







ORIGINAL ARTICLE

Current controversies in trichology: a European expert consensus statement

T. Meyer-Gonzalez,¹ D. Bacqueville,²  R. Grimalt,³  V. Mengeaud,² B.M. Piraccini,⁴ 
 L. Rudnicka,⁵  D. Saceda-Corralo,⁶  A. Vogt,⁷ Trichology Experts Network Group,[†]
 S. Vano-Galvan^{6,*} 

¹Trichology Unit, Dermatology Service Hospital Dr. Gálvez, Malaga, Spain

²Pierre Fabre Laboratories, Centre R&D Pierre Fabre Toulouse, Toulouse, France

³Department of Dermatology, Universitat Internacional de Catalunya, Barcelona, Spain

⁴IRCCS Azienda Ospedaliero-Universitaria di Bologna - Department of Experimental, Diagnostic and Specialty Medicine (DIMES) Alma Mater Studiorum, University of Bologna, Bologna, Italy

⁵Department of Dermatology, Medical University of Warsaw, Warsaw, Poland

⁶Trichology Unit, #TricoHRC Research Group, Dermatology Service, IRYCIS, Ramon y Cajal Hospital, University of Alcalá, Madrid, Spain

⁷Clinical Research Center for Hair and Skin Science, Department of Dermatology and Allergy, Charité-Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany

*Correspondence: S. Vañó-Galván. E-mail: drsergiovano@gmail.com

Abstract

Introduction Hair disorders are one of the most common conditions within dermatology practice but, although new diagnostic tools and therapeutic options have arisen, the management of these patients still represents a major clinical challenge.

Objective This study aimed at gathering information and achieving consensus on relevant recommendations on the latest advances in alopecia, trichoscopy and hair dermocosmetics.

Methods Experts of the steering committee consulted the available evidence on trichology-related areas from the past 5 years and formulated recommendations based on the evidence and their experience. A modified two-round Delphi procedure was performed among 45 European dermatologists experts in trichology to consult their degree of agreement on twenty recommendations, using a 4-point Likert scale. Consensus was defined as >80% of participants scoring either 1 (totally agree) or 2 (agree).

Results In the first round of the Delphi questionnaire, 75% of the recommendations reached consensus. Those that were not agreed upon were reformulated by the steering committee and voted again after an online meeting, where consensus was achieved in all recommendations.

Conclusions All recommendations reached consensus after the two-round Delphi questionnaire and may be useful in clinical practice for dermatologists. The participants agreed that besides this consensus, further clinical studies are needed to assess the benefits of the emerging tools and treatments and to clarify the controversies that still exist in the field, aiming at improving patients' quality of life.

Received: 10 June 2021; Accepted: 13 August 2021

Conflict of interest

Daniel Bacqueville and Valérie Mengeaud are current employees of Pierre Fabre Laboratories. Dr. Ramon Grimalt, Dr. David Saceda and Dr. Teresa Meyer declare that they have no conflict of interest. Dr. Bianca Maria Piraccini has received consulting fees from Difa Cooper, Pierre Fabre, L'Oréal, ISDIN, Legacy Healthcare, Pfizer, Almirall and Lilly; and has received honoraria for lectures and presentations from Difa cooper. Dr. Lidia Rudnicka has received consulting fees from Pierre Fabre, L'Oréal, Leo and Pfizer has received honoraria for lectures and presentations from Leo, Lilly and Abbvie; has had fiduciary roles in boards, societies or committees involving Polish Dermatological Society, European Academy of Dermatology and Venereology, American Academy of Dermatology and Venereology, International Dermoscopy Society and International Trichoscopy Society. Dr. Annika Vogt has been involved in the following sponsored as well as investigator-initiated research projects supported by Follicum AB, LEO Pharma, PPM Services S.A., Novartis Pharma AG, Johnson & Johnson

[†]Trichology Experts Network Group are listed in Appendix 1

Consumer Inc., PellePharm, Inc., Procter & Gamble. She received consulting fees and honoraria for lectures and presentations from Bayer, Galderma, Merck, Johnson & Johnson and Pierre Fabre Laboratories. She is board member in the Working Group Pediatric Dermatology within the German Society of Dermatology. Dr. Sergio Vañó-Galván has received grants from Novartis, Cantabria Labs, Fagron and DS Laboratories; consulting fees from Almirall, Pfizer, Janssen, Cantabria Labs, ISDIN, GSK, MSD, Pierre Fabre, Galderma, Ducray, L'Oréal, Abbott and FotoFinder; and honoraria for lectures and presentations from Almirall, Pfizer, Janssen, Cantabria Labs, ISDIN and GSK.

Funding source

This study was supported by DUCRAY Laboratoires Dermatologiques, Pierre Fabre Dermo-Cosmétique, France.

Introduction

Hair disorders, especially hair loss, are one of the most common conditions within dermatology practice that can significantly affect the patient's quality of life.¹ In recent years, new diagnostic tools and therapeutic options have been suggested, but whether they are effective and safe to treat hair disorders still remains controversial in some cases, as available evidence is limited.

