

Health-related quality of life in food and venom induced anaphylaxis and role of influencing factors

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Abstract

The impact on health-related quality of life (HRQL) plays a key role for patients suffering from allergies and anaphylaxis. In this narrative review we review the HRQL in allergic patients suffering from food and venom allergy, both being the most frequent elicitors of severe allergic, potential life-threatening reactions and provide an overview on the current knowledge and identified gaps.

The data show that for food and venom allergy standardized assessment tools to measure HRQL are available and have been successfully applied. Our analysis shows that multiple factors can modulate HRQL in these patient groups. These include sociodemographic data like patients' age and sex, fear of accidental reactions but also external factors like the social environment and the appreciation of the seriousness of the condition by others. External factors may have a significant impact on HRQL and should be considered in patient-related outcome assessments to avoid biased measurements possibly affecting the results. The assessment of the quality of life in the context of specific immunotherapy should consider lifestyle factors and ideally, the individual change in HRQL should be measured.

Although there are many data indicating a negative impact on HRQL in food allergic children and their caregivers, limited data are existing from adults with food allergy and venom allergic patients from all age groups. Also, the use of standardized questionnaires should be extended to allow for a better comparability of results between studies. Therefore, translation to additional languages is necessary.

Taken together, the eliciting allergen, the severity of the allergic disease but moreover multiple external factors impact the outcome in HRQL and should be considered in HRQL assessment.

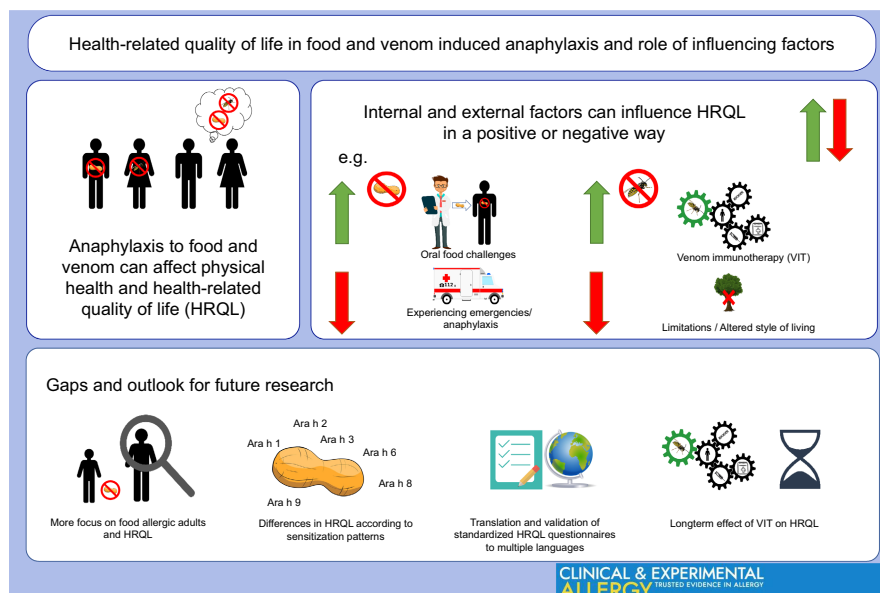
KEYWORDS

anaphylaxis, food allergy, health-related quality of life, venom allergy

Margitta Worm and Maria Beatrice Bilò contributed equally to this work.

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GRAPHICAL ABSTRACT

In this non-systematic narrative review, the literature on health-related quality of life (HRQL) in patients with food and venom induced anaphylaxis and the role of influencing factors was reviewed. Besides the negative influence of food or venom anaphylaxis as such, but also patient-specific and external factors can influence HRQL, for example the experience with emergencies, therapeutic interventions like venom immunotherapy (VIT) or participation in trials. Further research on HRQL is needed, especially in adult patients.

1 | INTRODUCTION

The impact on health-related quality of life (HRQL) plays a key role for patients suffering from allergies and anaphylaxis. Although affected patients are outside a reaction physically well, the fear of a severe allergic reaction has a great impact on patients' everyday life.¹⁻³ Anaphylaxis is unpredictable and patients' health status can change within minutes from fully functional to life-threatening situations, which can cause anxiety,⁴⁻¹¹ fear of accidental exposure,¹²⁻¹⁵ loss of control,^{16,17} social exclusion¹⁸ and bullying^{19,20} because every day-life situations are considered unsafe and/or the seriousness of the condition is not appreciated by others.^{8,17,21}

Therefore, it is essential to identify strategies to cope with anxiety, insecurity and other negative emotions on an individual basis. This may require finding the balance between the avoidance of accidental exposures, social functioning and HRQL.²² Possible coping mechanisms were reported recently in peanut allergic patients and categorized in three groups: daily monitoring and vigilance, communication about the allergic condition and planning.²³

