Outbreak of occupational allergic contact dermatitis from a smartphone screen protector glue

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Abstract

Background: Sensitization to acrylates is a concern in the occupational/environmental dermatology field.

Objective: To describe an occupational allergic contact dermatitis (ACD) outbreak from a smartphone screen protector glue.

Methods: Thirteen affected workers of a chain store selling phone screen protectors were investigated in five Spanish dermatology departments. The glue datasheet and label were assessed. A chemical analysis of the glue was performed. Based on this, some patients underwent additional testing.

Results: All patients (all female, mean age: 25) had severe fingertip dermatitis. The datasheet/label indicated that the glue contained isobornyl acrylate (IBOA), a “photoinitiator” and polyurethane oligomer. The company informed us that the ingredients were polyurethane acrylate, “methacrylate” (unspecified), acrylic acid, hydroxyethyl methacrylate, propylmethoxy siloxane, and photoinitiator 184. Isobornyl acrylate (or IBOA) and N,N-dimethylacrylamide (DMAA) were patch tested in eight and two cases, respectively, with negative results. A chemical analysis revealed 4-acryloylmorpholine (ACMO); isobornyl methacrylate (IBMA), and lauryl acrylate in one glue sample. Seven patients were patch tested with dilutions of the identified substances and six of seven were positive for ACMO 0.5% pet.

Conclusion: An outbreak of occupational ACD, likely from ACMO in a glue is described. Further investigations are needed to corroborate the role played by each compound identified in the chemical analyses.

Keywords
4-acryloylmorpholine, ACMO, acrylates, allergic contact dermatitis, case series, glue, isobornyl acrylate (IBOA), isobornyl methacrylate (IBMA), lauryl acrylate, smartphone
1 | INTRODUCTION

Occupational allergic contact dermatitis (ACD) from constituents of glues and adhesives have been described involving a variety of allergens such as acrylates and epoxy compounds; biocides (eg, 3-dibromo-2,4-dicyanobutane; N-methylol-chloroacetamide, chloromethylisothiazolinone/methylisothiazolinone; 1,2-benzisothiazolin-3-one; colophony, and so on). A variety of professions has been described to develop ACD from glues such as beauticians, cloggers and shoe manufacturers, workers performing manual or automatized labeling, carpenters, machinists, physiotherapists, upholsterers, carpenters, machinists, and so on. A mixture of a drop of the glue with a similar volume of pentamethylisothiazolinone, labels of the containers of the glue product and contacted the phone as manicure products with acrylates). A variety of professionals has been described to develop ACD from glues such as beauticians, cloggers and shoe manufacturers, workers performing manual or automatized labeling, carpenters, machinists, physiotherapists, upholsterers, carpenters, machinists, and so on.

We hereby describe an outbreak of occupational ACD from a glue product designed to attach tempered glass screen protectors to curved smartphones screens. Several workers of a Spanish company selling mobile phone tempered glass screen protectors were involved. The glue is available in kits for professional use that include a small ultraviolet lamp. These kits are also available to be purchased by the general consumer.

There are two previous independently published case reports of ACD from the same glue product involving two women: one employee of the aforementioned phone screen protector chain store who glued tempered glass screen protectors to her customers’ curved phones at work and another woman who got her Apple watch glued to a tempered glass screen protector in a store of the same brand. Both were sensitized to isobornyl acrylate (IBOA), and the latter to many additional acrylates. Because IBOA was declared on the label, it was considered of current relevance in those cases.

2 | MATERIAL AND METHODS

We performed a descriptive study on a case series of occupational ACD from a glue product marketed to attach curved tempered glass screen protectors to smartphone screens. Several workers of a Spanish chain store selling mobile phone screen protectors were involved.