New advances in trichology have proposed low-dose oral minoxidil,^{2–7} bicalutamide,^{8–10} dustasteride¹¹ and platelet-rich plasma (PRP)^{12,13} for the treatment of different types of alopecia. Besides drug treatments, hair transplantation (HT) has also emerged as a therapeutic option for many patients with non-cicatricial alopecia, but its effectiveness in cicatricial alopecia remains uncertain.^{14,15} Also, the role of the skin microbiome in skin disorders has received increasing attention in recent years.

Another controversial area is the effectiveness of vitamins and minerals supplements for the treatment of hair disorders.^{16–24} Similarly, oxidative stress has been recognized as a trigger factor of hair ageing.^{25,26}

The objective of this study was to gather information and achieve consensus on relevant recommendations and statements on alopecia, trichoscopy and dermocosmetics, provided by a community of renowned specialists in trichology.

Methods

Participants

Two coordinators (S V-G and T M-G) were selected considering their expertise in trichology to supervise the whole process and a steering committee (SC), formed by the two coordinators and seven trichologists (five physicians and two academic researchers), was established. Participants were renowned European experts in trichology. Physicians had at least 7 years of experience in the area of trichology (average 17.5 years), visit at least 60 patients a month and have an average of 100 relevant research publications in the field. Academic researchers had 3 years of experience in trichology research.

Forty-six experts from 10 different countries were invited to participate as panellists in the modified Delphi questionnaire; 45 of them participated in both rounds. Their nationalities included

Spain (31) Portugal (3), Bulgaria (2), Poland (2), Russia (2), Belgium (1), India (1), Nigeria (1), Ukraine (1) and Georgia (1). They were selected given their expertise and interest in trichology. The majority (93.5%) had at least 5 years of professional experience and visit at least fifty patients a month, has published trichology-related articles (67.4%), and has participated in congresses (71.7%) and clinical studies (56.5%) with a special focus in trichology.

Procedure and consensus process

A two-step modified Delphi, conducted between September 2020 and March 2021, was used to know the panellists' degree of agreement on the recommendations formulated by the SC.

Controversy areas to discuss were selected given the novelty of the subject and the paucity of evidence; they were distributed among the SC in order to elaborate the items of the questionnaire. The SC conducted a review of the literature in the field from the past 5 years and elaborated two recommendations on each assigned topic based on their judgement and experience, and according to the available evidence.

The recommendations that composed the questionnaire were validated by all the members of the SC and voted on a first round by the panellists ($n = 46$); the first round was conducted between the 21st of September 2020 and the 7th of January 2021 on an Internet microsite. A Likert scale was used to indicate the level of agreement: totally agree (1) – agree (2) – disagree (3) – totally disagree (4).

The level of agreement for the consensus was set at 80%. Unanimity was considered when 100% of the participants scored either 1 (totally agree) or 2 (agree). For the purpose of the analysis, unanimity and consensus were considered together as a consensus. The recommendations that did not reach consensus were reformulated by the same experts; some of them were proposed as statements rather than recommendations. On the 5th and 6th of February 2021, an online meeting was held and all the evidence supporting the recommendations was presented and discussed. After the meeting, the second round was opened and the modified recommendations were voted again ($n = 45$); the online voting system was active for a month.

Table 1 Results of the first round of the modified Delphi ($n = 46$). The % of agreement is shown

Alopecia	Oral minoxidil 5 mg daily is a therapeutic option for male patients with androgenetic alopecia.	95.65%
	Oral bicalutamide must be considered in female pattern hair loss when other approved treatment options have failed	86.96%
	Mesotherapy with dutasteride is a useful treatment for androgenetic alopecia patients. A protocol should be established	100.00%
	Systemic therapy is advisable for moderate-to-severe alopecia areata due to its association with systemic activation of the immune system	97.83%
	Patients with frontal fibrosing alopecia who are worsening despite treatment may benefit from reducing the use of sunscreens.	65.22%
	Platelet-rich plasma can be used as an adjunctive anti-inflammatory treatment for patients with lichen planopilaris.	80.43%
Trichoscopy	Every patient treated for hair loss should have a trichoscopy examination performed by the physician at least once throughout the treatment process.	95.65%
	In cases of chronic telogen effluvium associated with trichoscopic inflammatory signs (perifollicular erythema or hyperkeratosis, etc.), a trichoscopy-guided biopsy should be recommended.	97.83%
	Recently described diffuse variants of lichenoid alopecias should be considered in the differential diagnosis of patients complaining of scalp pruritus. In these patients, a trichoscopy-guided biopsy is recommended	97.83%
Scalp pruritus	Patients with alopecias associated with scalp dysesthesia could benefit from treatment with naltrexone.	78.26%
Microbiome and the scalp	Balance between bacteria and yeast might lead to a healthy skin.	93.48%
	Mild forms of scalp psoriasis could also be related to the type and quantity of bacteria living in our skin.	63.04%
	Hair transplant should be considered in patients with frontal fibrosing alopecia.	63.04%
Hair ageing	Among hair disorders, hair ageing is an entity of its own requiring specific patient education and management	89.13%
	Intake or topical application of antioxidants could be a supportive measure for individuals suffering from clinical signs of hair ageing.	76.09%
Hair cosmetics	An innovative generation of in vitro models is needed to closely reproduce native hair follicle by using long-term organ culture and tissue engineering. They will be useful to better understand hair follicle biology and to improve alopecia treatment before clinical trials in patients.	100.00%
	The identification of active ingredients that specifically target both intra- and extra-follicle signalling pathways (as for example Wnt/B catenin pathway, microcirculation, growth factors, cytokines, hormones, enzymes) could help to improve hair loss treatment.	100.00%
	Nutritional deficiencies should be corrected by diet supplementation or nutricosmetics to improve Telogen Effluvium	97.83%
	Patients with telogen effluvium could benefit from oral iron supplementation in order to reach ferritin levels $>40 \mu\text{L}$	97.83%
	Topical dermo-cosmetic formulations may improve hair loss by using specific active ingredients targeting the hair follicle, but also help to improve the quality of life of patients.	84.78%