Food and venom allergy can present with various symptoms ranging from mild local symptoms up to systemic multi-organ reactions, sometimes with even fatal outcomes.^{24,25} The risk of fatal anaphylactic reactions to food or venom is low and accounts for 1% of the total mortality risk of patients with a known allergy to those allergens.²⁶ To avoid accidental allergic reactions due to food a strict elimination diet is mandatory.^{27,28} Other main strategies of food and venom allergy management are educational measures to improve the recognition of symptoms of the allergic reaction and the availability and handling of emergency medication.^{29,30} Currently, there

Key messages

- Anaphylaxis to food or venom impact health-related quality of life (HRQL)
- Patient-specific and environmental factors may influence HRQL and need consideration
- More research in adult patients suffering from anaphylaxis is necessary

is no curative treatment for food allergies, but the role of allergen immunotherapy for food allergy, lately via oral or epicutaneous route to increase the threshold dose is studied also with regard to patients HRQL.³¹⁻³⁴ Recently, the first product for the treatment of severe peanut allergy received FDA³⁵ (Review) and EMA approval.

Venom allergy has a reported prevalence of 0.3%–42.8% of anaphylaxis among systemic reactions (SR).³⁶ It is the primary cause of severe SR in adults in central Europe and the second frequent major cause in children according to data from the European Anaphylaxis Registry.³⁷ Subcutaneous immunotherapy (VIT) is available for venom allergy and reduces the risk of reactions after accidental exposure effectively.³⁸ VIT is indicated in children and adults with a SR involving organs other than the skin, in adults with systemic skin reactions in cases of high risk of exposure and/or impaired HRQL, and in patients with clonal mast cell disorder and a history of a SR.^{38,39} Adherence to VIT is high.⁴⁰

Food and venom allergy are also associated with a financial burden: Gupta et al. reported the annually financial burden for food

allergic children in the United States at \$24.8 billion or \$4184 per child and year.⁴¹ A major financial burden are costs for free from the respective allergen(s) foods reaching up to \$1.7 billion annual costs.⁴¹ The costs for VIT were assessed regarding cost-effectiveness from a working group in the United Kingdom (Pharmalgen® VIT, ALK Abelló).⁴² The data show an incremental cost-effectiveness ratio of £ 18'065'527 per quality-adjusted life-year gained for Pharmalgen® VIT with high dose antihistamines (HDA) and epinephrine autoinjectors (EAI) compared to high dose antihistamines and EAI alone in the overall venom allergic population.⁴² Only for the subgroup of patients with frequent stings (five per year) Pharmalgen® VIT + HDA + EAI was shown to be more effective and less expensive than HDA and EAI alone and for those with high anxiety, Pharmalgen® VIT was still considered to be cost effective.⁴²

Herewith we review the HRQL in food and venom allergic patients based on published data, provide an overview on the current knowledge and identify gaps. Both allergens are the most frequent elicitors of severe allergic reactions.

2 | METHODS

In this narrative, non-systematic review, we reviewed the literature on HRQL in food and venom allergic patients independent of age using PubMed online databank from April 2021–August 2022. As search terms we used combinations of the following keywords: “food allergy”, “food anaphylaxis”, “venom allergy”, “venom anaphylaxis”, “anaphylaxis” in various combinations with “quality of life” and “health-related quality of life”. We selected food and venom allergy for this review only. We thought that food and venom pose similar risk for accidental exposure and require constant vigilance and carrying of the emergency medication.

Literature search was performed by using PubMed online databank: search criteria were considering RCT and CT for anaphylaxis and HRQL ($n = 21$), food allergy and HRQL ($n = 57$) and venom allergy and HRQL (9 if CT and RCT restricted and $n = 60$ without restrictions (all 60 publications were reviewed)).

We identified and extracted factors that have been shown to significantly impact on HRQL. We categorized, summarized and illustrated the identified factors (Tables 1 and 2 and Figures 2 and 3). Based on this analysis we identified gaps in the research. Figure 1 shows the flow chart of the study procedure.

