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REVIEW ARTICLE

Skin Problems due to Treatment with Diabetes Technology: A Narrative Review

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ABSTRACT:
Diabetes devices, such as insulin pumps, glucose sensors, and integrated automated insulin delivery systems, have brought about a transformative impact on the management of diabetes. This impact has been particularly significant for individuals with type 1 diabetes and increasingly for those with type 2 diabetes. These devices are designed for continuous wear, necessitating the consistent use of infusion sets, patch pumps, or glucose sensors that are inserted into the skin.
Regrettably, numerous studies have highlighted that skin-related issues stemming from diabetes devices are rather common. These problems encompass various forms of skin injury, allergic and irritative contact dermatitis, itching, wound formation, scarring, and lipodystrophies. The utilization of diabetes devices, both in the present and the foreseeable future, faces significant challenges due to these skin complications, but preventive strategies exist for especially skin injuries including use of a skin care regimen or patches. These challenges culminate not only in the discontinuation of device usage but also in decrease in quality of life and heavier disease burden.
This narrative literature review comprehensively synthesizes existing knowledge about skin problems triggered by diabetes devices, encompassing children, adolescents, and adults. The review delves into definitions, underlying causes, prevention strategies, and treatment approaches. Finally, the review provides recommendations for future research directions in skin problems and suggestions for advancement of in the part of diabetes devices in close contact with the skin to reduce device-related skin problems.
Abbreviations: AID: Automated Insulin Delivery, T1D: Type 1 Diabetes

Introduction

More than 8 million individuals worldwide are currently living with type 1 diabetes (T1D)[1], a chronic autoimmune condition characterized by dysfunctional pancreatic beta-cells, resulting in insufficient insulin production leading to hyperglycemia and necessitating lifelong treatment[2]. The primary approach to managing T1D involves the precise administration of insulin to achieve near normal blood glucose levels, avoiding both hyperglycemia and hypoglycemia[3]. Over the past decades, an increasing number of people have been turning to diabetes devices, such as insulin pumps, glucose sensors, or a combination of both, to optimize their glycemic control[4]. These devices offer added advantages, making them easier to integrate into daily life for individuals of all ages, whether at home, at work, in kindergarten, or at school[5,6].

One such advancement in this field is the automated insulin delivery (AID) system, which integrates an insulin pump, a glucose sensor, and an artificial intelligence algorithm. This system is designed to automate insulin dosing based on real-time glucose levels, enhancing the management of T1D[4]. In a recent cross-sectional study based on more than 3000 participants from our center, we have shown how AID are highly superior to other treatment modalities with CGM and therefore must be considered as the preferred treatment choice, at least when insulin pump treatment is chosen[7].

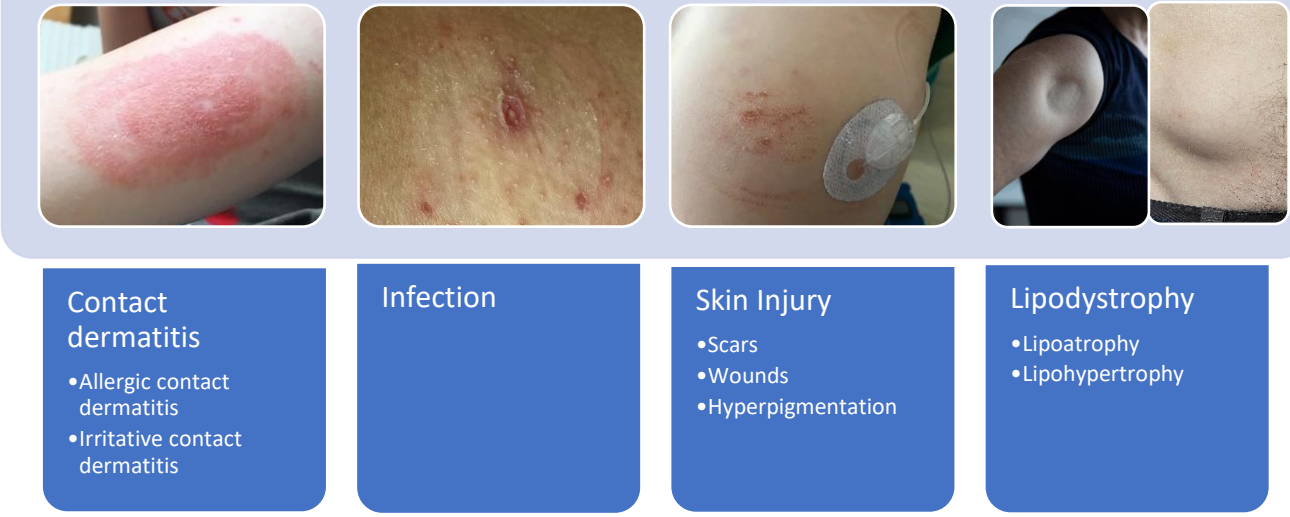
The function of an AID system or even just a glucose sensor or an insulin pump rely on the continuous adhesion to the skin from the patch of the insulin pump and/or the glucose sensor[8]. Unfortunately many studies have demonstrated the occurrence of different skin problems due to the use of these devices and thereby potentially limiting the use of diabetes devices[9]. Therefore, the purpose of this review is to summarize current knowledge and recent research within the field of skin problems due to diabetes devices.