GREEN: Consensus, GREY: no Consensus.

Results

In the first round, 75% of the recommendations (15/20) reached consensus (15% unanimously; Table 1). Four out of the five recommendations without consensus were modified before the second round in order to improve clarity, and some of them were proposed as statements rather than recommendations. One of the recommendations was not changed, but the supporting evidence was presented during the meeting. After the second round, an agreement was achieved for all of them (Table 2).

Discussion

This study provides the opinion of 45 experts on 20 recommendations and statements about the latest advances in trichology in a two-round modified Delphi. The second round was performed after an online meeting where the SC presented the scientific supporting evidence. Several concerns and controversies were raised and discussed during the meeting, but at the end, a consensus was achieved in all recommendations.

Non-cicatricial alopecia

Oral minoxidil 5 mg daily is a therapeutic option for male patients with androgenetic alopecia The safety and efficacy of oral minoxidil at low dose for the treatment of androgenetic alopecia have been evaluated in recent studies.^{2,3,7,27,28} Although experts agreed on the recommendation, several concerns were raised during the meeting, like the fact that low doses are not commercially available in most countries and the drug needs to be compounded in the pharmacy. Oral minoxidil is used for the treatment of hypertension, so any alteration in the compounding could lead to cardiovascular complications. Depending on the severity of the alopecia and comorbidities of the patient, lower doses (2.5 mg daily or even less) can be considered.

Oral bicalutamide must be considered in female pattern hair loss when other approved treatment options have failed Some studies have shown the off-label use of bicalutamide, a

Table 2 Results of the first ($n = 46$) and second ($n = 45$) round of the modified Delphi of the modified recommendations and statements. The % of agreement is shown

Alopecia	1st round results	Patients with frontal fibrosing alopecia who are worsening despite treatment may benefit from reducing the use of sunscreens.	65.22%
	2nd round results	It is controversial whether patients with frontal fibrosing alopecia who are worsening despite treatment may benefit from reducing the use of sunscreens.	84.44%
Scalp pruritus	1st round results	Patients with alopecias associated with scalp dysesthesia could benefit from treatment with naltrexone.	78.26%
	2nd round results	In case of alopecias associated with scalp dysesthesia, Naltrexone represents a promising option in patients unresponsive to conventional treatments.	93.33%
Microbiome and the scalp	1st round results	Mild forms of scalp psoriasis could also be related to the type and quantity of bacteria living in our skin.	63.04%
	2nd round results	Mild forms of scalp psoriasis could also be related to the type and quantity of bacteria living in our skin.	82.22%
Hair transplantation	1st round results	Hair transplant should be considered in patients with frontal fibrosing alopecia.	63.04%
	2nd round results	Hair transplant should be considered in some cases of frontal fibrosing alopecia.	91.11%
Hair ageing	1st round results	Intake or topical application of antioxidants could be a supportive measure for individuals suffering from clinical signs of hair ageing.	76.09%
	2nd round results	Experimental evidence supports the need for clinical studies to assess whether antioxidants could be a supportive measure for individuals suffering from clinical signs of hair ageing.	88.89%

GREEN: Consensus, RED: no Consensus.

nonsteroidal antiandrogen, for female androgenetic alopecia with a good safety profile with maximum efficacy at approximately 12 months.^{8–10} Experts agreed on this recommendation, but during the discussion, they mentioned the need to perform a blood test every 3–4 months in order to monitor the liver enzymes, as mild hypertransaminasaemia seems to be the most frequent adverse effect in the published studies.^{8–10} So, oral bicalutamide might be an option in female pattern hair loss when other therapies have failed. Woman with childbearing potential must maintain contraceptive measures during the treatment and at least 2 months after stopping it.

Mesotherapy with dutasteride is a useful treatment for androgenetic alopecia patients. A protocol should be established Dutasteride is an antiandrogen that has been used off-label for the treatment of androgenetic alopecia for several years, and 0.5 mg a day has proved to be effective and safe to treat male pattern hair loss.²⁹ Mesotherapy with dutasteride has also been used in some prospective and placebo-controlled studies to treat patients with androgenetic alopecia.^{30–34} Experts agreed that dutasteride microinjections are a promising therapeutic option for male and female patients with androgenetic alopecia but that comparative studies should be performed to establish the best protocol, as studies performed to date use different therapeutic regimens.

