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Allergic contact dermatitis caused by 2-hydroxyethyl methacrylate and ethyl cyanoacrylate contained in cosmetic glues among hairdressers and beauticians who perform nail treatments and eyelash extension as well as hair extension applications: a systematic review

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Abstract and keywords

Current cosmetic regulations primarily focus on protecting consumers, not the professional user who is subjected to a partly different, and certainly more intense exposure to hazardous substances. Against this background, the present systematic review aims to compile and appraise evidence regarding skin toxicity of 2-hydroxyethyl methacrylate (HEMA; CAS no. 212-782-2) and ethyl cyanoacrylate (ECA; CAS no. 7085-85-0) contained in cosmetic glues used among hairdressers and beauticians who perform nail treatments and eyelash extension as well as hair extension applications. This systematic review followed the PRISMA 2020 recommendations for reporting systematic reviews and meta-analysis. In total, 6 publications from 6 countries were eligible for this systematic review. Meta-analysis revealed that hairdressers and beauticians have a 9-fold increased risk of developing contact allergy to HEMA compared to controls who are not hairdressers and beauticians. Results for ECA are lacking. The present systematic review clearly shows that – regarding contact allergy to acrylates – it is not appropriate to apply risk assessment for consumers to hairdressers and beauticians who occupationally handle cosmetic glues. The regulations in existence do not adequately address occupational risks for hairdressers and beauticians connected with the use of acrylate-containing cosmetic substances and need reconsideration.

Keywords: contact dermatitis, ECA, ethyl cyanoacrylate, glue, hairdresser, HEMA, occupational, occupational diseases, skin diseases, 2-hydroxyethyl methacrylate

1 Introduction

Hairdressers and beauticians constitute a high-risk cohort for developing work-related skin damage and consequently occupational skin diseases (OSD). Hand dermatitis (hand eczema, HE) is thereby the most common OSD.^{1,2} The most relevant factors that contribute to the pathogenesis of HE in this occupational group are wet work and skin contact with irritants and allergens.³⁻⁵ This skin strain in everyday working life leads to impairment of the epidermal barrier function concomitant with the induction of a proinflammatory milieu so that the risk of developing occupational contact dermatitis is increased. Initial irritant HE can easily lead to the development of allergic HE due to the fact that allergens penetrate the impaired skin barrier more easily.⁶ An adequate risk assessment regarding hazardous substances, namely allergens, is indispensable in order to initiate appropriate protective measures and to ultimately protect the (skin) health of hairdressers and beauticians.

Occupational exposure is constantly changing due to changing compositions of products at work, which presents a major challenge for conducting risk assessment in the cosmetics sector. Whilst taking the cosmetic products' instructions of use into account, it is important to consider that hairdressers and beauticians are exposed regularly and for significant hours and long periods to hazardous substances. The European Cosmetics Regulation, adopted in 2009,⁷ is primarily focused on protecting consumers, not professional users. The Scientific Committee on Consumer Safety (SCCS) does normally not assess the risk of occupational exposures and therefore almost exclusively deals with 'consumer' aspects, targeting the general public.⁸ Thereby, occupational risks associated with the use of cosmetic products are not sufficiently recognized. As one consequence, the European Commission is unable to initiate appropriate occupational risk management to adequately protect hairdressers and beauticians. This has to be regarded as highly problematic since OSD do not only entail suffering due to illness on an individual level but also present a macrosocial problem as OSD may further result in high medical treatment costs for the social insurance system as well as social consequences such as a necessary occupational change or at worst, a premature withdrawal from the labour market.⁹⁻

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Within the framework of the project "Promoting the autonomous implementation of the European framework agreement on occupational health and safety in the hairdressing sector", a series of systematic reviews has been performed.¹² One of the product categories on which a focus has been put are cosmetic glues, used in the beauty sector for applying hair extensions,

conducting nail treatments which involve the use of cosmetic (nail) glues / applying nail art, and applying eyelash extensions (Figure 1). 2-Hydroxyethyl methacrylate (HEMA; CAS no. 212-782-2) and ethyl cyanoacrylate (ECA; CAS no. 7085-85-0) were identified as target substances in cosmetic glues.

The present systematic review aims to compile and appraise clinical evidence regarding skin toxicity of HEMA and ECA contained in cosmetic glues.

2 Methods

2.1 Eligibility criteria

Eligibility criteria for studies to be included in the systematic review are reported following the PECOS scheme adapted from the *CRD's (Centre for Reviews and Dissemination) guidance for undertaking reviews in health care*¹³ (Table 1).

2.2 Information sources

Systematic searches were conducted within the electronic databases Pubmed/Medline and Web of Science–Core Collection (WoS). Assessment of risk of bias within included studies and quality of evidence assessment has been described in the protocol for this systematic review.¹² As we expected large heterogeneity in methods and outcomes, we conducted a narrative synthesis of results instead of a meta-analysis, except where quantitative pooling was feasible.

2.3 Search strategy

Searches were performed in February 2021. Furthermore, we hand searched the bibliographies of all studies identified through the electronic database search and meeting the inclusion criteria. We also performed forward-snowballing by using the six most important references identified, and checked all references citing any of these publications. This citation analysis was performed based on the WoS database. We used English search terms only. Generally, we searched for title, abstract and key words.¹² Only accepted publications newer than 1999 (i.e., 2000 and following) were considered.

2.4 Selection process

For one search query, the search results were exported from Medline and WoS in a suitable format and imported into Zotero libraries, documenting the number of references contributed by each ex-/import set. In the Zotero library, bibliographical duplicates were identified and the

entry including less information (e.g., no abstract) were discarded.¹² In case of discordant results, the entry was reviewed by a third experienced reviewer and a final decision was made. Reasons for non-inclusion were documented, and summarized at the end for use in the PRISMA-P flowchart.¹⁴

The final set of references eligible for full text screening by two reviewers were imported into a Zotero cloud-based reference database, after the initial set of references had been archived. Full text articles were, again, scrutinized and extracted independently by two reviewers, with a third senior reviewer consensualizing divergent results between the two initial reviewers. All decisions and reasons leading to the exclusion of studies were documented, providing information on the individual assessments by both initial reviewers and the final decision. At the end of this process, a set of full text articles to be included in the systematic review was identified.

2.5 Data collection process and data items

Two reviewers independently extracted the data from studies meeting the inclusion criteria using a standardized, pre-piloted publication record form (PRF). In this review, only one PRF was used for clinical patch test studies since other study types did not apply. A third senior reviewer reviewed the extracted data and made final decisions in contradictory cases. The finalized PRF was preserved and is attached as supplemental material to this systematic review.