3 | FOOD-INDUCED ANAPHYLAXIS

3.1 | Tools to determine food allergy-related quality of life

Besides negative physical health when experiencing an anaphylactic reaction, food allergies affect the HRQL of patients, their caregivers and families. HRQL can be measured by generic and disease-specific questionnaires. Generic questionnaires allow for comparability

between the influence of various diseases and healthy controls on HRQL, but do not optimally address the barriers associated with food allergy, since food allergic patients are usually overall physical well-being outside the acute reaction. Therefore, disease-specific questionnaires considering the influence of food allergies on the HRQL have been developed.¹ The food allergy quality of life questionnaire (FAQLQ) and the Food Allergy Independent Measurement (FAIM), in the parent- and/or age-appropriate patient form (children-, teen-age-, adult form) are most commonly used.^{1,43–45} Another validated food allergy-specific quality of life questionnaire is the Food Allergy Quality of Life—Parental Burden-Questionnaire (FAQL-PB).⁴⁶ Those questionnaires cover multiple disease-relevant areas, like the emotional impact of food allergy, the risk of an accidental allergen exposure, the fear of having an allergic reaction and expected outcome of an accidental reaction and social and dietary restrictions.¹ Patients with food allergies but also their caregivers often experience high levels of anxiety. When the level of anxiety is very high, a significant impairment of physical and mental functions may occur. Recently, a new questionnaire to measure anxiety in a food allergy-specific way, the Food Allergy Anxiety Scale has been developed.²² With regard to parent-proxies, some studies showed an overrating of the patients HRQL, when comparing parent-perceived patient-specific HRQL to children perceived HRQL.^{47,48} Taking these observations into account, results from parent or caregiver-reported questionnaires have to be interpreted with caution. Moreover, food allergic individuals, who seek for help and present in specialized allergy centres have lower HRQL.⁴⁹ They seek help, because they perceive avoiding and other food allergy-specific measures as more troublesome than those not seeking help.⁴⁹ This may result in a bias, as study participants are mostly recruited at specialized allergy centres.

In addition, the Anaphylaxis Quality of Life Scale for Adults (A-QoL-Adults) has been suggested as a new tool to assess the HRQL of adults suffering from anaphylaxis, independent of the eliciting allergen.⁵⁰ The questionnaire includes 21 questions focused on consequences and emotions due to anaphylaxis in general and adds two elicitor-specific questions for food, drugs, insect venom or spontaneous anaphylaxis.⁵⁰ This is the first disease-specific questionnaire that allows to compare the impact of anaphylaxis due to different eliciting allergens on HRQL.⁵⁰

3.2 | Factors influencing the quality of life of food allergic patients

Many factors have been described to influence the HRQL in food allergic patients and are summarized in Table 1 and illustrated in Figure 2. However, most studies were conducted in children, caregivers and adolescents, while only limited data on food allergic adults exist.

The objective severity of a previous reaction was found to have an effect on HRQL in most studies.^{8,21,51–54} However, some studies reported a stronger effect of the patient- or parent-perceived severity than the objective severity of the reaction on HRQL or found even no influence of reaction severity on HRQL.^{9,52,55}

TABLE 1 Factors influencing health-related quality of life (HRQL) in food allergic patients

Category	Factors influencing HRQL in food allergic patients	Effect on HRQL	References
Experiences due to food allergy	Previous anaphylaxis	↓	[45,47,51,53,56,80–84]
	Having had to use epinephrine autoinjector (EAI)/visit emergency department due to allergy	↓	[21,51]
	Experiencing cardiovascular or respiratory symptoms in previous reactions	↓	[83]
	Experiencing multiple episodes of allergic reactions	↓	[53]
	Reaction happened more recently	↓	[21]
Measures due to food allergy	Prescription of EAI:	↑ ¹	¹ [12,13,51]
	• Mostly reported to reduce anxiety and stress, increase freedom, make patient feel safe ¹	↓ ²	² [16,48,80,85]
	• On the other hand, fear and hesitation when and how to use EAI/ suboptimal adherence/ being afraid of consequences (calling an ambulance, going to the hospital) ²		
	Constant vigilance	↓	[17]
	Oral food challenges, in some patient groups irrespective of the outcome ¹ , in others significant improvements after negative challenges ²	↑	¹ [86]; ² [87,88]
	Application of EAI by patient his- or herself during oral food challenge → experience of self-effectiveness	↑	[86]
	Preparation of meals at home for safety reasons: time consuming, career and productivity of caregivers can be affected, sometimes reduction of working hours required	↓	[8,16]
Patient-specific factors	Additional financial burden due to buying “free from...” products	↓	[89]
	More than one family member with food allergy	↓	[53]
	Having multiple food allergies	↓	[21,45,47,53,56,82]
	Having comorbidities (e.g. asthma, atopic dermatitis, allergic rhinoconjunctivitis)	↓	[84,90,91]
	Uncertainty about the diagnosis (Certainty about diagnosis is not a predictor of better quality of life)	↓	[55]
	More time elapsed since diagnosis (lower impact on quality of life over time because social support increases)	↑	[92]
	Female sex	↓	[13,47,48,52]
	Increasing patient's age	↓	[47,48,80,84,89,93]
	Parent-perceived increase of patients burden with increasing patient's age		
Emotional impact	Being able to eat products with a precautionary label for traces of the allergen	↑	[13]
	Fear of accidental ingestion and subsequent allergic reactions	↓	[12–15]
	High level of stress and anxiety	↓	[8–11]
	Worried about accidental contamination of food when eating out in a restaurant or a friends' house, although discussing allergy before eating	↓	[82,94]
	Fear of leaving food allergic child in care of others	↓	[15,51]
	Afraid of letting food allergic child participate in school, camps, birthday parties	↓	[82]
	Feeling awkward and different because of having to ask in a restaurant or carry emergency medication	↓	[19,20,94]
	Lack of control	↓	[16,17]