Systemic therapy is advisable for moderate-to-severe alopecia areata due to its association with systemic activation of the immune system Whether alopecia areata is an autoimmune disease still remains controversial³⁵ but many studies have

shown that severe cases are associated with a systemic activation of the immune system.^{36–39} While topic or local therapies may cause hair regrowth, they are unlikely to target the cause of the disease; the use of systemic therapy is recommended for those patients. The specific therapy (i.e. systemic corticosteroids, classical immunosuppressive drugs, JAK inhibitors. . .) will depend on the patient's features, benefit–risk ratio and availability of the treatment.

Cicatricial alopecia

It is controversial whether patients with frontal fibrosing alopecia who are worsening despite treatment may benefit from reducing the use of sunscreens A very recent and controversial topic in dermatology is the link between sunscreens and the development of FFA. Despite some studies support this association,^{40–43} data on this topic are still scarce and no agreement was reached on whether sunscreens should be avoided in patients with FFA. However, a survey by the American Hair Research Society shows that most specialists recommend avoiding the use of sunscreens (either chemical or physical) in patients with FFA.⁴⁴ Further research is required to provide an evidence-based recommendation.

Platelet-rich plasma can be used as an adjunctive anti-inflammatory treatment for patients with lichen planopilaris Platelet-rich plasma (PRP) has recently been described as a useful therapy for some autoimmune dermatoses like lichen sclerosus, as its high levels of growths factors have anti-inflammatory effects.⁴⁵ Though evidence is limited and the

number of patients included in recent studies is low,¹³ preliminary data show that PRP might be an interesting second-line therapeutic approach for LPP patients.

Trichoscopy

Every patient treated for hair loss should have a trichoscopy examination performed by the physician at least once throughout the treatment process Trichoscopy is an effective and non-invasive technique to examine the hair and the scalp. It can be used for a more effective and accurate diagnosis of hair disorders, but it might also assist in the diagnosis of other unperceived illnesses, as hair loss could be a symptom of severe local or systemic diseases. Over the past 10 years, studies about the role of trichoscopy in the diagnosis of different hair disorders have increased considerably,^{46–48} and nowadays, this technique is commonly used by dermatologists in patients with hair loss.

In cases of chronic telogen effluvium associated with trichoscopic inflammatory signs (yellow dots, perifollicular erythema or hyperkeratosis, etc.), a trichoscopy-guided biopsy should be recommended Diagnosis of telogen effluvium is usually based on patient history, physical examination and trichoscopy. However, telogen hair loss might be observed in other types of hair or systemic disorders.^{49–52} Therefore, it was agreed that in patients with signs of chronic hair loss associated with trichoscopic scalp inflammation and perifollicular pigmentation, a scalp trichoscopy-guided biopsy should be performed in order to rule out an associated cicatricial alopecia, such as fibrosing alopecia in a pattern distribution (FAPD) or lichen planopilaris diffuse pattern (LPPDP).

Recently described diffuse variants of lichenoid alopecias should be considered in the differential diagnosis of patients complaining of scalp pruritus. In these patients, a trichoscopy-guided biopsy is recommended Scalp pruritus is a frequent complaint in the dermatological area and might be a sign of different local or systemic diseases. Recently described scalp diseases, including FAPD and LPPDP, might also be associated with scalp itching.^{51–53} These types of alopecia can be easily mistaken for other dermatological issues: trichoscopy-guided biopsies are recommended in these cases as they might help with the diagnoses and management of these types of scarring alopecia.

Scalp pruritus

In case of alopecias associated with scalp dysesthesia, Naltrexone represents a promising option in patients unresponsive to conventional treatments In recent years, some studies have suggested that naltrexone at low doses (1–5 mg) could be a potential alternative to the standard therapeutic regimen of scalp pruritus.^{54,55} However, other studies using topical

steroids combined with either 3 mg of naltrexone or placebo failed to show any significant difference in the improvement of LPP.⁵⁶ Up to 5 mg of naltrexone a day preserves its anti-inflammatory properties;⁵⁷ thus, it could be a potential therapeutic option for patients with scalp dysesthesia; a large clinical study (NCT04409041) to test this hypothesis has started.

Microbiome and scalp: seborrhoeic dermatitis, alopecia areata and psoriasis

Balance between bacteria and yeast might lead to a healthy skin The microorganisms living in our skin have been shown to protect against invading pathogens, and its role in some skin disorders has been recently studied by many researchers. In seborrhoeic dermatitis, some studies show that decreasing specific microorganisms of our skin might be beneficial for the course of the disease,⁵⁸ while other papers have found healthy bacteria that might protect against disease development.⁵⁹ In alopecia areata, the role of the skin microbiome is still unclear^{60,61} and, even though some bacterial biomarkers are associated with the disease, further studies are necessary to prove their involvement in the pathophysiology of the disease and to test its potential as a diagnostic tool.

Mild forms of scalp psoriasis could also be related to the type and quantity of bacteria living in our skin The role of the skin microbiome in scalp psoriasis has not been studied extensively, although some characterization of the microbiome in psoriatic lesions has been performed, finding a relative imbalance of *Streptococcus*, *Staphylococcus* and *Malassezia* compared with healthy skin.^{62,63} This recommendation did not reach consensus on the first round of the Delphi-like questionnaire. However, after exposing the evidence on the role of the microbiome in seborrhoeic dermatitis^{58,59} and considering the similarities between seborrhoeic dermatitis and mild psoriasis, experts agreed on this recommendation.