The following basic data were extracted: Publication ID, year of study execution, country of origin, study design, methods, study setting and population involved, information on basic characteristics of participants (e.g., age, gender, ethnicity), number of participants, number of positive outcome(s), and funding source. Data on skin toxicity were sought for the outcome of skin sensitization/contact allergy in humans (e.g., numbers tested, numbers positive, test methods).

2.6 Study risk of bias assessment, reporting bias assessment and certainty assessment

Suitable criteria for assessing risk of bias (ROB) and quality of evidence were applied. Two reviewers independently appraised studies meeting the inclusion criteria after full text scrutiny without being blinded to the studies. Detailed criteria for the evaluation of quality and ROB were chosen according to Anon (2003), Pluye *et al.* (2009), and Sterne *et al.* (2019).¹⁵⁻¹⁷

2.7 Effect measures

The risk ratio regarding skin sensitization/contact allergy for hairdressers and beauticians who perform nail treatments and eyelash extension as well as hair extension applications vs. comparators/controls, i.e., people not working as hairdressers or beauticians, is provided by dividing contact allergy prevalences observed in hairdressers and beauticians by those observed in different comparator groups.

2.8 Synthesis methods

A substantial heterogeneity both in methodologies (even in the sub-categories of “experimental” and “clinical” research) and in outcomes was to be expected. Instead of a meta-analysis, we primarily conducted a narrative synthesis following guidance from the CRD.¹³ Summary tables present the main characteristics of the included studies, their finding as well as their quality rating. Notwithstanding, for a subset of eligible studies, namely those clinical patch test studies stratifying for hairdressers and beauticians who perform nail treatments and eyelash extension as well as hair extension applications vs. other “comparator” patients, a quantitative summary was feasible, in view of sufficiently uniform methodology and outcome definition. Here, graphical summaries as Forest plots with an assessment of heterogeneity (I^2) are presented.

3 Results

3.1 Study selection and study characteristics

A flow diagram of the study selection is presented in Figure 2. The initial search yielded 579 study records. Following the removal of bibliographic duplicates, 163 records were left to be screened on the full-test level. Another 8 references were found by manually searching references (i.e., backward and forward snowballing). A number of studies appeared to meet the inclusion criteria at first,¹⁸⁻³⁴ but they had to be omitted since they focused on a population that was inappropriate for this review. Case reports³⁵⁻³⁸ and case series³⁹⁻⁴⁴ were not included in the actual review, but compiled and extracted as supplemental information in case they were relevant in terms of including hairdressers and beauticians. We arrived at a final number of 6 papers after excluding publications that were extraneous to this review.

Characteristics of the included studies were recorded using a PRF (Table S 1). All included studies (n=6) were multicentric, retrospective patch test studies.⁴⁵⁻⁵⁰ Regarding the patch testing context, special series was tested in 4 studies,^{46-48,50} consecutive patients were tested in 1

study,⁴⁹ and an epidemiological sample was tested in 1 study.⁴⁵ The tested population comprised all patch test patients (n=5)^{45-48,50} or patients patch tested for occupational contact dermatitis only (n=1).⁴⁹

All of the 6 included studies reported on patch testing results for HEMA in hairdressers and beauticians who perform nail treatments and eyelash extension as well as hair extension applications.⁴⁵⁻⁵⁰ 4 of these studies also provided a comparator/control, i.e., patch test results with other occupations or without occupational context.^{46-48,50} Because of their oftentimes comparable exposure to cosmetic glues while performing diverse work tasks (nail treatments/nail art, make-up services including the application of artificial eyelashes etc.), occupational groups related to hairdressers within the cosmetic sector (manicurists, beauticians, aestheticians, nail designers etc.) were considered relevant for this systematic review.

The included studies were conducted in the European Union (EU) (n=4) (namely, Germany (n=1)⁴⁶, Portugal (n=1)⁴⁸, Spain (n=1)⁵⁰, and Sweden (n=1)⁴⁷), Australia (n=1)⁴⁹, and the United States of America (n=1)⁴⁵. All studies report on a high share of female participants (>50% for all studies).⁴⁵⁻⁵⁰

All of the 6 studies included gave information on HEMA, but none offered information on ECA regarding the inclusion criteria/target population of hairdressers and beauticians who perform nail treatments and eyelash extension as well as hair extension applications. Wetter *et al.* (2010) reported on patch test data from the Mayo Clinic, Rochester, Minnesota, USA and Scottsdale, Arizona, USA (2000-2007) concerning allergens in personal care products, whereby 1.1% of 871 patients tested with ECA gave a positive test result.⁵¹ Warshaw *et al.* (2015) looked at patch test results of the North American Contact Dermatitis Group (2011-2012) and found that of 4230 people tested for ECA, 0.3% had a positive result.⁵² Warshaw *et al.* (2020) further conducted an analysis of patch test data from the North American Contact Dermatitis Group (2001-2016) regarding contact dermatitis associated with nail care products and reported on 6.9% of 175 people tested with ECA showing a positive result.¹⁸ Results regarding patch testing of ECA in hairdressers and beauticians are lacking.

3.2 Risk of bias in studies, reporting biases, and certainty of evidence

Quality and ROB assessment (appropriate design, sampling and sample; justification of methodology; justification/presentation of results) for the 6 studies included in the present

systematic review is presented in Table S 2. All of the studies (n=6) received high scores regarding appropriate design, sampling and sample description, justification of methodology, and justification/presentation of results. As a result, we found the ROB to be low in all of the reports.

3.3 Results of individual studies

Gatica-Ortega *et al.* (2017) analyzed the files of patients diagnosed with allergic contact dermatitis caused by (meth)acrylates in long-lasting nail polish between January 2013 and June 2016 at four dermatological departments in Spain.⁵⁰ 39 of 40 (97.50%) hairdressers and beauticians who perform nail treatments and eyelash extension as well as hair extension applications were tested positive for HEMA, whereas of 2,313 other people tested 4 (0.17%) had a positive patch test result.⁵⁰

Ramos *et al.* (2014) examined data from January 2006 to April 2013 of the Dermatology Department, Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal with the aim to evaluate and correlate epidemiological and clinical parameters and positive patch test results against (meth)acrylates.⁴⁸ 20 of 35 (57.15%) tested hairdressers and beauticians who perform nail treatments and eyelash extension as well as hair extension applications had positive HEMA patch test results; 10 of 87 (11.50%) other people tested had a positive HEMA patch test result.⁴⁸

Over a ten-year period, Teik-Jin Goon *et al.* (2007) looked into patients tested to the acrylate and nail acrylics series at the Department of Occupational and Environmental Dermatology, Malmö University Hospital, Malmö, Sweden, to see if screening allergens could be discovered.⁴⁷ Of 13 included hairdressers and beauticians who perform nail treatments and eyelash extension as well as hair extension applications 8 (61.54%) were tested positive for HEMA, of 24 others tested 1 (4.16%) showed a positive test result.⁴⁷