TABLE 1 (Continued)

Category	Factors influencing HRQL in food allergic patients	Effect on HRQL	References
External factors	Others do not appreciate the seriousness of the food allergy, leading to frustration	↓	[8,17,21,23]
	Social negativity (e.g. exclusion from social events, negative attitudes and behaviours to food allergic individuals)	↓	[23,92]
	Bullying at school or leisure time activities due to food allergy	↓	[19,20,23]
	Access to support systems like activity holidays for food allergic children/ access to a 24-hour hotline in case of allergy-questions	↑	[95,96]
	Participation in clinical trials investigating OIT and achieving an increase in eliciting dose ¹	↑	¹ [34,97] ² [33]
	Longer duration of OIT (further increase in eliciting dose, less side effects, less accidental reactions) ²		

Note: ↓, factor associated with a decrease in HRQL; ↑, factor associated with an increase in HRQL.

Abbreviations: EAI, Epinephrine autoinjector; HRQL, Health-related quality of life; OIT, Oral immunotherapy.

TABLE 2 Factors influencing quality of life in venom allergic patients.

Category	Factors influencing quality of life in venom allergic patients	Effect on quality of life	References
Measures due to venom allergy	VIT ¹ (together with professional explanation and reassurance of protection) ²	↑	¹ [60–62,71,75] ² [77]
	Conventional protocol for VIT (longer treatment duration) in children and adolescents	↑	[5]
	Treatment with the EAI alone (no additional immunotherapy)	↓	[7,18,71,75,79]
	Sting challenges (confirming protection against the insect venom) during VIT	↑	[62,72,78]
Patient-specific factors	Female sex in adult patients	↓	[7,62,71,72]
	Being a beekeeper or having a beekeeper within the family in bee-venom allergic individuals	↑	[65]
Emotional impact	Anxiety	↓	[4–7]
	Caution & alertness in daily activities	↓	[4–6,18]
	Limitations & discomfort in daily activities, altered style of living	↓	[4–6,18]
	Uncertainty	↓	[7]
	Trying to protect the child from a sting	↓	[98]
External factors	Social exclusion	↓	[18]

Note: ↓, factor associated with a decrease in quality of life; ↑, factor associated with an increase in quality of life.

Abbreviations: EAI, Epinephrine autoinjector; VIT, Venom immunotherapy.

Ethnicity and country of origin seem to impact HRQL in food allergic patients.^{9,15,56,57} One study reported on Hispanic fathers with a reduced HRQL, while non-Hispanic, white ethnicity was associated with a better HRQL in mothers and fathers.¹⁵ Another study described that Asian-American parents have higher anxiety with regard to food allergy compared to African American, Caucasian or Hispanic caregivers.⁵⁷ Among European countries differences of HRQL in food allergic patients were related to cultural attitudes towards food.⁹ Patients with food allergy from the United States showed a significantly more impaired quality of life than patients from the Netherlands.⁵⁶ As potential underlying reasons, the authors suggest a greater variety of foods in the USA and, therefore, a higher risk of accidental allergen exposure, a more stringent use of the precautionary allergen labelling in the USA, differences in the

practice of eating out (Americans eat out more often than the Dutch), and more patients from the United States were prescribed an EAI, which may according to the authors remind patients of their disease more often.⁵⁶

One recent study investigated the challenges of the COVID-19 pandemic for families with food allergic individuals. On the one hand, families consumed their meals almost always at home, leading to an increased feeling of safety and control about the food intake. On the other hand, families had to deal with problems during grocery shopping, especially in the beginning of the pandemic, when staple foods, needed to prepare allergen-free meals at home, were not available due to hoarding. In addition therapies or diagnostic procedures were sometimes delayed as they were considered to be elective procedures.⁵⁸

4 | HYMENOPTERA VENOM

4.1 | Tools to determine hymenoptera venom allergy-related quality of life

A specific HRQL questionnaire was developed and validated in Dutch and English version for untreated adult patients allergic to