Hair transplantation

Hair transplant should be considered in some cases of frontal fibrosing alopecia The effectiveness of HT in androgenetic alopecia and secondary scarring alopecia is well established, but whether other types of alopecia could also benefit remains controversial. A systematic review¹⁴ showed both positive and negative results in patients with FFA and LPP: patients stabilized for at least 2 years and treated with anti-inflammatory drugs pre- and post-transplant had better results than those who did not. In a multicentre review of 51 FFA patients, stabilized patients (no progression of the alopecia on the frontotemporal hairline after 12 months)

that underwent HT experienced good but temporary results – only 41% of the grafts survived after 5-year follow-up, despite maintaining the medical therapy.¹⁵ However, 82% of patients were globally satisfied with the procedure. Hair transplantation in FFA patients is challenging, as the affected area is not well defined and the donor area should be accurately selected with dermoscopy. Therefore, the experts agreed that HT should only be considered in some selected cases of FFA, after a careful discussion with the patients about the expected results and durability of the transplanted hairs.

Hair ageing

Among hair disorders, hair ageing is an entity of its own requiring specific patient education and management Age-related hair loss has been widely debated over the years, and several clinical and pre-clinical studies have been conducted in this area. A new focus has arisen around the role of the hair follicle environment in hair ageing.^{64,65} A study by Cao *et al.*⁶⁶ used mice to transplant hair follicles from an old tissue environment to a young one and showed that some molecular processes could be reversed. Due to our lifespan, ageing studies in humans are more complicated and data are rather limited.^{67,68} Further research should focus on discerning the differences between hair ageing and androgenetic alopecia, which are commonly confused. All experts agreed on hair ageing being a specific field among hair disorders that should be managed accordingly.

Experimental evidence supports the need for clinical studies to assess whether antioxidants could be a supportive measure for individuals suffering from clinical signs of hair ageing Oxidative stress has been studied as a trigger factor in hair ageing for some time, but whether supplementation of antioxidants could restore the redox imbalance and reverse the ageing process in humans remains unknown^{25,26} and further research is needed.

Evidence-based hair cosmetics

An innovative generation of in vitro models is needed to closely reproduce native hair follicle by using long-term organ culture and tissue engineering. They will be useful to better understand hair follicle biology and to improve alopecia treatment before clinical trials in patients A better understanding of the molecular mechanisms of hair follicles and new screening tools might discover new therapeutic options that could be ultimately used to treat patients with different types of alopecia. To date, cell culture models – 2D or 3D tissue engineering models – are the most used in basic research.^{69–71} However, experts demand new hair follicle models that mimic the complexity of this biological structure. Recent work^{72,73} suggests that entire hair follicle might soon be generated from

cultured human cells. This could imply a revolutionary treatment for hair loss: to generate enough hair follicles in a dish that can be then implanted into patients.

The identification of active ingredients that specifically target both intra- and extra-follicle signalling pathways (as for example Wnt/B catenin pathway, microcirculation, growth factors, cytokines, hormones and enzymes) could help to improve hair loss treatment Active ingredients that target key signalling pathways of hair biology are becoming complementary therapies for hair loss,^{74–76} but further research is needed to identify new molecules that target specific signalling pathways. Basic research and hair follicle models could be used to both identify new key players in hair biology and to screen active ingredients and select the better extract to further do clinical trials.

Nutritional deficiencies should be corrected by diet supplementation or nutricosmetics to improve Telogen Effluvium Even though several studies have shown that patients with alopecia present low levels of ferritin, iron, vitamin D or zinc,^{16,17,20,22,77} the role of the micronutrients in hair loss has been widely debated. However, nutricosmetics could be a useful supplement to improve the management of some hair disorders, like telogen effluvium. Well-designed clinical trials are crucial to elucidate the efficacy and safety of nutritional supplementation.

Patients with telogen effluvium could benefit from oral iron supplementation in order to reach ferritin levels >40 µ/L A controversial aspect of telogen effluvium and other hair loss disorders is the contribution of vitamins and minerals supplementation on the course of the disease. Several studies have been performed, but conclusions are inconsistent.^{16,19,21,78,79} Regardless, many dermatologists routinely prescribe iron supplementation for patients with telogen effluvium and the panellists agreed on maintaining ferritin levels above 40 µ/L in these patients.

Topical dermo-cosmetic formulations may improve hair loss by using specific active ingredients targeting the hair follicle, but also help to improve the quality of life of patients Experts agreed on this recommendation and emphasized the need for robust clinical trials to evaluate the efficacy of topical cosmetics to improve hair loss. Some indications that topical hair lotions and shampoos containing active ingredients improve hair density and prevent hair loss have already been proposed but scientific evidence is still missing.

Overall, this study has reached consensus in emerging topics in trichology, in areas with limited evidence and variability in the clinical practice. However, our study also has some limitations: the recommendations are not based on an exhaustive systematic review so some evidence may have been missed. On the other hand, the Delphi technique only provides qualitative

results, from the punctuation on the degree of agreement of the panellists with the recommendations and statements. Besides, considering that most panellists were Spanish (69%), they may not be representative of the whole specialist population.