Uter and Geier (2015) performed an analysis of patch test results with (meth)acrylates using patch test data of the Information Network of Departments of Dermatology from 2004 to 2013 to analyze the frequency of allergic contact dermatitis caused by (meth)acrylates used in artificial nails, comparing nail artists and consumers.⁴⁶ 27 of 87 hairdressers and beauticians who perform nail treatments and eyelash extension as well as hair extension applications (31.03%) and 47 of 72,157 others (0.07%) tested provided positive patch test results for HEMA.⁴⁶

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In the studies of Lyons *et al.* (2013)⁴⁹ and Warshaw *et al.* (2012)⁴⁵ a comparator/control was not available. Lyons *et al.* (2013) assessed patch testing results of hairdressers and beauticians who perform nail treatments and eyelash extension as well as hair extension applications and trainees attending the Department of Occupational Dermatology Research and Education Centre, Carlton, Australia from January 1993 to December 2010.⁴⁹ Of 164 hairdressers and beauticians who perform nail treatments and eyelash extension as well as hair extension applications, 8 (4.88%) showed positive patch test results for HEMA.⁴⁹ Warshaw *et al.* (2012) conducted an analysis on patch test data from the North American Contact Dermatitis Group generated between 1994 and 2010 and found that of 57 hairdressers and beauticians who perform nail treatments and eyelash extension as well as hair extension applications 15 (26.32%) were tested positive for HEMA.

Case reports on sensitization against HEMA are summarized in Table S 3. In 2008, Andersen *et al.* (2009) reported on a 35 old female manicurist with 14 working years in Denmark with positive patch test results against HEMA.³⁸ Kiec-Swierczynska *et al.* (2013) present a case of a 32 year old female manicurist with 3 working months in 2013 in Poland who was tested positive for HEMA as well as 2-hydroxypropyl-methacrylate (HPMA).³⁷ In 2019, Nakagawa *et al.* (2019) report on a case of a 41 year old female manicurist with 2 working years in Japan in 2019 showing a positive patch test result against HEMA and ethylene glycol dimethacrylate (EGDMA).³⁶ In Finland, it was reported by Pesonen *et al.* (2012) in 2011 about a 34 year old female cosmetician with >8 working years who had a positive patch test reaction against HEMA.³⁵

A summary of case series on sensitization against HEMA is displayed in Table S 4. DeKoven *et al.* (2017) presented a case series in which 6 female nail technicians from Canada with an age ranging from 38 to 58 years were tested positive for HEMA from 2015 to 2016.⁴⁴ Le *et al.* (2015) report in 2014 on 2 female beauticians (23 and 25 years of age) and 1 female beauty therapist (20 years of age) in Australia showing positive patch test results for HEMA, methyl methacrylate (MMA), and EGDMA.⁴³ Maio *et al.* (2012) describe the cases of 2 female nail beauticians from Portugal in 2011 with an age of 35 and 50 years who have shown positive patch test results for HEMA and HPMA.⁴² Minamoto (2014) have reported in 2013 in Japan on 1 female manicurist (35 years old) showing positive patch test results for HEMA and EGDMA.⁴¹ In 2011, Patruno *et al.* (2012) found positive patch test results against HEMA,

EGDMA, and triethylene glycol dimethacrylate (TREGMA) in 13 female beauticians in Italy.⁴⁰ Vazquez-Osorio *et al.* (2014) reported on 2 female manicurists aged 27 and 52 years in Spain in 2014 showing positive patch test results for HEMA, EGDMA, and hydroxyethyl acrylate (HEA).³⁹

There were no reports of active sensitization (i.e., the patient being newly sensitized due to the patch test procedure) in the studies reviewed.

3.4 Results of syntheses

Figure 3 presents a forest plot depicting the risk of contact allergy to HEMA of hairdressers and beauticians who perform nail treatments and eyelash extension as well as hair extension applications vs. comparators/controls. In this meta-analysis, 2 studies were included which provided data about hairdressers and beauticians who perform nail treatments and eyelash extension as well as hair extension applications as well as comparators/controls.^{46,48} The studies of Ramos *et al.* (2014)⁴⁸ and Uter and Geier (2015)⁴⁶ present narrow CIs indicating high precision. The pooled risk ratio is 8.47 [95% CI 4.70, 15.27]. Thus, hairdressers and beauticians seem to have a 9-fold increased risk of developing contact allergy to HEMA compared to controls who are not hairdressers or beauticians.

4 Discussion

In this unprecedented systematic review, aiming to compile and appraise evidence regarding skin toxicity of HEMA and ECA contained in cosmetic glues, it was found that hairdressers and beauticians who perform nail treatments and eyelash extension as well as hair extension applications are subjected to a substantially higher risk of developing contact allergy against HEMA – representing a marker allergen within the group of (meth)acrylates – compared to other people not working as hairdressers or beauticians. All included studies provided clear evidence that occupational skin contact with cosmetic glues in the beauty sector might lead to elicitation of contact dermatitis; it further cannot be ruled out that a proportion of hairdressers and beauticians might even be sensitized within their occupational surroundings. This is especially true for hairdressers and beauticians who do not appropriately protect their hands by using gloves, but even wearing gloves would not eliminate the substantial risk of sensitization because of the short break-through durations (<10min)^{53,54} of acrylates for typical gloves used in the cosmetics sector.

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It was deduced that occupational groups related to hairdressers within the cosmetic sector (manicurists, beauticians, aestheticians, nail designers etc.) have a comparable exposure as hairdressers, since exposure to cosmetic glues while performing diverse work tasks (nail treatments / nail art, make-up services including the application of artificial eyelashes etc.) is similar. An overview of selected European countries in which nail treatments and make-up services are part of the training as hairdresser shows that nail treatments are structurally integrated into the training as a hairdresser in Austria, Germany, Spain, and Switzerland; for make-up services this is the case in Austria, Denmark, and Germany (Table 2). This shows that a considerable proportion of hairdressers has a similar exposure to cosmetic glues used for conducting nail treatments and make-up services as in other occupations, e.g., cosmeticians, make-up artists etc., and that the aforementioned consideration seems to be valid.