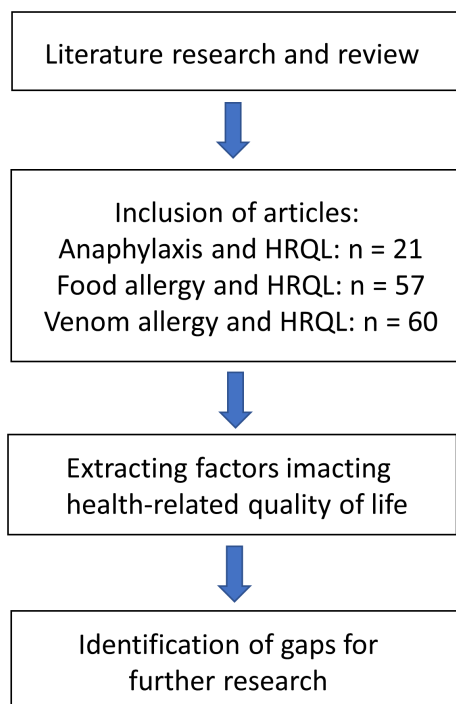


FIGURE 1 Methodologic process

yellow jackets (the Vespidae Allergy Quality of Life Questionnaire: VQLQ); this instrument is made of 14 items, divided into four domains (anxiety, caution, limitations and discomfort) and shows the scale as a one-dimensional measurement tool.⁵⁹ German, Spanish, Polish, Turkish and Portuguese translation, cultural adaption and validation of the original VQLQ were made to evaluate the quality of life of adults allergic to vespids, including *Polistes dominula* in the Mediterranean area.^{60–65} Also, the newly developed A-QoL-Adults represents a new tool to assess the impact of anaphylaxis due to insect venom on the HRQL.⁵⁰

Venom allergy in children may have a considerable impact on the HRQL of the parents of patients, as parents will try to protect their child from a sting, or its consequences.⁶⁶ Therefore, the VQLQ was adapted and validated in Polish venom allergic children and adolescents (Children's Hymenoptera Venom Allergy Quality of Life Scale - CHVAQoLS), as well as their parents (Parents of Children with Hymenoptera Venom Allergy Quality of Life Scale - PoCHVAQoLS).^{66–68} In the CHVAQoLS questionnaire, a new scale for children and adolescents was developed, measuring six dimensions of HRQL (anxiety, caution, limitations, discomfort, support received from parents, feeling of safety).⁶⁸

In some studies, in adult and children the VQLQ was also used to measure HRQL of bee-venom allergic patients.^{60,64,65,69,70} Bee-venom allergic patients may face different problems than vespidae venom allergic patients, as the risk of being stung differs between both patient groups.⁵⁹ In addition, many bee-venom allergic patients are beekeepers or family members of those.⁵⁹ As suggested during the development of the VQLQ and later shown in another study, the impact on HRQL differs between honeybee-allergic beekeepers and non-beekeepers but the impact on HRQL of honeybee-allergic