2.1 | Epidemiological and clinical data assessment

Epidemiological and clinical data (such as age, sex, latency time from the first exposure to the beginning of the lesions, symptoms, body sites involved, evolution, patch test results, exposure to other sources of acrylates and associated reactions from them) were evaluated retrospectively from the clinical histories. We specifically evaluated the prior exposures and reactions from nail aesthetic materials containing acrylates (a variety of techniques applied to the nails with aesthetic purposes containing acrylates or methacrylates including acrylic nails, gel nails, long-lasting nail polish, and fake nails, hereafter referred to as manicure products with acrylates).

In addition, we assessed the technical datasheets as well as the labels of the containers of the glue product and contacted the phone protector company to request additional information regarding the composition of the product.

2.2 | Patch test investigations

We performed patch tests with the Spanish Contact Dermatitis Research Group (GEIDAC) and the acrylate series (Table S1). In addition, in some patients, patch tests were performed with samples of their own glue brought in by them to our office. We also patch tested IBOA 0.1% pet. from Chemotechnique Diagnostics (Vellinge, Sweden) and N,N-dimethyl acrylamide (DMAA) 0.1% pet. obtained from Department of Occupational and Environmental Dermatology, Malmö (Sweden) in eight cases and two cases, respectively; and the isocyanate series in one patient (case 9); and the plastic and glue series, in another patient (case 11). Occlusion times, reading times, and scoring of the reactions were performed according to the European Guidelines. A mixture of a drop of the glue with a similar volume of petrolatum was either patch tested in a semi-open fashion or in patch test chambers occluded for 48 hours. The mixing was performed at room temperature on top of a piece of paper with a cotton swab before applying the mixture to the test chamber.

2.3 | Chemical analyses and additional patch test investigations

Chemical analysis of three samples of the glue provided by two different patients (one sample of an older glue provided by one patient in 2019 and two samples of a newer glue recently provided by another patient) was performed by gas chromatography-mass spectrometry (GC-MS). The library of mass spectra of the National Institute of Standards and Technology (Gaithersburg, Maryland) was used for identification of substances. Dilutions of the identified substances in acetone (all from Sigma-Aldrich, Steinheim, Germany) were used as reference standards.

In seven patients, additional patch tests with dilutions of the individual ingredients identified through the chemical analysis were performed. Controls were performed in consecutive eczema patients.

2.4 | Statistical calculations

We performed statistical calculations using Fisher’s exact test, two-sided, concerning the number of positive reactors to ACMO among the patients and controls.

2.5 | Ethical considerations

Informed consent for participation was obtained from the controls and the other patients agreed to participate in a case report.
3  |  RESULTS

3.1  |  Epidemiological and clinical features

Thirteen cases in five dermatology departments across Spain had a severe blistering fingertip dermatitis with a clear-cut relationship to work (Figure 1A). With the repetitive exposure, lesions became more hyperkeratotic and less vesicular (Figure 1B,C). All patients were women with a mean age of 25 (20-33). One patient began experiencing lesions as of 2018, nine patients in 2019, and three patients in 2020. Mean latency time from first exposure to the beginning of their symptoms was 15 weeks (3-32). Fingertips (Figure 1D,E) were involved in all patients, and the first three fingers were predominantly affected. In eight patients, lesions also involved other locations such as the face, dorsal aspects of the hands, the lateral aspects of the fingers, wrists, and the areas in contact with the workplace surfaces such as the volar aspects of the forearms. All patients attributed their lesions to the contact with the glue at work. All continued working except for four patients who lost their jobs. Lesions resolved upon avoidance of exposure to the glue in all cases except for three women who continued being in contact with the glue at work and had persisting dermatitis. We suggested that they used Silver Shield/4H (Honeywell Safety Products, Charlotte, NC, United States) gloves or fingerstalls but none of them complied with this recommendation. This may be due to the fact that the Silver Shield/4H gloves are rigid and difficult to work with, expensive, and difficult to find. Instead, the three patients tried to handle the glue more carefully avoiding direct contact to it and sometimes wore nitrile gloves. Accidental contact with the glue, however, occasionally occurred. The patients who were being in continuous contact with the glue had the perception that the severity of the reactions decreased over time and suspected that “the composition of the glue could have changed.”