Definition of skin problems

Skin problems or dermatological complications due to diabetes devices are a whole range of different types of reactions all found on the skin visually after removal of the diabetes device. Overall, the reactions can be separated in four distinct types of reactions: eczema (allergic or irritative), infection, skin injury and lipodystrophy, where the latter includes both lipoatrophy and lipohypertrophy and is found only relevant as a reaction to the injection or infusion of insulin and not in relation to glucose sensors[9]. Most do judge the patches and the medical adhesives to be responsible for reactions of both irritative and allergic eczema as well as wounds[9,10], whereas infections are caused by microbial contamination and can theoretically be seen at both insulin pump and glucose sensor sites, but are primarily seen in relation to insulin pump usages[11,12]. The specific eczema reactions in relation to diabetes devices are characterized as contact dermatitis[13], whereas other dermatological manifestations include the unspecific group of skin injury including scars and wounds which could be speculated to be later manifestations of contact dermatitis in some circumstances or just an unspecific skin injury. Itching is a very important symptom related to especially contact dermatitis but also infections and skin injury, especially in children and adolescents itching is crucial interfering with other daily life and resulting in further dermal manifestations due to scratching[11,14].

When it comes to the frequency of skin problems, studies have shown that 90% of pediatric insulin pump users and 80% of pediatric glucose sensor users had experienced some kind of skin problem over the time[15], compared to 80% of adult insulin pump users and 71% of adult glucose sensor users[16]. This highlights the magnitude of these reactions in users of diabetes devices with children and adolescents being more affected than adults. A recent study, utilizing the UK general practice database, examined skin problems in individuals using insulin pumps and those using apomorphine pumps as treatment for Parkinson's disease. They found similarly that approximately 40% experienced skin events and that infections and contact dermatitis were the most frequent in both groups independent of time between change of infusions sets that varied from daily for apomorphine infusion sets to up to 7 days for different sets for insulin infusion[17]. The intensity, severity and consequences of skin problems vary significantly, and many gaps in our knowledge about the pathophysiology, treatment, and prevention of these issues still exist.

Figure: Types of Skin Problems in four major groups



Itching

Itching is a commonly reported symptom in many users of both insulin pumps and glucose sensors[11,15,16]. It can be found without further visual symptoms or in relation to contact dermatitis, scars, wounds or lipodystrophies[18]. Dry skin and itching symptoms are also in general more commonly observed in children with T1D compared to their healthy peers[19], even though the skin barrier is not found to be impaired neither in children and adolescents nor in adults with T1D[20]. Itching can be a very frustrating symptom interfering with everyday life and in children, it have been associated with sleep disturbances, difficulty in concentration and attempts to scratch off the device[14]. Itching can ultimately result in the vicious circle of skin barrier defect by scratching and thereby increase allergen penetration and increase susceptibility to contact dermatitis[21].

Contact dermatitis

One of the most persisting reactions towards diabetes devices are the contact dermatitis, which is an inflammatory skin reaction caused by either irritative or allergenic substances where reactions therefore are characterized as either irritant or allergic contact dermatitis[22]. The distinction between the two types is based on a proven allergic reaction through a positive patch test towards a panel of allergens and the patients' devices, and irritant contact dermatitis is therefore an exclusion criterion. Though, knowledge on specific allergens are needed in order to patch test for the relevant panel of allergens[23]. The most frequent allergens are in a recent systematic review found to be colophony and acrylates both being important substances in the production of a medical adhesive[10].

The frequency of contact dermatitis in cross-sectional studies depend on methods and definitions used. For example, a German study in 2020 examined children and adolescents and found 14% of insulin pump users and 18% of glucose sensor users had current contact dermatitis[11]. In a survey study, 35.9% reported experiencing "local skin irritation"[24] while another study described that approximately 20% recognized their skin as "*red and itchy*"[25]. A cross-sectional study of self-reported prevalence of contact dermatitis discovered around 25-33% in children and adolescents[15] and 16-25% in adults[16]. The first prospective study of skin problems have revealed more than 20% experiencing at least 1 visible contact dermatitis during the first year of device use in a pediatric cohort[12]. All in all, the conclusion is that between 14-35% of users of both insulin pump and glucose sensors do evolve contact dermatitis but the real prevalence of irritative vs. allergic contact dermatitis is difficult to establish since this requires a patch test. One study saw in 17/52 (33%) a negative patch test indicating these were irritative or the allergen were not included in the patch test series[26]. Another study found 9/24 (24%) had negative patch tests with a broader panel of allergens[23]. Investigation of the prevalence of allergic contact dermatitis in general diabetes populations are only available from glucose sensor users showing 3.8 to 5.3 % in respectively Freestyle libre® users[27] and a mix of glucose sensor users[28]. A recent study of dermis with optical coherence tomography did find inflammation, lymphocyte infiltration and fibrosis as signs of allergic

sensitization of insulin pump sites compared to control sites[29].

Infections

For skin infections most studies show that the rates of infections due to insulin pump usage were much higher in the early years of insulin pump use around 29% per year, whereas more recent studies in both children and adolescents reveal 2-7% per year with infections with tendency to more infections due to CSII compared to CGM[15,16,25,30]. The historical variation in these figures may be attributed to improved hygienic procedures or advancements in the design of infusion sets, whereas the differences between device types may be influenced by factors as device size, length of attachment or insertion procedures. Microbial colonization of the catheter is thought to be important here, and natural cutaneous bacteria as *Staphylococcus* and *Streptococcus* are typical the guilty microbial agents[31], also shedding light on importance of a natural and healthy skin microbiome[32]. A consensus document regarding medical adhesive has also concluded that overgrowth of microorganisms are seen under medical adhesives[33]. Secondary wound infections can also be observed as a result of contact dermatitis, particularly due to the associated itching and subsequent scratching[34]. A prospective study of 170 children and adolescents only reported eight infections during 12 months of study period, all related to use of insulin pump[12]. The recent ADA Standards of Care describe infections at pump sites as potential complication accordingly, but do not mention it at sensor sites at all[4].