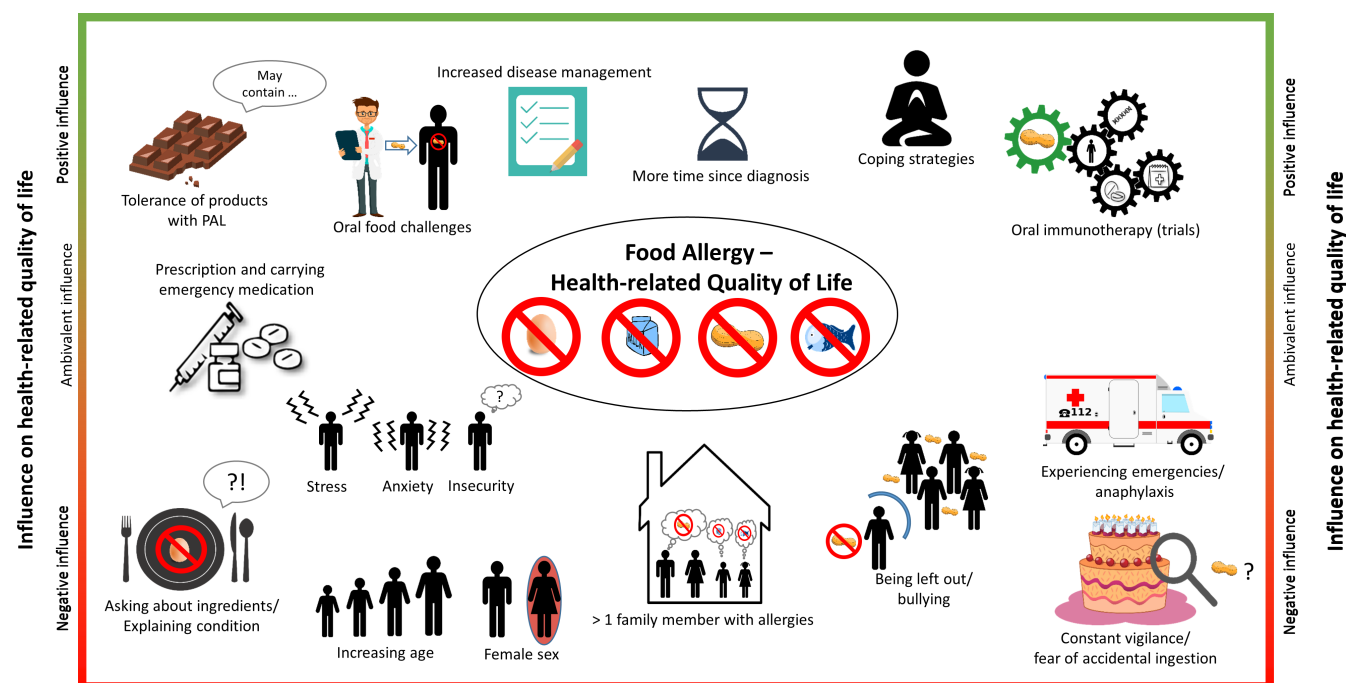


FIGURE 2 Factors influencing quality of life in food allergic patients. See Table 1 for referencing.

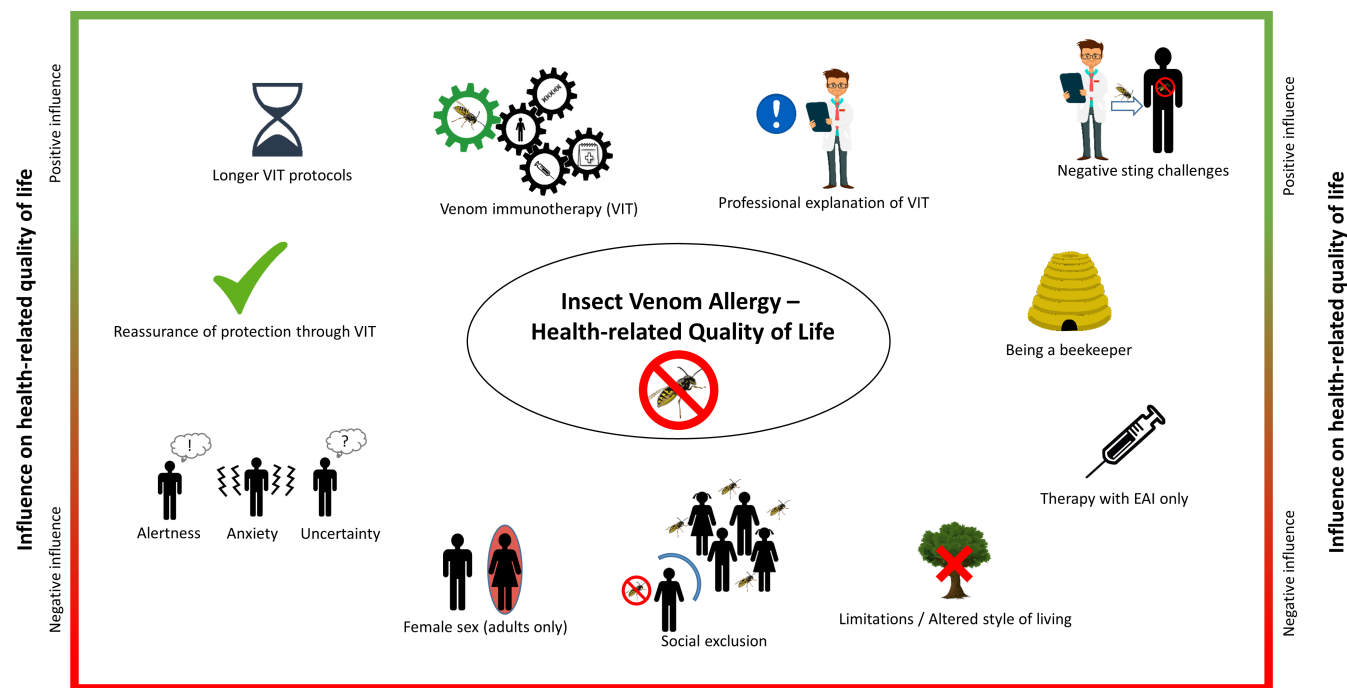


FIGURE 3 Factors influencing quality of life in venom allergic patients. See Table 2 for referencing.

non-beekeepers is comparable to the impact perceived by patients allergic to vespid venom.^{65,71} Without distinguishing between the beekeeper-status, some⁷⁰ but not all studies^{69,72} observed a lower impairment of HRQL in bee-venom allergic patients compared to those allergic to wasp venom.