Even though published results specifically on hairdressers and beauticians who perform nail treatments and eyelash extension as well as hair extension applications are very limited regarding sensitization to HEMA and non-existent in case of ECA, an overall substantial risk is to be expected from present data that cannot yet be fully quantified. The numerous case reports³⁵⁻³⁸ and case series^{24,39-44} on contact allergy against acrylates in those occupationally exposed in the beauty industry support this notion. Further, others acrylates such as MMA, EGDMA, TREGDMA, HPMA, and HEA were reported to be the source of allergic contact dermatitis in people working in the beauty industry.^{36,37,39-43} This highlights the prevailing problem of cross-reactions, i.e., sensitization induced by one acrylic compound extending to one or more other acrylics.^{34,55} As a result, many people sensitized to acrylics are multiply sensitized and, as a consequence, need to strictly avoid exposure to many other acrylics,⁵⁵ with the notable exception of cyano- vs. other acrylates/methacrylates which seem to not cross-react,⁵⁶ although past studies provided conflicting clinical results.^{57,58}

In view of a lack of hairdresser-specific results on ECA, we examined a random sample of eyelash glues for temporary and permanent application of eyelash extensions, nail glues, and hair extension glues regarding their ingredients. Eyelash glues for temporary application of eyelash extensions mostly comprised ethylhexyl acrylate copolymer and ammonium acrylates copolymer (Table 3); in eyelash glues for permanent application of eyelash extensions, mostly ECA was found (Table 3). All of the nail glues within our random sample contained ECA (Table 4). Cases of ECA contact allergy in the context of false eyelashes reported by Shanmugam and Wilkinson (2012) as well as Sato *et al.* (2017) illustrate that cosmetic use of

ECA might entail some risk of sensitization and a risk of elicitation in sensitized individuals.^{59,60} Hair extension glues, like eyelash glues for temporary application, have also been shown to contain acrylates (Table 5). Although acrylate (co-)polymers are generally considered safe in terms of sensitization risk, residual monomers might pose a – yet unfathomed – risk at least for those already sensitized to the respective monomer from other sources. The sparse data situation on sensitization to specific acrylates in hairdressers and beauticians however points to an existing research gap which should be examined in further studies. Regarding inclusion of ECA in a hair cosmetic patch test series, only anecdotal evidence is yet available concerning actual sensitisation and allergic contact dermatitis due to cosmetic products containing ECA. Hence, despite the considerable exposure, we would at present not recommend to add ECA to a hair cosmetic series, but suggest aimed testing in case of a – usually very clear – history.

Current articles by Romita *et al.* (2020) and Sterkens *et al.* (2021) report on the increasing use of (meth)acrylates in gel nail polishes – such as daylight curing ‘hybrid’ gel nail polish – and their role as sensitizers.^{61,62} This again stresses how (occupational) exposure is always shifting due to changing product compositions especially at work, posing a significant obstacle for completing a health risk assessment in the beauty industry. At this point it should be mentioned that in terms of exposure hairdressers and beauticians might be burdened twofold – as professionals and as consumers themselves. It further might be assumed that a proportion of hairdressers and beauticians is presumably not aware of the health risk that cosmetic glues can pose. A case report by Isaksson *et al.* (2007) stresses the importance of preventing sensitization against acrylates as – in this presented case – allergic contact dermatitis elicited by ECA used whilst applying artificial nails led to months of sick leave.⁶³ Moreover, the reported risk of severe burns by nail glues should be mentioned which can happen when cyanoacrylate-containing glues get on textiles/clothes in contact with skin.⁶⁴⁻⁶⁶

By dint of the results of the present systematic review it seems appropriate that prevention strategies are developed for raising awareness in hairdressers and beauticians about the risk that handling cosmetic glues – especially without adequate protection – might entail. Such topical information (in any medial format) could be prepared under health pedagogical considerations and might be then presented within the framework of health education programs. This might also apply to other occupational fields for which relevant acrylate exposure has been evidenced in previous studies, such as dental personnel.⁶⁷⁻⁷² The German Social Accident Insurance (DGUV) has recognized the problem for dental personnel and initially launched information

brochures about acrylate allergy and its prevention. These existing informational materials might serve as a point of entry for developing potential awareness campaigns and future training measures tailored to the needs of workers in occupational groups exposed to acrylates.⁷³

The present systematic review clearly shows that it is not appropriate to assess the risk of hairdressers and beauticians who handle cosmetic glues within their occupational surroundings regarding contact allergy to acrylates the same way as the risk of other people not working as hairdressers and beauticians such as consumers or clients. It was confirmed that the occupational risks associated with the use of cosmetic products are not sufficiently recognized by the regulations in force. The current SCCS opinion on the use of HEMA for nail cosmetics (SCCS/1592/17) seems not to be satisfactory for protecting hairdressers and beauticians who perform nail treatments and eyelash extension as well as hair extension applications.⁷⁴ The results of this paper point in favour of the notion that presumably an increase of the prevalence of sensitization against acrylates – such as HEMA – and consequently of contact dermatitis from cosmetic products containing acrylates might be expected in the future.⁷⁴ The proven higher risk of hairdressers and beauticians regarding development of contact allergy against acrylates should lead to reconsidering current risk assessment. Only this way it will be possible to efficiently contribute to prevention of OSD in terms of HE in hairdressers and beauticians – according to the minimum standards set out in the position paper of the COST Action StanDerm (TD 1206)⁷⁵ – to obviate personal suffering due to illness as well as high costs for the social insurance system and consequently the general population.

5 Other information

5.1 Registration and protocol

This systematic review has been registered in the International Prospective Register of Systematic Reviews (PROSPERO) under the registration number CRD42021238118.⁷⁶ The protocol has been published elsewhere.¹² No amendments to the information provided at registration or in the protocol were made.

5.2 Support

This systematic review is supported by a grant from Uni Europa–The European Global Services Union (Project VS/2019/0440: “Promoting the autonomous implementation of the European framework agreement on occupational health and safety in the hairdressing sector”). Other than being given the opportunity to provide input in the initial Delphi process to identify relevant

substances, the sponsor had no role in the development, nor in the performance of the systematic review and the publication of its results.

5.3 Competing interests

W.U. has received an honorarium for a lecture on contact allergy from mixed dermatopharmaceutical sponsors (GEIDAC, Toledo, Sept. 2018) and travel reimbursement for participation in study meetings of the IDEA project (IFRA). W.U. is external expert for the SCCS. Other authors: None to declare.

5.4 Availability of data, code and other materials

Data, code and other materials other than included in the PROSPERO registration⁷⁶ and the previously published protocol¹² are available from the corresponding author upon reasonable request.