Lipodystrophies

Lipodystrophies is a well-known complication to the treatment with insulin which affect insulin absorption and are seen in the subcutaneous layer of the skin where most other skin problems do at least initiate in the epidermis of dermis layer of the skin[18]. It can be sub-divided in lipohypertrophy and lipoatrophy, where lipohypertrophy is characterized as a soft swelling with hypertrophy of the adipose tissue of subcutis, lipoatrophy is a depression with loss of adipose tissue of subcutis[9]. The prevalence of both lipodystrophies depend a lot on study characteristics and there is also an urgent need for better identification and definition of both reactions which have been known for decades also to use of insulin syringes or pens, but are seen nowadays in relation to insulin pumps as well[35]. Earlier use of animal insulin were associated with high rates of lipoatrophy, but from the 80s human insulins were introduced which were causing more lipohypertrophy than lipoatrophy[36]. Most studies nowadays also find lipohypertrophy way more frequent than lipoatrophy[11]. The self-reported rates of lipohypertrophy are very low[15] compared to dermatological investigated rates[11]. This indicates unawareness regarding examining for lipohypertrophy since it can be visually seen but often require palpation to be sure[36].

Lipohypertrophy is thought to result from the anabolic effects of insulin. However, over time, the skin in lipohypertrophic areas becomes hyposensitized making infusion set insertion in those areas more comfortable and less painful[18]. Most studies show that proper injection technique with rotation of infusion set position is crucial for prevention of lipohypertrophy and that the insulin absorption is impaired when injected in lipohypertrophic areas[36].

Lipoatrophy is with the modern insulins described as a rare skin complication, which in most studies show prevalence around 1-3%[37,38], but again the complication can be underrated. The etiology of lipoatrophy is not well-established but thought to be heterogenous including autoimmune response towards insulin. This explains why other insulin types are tried in the treatment or secondary prevention of new lipoatrophic areas[38,39]. Sodium cromoglycate are also used in the treatment of lipoatrophy and even laser treatment or use of steroid injections although evidence is sparse since only few studies with the treatment of only a few patients do exist[37].

Ultrasound have been found helpful in assessment of lipohypertrophy and are more sensitive than palpation alone besides it can also have educational properties in showing the reactions to persons with diabetes and thereby helping showing the need for behavioral changes[36]. A recent study of 74 people with diabetes showed a high variety of heterogenous findings with ultrasound in insulin-exposed tissue which resulted in a model of lipohypertrophy in different grades according to disruption of the skin[40]. Ultrasound have also been used in a study of both insulin pump and glucose sensor sites, where hyper echogenicity were found in 70% of all insulin pump sites after 12 months of use compared to only 4% of glucose sensor sites[41], again emphasizing the insulin as important guilty agent in these reactions. To what extent hyper echogenicity is a mild grade of lipohypertrophy is still not investigated properly.

Skin injury

Besides the specific contact dermatitis, infections and lipodystrophies, other skin problems exist which we here have defined as more unspecific skin injury, which includes wound, hyperpigmentation, and scars, but also the small “dots” seen frequently after

having removed the infusion set. Most of these reactions are anticipated to be related to the medial adhesive or the device itself which therefore categorizes these reactions including contact dermatitis as MARSI: Medical Adhesive-Related Skin Injury[33]. The wounds are typically caused by mechanical issues causing skin stripping, tension injury or skin tears where some wounds simply arise by the ungentle removal of the diabetes device[33]. Scars can be accompanied by hyperpigmentation but also often is a response to continuous use of the same site for either insulin pump or glucose sensor leading to more chronic disruption of the skin[9]. Wounds and especially scars can also be a later clinical presentation of chronic itching, infections or contact dermatitis[42]. Some do also argue that these more minor skin problems are a natural consequence of continuously use of patches on the skin and these issues are therefore typically tolerated by the diabetes device users[42].

Causes of skin problems

It has been speculated whether a more vulnerable skin barrier in persons with T1D could explain the high rates of skin problems. One study investigated the skin barrier and found similar skin barrier among children and adolescents with T1D, nonetheless small differences in the group of few adults with long-term T1D were found for small skin barrier molecules, but without mechanical measurable impairment of the skin barrier making impaired skin barrier a less likely reason for skin problems due to diabetes devices[20]. Comparison of insulin pumps with apomorphine pumps do also emphasize similar frequencies overall of skin problems irrespective of patient population, although infections specifically were more frequent in the apomorphine population which though had more frequent intervention (daily shift), were much older and more infection-vulnerable[17]. When it comes to the infections, part of the skin microbiome on the buttocks were different in the above mentioned skin barrier study[20], which suggest this as a reason for infections. The insulin is the suspected cause for both lipoatrophy and lipohypertrophy and both reactions are subsequently also seen with insulin injections[18], no direct comparative studies have been found comparing frequencies of these reactions with use of pen versus insulin pump.

The design of the devices is in many reviews and studies thought to be the major cause of skin problems including the adhesives, also highlighting why especially skin injury and contact dermatitis were literally not seen with insulin injections. For the allergic contact dermatitis of course the important allergens are the major causes of reactions, but here not only allergens from the medical adhesive touching the skin but also allergens from glue in the housing part of device are found responsible[23]. The adhesive needs to be strong enough to ensure proper adhesion so extra patches is not needed in order to keep the device situated in the full wear-time, and often more reactions are seen when a device is changed to longer wear-time[43]. In a recent and comprehensive literature review conducted by Convatec Infusion Care, a leading global manufacturer of infusion sets, several previously unexplored factors related to the design and materials of these infusion sets were examined and shed significant light on how these factors can impact both skin reactions and the subcutaneous response[44].