Seven patients used manicure products with acrylates prior to the reactions from the glue. However, six of them never recalled reactions from manicure materials. On the other side, one patient (case 2) perceived reactions from manicure materials when she attended certain aesthetic salons but not others. She denied applying manicure products with acrylates to herself or other people. That patient clearly related her lesions to the contact with the glue.
3.2 | Patch test results

Patch tests were performed in 12 of the 13 cases. The glue was patch tested in six patients and positive results were obtained in all of them (3+, 2+, and 1+ reactions in four, one, and one patients, respectively) (Figure 2A). Since three patients who continued contact with the glue had the perception that the intensity of their skin reactions to the glue decreased over time as if the composition had been changed, we performed tests with samples of a newer glue in two of the patients (samples provided by case 2). The newer glue triggered less-intense patch test reactions than the older glue (Figure 2B) (Table S1). In addition, semi-open tests with the glue were performed in two patients, with positive reactions (1+) in both (Table S1).

Twelve of 13 cases were patch tested with the Spanish Contact Dermatitis Research Group (or GEIDAC) baseline and acrylate series, with positive results for nickel sulfate in 2 of 12, p-tert butylphenol formaldehyde resin in 1 of 12, and various acrylates in 3 of 12 (Table S1). Isocyanate series were patch tested in one patient and plastic and glue series in another patient with negative results. All patients reacting to components of the acrylate series used manicure products.

IBOA 0.1% pet. and DMAA 0.1% pet. were patch tested in eight and two cases, respectively, with negative results.

3.3 | Datasheet and label assessment

The color of the kit boxes and the lamps changed over time, even though the external aspect and label of the glue container did not change. Three versions of the kits, consecutively available from 2019 are currently coexisting in the stores according to one of our patients (Figure 3A,B). The information regarding the composition in the label,
 datasheets, and documents provided by the smartphone screen protector company were contradictory. On one side, the label and datasheet indicated that the glue contained IBOA, a “photoinitiator” and polyurethane oligomer. On the other side, we were subsequently informed by the company that the actual ingredients of the glue were polyurethane acrylate, “methacrylate” (unspecified), acrylic acid, hydroxyethylmethacrylate (HEMA), propyltrimethoxysiloxane, and photoinitiator 184 (1-hydroxycyclohexyl phenyl ketone). This unanticipated change of the information regarding the composition along with the negative patch tests with IBOA prompted us to pursue a chemical analysis of the product.

3.4 Chemical analysis

Chemical analysis was performed on three glue samples: one sample of an older glue provided by one patient evaluated in 2019 and samples of two containers of a newer glue recently provided by another patient.

In the GC–MS analysis of the old glue sample, three substances were identified: 4-acryloylmorpholine (or ACMO), isobornyl methacrylate (or IBMA), and lauryl acrylate. The presence of these substances in the glue was confirmed by analyses of acetone solutions of the individual substances. The concentration in the glue was estimated to be ~20% for each of the three substances. An additional unidentified peak was observed, which possibly could be another acrylate. Furthermore, small amounts of IBOA (<0.1%) were detected in the old glue sample. The two new glue samples contained 70%-80% ACMO, but no (<0.01%) IBMA, lauryl acrylate, or IBOA. No other methacrylates were observed in these two samples.

In the old glue sample, there was an indicated presence of isophorone diisocyanate, which in turn may indicate the presence of polyurethane acrylate or polyurethane. Photoinitiator 184 was not observed in any of the glue samples.

3.5 Patch tests with the individual identified ingredients

Patch tests with petrolatum preparations in w/w of the individual identified ingredients (ACMO 0.50%, 0.16%, and 0.05%; IBMA 2.0%, 0.063%, and 0.20%; and lauryl acrylate 0.30%, 0.095%, and
The figure shows the structure of the ACMO molecule as well as the structure of the N,N-dimethylacrylamide (DMAA), and their resemblance

0.03% obtained from Department of Occupational and Environmental Dermatology, Malmö, Sweden) were performed in seven patients.