4.2 | Factors influencing the quality of life of hymenoptera venom allergic patients

As it was shown in Dutch patients using the VQLQ, an allergic reaction after an insect sting results in uncertainty and as a further consequence in a diminished HRQL.⁷ The impairment in HRQL correlates positively with the anxiety level.⁷ Nevertheless, also patients with a higher anxiety level at the beginning were able to improve their HRQL due to VIT.⁷ Irrespective of the general anxiety level, the time elapsed since the allergic reaction, reaction severity or age, women showed a stronger impairment in their HRQL than men.⁷ Many studies confirmed this correlation of female sex and a stronger impairment on HRQL.^{62,71,72} In a German study using sociodemographic and disease-specific characteristics as well as the HADS, also female patients with mild SRs showed higher disease-related anxiety levels than men.⁷³ As higher anxiety levels in female patients were reported in many studies, not only related to anaphylaxis, it is suggested that differences between sex with regard to mood disorders might be related to hormonal differences and diversities in the immune system.^{73,74}

With the use of CHVAQoLS in Polish children, a higher anxiety in girls within the group of dermal reactors was shown, but higher levels of anxiety in boys than girls with grade II reactions were

observed,⁴ while other studies did not find any significant differences between girls and boys.⁶⁹ A significant association between the severity of the anaphylactic reaction (Mueller's grade IV compared to grade III) and anxiety was reported,⁵ but not confirmed by others.⁶⁹ Several studies showed a significant positive relationship between anxiety and caution as well as caution, limitations and discomfort, meaning that the more anxious the patient feels about a future reaction to an insect sting, the more measures they will invest in its avoidance, and therefore, they will experience more limitations.^{4–6} The level of parental caution seemed to decrease slightly with increasing age of the venom allergic child.⁶ Also, an association between the level of caution and the place of residence was revealed, showing that adolescents from a rural area had lower levels of caution.^{5,6} This might be caused by a higher accustomation to hymenoptera but also by a higher number of beekeepers in rural areas⁵ and another study in children and adolescents found no difference in the levels of limitations due to wasp allergy between patients living in rural or urban areas.⁴

Having a child or an adolescent allergic to hymenoptera venom has an undoubted impact on the HRQL of parents. The levels of HRQL in children and their parents per dimension were strongly dependent.⁶ Caution and anxiety showed a positive association and both influenced the level of perceived limitations as well as discomfort in parents.⁶ The support given to their children was depending on the severity of the allergic reaction as well as the gender of the parent: for mothers, a higher level of support was associated with higher levels of limitations and discomfort.⁶

Many studies showed an improvement in HRQL in patients receiving VIT,^{60–62,71} even in patients who previously only reacted with dermal symptoms,⁷⁵ as the anxiety and the fear of a resting

decrease.⁶¹ This suggests that the expectations of patients should change, after a clinician provides them with information about VIT and its effect.² Nevertheless, patients under immunotherapy still held debilitating beliefs, which had a negative impact on HRQL and were associated with a higher level of distress.⁷⁶ Receiving VIT over a 1-year period together with a professional explanation and the reassurance of protection induced a reduction in dysfunctional beliefs in 2/3 of patients and an improvement in HRQL.⁷⁷ This effect was also shown by other authors, where standardized patient information together with VIT in adults were able to improve the HRQL, regardless of gender, general anxiety and recent stings after an one-year treatment in two out of three adults.^{2,71} As adequate information helps patients to adjust their expectations and, therefore, improve their HRQL, it would be beneficial to improve educational strategies and measure their outcome via the change in HRQL.²

Sting challenges in patients receiving VIT are also associated with a significant improvement in HRQL, meaning that some patients trust their therapy only after the demonstration of its efficacy through a sting challenge.^{62,72,78}

In contrast to VIT, therapy with the EAI alone was shown to negatively impact HRQL of adult patients,^{71,75} to be experienced as burdensome² and to be associated with a higher level of anxiety and depression.⁷⁹ Some patients with a negative attitude towards the EAI were not willing to use the EAI if necessary and some of them were afraid of possible side effects.^{2,7} Therefore, injectable epinephrine as the only treatment seems not to be the right approach in patients with VIT from the point of HRQL.²

Improvement of HRQL has been also observed in children, adolescents as well as their parents during VIT, mainly related to a lower level of anxiety.^{5,6,69} The VIT protocol seems to have an effect on HRQL of treated patients, where patients treated with a conventional, longer lasting protocol showed a lower level of discomfort.⁵ This may suggest a broader sense of burden of treatment and disease itself, and it might be necessary to improve the medical information on the advantages of shorter protocols.⁵ The longest duration of VIT in children and adolescents was also related to a decrease of parents' anxiety.⁶

An overview of factors influencing HRQL in patients allergic to hymenoptera venom is displayed in Table 2 and illustrated in Figure 3.