Cross-sectional studies have revealed different association factors to skin problems including atopic disposition, longer duration of device use and low number of skin sites being used[11,15,16,30]. Regarding age most studies show higher frequencies of skin problems in children and adolescents compared to adults, but the comparability between age groups, indications for device use and inclusion in the studies could cause bias making comparisons difficult even with use of exact same questionnaire[15,16]. It could be speculated that younger children would present with more skin problems than older children due to smaller skin surface to be used for the same devices as in adults and maybe also higher demands for adhesion, but no studies have confirmed any differences in skin problems according to different age groups within childhood and adolescence[15,30].

Prevention of skin problems

The most effective way to prevent skin problems associated with diabetes devices is undoubtly to develop and produce devices that are gentle to the skin. This includes the use of less allergenic molecules, use of adhesives in the lowest necessary concentration. Furthermore, will a full declaration of ingredients in the devices help avoiding problematic compounds for those patients with a proven allergy towards specific allergens. Numerous studies particular in the field of contact dermatitis, have reached this conclusion[8,45]. Although this may entail higher production costs due to the use of more skin-friendly adhesives, a cost analysis has attempted to demonstrate that the increased expenses related to skin problems justify this investment[46]. However, the compelling business case may not be enough for manufacturers to feel a strong motivation to switch to skin-friendly materials or designs for diabetes devices because the rate of discontinuation due to skin issues remains relatively low[9]. Nevertheless, there are alternative preventive options that can be employed, as outlined in both the medical adhesive consensus

statement[33] and the recent Guidelines for pediatric diabetes[47]. These strategies include maintaining skin hydration, using proper removal technique, rotating the device placement site, ensuring correct device placement, and implementing prophylactic skin care routines. A recent intervention study has investigated a skin care program that involved avoiding disinfection, ensuring proper device removal and use of lipid lotion. This program successfully prevented 2/3 of all skin wounds but only few of the contact dermatitis, emphasizing the role of allergens in the latter[12]. In adults the possibility of using an implantable glucose sensor is possible, although with no current connection to insulin pumps, but this has in literature been advised as possible strategy[48].

Treatment of skin problems

Once skin problems have manifested, there is a strong correlation with the likelihood of further skin issues, as most of these skin problems tend to persist or are strongly associated with the occurrence of future skin problems[49,50], especially with continued use of the device. Therefore, the treatment of skin problems includes not only the acute treatment of the exact reaction, but also secondary prevention of new reactions. The first and most important advice is to avoid use of the skin site with any skin problem for insertion of the next couple of devices in order to achieve proper healing[47], the only exemption from this is that glucose sensors may be inserted in areas of lipohypertrophy[51]. Most skin problems will heal consequently over time due to natural healing process and do not need acute treatment besides avoidance of the site. Though, for some reactions of contact dermatitis use of topical steroids can be necessary at least temporary for up to four weeks[22,33]. The problem with use of continuous or long-term topical steroids are the risk of steroid-induced skin atrophy which consequently impair the skin barrier and thereby result in a vicious circle of more vulnerability towards new skin problems[52]. Alternatively topical calcineurin inhibitors can be used although they are less effective in controlling the eczematous reactions. A hydrocolloid patch have been proposed and tested in a small explorative manner in order to treat irritative contact dermatitis by hydrocolloid patch with occlusion technique to avoid use of steroids[53].

For the secondary prevention of new skin problems the skin care program may be used[12]. Alternatively, barrier lotion, film or patches are needed under the devices to avoid that the original device touches the skin, which is also the strategy even with allergic contact dermatitis[47], if the devices for which an allergy has been proven cannot be avoided. In most cases that is the case since there is cross reactivity between acrylates and so far, all diabetes devices contain acrylates. Many studies also do show that users already uses different patches or silicone film between device and skin[54–57]. Overall, the advice are "try-and-error" approaches with different patches containing different medical adhesives or chemicals based on acrylate, silicone, or hydrocolloid, but no formal recommendations on which are superior are available. Research has explored the use of local corticosteroids designed for nasal application, administered as a spray on the skin prior to inserting a diabetes device, as a secondary preventive approach, which involved 12 children and adolescents, with a successful response observed in 10 out of the 12 individuals, and no reported glycemic adverse events[58]. Taking the skin-atrophic potential of steroids in mind[52], it must though be investigated which long-term consequences of skin barrier are seen when used under occlusion, but the willingness to try these type of strategies highlights the need for better treatment and secondary prevention of skin problems.

Consequences of skin problems

Many consequences of skin problems exist, some well-established and some more speculative. The ultimate consequence of skin problems is the discontinuation of device use limiting the person by not achieving the great treatment potential and flexibility by using the modern diabetes devices. Discontinuation rates because of skin problems differs in literature but are typically low compared to the amount of skin problems[59]. Quality of life are found impaired with severe skin problems in both children, adolescents and adults[49,50]. Economic consequences of skin problems include extra costs due to pre-term change of devices for the health-care-system or private economy depending on healthcaresystem[46]. The consequence of skin problems on glycemic values like time in range or hba1c is only studied for lipodystrophy[36], where a study do show association to higher hba1c with skin problems[11], while other studies reject these hypotheses[15,16].

The occlusion of the skin area may also have consequences, which have been shown in other areas but not investigated in diabetes devices. Several studies have demonstrated that prolonged occlusion with gloves, even for just six hours a day, can have detrimental effects on the skin barrier[60]. In this context, "long-term" typically refers to a duration of at least two weeks. Given this, it's reasonable to speculate that the impact on the skin barrier could be even more significant when it comes to diabetes devices. However, our understanding of the effects on the skin barrier when occlusion intervals extend beyond 6 hours a

day and instead span 3 to 14 days, as is the case with diabetes devices, remains incomplete. To potentially mitigate the adverse effects on the skin barrier caused by prolonged occlusion, a simple skincare regimen involving the use of moisturizers could prove to be essential.