ACMO 0.5% was positive in six patients: three patients with prior positive patch test reactions to the glue (3+ in one case [Figure 2A]; and 1+ in two cases) and three patients (1+) who had not been patch tested with the glue. ACMO was negative in one of seven cases involving one patient with positive patch and semi-open test reactions to the glue (3+ to the older glue and 1+ to the newer glue) as well as many acrylates: HEMA, 2-hydroxyethyl acrylate (2-HEA), 2-hydroxypropyl methacrylate (2-HPMA), ethyl acrylate (EA), ethylene glycol dimethacrylate (EGDMA), ethyl methacrylate (EMA), and tetrahydrofurfuryl methacrylate (THFMA). She had a past history of exposure to manicure products with acrylates with good tolerance to them except for occasional reactions to manicure materials applied in certain beauty salons (case 2) (Table S1).

One patient (case 9) developed a flare up reaction on day (D)3 involving papules on the lateral aspects of the fingers at the locations previously affected by the dermatitis. Regarding this particular case, the acrylate series were tested with negative results and no positive patch test reactions other than ACMO were observed, thus the flare up reaction was attributed to ACMO.

Patch tests with the lower concentrations of ACMO (0.16% and ACMO 0.05%) were only positive in the patient with stronger (3+) reactions to ACMO 0.5% (Table S1). Patch tests with the dilutions of IBMA or lauryl acrylate were negative.

3.6 | Patch tests with ACMO in controls

Twenty-five controls with ACMO 0.5% pet. were performed. Twenty-five consecutive eczema patients attending three contact dermatitis patch test departments to be investigated for unrelated eczema without previous exposure to the suspected glue agreed to act as controls. Twenty-one were negative, three were positive, and one developed a late reaction to it (on D18).

The positive controls involved three individuals under investigation for reactions to long-lasting nail polish and other manicure products with acrylates who also had strong concomitant reactions to many acrylates such as HEMA, HPMA, and EGDMA, among others (Figure 2C) (Table S2).

Statistical calculations using Fisher’s exact test, two-sided, concerning the number of positive reactors to ACMO among the patients and controls based on positive reactions registered on the ordinary reading days yielded significant values independent on inclusion of the controls under investigation for a possible acrylate allergy or not (6/7 versus 3/25, \( P = .0006; 6/7 \) versus 0/22, \( P < .0001 \)).

A late reaction to ACMO was observed involving one patient who was being investigated for reactions from phenylethyl resorcinol in a photoprotector. The said patient denied a prior exposure to the smartphone screen protector glue but recalled past exposure to manicure products with acrylates once 2 years before with good tolerance to them. The patient came back on D18 after noting new 2+ reactions involving the areas where we had patch tested ACMO and HEMA (as part of the GEIDAC extended baseline series at the time) on her back. Reactions followed a crescendo pattern over the following days (3+ on D36). The patient accepted further patch tests 3 months thereafter and both substances became positive on D2 and D4. She was diagnosed as having a late reaction to HEMA and ACMO.

4 | DISCUSSION

4-Acryloylmorpholine (ACMO, Figure 4) (IUPAC name: 1-morpholin-4-ylprop-2-en-1-one; CAS no. 5117-12-4; molecular weight 141.17) is a monofunctional monomer. Indirect uses of this molecule include adhesives and sealants, coating products, inks, toners, pharmaceuticals, photo-chemicals, manufacturing of plastic products, ultraviolet curable resins (as a reactive diluent because of its low viscosity and high curability) and oil field polymers. ACMO is also used in decorative nail products.

ECHA has no public registered data indicating whether or in which chemical products the substance might be used at a consumer level. ACMO is registered under the REACH Regulation and is manufactured in and/or imported to the European Economic Area, at ≥ 100 tons per annum.