4.3 | Gaps and outlook

In summary, although standardized HRQL assessment tools are available for food and venom allergy, we identified gaps and future research fields in this area. First, as regards food allergy more data on HRQL from adults with food allergy in general is required. As the sensitisation pattern and consecutively the severity are possible influencing factors different cohorts should be studied to delineate this in more detail (e.g. storage protein sensitisation versus lipid-transfer-protein (LTP) versus Pathogen-related-protein-10;

cofactor-dependent allergy (e.g. wheat-dependent exercise induced anaphylaxis/LTP) vs. non-cofactor-dependent allergy).

Besides the affected individual patient, food allergy, but also venom allergy may also impact the HRQL of other family members. Again, profound data on parents and caregivers from food allergic patients has been published but only limited data are available, for example from their siblings or the children of adult food or venom allergic parents.

Also standardized tools to assess elicitor-specific allergy HRQL worldwide are largely missing and would require a translation and validation of existing questionnaires e. g. FAQLQ/VQLQ in the age-appropriate form to multiple languages. Such use of standardized questionnaires may facilitate an intercultural comparison of HRQL and may result in the identification of factors improving the HRQL (e.g. factors in the health care system). The recently published A-QoL-Adults might fill this gap and also allows to compare the impact of anaphylaxis with different underlying eliciting allergens, but it needs to be validated in larger cohorts and translated to multiple languages in order to increase its international usage.

Regarding allergen immunotherapy and HRQL long-term data is largely missing, for example are positive effects of VIT/OIT on HRQL stable even after cessation of the treatment.

Lifestyle and socioeconomic factors but also cultural factors can largely affect HRQL and their impact on the outcome of HRQL should be first better elucidated and moreover require consideration in the development of HRQL assessment tools. Maybe new e-health digital technologies (e.g. e-diaries) can support to gain more data worldwide and may build the basis for the development of novel HRQL assessment tools also considering current environmental influences.

5 | CONCLUSION

Our analysis reveals the eliciting allergen, the severity of the allergic disease, but moreover multiple external factors impact the outcome in HRQL in food, but also venom allergic patients and should be considered in HRQL assessment.

There is robust data that food allergic paediatric patients, especially those who did experience anaphylaxis in the past, have an impaired HRQL, due the fear of repetitive anaphylactic reactions and the actions taken to avoid reactions, such as constant vigilance and carrying emergency medication. Several external factors have been shown to modulate HRQL in both, positive and negative ways. Bullying due to food allergy or if others are not appreciating the seriousness of the disease, lead to diminished HRQL. Social support, oral food challenges, the tolerance of products with precautionary allergen labelling, oral immunotherapy and the experience of self-effectiveness improve HRQL. As most data on food allergy HRQL are reflecting children and their caregivers, more data on HRQL of food allergic adults is urgently needed. Also, an allergic reaction to Hymenoptera venom can have a negative impact on the HRQL of

patients as well as their relatives, irrespective of the severity of the reaction or patients' age. However, in comparison to food allergy, by far less data is available.

Hymenoptera venom allergy has been shown to cause emotional distress, fear and anxiety as well as restrictions in social life and everyday activities. This may lead to a perceived loss of safety and uncertainty. The extent of the perceived burden is associated with sociodemographic factors like patients' sex but also medical factors like the severity of the previous reaction(s). Therefore, the measurement of HRQL with disease-specific questionnaires that capture the concerns associated with hymenoptera venom allergy is important. Age-appropriate validated questionnaires for patients as well as their parents have been developed, translated and adapted in several languages. VIT together with proper information about the therapy and reassurance of its effectiveness improve HRQL of vespid allergic patients irrespective of the initial reaction severity, while the EAI alone does not lead to an improved HRQL. Therefore, HRQL should be one of the reasons to offer immunotherapy.

AUTHOR CONTRIBUTIONS

VH performed literature research and review, wrote the manuscript and designed the figures. MM assisted in literature research and review. SDB assisted in literature research and review as well as figure design. MW and MBB conceptualized the manuscript, wrote the manuscript and supervised the process. All authors read and approved the final version of the manuscript.

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CONFLICT OF INTEREST

VH, MM, SDB, MW and MBB have no relevant conflict of interest to disclose with regard to this manuscript.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

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