment (years)		
≤5	39(11.6)	28(17.1)
>5-10**	135(40.1)	32(19.5)
>10-15	49(14.5)	17(10.4)
>15-20	24(7.1)	20(12.2)
>20*	90(26.7)	67(40.9)
Sex **		
Female	309(91.7)	95(57.9)
Male	28(8.3)	69(42.1)
Job Title (yes)		
Administrative		164(100.0)
Professional nurses	123(36.5)	
Enrolled nurses	141(41.8)	
Enrolled nursing assistants	73 (21.7)	
Medical and Personal History		
Personal history of Allergy Disease (yes)	147(43.6)	83(50.6)
Family history of Allergy Disease (yes)	197(58.5)	102(62.2)
Fruit allergy (yes)	29(8.6)	9(5.5)
Previous open surgery (yes)*	168(49.8)	61(37.2)
Work-related allergy symptoms(yes)*	138(40.9)	52(31.7)
Non-occupational latex exposure (yes)	161(47.8)	76(46.3)
Latex sensitisation (yes)	24(7.1)	5(3.1)
Current latex allergy (yes)*	20(5.9)	3(1.8)
Chi square, *p<0.05, **p<0.001		

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518 **Table 2: Comparison of risk factors between latex sensitised (skin prick test positive) and non-**
 519 **sensitised (skin prick test negative) healthcare workers at King Edward VIII Hospital, KwaZulu-**
 520 **Natal South Africa (n=501)**

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Characteristics	Latex SPT +ve [†] (29) N (%)	Latex SPT -ve [†] (472) N (%)	522 523 524
Demographics			525
Age (years.)			526
≤30	1 (3.5)	48(10.2)	527
>30-40	13 (44.8)	148(31.4)	528
>40-50	8 (27.6)	152(32.2)	529
>50	7 (24.1)	124(26.3)	530
Duration of employment			531
≤5	3(10.3)	64(13.6)	532
>5-10	16(55.2)	151(31.9)	533
>10-15	3(10.3)	63(13.4)	534
>15-20	1(3.5)	43(9.1)	535
>20	6(20.7)	151(31.9)	536
Sex (yes)			537
Male	5(17.2)	118(25.0)	538
Female	24(82.8)	354(75.0)	539
Job Title (yes)			540
Administrative	5(17.2)	159(33.7)	541
Professional nurses	5(17.2)	118(25.0)	542
Enrolled nurses	14(48.3)	127(26.9)	543
Enrolled nursing assistants	5(17.2)	68(14.4)	544
Latex Exposure			545
Exposure status(yes)	24 (82.8)	313(66.3)	546
Type of gloves			547
None	5(17.2)	165(34.6)	548
Exclusive powdered latex glove (yes)	2(6.9)	36(7.6)	549
Exclusive powder free latex glove (yes)*	11(37.9)	77(16.3)	550
Mixed (yes)	11(37.9)	198(41.9)	551
Medical and Personal History			552
Personal history of Allergy Disease (yes)	16(55.2)	214(45.3)	553
Family history of Allergy Disease (yes)	18(62.1)	281(59.5)	554
Fruit allergy (yes)*	5(17.2)	33(6.9)	555
Previous open surgery (yes)	18(62.1)	211(44.7)	556
Non-occupational latex exposure (yes)	12(41.4)	225(47.7)	557
Reaction to other latex medical devices (yes)*	3(10.3)	8(1.7)	558
Chi Square, *p<0.05			559
†Latex Skin Prick Test Positive			560
#Latex Skin Prick Test Negative			561
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567 **Table 3: Crude Odds Ratios (OR) (95%CI) of demographics, exposure status, medical and personal**
 568 **history and latex sensitisation and latex allergy amongst healthcare workers at King Edward VIII**
 569 **Hospital, KwaZulu-Natal South Africa, (n=501)**