Conclusions

Despite the extensive number of studies published, hair disorders still represent a common complaint in the clinics, probably due to the specific characteristics of each type of hair disease. The recommendations agreed in this study may be useful in clinical practice for dermatologists. However, further studies should be conducted to validate the benefits of some of the new treatments and techniques, and to establish protocols that would improve the management of these diseases.

Acknowledgements

The authors would like to thank Ducray for their economic and logistic support for this project, and GOC Health Consulting team for their methodologic and logistic support for this project and for the assistance on writing this manuscript.

Author contributions

All authors made substantial contributions to conception and design and acquisition of data; took part in drafting the article or revising it critically for important intellectual content; gave final approval of the version to be published; and agreed to be accountable for all aspects of the work.

References

- Urban J, Qi L, Zhao H, Rybak I, Rauhen KA, Kiuru M. Comparison of hair manifestations in cardio-facio-cutaneous and Costello syndromes highlights the influence of the RAS pathway on hair growth. *J Eur Acad Dermatol Venereol* 2020; **34**: 601–607.
- Panchaprateep R, Lueangarun S. Efficacy and safety of oral minoxidil 5 mg once daily in the treatment of male patients with androgenetic alopecia: an open-label and global photographic assessment. *Dermatol Ther (Heidelb)* 2020; **10**: 1345–1357.
- Jimenez-Cauhe J, Saceda-Corralo D, Rodrigues-Barata R *et al.* Effectiveness and safety of low-dose oral minoxidil in male androgenetic alopecia. *J Am Acad Dermatol* 2019; **81**: 648–649.
- Sanabria B, Vanzela TN, Miot HA, Müller RP. Adverse effects of low-dose oral minoxidil for androgenetic alopecia in 435 patients. *J Am Acad Dermatol* 2021; **84**: 1175–1178.
- Perera E, Sinclair R. Treatment of chronic telogen effluvium with oral minoxidil: A retrospective study. *F1000Res* 2017; **6**: 1650.
- Vano-Galvan S, Trindade de Carvalho L, Saceda-Corralo D *et al.* Oral minoxidil improves background hair thickness in lichen planopilaris. *J Am Acad Dermatol* 2021; **84**: 1684–1686.
- Vañó-Galván S, Pirmez R, Hermosa-Gelbard A *et al.* Safety of low-dose oral minoxidil for hair loss: a multicenter study of 1404 patients. *J Am Acad Dermatol* 2021; **84**: 1644–1651.
- Ismail FF, Meah N, Trindade de Carvalho L, Bhojru B, Wall D, Sinclair R. Safety of oral bicalutamide in female pattern hair loss: A retrospective review of 316 patients. *J Am Acad Dermatol* 2020; **83**: 1478–1479.
- Fernandez-Nieto D, Saceda-Corralo D, Rodrigues-Barata R *et al.* Oral bicalutamide for female pattern hair loss: a pilot study. *Dermatol Ther* 2019; **32**: e13096.
- Fernandez-Nieto D, Saceda-Corralo D, Jimenez-Cauhe J *et al.* Bicalutamide: a potential new oral antiandrogenic drug for female pattern hair loss. *J Am Acad Dermatol* 2020; **83**: e355–e356.
- Pindado-Ortega C, Saceda-Corralo D, Moreno-Arrones Ó *et al.* Effectiveness of dutasteride in a large series of patients with frontal fibrosing alopecia in real clinical practice. *J Am Acad Dermatol* 2021; **84**: 1285–1294.
- Jha AK. Platelet-rich plasma for the treatment of lichen planopilaris. *J Am Acad Dermatol* 2018; **79**: e95–e96.
- Svigos K, Yin L, Shaw K *et al.* Use of platelet-rich plasma in lichen planopilaris and its variants: a retrospective case series demonstrating treatment tolerability without koebnerization. *J Am Acad Dermatol* 2020; **83**: 1506–1509.
- Ekelem C, Pham C, Atanaskova MN. A Systematic review of the outcome of hair transplantation in primary scarring alopecia. *Skin Appendage Disord* 2019; **5**: 65–71.
- Vañó-Galván S, Villodres E, Pigem R *et al.* Hair transplant in frontal fibrosing alopecia: a multicenter review of 51 patients. *J Am Acad Dermatol* 2019; **81**: 865–866.
- Cheung EJ, Sink JR, English Iii JC. Vitamin and mineral deficiencies in patients with telogen effluvium: a retrospective cross-sectional study. *J Drugs Dermatol* 2016; **15**: 1235–1237.
- Deloche C, Bastien P, Chadoutaud S *et al.* Low iron stores: a risk factor for excessive hair loss in non-menopausal women. *Eur J Dermatol* 2007; **17**: 507–512.
- Park SY, Na SY, Kim JH, Cho S, Lee JH. Iron plays a certain role in patterned hair loss. *J Korean Med Sci* 2013; **28**: 934–938.
- Rasheed H, Mahgoub D, Hegazy R *et al.* Serum ferritin and vitamin d in female hair loss: do they play a role? *Skin Pharmacol Physiol* 2013; **26**: 101–107.
- Sanke S, Samudrala S, Yadav A, Chander R, Goyal R. Study of serum vitamin D levels in men with premature androgenetic alopecia. *Int J Dermatol* 2020; **59**: 1113–1116.
- Sant'Anna Addor FA, Donato LC, Melo CSA. Comparative evaluation between two nutritional supplements in the improvement of telogen effluvium. *Clin Cosmet Investig Dermatol* 2018; **11**: 431–436.
- Conic RRZ, Piliang M, Bergfeld W, Atanaskova-Mesinkovska N. Vitamin D status in scarring and non-scarring alopecia. *J Am Acad Dermatol* 2018; **18**: 577–584.
- Dhurat R, Chitallia J, May TW *et al.* An open-label randomized multicenter study assessing the noninferiority of a caffeine-based topical liquid 0.2% versus minoxidil 5% solution in male androgenetic alopecia. *Skin Pharmacol Physiol* 2017; **30**: 298–305.
- Pekmezci E, Dündar C, Türkoğlu M. A proprietary herbal extract against hair loss in androgenetic alopecia and telogen effluvium: a placebo-controlled, single-blind, clinical-instrumental study. *Acta Dermatovenerol Alp Pannonica Adriat* 2018; **27**: 51–57.
- Lim KM, An S, Lee OK *et al.* Analysis of changes in microRNA expression profiles in response to the troxerutin-mediated antioxidant effect in human dermal papilla cells. *Mol Med Rep* 2015; **12**: 2650–2660.
- Gherardini J, Wegner J, Chéret J *et al.* Transepidermal UV radiation of scalp skin ex vivo induces hair follicle damage that is alleviated by the topical treatment with caffeine. *Int J Cosmet Sci* 2019; **41**: 164–182.
- Saoraya Lueangarun RP, Tempark T, Noppakun N. Efficacy and safety of oral minoxidil 5 mg daily during 24-week treatment in male androgenetic alopecia. *J Am Acad Dermatol* 2015; **72**(Suppl. 1): AB113.
- Pirmez R, Salas-Callo CI. Very-low-dose oral minoxidil in male androgenetic alopecia: a study with quantitative trichoscopic documentation. *J Am Acad Dermatol* 2020; **82**: e21–e22.
- Eun HC, Kwon OS, Yeon JH *et al.* Efficacy, safety, and tolerability of dutasteride 0.5 mg once daily in male patients with male pattern hair loss: a randomized, double-blind, placebo-controlled, phase III study. *J Am Acad Dermatol* 2010; **63**: 252–258.