6 References

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7 Tables

Table 1: Eligibility criteria following the PECOS scheme

Criterion	Inclusion	Exclusion
Participants	Hairdressers and beauticians who perform nail treatments and eyelash extension as well as hair extension applications†, Patients, Products	None
Exposure	Exposure to (an) eligible chemical(s)‡	n/a
Comparator	Clients, Consumers, normal Population (no or less exposure)	n/a
Outcome	Skin toxicity event (contact allergy, irritancy)	n/a
Study design	Experimental studies Observational studies	Qualitative studies Case reports Case series

†, hairdressers and related occupational groups (manicurists, beauticians, aestheticians, nail designers etc.) do oftentimes have a comparable exposure to cosmetic glues whilst conducting diverse work tasks (nail treatments / nail art, make-up services including the application of artificial eyelashes etc.); ‡, 2-Hydroxyethyl methacrylate (HEMA, substance identifiers: 2-Hydroxyethyl methacrylate, 868-77-9, HEMA, methacrylic acid, 2-hydroxyethyl ester (6CI,8CI), methacrylic acid, ester with glycol (7CI), 2-(Methacryloyloxy)ethanol, 2-HEMA, 2-Hydroxyethyl 2-methylprop-2-enoate, ethylene glycol methacrylate, ethylene glycol monomethacrylate, glycol methacrylate, glycol monomethacrylate, β -Hydroxyethyl methacrylate) and ethyl cyanoacrylate (ECA, substance identifiers: ethyl cyanoacrylate, 7085-85-0, acrylic acid, 2-cyano-, ethyl ester (6CI,7CI,8CI), 2-Cyano-2-propenoic acid ethyl ester, 2-Cyanoacrylic acid ethyl ester, ethyl 2-cyanoacrylate, ethyl 2-cyanopropenoate, ethyl α -cyanoacrylate);¹² n/a, not applicable.

Table 2: Overview of selected European countries in which nail treatments and make-up services are part of the training as hairdresser

Country	Nail treatments†		Make-up services‡	
	Included?	Structural integration within the training	Included?	Structural integration within the training
Austria	yes	Framework curriculum for the apprenticeship as hairdresser: specialized classes / specialist knowledge and specialized internship	yes	Framework curriculum for the apprenticeship as hairdresser: specialized internship
Croatia	no	n/a	no	n/a
Denmark	no	n/a	yes	Framework curriculum for the apprenticeship as hairdresser: make-up course
France	no	n/a	no	n/a
Germany	yes	Framework curriculum for the apprenticeship as hairdresser: learning area 10: hand care and nail design	yes	Framework curriculum for the apprenticeship as hairdresser: learning area 11: using decorative cosmetics
Netherlands	no	n/a	no	n/a
Portugal	no	n/a	no	n/a
Spain	yes	Framework curriculum for the apprenticeship as hairdresser: professional module 10 (includes manicure and pedicure)	no	n/a
Switzerland	yes	Framework curriculum for the apprenticeship as hairdresser: elective manicure	no	n/a
United Kingdom	no	n/a	no	n/a

† manicures, artificial nails / nail design etc.; ‡ day make-up, evening make-up, bridal make-up etc.; n/a, not applicable

Table 3: Random sample of eyelash glues for temporary and permanent application of eyelash extensions sold within the European Union (EU) in local drugstores and/or perfumeries or in online shops along with their ingredients according to the International Nomenclature of Cosmetic Ingredients (INCI)

Product name	Manufacturer	Ingredients†
Eyelash glues for temporary application (around 24h) of eyelash extensions		
Artdeco Eyelash Adhesive	Artdeco cosmetic GmbH, Karlsfeld, Germany	acrylates/ethylhexyl acrylate copolymer, aqua (water), alcohol, propylene glycol, sodium benzoate
Adhesive Naomi Jon Tool Set	Melody Lashes GmbH, Hamburg, Germany	acrylate copolymer, aqua, hydroxypropylcellulose, CI 77491, fragrance
Catrice Lash Glue 010	cosnova GmbH, Sulzbach am Taunus, Germany	acrylates/ethylhexyl acrylate copolymer, aqua (water), phenoxyethanol

Product name	Manufacturer	Ingredients†
DUO Quick Set Adhesive Clear	bacodi GmbH, Wiesbaden, Germany	acrylates/ethylhexyl acrylate copolymer, alcohol denat, amp-acrylates copolymer, phenoxyethanol, ethylhexylglycerin
DUO Quick Set Adhesive Dark	bacodi GmbH, Wiesbaden, Germany	acrylates/ethylhexyl acrylate copolymer, alcohol denat, amp-acrylates copolymer, phenoxyethanol, ethylhexylglycerin, citric acid, sorbitol, sodium carbonate, cetareth-25, carbon black (CI 77266)
DUO Eyelash Adhesive Line It Lash It	bacodi GmbH, Wiesbaden, Germany	water (aqua, eau), ammonium acrylates copolymer, glycerin, styrene/acrylates/ammonium methacrylate copolymer, 1,2-hexanediol, pentylene glycol, potassium sorbate, xanthan gum, butylene glycol, caprylyl glycol, c11-15 pareth-7, sodium laureth-12 sulfate, tetrasodium edta, sodium lauryl sulfate, disodium laureth sulfosuccinate, phenoxyethanol, iron oxides (CI77499)
Duo 2-in-1 Brush On Adhesive	Ardell International, Inc., California, USA	acrylates/ethylhexyl acrylate, copolymer, water (eau, aqua), retinol, ascorbic acid, tocopherol, cetareth-25, propylene glycol, peg-60 hydrogenated castor oil, glycerin, phenoxyethanol, iron oxides (CI 77499)
essence cosmetics Peel off Lash Glue	cosnova GmbH, Sulzbach am Taunus, Germany	rubber latex, aqua (water), sodium dodecylbenzenesulfonate, cellulose gum, dimethicone, ethylhexylglycerin, phenoxyethanol, sodium benzoate
Eylure 18H Lash Glue Latex Free Clear	Original Additions Beauty Products Ltd, Hayes, UK	acrylates/ethylhexyl acrylate copolymer, aqua / water, propylene glycol, bambusa vulgaris (bamboo) extract, camellia sinensis (tea) leaf extract, phenoxyethanol, ethylhexylglycerin, butylene glycol
Eylure 18H Lash Glue Latex Free Acrylic Black	Original Additions Beauty Products Ltd, Hayes, UK	acrylates/ethylhexyl acrylate copolymer, aqua / water, propylene glycol, bambusa vulgaris (bamboo) extract, camellia sinensis (tea) leaf extract, citric acid, sorbitol, cetareth-25, sodium carbonate, phenoxyethanol, ethylhexylglycerin, butylene glycol, carbon black
fesh! Eyelash Adhesive	KTN Dr. Neuberger GmbH, Wiesbaden, Germany	acrylates/ethylhexyl acrylate copolymer, aqua, propylene glycol, phenoxyethanol, ethylhexylglycerin
Hollybee Cosmetics Lash Glue	Kafa Safari GmbH, Berlin, Germany	water, cellulose gum, sodium dodecylbenzenesulfonate, rubber latex, parfum, formalin solution, ammonium hydroxide
Huda Beauty Lash Glue	HB USA Holdings, Inc., California, USA	rubber latex, sodium dodecylbenzenesulfonate, cellulose gum, methylparaben, carbon black / CI 77266
Kiss Everlasting Strip Eyelash Adhesive - Clear	Kiss products Inc., Washington, USA	acrylates/ethylhexyl acrylate copolymer, water (aqua), propylene glycol, butylene glycol, aloe barbadensis leaf extract, phenoxyethanol, triethanolamine, carbomer, ethylhexylglycerin, fragrance (parfum), citral, citronellol, limonene, geraniol, hexyl cinnamal, linalool