Characteristics	N=2 9	Latex Sensitisation OR (95%CI)	N=23	LA# OR (95%CI)	570 571 572
Demographics					
Age (years)					
≤30	1	0.3(0.0-1.9)	1	0.4(0.0-2.4)	573
>30-40	13	1.8(0.8-3.7)	11	2.0(0.9-4.6)	574
>40-50	8	0.8(0.4-1.8)	7	0.9(0.4-2.2)	575
>50	7	0.8(0.4-2.1)	4	0.6(0.2-1.7)	576
Duration of employment (years)					
<5	3	0.7(0.2-2.4)	3	0.9(0.3-3.2)	577
5-10	16	2.6(1.2-5.5)*	14	3.3(1.4-7.6)*	578
>10-15	3	0.7(0.2-2.4)	3	0.9(0.3-3.2)	579
>15-20	1	0.4(0.0-2.1)	1	0.5(0.0-2.8)	580
>20	6	0.5(0.2-1.4)	2	0.2(0.0-0.8)	581
Sex (yes)					
Female	24	1.6(0.6-4.1)	20	2.2(0.7-7.2)	582
Job Title (yes)					
Administrative	5	0.4(0.2-1.1)	3	0.3(0.1-0.9)*	583
Professional nurses	5	0.6(0.2-1.6)	4	0.6(0.2-1.8)	584
Enrolled nurses	14	2.5(1.2-5.3)*	11	2.4(1.1-5.6)*	585
Enrolled nursing assistants	5	1.2(0.5-3.3)	5	1.7(0.6-4.5)	586
Latex Exposure					
Exposure status (yes)	24	2.4(0.9-6.3)	20	3.4(1.1-10.8)	587
Type of gloves					
None	5	0.4(0.2-1.0)	3	0.3(0.1-0.9)	588
Exclusive Powdered latex glove (yes)	2	0.9(0.0-3.6)	2	1.2(0.0-1.7)	589
Exclusive Powder free latex glove (yes)	11	3.1(1.4-6.8)*	10	3.1(1.7-9.1)*	590
Mixed gloves(yes)	11	0.8(0.4-1.8)	8	0.7(0.3-1.7)	591
Medical and Personal History					
Personal history of Allergy Disease (yes)	16	1.4(0.7-3.1)	12	1.3(0.5-2.9)	592
Family history of Allergy Disease (yes)	18	1.1(0.5-2.4)	14	1.1(0.5-2.4)	593
Fruit allergy (yes)	5	2.8(1.0-7.5)	5	3.7(1.4-10.4)*	594
Previous open surgery (yes)	18	1.1(0.5-2.4)	14	1.5(0.7-3.1)	595
Chi square, *p<0.05					590
† Latex Skin Prick Test Positive					591
#Latex Skin Prick Test Positive and work related clinical symptoms of allergy					592

Table 4: Multivariate analysis of demographics, medical and personal history, exposure history and latex sensitisation (LS)[†] and latex allergy (LA)[#] amongst healthcare workers at King Edward III Hospital, KwaZulu-Natal South Africa, (n=501)

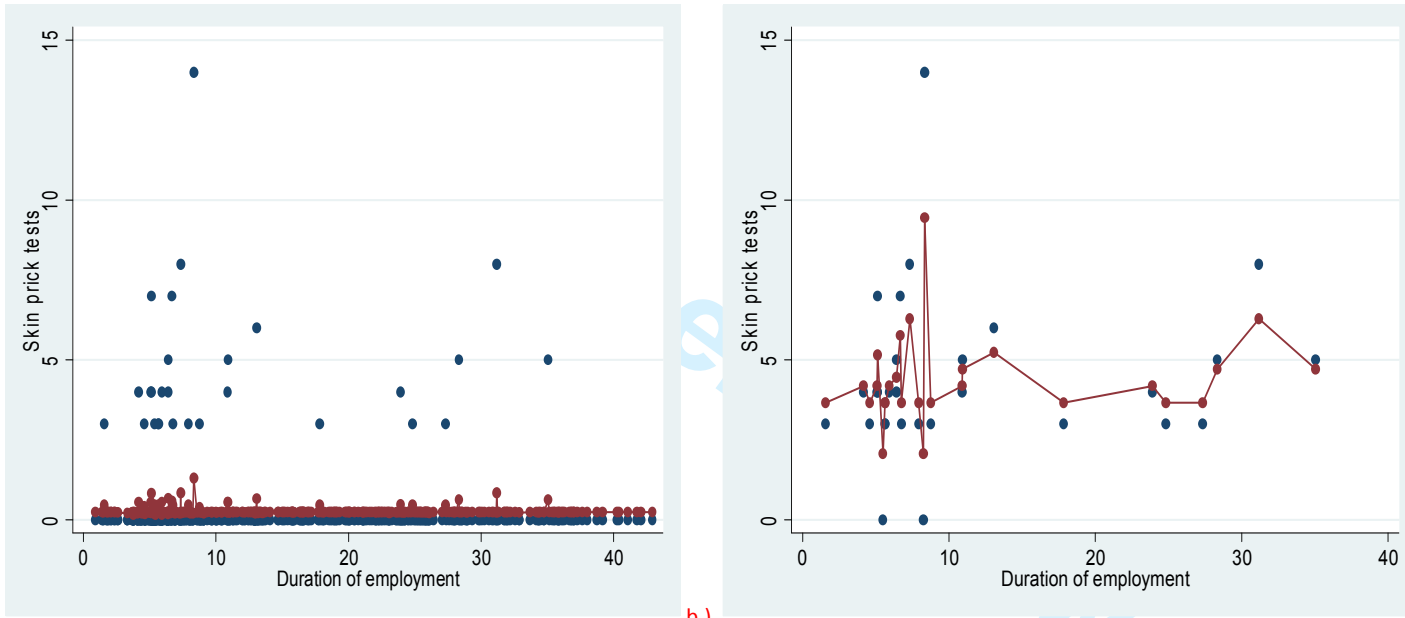
Characteristics	MODEL I* (n=501)		MODEL II** (n=501)		MODEL III***(n=202)		MODEL IV****(n=252)	
	LS OR (95%CI)	LA OR (95%CI)	LS OR (95%CI)	LA OR (95%CI)	LS OR (95%CI)	LA OR (95%CI)	LS OR (95%CI)	LA OR (95%CI)
Demographics								
Sex (female)	0.9(0.2-2.7)	1.1(0.3-4.4)	0.9(0.3-2.7)	1.1(0.3-4.5)	0.3(0.0-1.8)	0.3(0.0-3.1)	2.5(0.5-12.2)	2.5(0.5-12.2)
Duration of employment (years)	0.9(0.9-1.0)	0.9(0.8-0.9)	0.9(0.9-1.0)	0.9(0.8-0.9)	0.9(0.9-1.8)	0.7(0.5-1.0)	0.9(0.9-1.0)	0.9(0.9-1.0)
Latex Exposure								
Exposure status(yes)	2.2(0.7-6.7)	2.6(0.7-9.8)						
Type of gloves								
None			1	1				
Exclusive lightly powdered latex glove (yes)			1.6(0.3-9.8)	2.6(0.4-17.7)				
Exclusive Powder free latex glove (yes)			4.2(1.2-14.1)	5.1(1.2-21.2)				
Mixed gloves (yes)			1.7(0.5-5.6)	1.7(0.4-7.1)				