According to the harmonized classification, labeling and packaging of substances and mixtures (CLP Regulation) approved by the European Union, this substance is harmful if swallowed (classified as H302), causes serious eye damage (H318), may cause damage to organs through prolonged or repeated exposure (H373), may cause an allergic skin reaction (H317), and is identified as toxic if inhaled. Precautions that should be observed when handling this substance include wearing protective gloves and/or clothing, and eye and/or face protection, as specified by manufacturer/supplier. Proper removal technique without touching the outer surface and disposal of contaminated gloves after use in accordance with applicable laws and good laboratory practices must also be accomplished.

ACMO is structurally related to DMAA and other similar compounds (Figure 4); however, it is uncertain whether there are cross reactions between them in practice.

![Diagram of 4-Acryloylmorpholine and N,N-dimethylacrylamide](image-url)
According to in vivo assay-guinea pig, it may cause skin sensitization (Directive 67/548/EEC, Annex V, B.6). However, to our knowledge no previous cases of sensitization from ACMO have been published thus far.

We hereby report a case series of patients with occupational ACD from a glue used to attach screen glass tempered protectors to smartphones containing ACMO. The clinical picture of severe fingertip dermatitis was reminiscent of ACD from acrylates in manicurists but with a more bilateral and symmetrical involvement. Other body sites involved suggested ectopic ACD resulting from passive transfer of the allergen through the fingers (facial lesions) or from contact with contaminated workplaces surfaces (forearms). According to a press report, only women are hired by this company, which could be an explanation for the fact that all cases involved female patients.

Patch testing with new allergens is usually challenging because patch test concentrations and vehicles are not standardized. Thus, positive results require ruling out of irritancy and negative results involve ruling out false negative.

We believe ACMO is a culprit allergen in our case series because patch test reactions, although weak in most patients, were in crescendo and persistent; one patient experienced a flare up reaction; and most controls were negative. Furthermore, false-positive reactions to ACMO due to irritancy are highly unlikely as there was between those patients tested with ACMO and controls a highly statistically significant difference with a P-value below .0001 (.0006 including controls with suspected acrylate allergy). In addition, the latency time between exposure and onset of dermatitis was longer than 3 weeks in all patients, further supporting the allergic nature of the skin reactions.

Patch test reactions to ACMO were weak in most patients in comparison to the reactions observed with the glue as well as the dermatitis observed in the clinical setting. It is not possible to be certain of the concentration of acrylates in the glue preparation that were patch and semi-open tested in some of our cases due to the non-standardized method of performing the mixture. Appropriate dilutions should have been prepared to minimize the risks of irritancy and active sensitization.

We speculate that the differences in the ACMO concentration between patch test preparations (0.5% pet.) and the glue (~20%) are likely responsible for these differences. However, because one of our controls developed late reactions to both HEMA and ACMO, no further tests with higher concentrations were performed. Active sensitization to them is possible particularly as positive reactions to both of them were registered already on D2 and D4 at retesting. However, there is another possible explanation based on two findings reported in the literature. Patch testing with multiple tests of one sensitizer at the same concentration (dose in mg/cm²) may result in both positive and false negative reactions in those already sensitized, and late-appearing reactions beyond D7 may develop in those already sensitized to HEMA. Furthermore, the control with late-appearing reactions had been exposed to acrylate-containing cosmetics a few years earlier and might therefore have been silent sensitized to HEMA on such an occasion. Because ACMO may be present in artificial nail products she may also have been silently sensitized to ACMO.

Presently, it is not known whether there is any relationship between HEMA/test preparation with HEMA and ACMO/test preparation with ACMO. Active sensitization to ACMO in the control would be surprising based on experience with Kathon CG some decades ago.

In the 1980s, active sensitization from Kathon CG occurred rarely with an aqueous patch test solution at 300 ppm and more frequently with 1000 ppm, thus it needed to be 20 to 67 times higher than the use concentration (15 ppm in leave-on cosmetics) to actively sensitize. The phone store workers hands were constantly exposed to ACMO 20% (old glue) or 70% to 80% (newer glue).