- 30 Moftah N, Abd-Elaziz G, Ahmed N, Hamed Y, Ghannam B, Ibrahim M. Mesotherapy using dutasteride-containing preparation in treatment of female pattern hair loss: photographic, morphometric and ultrastructural evaluation. *J Eur Acad Dermatol Venereol* 2013; **27**: 686–693.
- 31 Reguero-Del Cura L, Durán-Vian C, de Quintana-Sancho A. RF-mesotherapy with dutasteride: a future alternative treatment for androgenetic alopecia. *Actas Dermosifiliogr* 2020; **111**: 419–420.
- 32 Saceda-Corralo D, Rodrigues-Barata AR, Vañó-Galván S, Jaén-Olasolo P. Mesotherapy with dutasteride in the treatment of androgenetic alopecia. *Int J Trichology* 2017; **9**: 143–145.
- 33 Abdallah M, El-Zawahry KA, Besar H. Mesotherapy using dutasteride-containing solution in male pattern hair loss: a controlled pilot study. *J Pan Arab Leag Dermatol* 2009; **20**: 137–145.
- 34 Sobhy N, Aly H, El Shafee A, El Deeb M. Evaluation of the effect of injection of dutasteride as mesotherapeutic tool in treatment of androgenetic alopecia in males. *Our Dermatol Online* 2013; **4**: 40.
- 35 Żeberkiewicz M, Rudnicka L, Malejczyk J. Immunology of alopecia areata. *Cent Eur J Immunol* 2020; **45**: 325–333.
- 36 Conic RZ, Tamashunas NL, Damiani G et al. Comorbidities in pediatric alopecia areata. *J Eur Acad Dermatol Venereol* 2020; **34**: 2898–2901.
- 37 Rudnicka L, Waśkiel-Burnat A. Systemic aspects of alopecia areata Comment to the article by Lai and Sinclair. *J Eur Acad Dermatol Venereol* 2021; **35**: e214–e215.
- 38 Shahidi-Dadras M, Bahraini N, Rajabi F, Younespour S. Patients with alopecia areata show signs of insulin resistance. *Arch Dermatol Res* 2019; **311**: 529–533.
- 39 Wang E, Chong K, Yu M et al. Development of autoimmune hair loss disease alopecia areata is associated with cardiac dysfunction in C3H/HeJ mice. *PLoS ONE* 2013; **8**: e62935.
- 40 Robinson G, McMichael A, Wang SQ, Lim HW. Sunscreen and frontal fibrosing alopecia: A review. *J Am Acad Dermatol* 2020; **82**: 723–728.
- 41 Moreno-Arrones OM, Saceda-Corralo D, Rodrigues-Barata AR et al. Risk factors associated with frontal fibrosing alopecia: a multicentre case-control study. *Clin Exp Dermatol* 2019; **44**: 404–410.
- 42 Debroy Kidambi A, Dobson K, Holmes S et al. Frontal fibrosing alopecia in men: an association with facial moisturizers and sunscreens. *Br J Dermatol* 2017; **177**: 260–261.
- 43 Aldoorni N, Dobson K, Holden CR, McDonagh AJ, Harries M, Messenger AG. Frontal fibrosing alopecia: possible association with leave-on facial skin care products and sunscreens; a questionnaire study. *Br J Dermatol* 2016; **175**: 762–767.
- 44 Tosti A, Bergfeld WF, Christiano AM, et al. Response from the American Hair Research Society to "Sunscreen and frontal fibrosing alopecia: A review". *J Am Acad Dermatol* 2020; **82**: 729–730.
- 45 Everts P, Onishi K, Jayaram P, Lana JF, Mautner K. Platelet-rich plasma: new performance understandings and therapeutic considerations in 2020. *Int J Mol Sci* 2020; **21**: 7794.