Product name	Manufacturer	Ingredients†
Kiss Lash Glue liner black	Kiss products Inc., Washington, USA	water (aqua), acrylates/ethylhexyl, acrylate copolymer, acrylate copolymer, alcohol, 1,2-hexanediol, peg-40, hydrogenated castor oil, sodium dehydroacetate
Kiss Lash Glue liner clear	Kiss products Inc., Washington, USA	water (aqua), acrylates/ethylhexyl, acrylate copolymer, acrylate copolymer, alcohol, 1,2-hexanediol, peg-40, hydrogenated castor oil, sodium dehydroacetate
Melody Lashes Glued Adhesive	Melody Lashes GmbH, Hamburg, Germany	rubber latex, acrylates copolymer, aqua, cellulose gum, ricinus communis (castor) seed oil, chamomilla recutita (matricaria) flower oil
Eyelash glues for permanent application (>1week) of eyelash extensions		
Ardell LashTite Adhesive Clear	Ardell International, Inc., California, USA	propylene glycol methyl ether acetate, nitrocellulose, sd alcohol 40-b, iron oxide
Artdeco Adhesive For Permanent Lashes	Artdeco cosmetic GmbH, Karlsfeld, Germany	methoxyisopropyl acetate, alcohol denat., nitrocellulose
DUO Individual Lash Adhesive clear	Ardell International, Inc., California, USA	water, rubber latex, cellulose gum, sodium dodecylbenzenesulfonate, ammonium hydroxide, fragrance, coumarin, geraniol, limonene, linalool, formaldehyde
Jolifin Lashes Eyelash Glue 1-2sec, high viscosity	Jolifin LJV GmbH, Babenhausen, Germany	ethyl-2-cyanoacrylate, polyurethane, BHA, diisononyl adipate, sorbic acid, carbon black
Lankiz Lash Extension Glue	Hymax Company Ltd., London, UK	cyanoacrylate, polymethylmethacrylate, carbon black
Lavertu Glue 0,5-1sec‡	Fresa Cosmetics B.V., Vught, The Netherlands	ethyl cyanoacetate, cyanoacrylate, polymethylmethacrylate, carbon black, poly isocyanate water, cyanoacrylate polymethyl methacrylate
Lavertu Glue 1-2sec§	Fresa Cosmetics B.V., Vught, The Netherlands	ethyl cyanoacetate, cyanoacrylate, polymethylmethacrylate, carbon black, poly isocyanate water, cyanoacrylate polymethyl methacrylate
Maxi Soft Glue	Eyemee The Beauty Co., Ltd., Seoul, Korea (South)	2-ethoxyethyl-2-cyanoacrylate, polymethyl methacrylate, CI 77866

† according to the International Nomenclature of Cosmetic Ingredients (INCI), as listed by the manufacturer; ‡ advertised longevity of 7-8 weeks; § advertised longevity of 8-9 weeks; UK, United Kingdom; USA, United States of America

Table 4: Random sample of nail glues sold within the European Union (EU) in local drugstores and/or perfumeries or in online shops along with their ingredients according to the International Nomenclature of Cosmetic Ingredients (INCI)

Product name	Manufacturer	Ingredients†
Ardell Nail Addict Professional Nail Glue	Ardell International, Inc., California, USA	ethyl cyanoacrylate, polymethyl methacrylate, BHA, red 7 (CI 15850)
Artdeco Nail Glue	Artdeco cosmetic GmbH, Karlsfeld, Germany	ethyl cyanoacrylate, polymethyl methacrylate
essence cosmetics fix it! nail glue violet	cosnova GmbH, Sulzbach am Taunus, Germany	ethyl cyanoacrylate, polymethyl methacrylate, aqua (water), alcohol
Elegant Touch Brush On Nail Glue	PDC Brands, Hayes, UK	ethyl cyanoacrylate, polymethyl methacrylate, BHT

Product name	Manufacturer	Ingredients†
Elegant Touch Quick Dry Nail Glue	PDC Brands, Hayes, UK	ethyl cyanoacrylate, polymethyl methacrylate, BHT, BHA
Kiss Maximum Speed Nail Glue	OBELIS S.A., Brussels, Belgium	ethyl cyanoacrylate, polymethyl methacrylate, BHA
Kiss Brush-On Nail Glue	OBELIS S.A., Brussels, Belgium	ethyl cyanoacrylate, polymethyl methacrylate, BHA, tetrahydrofuran, sulfur dioxide
Kiss Precision Nail Glue	Kiss products Inc., Washington, USA	ethyl cyanoacrylate, polymethyl methacrylate, BHA, undecylenic acid
Kiss Maximum Speed Nail Glue pink	Kiss products Inc., Washington, USA	ethyl cyanoacrylate, polymethyl methacrylate, BHA, tetrahydrofuran, red 7 lake (CI 15850:1)

† according to the International Nomenclature of Cosmetic Ingredients (INCI), as listed by the manufacturer; UK, United Kingdom; USA, United States of America

Table 5: Random sample of hair (extension) glues sold within the European Union (EU) in local drugstores and/or perfumeries or in online shops along with their ingredients according to the International Nomenclature of Cosmetic Ingredients (INCI)

Product name	Manufacturer	Ingredients†
Fidentia Bond Glue	Fidentia Professional Line, Weil der Stadt, Germany	xanthan gum, glycerin, water, acrylate copolymer, non phenol ethoxylate, colour white
Fidentia Bond Glue Pen	Fidentia Professional Line, Weil der Stadt, Germany	xanthan gum, glycerin, water, acrylate copolymer, non phenol ethoxylate, colour white
Walker 1.4 OZ Great White Adhesive	Walker Tape Co., West Jordan, USA	purified water, hydrophobic acrylic copolymer resins
Liquid Gold Extra Strong	Rapunzel of Sweden AB, Umeå, Sweden	p-chlorobenzonzoic acid, ethyl alcohol, methyl acetate, petroleum hydrocarbon resin, rosin ester and styrene-isoprene block copolymer

† according to the International Nomenclature of Cosmetic Ingredients (INCI), as listed by the manufacturer; USA, United States of America

8 Figures



Figure 1: Usual application of eyelash glue / adhesive onto a) so-called cluster eyelash extensions and b) a so-called eyelash band. The eyelash glue is usually placed on the back of the hand and the eyelash extension is then dipped into the glue with the help of tweezers. Oftentimes, the remaining eyelash glue dries on the hand and the residue will only be removed at the end of the working day exposing the hairdresser or beautician to the substances contained in the cosmetic glue for a considerable amount of time. Exposure might also be given when gloves are worn due to the short break-through times ($<10\text{min}$)^{53,54} of acrylates for most gloves used in the cosmetic sector. Thus, even wearing gloves would not alleviate the high risk of sensitization.