If 0.5% ACMO actively sensitized one control, the actively sensitizing concentration is 4 times lower (old glue) or 140 to 160 times lower (newer glue) than the ACMO concentration in the glue. The ratio for an actively sensitizing test concentration vs use concentration is ~1000 to 10 000 times higher for Kathon CG compared with ACMO, which we think is arguing against active sensitization to ACMO in the control.

Of interest, one patient who reacted intensely to the glue did not react to ACMO, IBMA, lauryl acrylate, or IBOA. The discrepancy in patch test reactivity to the glue and ACMO in this patient as compared to the other glue-positive patients indicates that there might be another sensitizer in the glue not yet identified. Because sensitization to IBOA can be underestimated by performing patch tests at a 0.1% pet., and currently higher concentrations (0.3% pet.) are recommended to increase sensitivity, we cannot rule out a possible contribution of IBOA to the clinical picture in this particular case (or in other cases). Furthermore, another ACD case from the same glue involving two patients sensitized to IBOA have been reported previously. We believe, however, that it is unlikely that IBOA is implicated in our cases because it was only marginally detected in the older glue sample and not detected in the newer glue, which was able to elicit patch test reactions in two patients and also clinical contact reactions in some patients who continued to use it at work.

We observed strong patch test reactions to ACMO in three positive controls corresponding to three patients allergic to manicure products who were intensely sensitized to multiple acrylates (Table S2).

Since, to our knowledge, no previous cases of sensitization to ACMO had been reported, and potential sources of exposure to ACMO are diverse, we used patients investigated for unrelated eczema lesions who lacked a previous exposure to the glue without other restrictions as controls.

In fact, the serendipitous finding of positive patch test results to ACMO involving patients allergic to acrylates in manicure materials is, in our opinion, very interesting and may lead to new lines of research. We could speculate that said reactions to ACMO in controls may occur after the exposure to manicure products containing ACMO or as a result of cross reactions with HEMA or other acrylate compounds. Particularly, cross reactions between ACMO and DMAA, which is also used in manicure products, would be expected due to the similarity of the molecules, but unfortunately this could not be confirmed because DMAA was not tested in any of the three ACMO-positive controls.
Apparently, there was no association between ACMO and HEMA among the cases: HEMA was tested in 12 of 13 cases, being negative in 11 of them (including the 6 ACMO-positive patients). On the other hand, HEMA was positive in the only case who tested negative to ACMO (case 2).

Contrary to the cases we reviewed, in the controls there seemed to be an association between HEMA and ACMO. Three controls (three women allergic to several acrylates in manicure products) were positive to both ACMO and HEMA, and one additional control developed late simultaneous reactions to both HEMA and ACMO (on D18). This synchronicity could be an indirect proof of cross-reactions between the two compounds, although past co-sensitization due to exposure to a common source is also possible. However, if cross-reactions to HEMA were the reason for the ACMO positive results in controls, one would expect HEMA to yield stronger reactions than ACMO in them (this occurred in only one case). In the remaining two, reactions to ACMO were equal or stronger than reactions to HEMA, respectively (Table S2).

Regarding alternative explanations, the purity of ACMO used for patch testing was confirmed, and contamination with HEMA ruled out (HEMA was not found in either ACMO or the glue), and, to our knowledge, ACMO is not a known by-product or degradation product of HEMA.

Regarding our cases, it is unlikely that sensitization to ACMO is related to manicure products because only two cases with positive patch test reactions to the glue reported prior exposure to manicure products and were sensitized to components of the acrylate series. In addition, only one of two patients reacting to the glue and being exposed to manicure materials reacted to ACMO.

Whether IBMA and lauryl acrylate contributed to the ACD in these cases cannot be totally clarified. Patch tests with them were negative in all cases but patch test concentrations for either IBMA and lauryl acrylate have not been standardized; thus, false negative reactions cannot be ruled out.