Future recommendations

The utilization of diabetes devices has been steadily rising, encompassing both children, adolescents, and adults with T1D. Furthermore, there is an emerging trend suggesting potential usage among a specific subset of individuals with Type 2 Diabetes in the future. This increasing adoption of diabetes devices has led to a corresponding increase in the prevalence of skin problems associated with their use. Most manufacturers in the diabetes technology sector are consistently moving towards extending the wear-time of their devices. This progressive shift not only serves to reduce the frequency of device changes but has also been supported by studies demonstrating a decrease in subcutaneous reactions when devices are worn for longer periods[61]. However, it's worth noting that this increase in wear-time may be contingent on a stronger adhesion or a higher concentration of adhesive substances. This, in turn, raises the concern of an increased risk of allergic reactions unless more skin-friendly adhesives are being used[43]. In essence, the selection of a medical adhesive involves striking a delicate balance between ensuring proper adhesion to secure the device in place for optimal function of both insulin infusion and glucose measures and avoiding excessively strong adhesion that could potentially lead to adverse skin reactions. To date, our experience with these devices only spans a relatively short timeframe of 10 to 15 years. This limited historical perspective underscores the critical importance of maintaining a steadfast focus on skin problems in the years to come. In the case of children and adolescents, the prevailing public health recommendation is to avoid products that may trigger allergies, the same apply for adults. However, when it comes to diabetes devices, adhering to this recommendation proves unfeasible due to their integral role in managing diabetes. The long-term dermatological and allergy-provoking consequences of utilizing diabetes devices remain largely unknown, emphasizing the need for ongoing research and vigilance in monitoring these effects.

Many knowledge gaps exist for skin problems and in future research it is recommended to study specifically how the skin barrier and microbiome milieu are influenced by the occlusion by patches as well as different types of medical adhesives. More information is needed to guide future design of devices. Especially, contact dermatitis needs further investigation in means of both prevention, treatment and handling in clinical practice, thirdly important risk factors still need to be established to stratify preventive treatment when diabetes devices are initiated. Lastly there is an imperative need to understand the consequences of topical steroid-use both for glucose excursions, measurement precision, insulin absorption and skin-atrophy.

Still, almost all diabetes devices include the same allergy-provoking substances based on acrylic adhesive and colophony, which in clinical practice leaves less potential for changing to other diabetes devices after an allergic contact dermatitis have been diagnosed. Therefore, it is intensely encouraged that future trials of diabetes devices with other more skin friendly medical adhesives based on hydrocolloid or silicone will be included, at least to be used in a subgroup of the population[33]. When it comes to the insulin being used in diabetes devices, studies are also needed after approval of new insulin comparing the tendency of resulting in both lipohypertrophy and lipoatrophy, and this may also be a perspective of the insulin designing process or using filters in infusions set to prevent precipitation products[62].

Lastly, the regulation of diabetes devices is included in the EU Medical Device Regulation, where there by now still are no legal requirement of declaration of exact product composition of diabetes devices, impairing the patch test process a lot since the exact potential allergens from many diabetes devices is not known, which therefore delays the diagnostic procedure of allergic contact dermatitis[63]. Legislation for full declaration of substances included in diabetes devices are clearly warranted and will help the future clinical practice.

Conclusions

In conclusion, the increasing use of diabetes devices that require skin attachment and the high prevalence of associated skin problems highlights the need for the development of more skin friendly products. This imperative applies for all, but especially to subgroups with existing skin issues or with a high risk of developing adhesive material allergies. Further research is warranted to gain a better understanding of the long-term consequences and the potential benefits of using more skin-friendly adhesives.

Conflict of Interest statement

AKB has received project grants from Medtronic and received speaking honoraria from Rubin Medical and Convatec.
CZ has no conflicts.
KN holds shares in Novo Nordisk; has been a paid consultant for Novo Nordisk and Medtronic; has

received speaker honorarium and honorarium for Advisory Board to her institution from Medtronic, Novo Nordisk, Insulet, Convatec, her institution has received research funding from Zealand Pharma, Novo Nordisk, Medtronic, and Dexcom.
JS serves as an adviser to Medtronic and Novo Nordisk. She owns shares in Novo Nordisk and has received fees for speaking on behalf of Medtronic, Sanofi Aventis, Rubin Medical and Novo Nordisk and funding from Medtronic and Novo Nordisk.