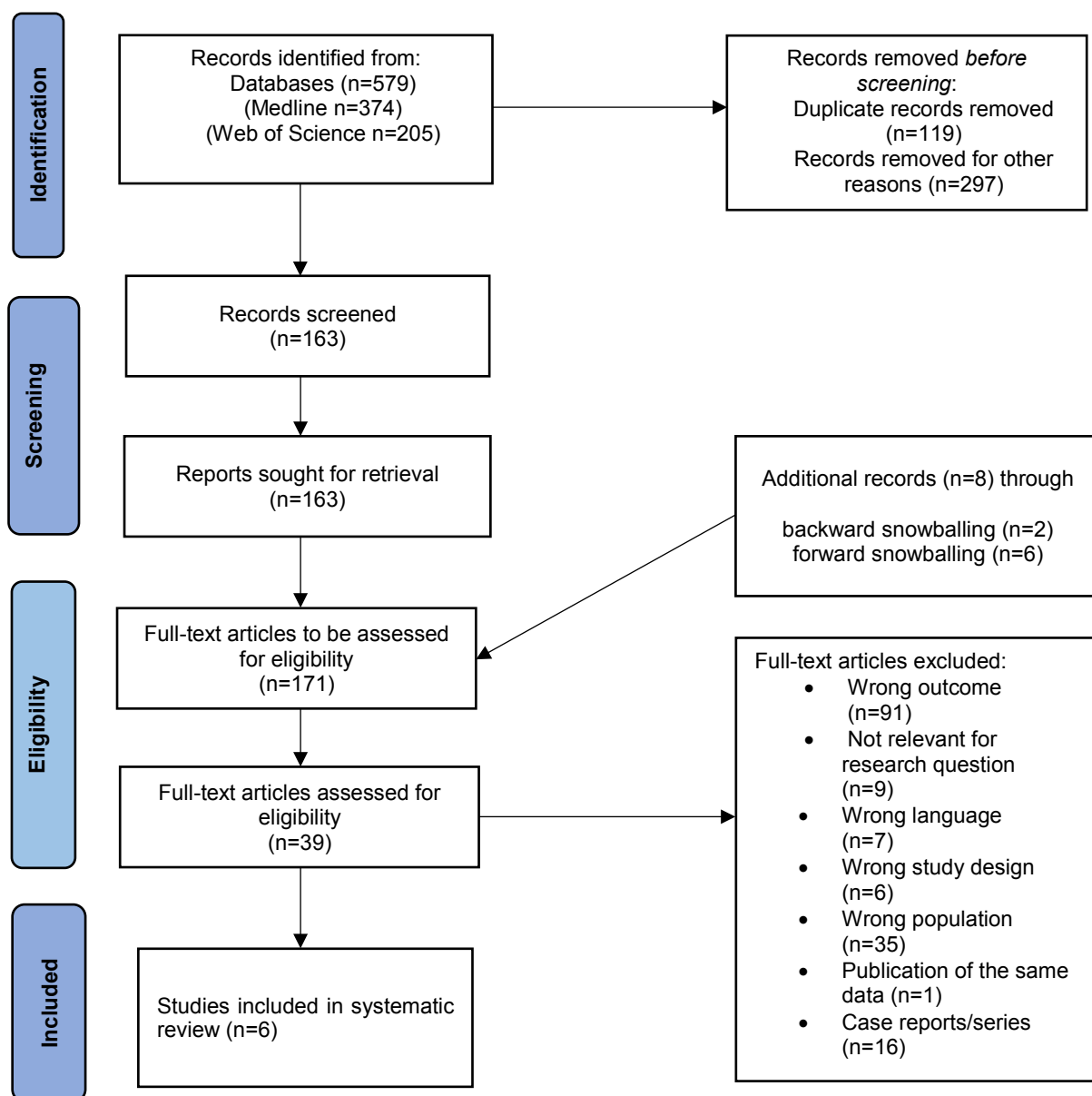
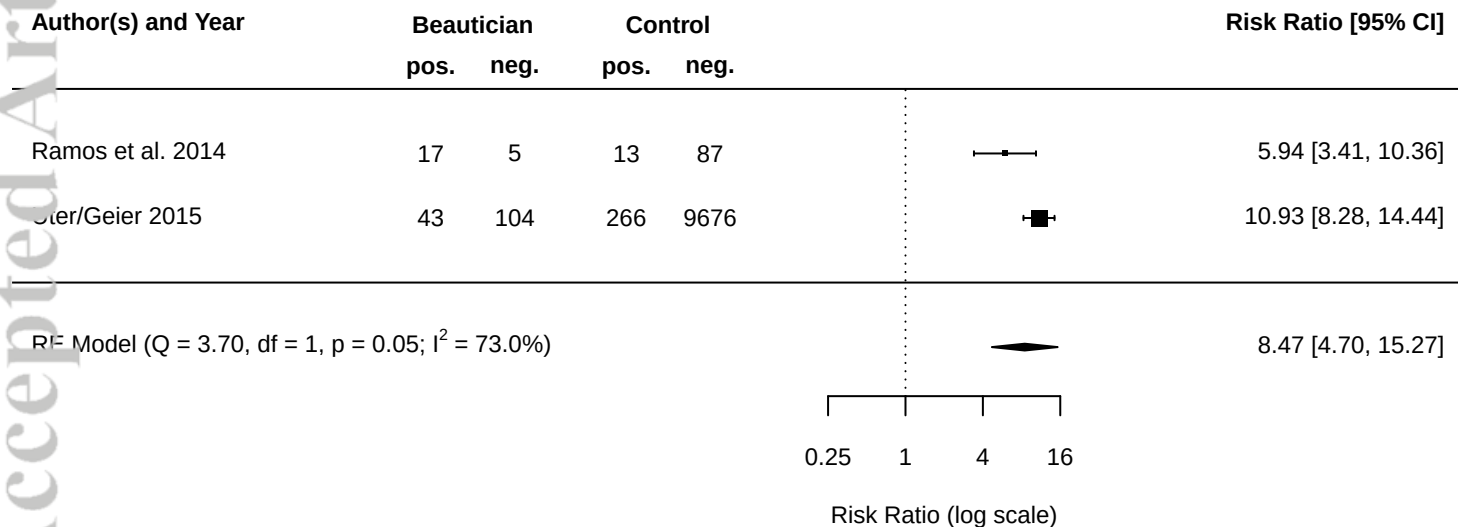


Figure 2: Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) 2020 flow diagram of literature search according to Page *et al.* (2021)⁷⁷

Figure 3: Forest plot regarding the risk ratio of hairdressers and beauticians who perform nail treatments and eyelash extension as well as hair extension applications vs. others/non-hairdressers and non-beauticians for HEMA. The controls comprise: other patch test patients patch tested with a special acrylate series, including consumers as well as occupationally exposed individuals in Ramos *et al.* (2014)⁴⁸ and Uter and Geier (2015)⁴⁶



9.2 Appendix 2 Quality and risk of bias (ROB) assessment

Table S 2: Quality and Risk of bias (ROB) assessment with reference to Anon (2003)¹⁶, Pluye *et al.* (2009)¹⁵, and Sterne *et al.* (2019)¹⁷ for the 6 studies included in the present systematic review.