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Pairs of Powdered latex Gloves in the last 7 days					1.1(1.0-1.2)	1.2(1.0-1.4)		
Pairs of Powder Free Latex Gloves in the last 7 days							1.0(0.9-1.1)	1.0(0.9-1.1)
Personal and Medical History								
Personal history of allergy disease (yes)	1.5(0.7-3.3)	1.4(0.6-3.2)	1.5(0.7-3.3)	1.3(0.6-3.2)	1.4(0.3-6.8)	1.6(0.2-11.6)	1.0(0.4-2.9)	0.9(0.3-2.8)
Family history of allergy disease (yes)	1.0(0.45-2.2)	0.9(0.4-2.2)	1.1(0.5-2.3)	0.9(0.4-2.3)	0.4(0.1-1.9)	0.5(0.1-3.6)	0.7(0.2-2.0)	0.8(0.3-2.7)
Fruit allergy (yes)	2.3(0.8-6.7)	3.1(1.1-9.2)	2.2(0.8-6.5)	3.0(0.9-9.1)	5.0(0.4-56.9)	9.7(0.6-163.0)	1.7(0.3-8.5)	2.0(0.4-10.4)
Previous open surgery (yes)	2.0(0.9-4.4)	1.9(0.8-4.6)	2.1(0.9-4.6)	1.9(0.8-4.7)	1.4(0.3-7.4)	1.2(0.1-11.1)	1.1(0.4-3.2)	1.2(0.4-3.8)

†Latex Skin Prick Test Positive
 ‡Latex Skin Prick Test Positive and work related clinical symptoms of allergy
 *Model included latex glove exposure status
 **Model included type of gloves
 ***Model included number of pairs of powdered latex gloves
 ****Model included number of pairs of powder free latex gloves

Only



a.) b.)
Figure 1: Exposure-response relationship between duration of employment and latex sensitisation using penalised splines including a.) All participants and b) Spt positive only

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60STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest
Outcome data	15*	Report numbers of outcome events or summary measures
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses

Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

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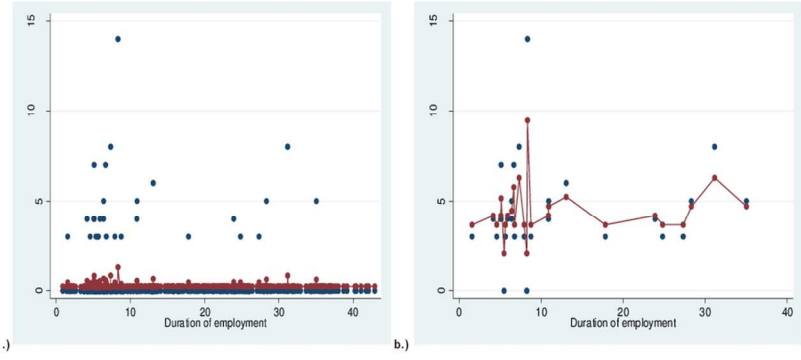


Figure 1: Exposure-response relationship between duration of employment and latex sensitisation using penalised splines including a.) All participants and b) Spt positive only

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