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References

1. Gregory GA, Robinson TIG, Linklater SE, et al. Global incidence, prevalence, and mortality of type 1 diabetes in 2021 with projection to 2040: a modelling study. *Lancet Diabetes Endocrinol*. 2022;10(10):741-760. doi:10.1016/S2213-8587(22)00218-2
2. Libman I, Haynes A, Lyons S, et al. ISPAD Clinical Practice Consensus Guidelines 2022: Definition, epidemiology, and classification of diabetes in children and adolescents. *Pediatr Diabetes*. 2022;23(8):1160-1174. doi:10.1111/pedi.13454
3. Cengiz E, Danne T, Ahmad T, et al. ISPAD Clinical Practice Consensus Guidelines 2022: Insulin treatment in children and adolescents with diabetes. *Pediatr Diabetes*. 2022;23(8):1277-1296. doi:10.1111/pedi.13442
4. American Diabetes Association Professional Practice Committee, Draznin B, Aroda VR, et al. 7. Diabetes Technology: Standards of Medical Care in Diabetes-2022. *Diabetes Care*. 2022;45(Suppl 1):S97-S112. doi:10.2337/dc22-S007
5. Sherr JL, Schoelwer M, Dos Santos TJ, et al. ISPAD Clinical Practice Consensus Guidelines 2022: Diabetes technologies: Insulin delivery. *Pediatr Diabetes*. n/a(n/a). doi:10.1111/pedi.13421
6. Tauschmann M, Forlenza G, Hood K, et al. ISPAD Clinical Practice Consensus Guidelines 2022: Diabetes technologies: Glucose monitoring. *Pediatr Diabetes*. 2022;23(8):1390-1405. doi:10.1111/pedi.13451
7. Nørgaard K, Ranjan AG, Laugesen C, et al. Glucose Monitoring Metrics in Individuals With Type 1 Diabetes Using Different Treatment Modalities: A Real-World Observational Study. *Diabetes Care*. Published online August 23, 2023:dc231137. doi:10.2337/dc23-1137
8. Hartsough EM, Hylwa SA. Wearable Woes: Allergens in Diabetic Devices. *Dermat Contact Atopic Occup Drug*. 2021;32(1):19-31. doi:10.1097/DER.0000000000000673
9. Jedlowski PM, Te CH, Segal RJ, Fazel MT. Cutaneous Adverse Effects of Diabetes Mellitus Medications and Medical Devices: A Review. *Am J Clin Dermatol*. Published online October 25, 2018. doi:10.1007/s40257-018-0400-7
10. Cameli N, Silvestri M, Mariano M, Messina C, Nisticò SP, Cristaudo A. Allergic Contact Dermatitis, an Important Skin Reaction in Diabetes Device Users: A Systematic Review. *Dermatitis*. 2022;Publish Ahead of Print. doi:10.1097/DER.0000000000000861
11. Burgmann J, Biester T, Grothaus J, Kordonouri O, Ott H. Pediatric diabetes and skin disease (PeDiSkin): A cross-sectional study in 369 children, adolescents and young adults with type 1 diabetes. *Pediatr Diabetes*. n/a(n/a). doi:10.1111/pedi.13130
12. Berg AK, Grauslund AC, Sørensen F, et al. A Skin Care Program to Prevent Skin Problems due to Diabetes Devices in Children and Adolescents: A Cluster-Controlled Intervention Study. *Diabetes Care*. Published online July 21, 2023:dc230462. doi:10.2337/dc23-0462
13. Alves da Silva C, Bregnhøj A, Mowitz M, Bruze M, Andersen KE, Sommerlund M. Contact dermatitis in children caused by diabetes devices. *Contact Dermatitis*. 2022;87(5):406-413. doi:10.1111/cod.14166
14. Berg AK, Simonsen AB, Svensson J. Perception and Possible Causes of Skin Problems to Insulin Pump and Glucose Sensor: Results from Pediatric Focus Groups. *Diabetes Technol Ther*. 2018;20(8):566-570. doi:10.1089/dia.2018.0089
15. Berg AK, Olsen BS, Thyssen JP, et al. High frequencies of dermatological complications in children using insulin pumps or sensors. *Pediatr Diabetes*. 2018;19(4):733-740. doi:10.1111/pedi.12652
16. Berg AK, Nørgaard K, Thyssen JP, et al. Skin Problems Associated with Insulin Pumps and Sensors in Adults with Type 1 Diabetes: A Cross-Sectional Study. *Diabetes Technol Ther*. 2018;20(7):475-482. doi:10.1089/dia.2018.0088
17. Jick SS, Oleske DM, Persson R, Zamudio J, Facheris MF. Epidemiology of skin event rates among users of pumps for the subcutaneous administration of drugs for chronic conditions. *Curr Med Res Opin*. 2021;37(9):1563-1571. doi:10.1080/03007995.2021.1953971
18. Passanisi S, Salzano G, Lombardo F. Skin Involvement in Paediatric Patients with Type 1

Diabetes. *Curr Diabetes Rev*. 2022;18(4):46-55. doi:10.2174/1573399817666210903153837