Study	AD: Appropriate design, sampling and sample†							JM: Justification of methodology‡				JR: Justification/presentation of results§				
	AD1	AD2	AD3	AD4	AD5	AD6	AD total	JM1	JM2	JM3	JM total	JR1	JR2	JR3	JR4	JR total
Gatica-Ortega <i>et al.</i> (2017)	1	1	2	1	1	1	7	1	2	1	4	1	0.5	1	1	3.5
Lyons <i>et al.</i> (2013)	1	1	1	1	1	1	6	1	2	1	4	1	1	1	1	4
Ramos <i>et al.</i> (2014)	1	1	2	1	1	1	7	1	2	1	4	1	1	1	1	4
Teik-Jin Goon <i>et al.</i> (2007)	1	0.5	2	1	1	0.5	6	1	2	1	4	1	0.5	1	1	3.5
Uter and Geier (2015)	1	1	2	1	1	1	7	1	2	1	4	1	1	1	1	4
Warshaw <i>et al.</i> (2012)	1	1	2	1	1	1	7	1	2	1	4	1	1	1	1	4

† maximum score: 7 points; ‡ maximum score: 4 points; § maximum score: 4 points; AD1, appropriate, scientifically based study design; AD2, appropriate sample size; AD3, appropriate sample description; AD4, selection bias; AD5, information bias; AD6, funder/sponsoring documented; JM1, appropriate, scientifically based methodology; JM2, adequate use and description of methods; JM3, validation/standardization of used methods; JR1, results clearly and completely documented; JR2, appropriate statistical techniques; JR3, all measurements mentioned in the methods are reported; JR4, independent peer review

9 Appendices

9.1 Appendix 1: Publication record form (PRF)

Table S 1: Publication record form (PRF) for documenting key characteristics of the 24 studies included in this systematic review. Results regarding 2-hydroxyethyl methacrylate (HEMA) are displayed

Study	Year (range)	Country	Study design	Patch testing†	Patch testing context	Population tested	Female (%)	Age (years)	No. of hair-dressers and beauticians who perform nail treatments and eyelash extension as well as hair extension applications tested	No. of hair-dressers and beauticians who perform nail treatments and eyelash extension as well as hair extension applications with a positive result‡	No. of others tested	No. of others tested with a positive result‡	Funder
Gatica-Ortega <i>et al.</i> (2017)	2013-2016	Spain	multicentric, retrospective	yes	special series	all patch test patients	64.3	63.2% >40 years	40	39	2,313	4	n/a
Lyons <i>et al.</i> (2013)	1993-2010	Australia	monocentric, retrospective	yes	consecutive patients	occupational patch test patients	95.7	23 (mean)	164	8	none	none	n/a
Ramos <i>et al.</i> (2014)	2006-2013	Portugal	monocentric, retrospective	yes	special series	all patch test patients	91.8	n/a	35	20	87	10	none
Teik-Jin Goon <i>et al.</i> (2007)	1995-2004	Sweden	monocentric, retrospective	yes	special series	all patch test patients	57.7	19-63, mean: 41.5	13	8	24	1	Avtal om Läkarutbildning och Forskning (ALF), Sweden, and the ExxonMobil—National University of Singapore (NUS) Research Fellowship for clinicians, Singapore
Uter and Geier (2015)	2004-2013	Germany	multicentric, retrospective	yes	special series	all patch test patients	63.1	n/a	87	27	72,157	47	n/a
Warshaw <i>et al.</i> (2012)	1994-2012	United States of America	multicentric, retrospective	yes	epidemiological sample	all patch test patients	64.7	n/a	57	15	n/a	n/a	none

† other methods than patch testing were not used within the presented set of studies; ‡ regarding acrylates; n/a, not available

9.3 Appendix 3: Case reports and case series

Table S 3: Case reports

Study	Year(s)	Country	Age	Gender	Occupation	Working years	Results of own products tested	Positive PT results†
Andersen <i>et al.</i> (2009)	2008	Denmark	35	female	manicurist	14	n/t	HEMA
Kiec-Swierczynska <i>et al.</i> (2013)	2013	Poland	32	female	manicurist	3 months	n/t	HEMA, HPMA
Nakagawa <i>et al.</i> (2019)	2019	Japan	41	female	manicurist	2	n/t	HEMA EGDMA
Pesonen <i>et al.</i> (2012)	2011	Finland	34	female	cosmetician	>8	n/t	HEMA

† regarding acrylates; EGDMA, ethylene glycol dimethacrylate; HEMA, 2-hydroxyethyl methacrylate; HPMA, 2-hydroxypropyl-methacrylate; n/t, not tested; PT, patch test

Table S 4: Case series

Study	Year(s)	Country	Age (years)	Gender	Occupation	Working years	Results of own products tested	Positive PT results†
DeKoven <i>et al.</i> (2017)	2015-2016	Canada	38-58	female	6 nail technicians	>5	n/t	HEMA
Le <i>et al.</i> (2015)	2014	Australia	23, 35, 20, 24	female	2 beauticians, 1 beauty therapist, 1 nurse	n/a, 18 months, 4 years, n/a	yes, no, yes, n/t	HEMA, MMA, EGDMA
Maio <i>et al.</i> (2012)	2011	Portugal	35, 50	female	2 nail beauticians	n/a	yes	HEMA, HPMA
Minamoto (2014)	2013	Japan	35, 30	female	1 manicurist, 1 dental hygienist	n/a, 7	n/t, yes	HEMA, EGDMA
Patruno <i>et al.</i> (2012)	2011	Italy	n/a	female	13 beauticians	n/a	n/t	TREGDMA, HEMA, EGDMA
Vazquez-Osorio <i>et al.</i> (2014)	2014	Spain	27, 52	female	2 manicurists	n/a	n/t	HEMA, EGDMA, HEA

† regarding acrylates; EGDMA, ethylene glycol dimethacrylate; HEA, hydroxyethyl acrylate; HEMA, 2-hydroxyethyl methacrylate; HPMA, 2-hydroxypropyl-methacrylate; MMA, methyl methacrylate; n/a, not available; n/t, not tested; PT, patch test; TREGDMA, triethylene glycol dimethacrylate