Three patients continued to use the glue at work. They tried to handle it more carefully but hardly ever used nitrile gloves and never used Silver Shield/4H gloves. However, these patients noted a lessening of the severity of the skin reactions over time upon accidental contact with the glue. In addition, in two of them, patch tests with newer samples of the glue rendered weaker reactions than patch tests with older samples of the glue. We thus speculated that the composition of the product was changed over time without the labeling being updated.

A change in the composition of the glue was confirmed when analyzing old and new glue samples. Of interest, in case ACMO was the major sensitizer in those individuals patch tested with samples of both an older and a newer glue, one would expect a stronger rather than a weaker reaction to the new glue, as it contained 3-4 times more ACMO (20% vs 70% to 80%). Thus, this result with weaker reactions to the new glue possibly indicates that there may be another sensitizer (sensitizers) in the glue with a lower concentration in the new glue as compared to the old one. Other possible explanations involve variations in the method that may have impacted the patch test results (eg, uniformity of the test substance distribution, state of the skin, other acrylates or substances in the older glue playing a role in intensifying the reaction, and so on).

To summarize, an outbreak of professional allergic contact dermatitis from a mislabeled glue containing three non-declared ingredients, namely, IBMA, lauryl acrylate, and ACMO is reported. Further patch tests to these substances and other possible ingredients are needed to corroborate the specific role played by each of them.

This case series further illustrates the lack of reliability of the datasheets/labels.

We reiterate the urgent need to develop legislation so that manufacturers provide transparent and reliable information regarding the composition of consumer products and actively cooperate in the investigation of the cases of ACD.

**AUTHOR CONTRIBUTIONS**

Francisca Herreros-Montejano: Conceptualization (lead); formal analysis (lead); investigation (lead); methodology (lead); supervision (lead); validation (lead); visualization (lead); writing – review and editing (lead). Martin Mowitz: Conceptualization (lead); formal analysis (lead); investigation (lead); methodology (lead); resources (lead); supervision (lead); validation (lead); visualization (lead); writing – review and editing (lead). Felipe Heras-Mendaza: Conceptualization (lead); formal analysis (lead); investigation (lead); methodology (lead); supervision (lead); validation (lead); visualization (lead); writing – review and editing (lead). Tatiana Sanz-Sánchez: Conceptualization (lead); formal analysis (lead); investigation (lead); methodology (lead); supervision (lead); validation (lead); visualization (lead); writing – review and editing (lead). María Elena Gatica-Ortega: Conceptualization (lead); formal analysis (lead); investigation (lead); methodology (lead); supervision (lead); validation (lead); visualization (lead); writing – original draft (lead); writing – review and editing (lead). Ana López-Mateos: Investigation (supporting). Cristian Valenzuela-Oñate: Investigation (supporting). Cristina Faura-Berruga: Investigation (supporting). Violeta Zaragoza-Ninet: Investigation (supporting). Cecilia Svedman: Conceptualization (lead); formal analysis (lead); investigation (lead); methodology (lead); resources (lead); software (lead); supervision (lead); validation (lead); visualization (lead); writing – review and editing (lead). Cecilia Svedman: Conceptualization (lead); formal analysis (lead); investigation (lead); methodology (lead); resources (lead); supervision (lead); validation (lead); visualization (lead); writing – review and editing (lead). María Antonia Pastor-Nieto: Conceptualization (lead); formal analysis (lead); investigation (lead); methodology (lead); resources (lead); supervision (lead); validation (lead); visualization (lead); writing – review and editing (lead).

**CONFLICT OF INTEREST**

As authors, we declare that we do not have any potential conflicts of interests to declare regarding this article.

**DATA AVAILABILITY STATEMENT**

Author elects to not share data
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SUPPORTING INFORMATION
Additional supporting information may be found in the online version of the article at the publisher’s website.

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