19. Pavlović MD, Milenković T, Dinić M, et al. The prevalence of cutaneous manifestations in young patients with type 1 diabetes. *Diabetes Care*. 2007;30(8):1964-1967. doi:10.2337/dc07-0267
20. Berg AK, Grauslund AC, Nørgaard K, et al. Similar Skin Barrier Function in Persons with Type 1 Diabetes Compared with Healthy Controls. *JID Innov*. 2023;3(4). doi:10.1016/j.xjidi.2023.100200
21. Elias PM. Skin barrier function. *Curr Allergy Asthma Rep*. 2008;8(4):299-305. doi:10.1007/s11882-008-0048-0
22. Novak-Bilić G, Vučić M, Japundžić I, Meštrović-Štefekov J, Stanić-Duktaj S, Lugović-Mihić L. IRRITANT AND ALLERGIC CONTACT DERMATITIS - SKIN LESION CHARACTERISTICS. *Acta Clin Croat*. 2018;57(4):713-720. doi:10.20471/acc.2018.57.04.13
23. Ahrensbøll-Friis U, Simonsen AB, Zachariae C, Thyssen JP, Johansen JD. Contact dermatitis caused by glucose sensors, insulin pumps, and tapes: Results from a 5-year period. *Contact Dermatitis*. 2020;n/a(n/a). doi:10.1111/cod.13664
24. Al Hayek AA, Robert AA, Al Dawish MA. Skin-Related Complications Among Adolescents With Type 1 Diabetes Using Insulin Pump Therapy. *Clin Med Insights Endocrinol Diabetes*. 2018;11:1179551418798794. doi:10.1177/1179551418798794
25. Rigo RS, Levin LE, Belsito DV, Garzon MC, Gandica R, Williams KM. Cutaneous Reactions to Continuous Glucose Monitoring and Continuous Subcutaneous Insulin Infusion Devices in Type 1 Diabetes Mellitus. *J Diabetes Sci Technol*. Published online May 9, 2020:1932296820918894. doi:10.1177/1932296820918894
26. Herman A, Montjoye L de, Baeck M. Adverse cutaneous reaction to diabetic glucose sensors and insulin pumps: Irritant contact dermatitis or allergic contact dermatitis? *Contact Dermatitis*. 2020;83(1):25-30. doi:10.1111/cod.13529
27. Pyl J, Dendooven E, Van Eekelen I, et al. Prevalence and Prevention of Contact Dermatitis Caused by FreeStyle Libre: A Monocentric Experience. *Diabetes Care*. Published online February 13, 2020:dc191354. doi:10.2337/dc19-1354
28. Vidal-Albareda C, Yelmo-Valverde R, Solórzano-Zepeda C, Rodríguez-Muñoz N, de-la-Hoz-Caballer B, González-de-Olano D. Prevalence of contact dermatitis to glucose sensors in pediatric population and the main allergens involved. *Contact Dermatitis*. 2020;83(1):47-49. doi:10.1111/cod.13511
29. Kalus A, Shinohara MM, Wang R, et al. Evaluation of Insulin Pump Infusion Sites in Type 1 Diabetes: The DERMIS Study. *Diabetes Care*. 2023;46(9):1626-1632. doi:10.2337/dc23-0426
30. Schober E, Rami B. Dermatological side effects and complications of continuous subcutaneous insulin infusion in preschool-age and school-age children. *Pediatr Diabetes*. 2009;10(3):198-201. doi:10.1111/j.1399-5448.2008.00477.x
31. Nowakowska M, Jarosz-Chobot P, Polańska J, Machnica Ł. Bacterial strains colonizing subcutaneous catheters of personal insulin pumps. *Pol J Microbiol*. 2007;56(4):239-243.
32. Lee HJ, Kim M. Skin Barrier Function and the Microbiome. *Int J Mol Sci*. 2022;23(21):13071. doi:10.3390/ijms232113071
33. McNichol L, Lund C, Rosen T, Gray M. Medical adhesives and patient safety: state of the science: consensus statements for the assessment, prevention, and treatment of adhesive-related skin injuries. *J Wound Ostomy Cont Nurs Off Publ Wound Ostomy Cont Nurses Soc*. 2013;40(4):365-380; quiz E1-2. doi:10.1097/WON.0b013e3182995516
34. Patel B, Priefer R. Infections associated with diabetic-care devices. *Diabetes Metab Syndr Clin Res Rev*. 2021;15(2):519-524. doi:10.1016/j.dsx.2021.02.023
35. Gentile S, Strollo F, Ceriello A, et al. Lipodystrophy in Insulin-Treated Subjects and Other Injection-Site Skin Reactions: Are We Sure Everything is Clear? *Diabetes Ther*. 2016;7(3):401-409. doi:10.1007/s13300-016-0187-6
36. 36. Tian T, Aaron RE, Huang J, et al. Lipohypertrophy and Insulin: An Update From the Diabetes Technology Society. *J Diabetes Sci Technol*. Published online August 9, 2023:19322968231187660. doi:10.1177/19322968231187661
37. Xatzipsalti M, Alvertis H, Kourousi G, et al. Lipoatrophy, a rare complication of diabetes: a single-center experience. *Horm Athens Greece*. Published online October 21, 2021. doi:10.1007/s42000-021-00324-z
38. Kordonouri O, Biester T, Schnell K, et al. Lipoatrophy in children with type 1 diabetes: an increasing incidence? *J Diabetes Sci Technol*. 2015;9(2):206-208. doi:10.1177/1932296814558348
39. Kordonouri O, Biester T, Weidemann J, et al. Lipoatrophy in children, adolescents and adults with insulin pump treatment: Is there a beneficial

effect of insulin glulisine? *Pediatr Diabetes*. 2020;21(7):1285-1291. doi:10.1111/pedi.13094

40. Hashem R, Mulnier H, Ghazaleh HA, et al. Characteristics and morphology of lipohypertrophic lesions in adults with type 1 diabetes with ultrasound screening: an exploratory observational study. *BMJ Open Diabetes Res Care*. 2021;9(2):e002553. doi:10.1136/bmjdrc-2021-002553
41. Sørensen FMW, Svensson J, Kinnander C, Berg AK. Ultrasound Detected Subcutaneous Changes in a Pediatric Cohort After Initiation of a New Insulin Pump or Glucose Sensor. *Diabetes Technol Ther*. Published online June 6, 2023. doi:10.1089/dia.2023.0137
42. Pleus S, Ulbrich S, Zschornack E, Kamann S, Haug C, Freckmann G. Documentation of Skin-Related Issues Associated with Continuous Glucose Monitoring Use in the Scientific Literature. *Diabetes Technol Ther*. 2019;21(10):538-545. doi:10.1089/dia.2019.0171
43. Oppel E, Högg C, Oschmann A, Summer B, Kamann S. Contact allergy to the Dexcom G6 glucose monitoring system—Role of 2,2′-methylenebis(6-tert-butyl-4-methylphenol) monoacrylate in the new adhesive. *Contact Dermatitis*. 2022;87(3):258-264. doi:10.1111/cod.14141
44. Hendel K, Stumpe T, Ozer K. Impact of Infusion Set Materials and Designs on the Subcutaneous Response in People With Diabetes: A Rapid Review of the Literature. *J Diabetes Sci Technol*. Published online November 18, 2022: 19322968221138076. doi:10.1177/19322968221138076
45. Kamann S, Wagner N, Oppel E. Modern diabetes devices for continuous blood sugar measuring: Limitations due to contact allergies. *J Dtsch Dermatol Ges J Ger Soc Dermatol JDDG*. 2021;19(12):1715-1721. doi:10.1111/ddg.14621
46. Berg AK, Thorsen SU, Thyssen JP, Zachariae C, Keiding H, Svensson J. Cost of Treating Skin Problems in Patients with Diabetes Who Use Insulin Pumps and/or Glucose Sensors. *Diabetes Technol Ther*. 2020;22(9):658-665. doi:10.1089/dia.2019.0368
47. Fröhlich-Reiterer E, Elbarbary NS, Simmons K, et al. ISPAD Clinical Practice Consensus Guidelines 2022: Other complications and associated conditions in children and adolescents with type 1 diabetes. *Pediatr Diabetes*. 2022;23(8):1451-1467. doi:10.1111/pedi.13445
48. Oppel E, Kamann S, Heinemann L, Reichl FX, Högg C. The implanted glucose monitoring system Eversense: An alternative for diabetes patients with isobornyl acrylate allergy. *Contact Dermatitis*. n/a(n/a). doi:10.1111/cod.13392
49. Weng AT, Zachariae C, Christensen KB, Svensson J, Berg AK. Five-Month Follow-up Shows No Improvement in Dermatological Complications in Children With Type 1 Diabetes Using Continuous Glucose Monitoring Systems and Insulin Pumps. *J Diabetes Sci Technol*. Published online October 16, 2019:1932296819882425. doi:10.1177/1932296819882425
50. Christensen MO, Berg AK, Rytter K, et al. Skin Problems Due to Treatment with Technology Are Associated with Increased Disease Burden Among Adults with Type 1 Diabetes. *Diabetes Technol Ther*. 2019;21(4):215-221. doi:10.1089/dia.2019.0007
51. DeSalvo DJ, Maahs DM, Messer L, et al. Effect of lipohypertrophy on accuracy of continuous glucose monitoring in patients with type 1 diabetes. *Diabetes Care*. 2015;38(10):e166-167. doi:10.2337/dc15-1267
52. Aschoff R, Schmitt J, Knuschke P, Koch E, Bräutigam M, Meurer M. Evaluation of the atrophogenic potential of hydrocortisone 1% cream and pimecrolimus 1% cream in uninvolved forehead skin of patients with atopic dermatitis using optical coherence tomography. *Exp Dermatol*. 2011;20(10):832-836. doi:10.1111/j.1600-0625.2011.01335.x
53. Berg AK, Sørensen MH, Knoth HS, Svensson J. An Occlusive Hydrocolloid-Based Patch Is Effective, Feasible, and Safe As a Treatment of Irritant Contact Dermatitis due to Diabetes Devices in Children and Adolescents with Type 1 Diabetes. *Diabetes Technol Ther*. Published online June 19, 2023. doi:10.1089/dia.2023.0224
54. Passanisi S, Salzano G, Galletta F, et al. Technologies for Type 1 Diabetes and Contact Dermatitis: Therapeutic Tools and Clinical Outcomes in a Cohort of Pediatric Patients. *Front Endocrinol*. 2022;13:846137. doi:10.3389/fendo.2022.846137
55. Ng KL, Nixon RL, Grills C, Tam MM. Solution using Stomahesive® wafers for allergic contact dermatitis caused by isobornyl acrylate in glucose monitoring sensors. *Australas J Dermatol*. 2022;63(1):e56-e59. doi:10.1111/ajd.13675
56. Kamann S, Heinemann L, Oppel E. Usage of Hydrocolloid-Based Plasters in Patients Who Have Developed Allergic Contact Dermatitis to Isobornyl Acrylate While Using Continuous Glucose Monitoring Systems. *J Diabetes Sci*

Technol. 2020;14(3):582-585. doi:10.1177/1932296819876964

57. Messer LH, Berget C, Beatson C, Polsky S, Forlenza GP. Preserving Skin Integrity with Chronic Device Use in Diabetes. *Diabetes Technol Ther*. 2018;20(S2):S2-54-S2-64. doi:10.1089/dia.2018.0080
58. Paret M, Barash G, Rachmiel M. "Out of the box" solution for skin problems due to glucose-monitoring technology in youth with type 1 diabetes: real-life experience with fluticasone spray. *Acta Diabetol*. Published online November 8, 2019. doi:10.1007/s00592-019-01446-y
59. Asarani NAM, Reynolds AN, Boucher SE, de Bock M, Wheeler BJ. Cutaneous Complications with Continuous or Flash Glucose Monitoring Use: Systematic Review of Trials and Observational Studies. *J Diabetes Sci Technol*. Published online August 27, 2019:1932296819870849. doi:10.1177/1932296819870849
60. Tiedemann D, Clausen ML, John SM, Angelova-Fischer I, Kezic S, Agner T. Effect of glove occlusion on the skin barrier. *Contact Dermatitis*. 2016;74(1):2-10. doi:10.1111/cod.12470
61. Kastner JR, Eisler G, Torjman MC, et al. In Vivo Study of the Inflammatory Tissue Response Surrounding a Novel Extended-Wear Kink-Resistant Insulin Infusion Set Prototype Compared With a Commercial Control Over Two Weeks of Wear Time. *J Diabetes Sci Technol*. Published online May 9, 2022:19322968221093360. doi:10.1177/19322968221093362
62. Zhang G, Romo-Anselmo E, Kwa T, Cohen O, Vigersky R, Chattaraj S. Advances in Insulin Infusion Set in the New Era of Automated Insulin Delivery: A Systematic Review. *J Diabetes Sci Technol*. 2023;17(2):302-313. doi:10.1177/19322968221145731
63. Herman A, Uter W, Rustemeyer T, et al. Position statement: The need for EU legislation to require disclosure and labelling of the composition of medical devices. *J Eur Acad Dermatol Venereol*. n/a(n/a). doi:https://doi.org/10.1111/jdv.17238