- 46 Alessandrini A, Brattoli G, Piraccini BM, Di Altobrando A, Starace M. The Role of Trichoscopy in Keratosis Follicularis Spinulosa Decalvans: Case Report and Review of the Literature. *Skin Appendage Disord* 2021; **7**: 29–35.
- 47 Waśkiel-Burnat A, Rakowska A, Sikora M, Ciechanowicz P, Olszewska M, Rudnicka L. Trichoscopy of tinea capitis: a systematic review. *Dermatol Ther (Heidelb)* 2020; **10**: 43–52.
- 48 Saceda-Corralo D, Moreno-Arrones OM, Rodrigues-Barata R et al. Trichoscopy activity scale for folliculitis decalvans. *J Eur Acad Dermatol Venereol* 2020; **34**: e55–e57.
- 49 Chanprapaph K, Udornpanich S, Visessiri Y, Ngamjanyaporn P, Suchonwanit P. Nonscarring alopecia in systemic lupus erythematosus: A cross-sectional study with trichoscopic, histopathologic, and immunopathologic analyses. *J Am Acad Dermatol* 2019; **81**: 1319–1329.
- 50 Alessandrini A, Starace M, Bruni F et al. Alopecia Areata incognita and diffuse alopecia areata: clinical, trichoscopic, histopathological, and therapeutic features of a 5-year study. *Dermatol Pract Concept* 2019; **9**: 272–277.
- 51 Starace M, Alessandrini A, Brandi N, Piraccini BM. Preliminary results of the use of scalp microneedling in different types of alopecia. *J Cosmet Dermatol* 2020; **19**: 646–650.
- 52 Griggs J, Trüeb RM, Gavazzoni Dias MFR, Hordinsky M, Tosti A. Fibrosing alopecia in a pattern distribution. *J Am Acad Dermatol* 2020. doi: 10.1016/j.jaad.2019.12.056. Online ahead of print.
- 53 Du X, Li Y, Zhu Q et al. Focal and diffuse fibrosing alopecias: Classical lichen planopilaris, frontal fibrosing alopecia, fibrosing alopecia with a pattern distribution, cicatricial pattern hair loss, and lichen planopilaris diffuse pattern. *JAAD Case Rep* 2020; **6**: 403–410.
- 54 Ekelem C, Juhasz M, Khera P, Mesinkovska NA. Utility of naltrexone treatment for chronic inflammatory dermatologic conditions: a systematic review. *JAMA Dermatol* 2019; **155**: 229–236.
- 55 Strazzulla LC, Avila L, Lo Sicco K, Shapiro J. Novel treatment using low-dose naltrexone for lichen planopilaris. *J Drugs Dermatol* 2017; **16**(11): 1140–1142.
- 56 Lajevardi V, Salarvand F, Ghiasi M, Nasimi M, Taraz M. The efficacy and safety of oral low dose naltrexone versus placebo in the patients with lichen planopilaris: a randomized controlled clinical trial. *J Dermatol Treat* 2020; doi: 10.1080/09546634.2020.1774488. Online ahead of print.
- 57 Wang X, Zhang Y, Peng Y et al. Pharmacological characterization of the opioid inactive isomers (+)-naltrexone and (+)-naloxone as antagonists of toll-like receptor 4. *Br J Pharmacol* 2016; **173**: 856–869.
- 58 Van TN, Thi NH, Van TH et al. Efficacy of oral itraconazole in the treatment of seborrheic dermatitis in vietnamese adults patients. *Open Access Maced J Med Sci* 2019; **7**: 224–226.
- 59 Park HK, Ha MH, Park SG, Kim MN, Kim BJ, Kim W. Characterization of the fungal microbiota (mycobiome) in healthy and dandruff-afflicted human scalps. *PLoS ONE* 2012; **7**: e32847.
- 60 Moreno-Arrones OM, Serrano-Villar S, Perez-Brocal V et al. Analysis of the gut microbiota in alopecia areata: identification of bacterial biomarkers. *J Eur Acad Dermatol Venereol* 2020; **34**: 400–405.
- 61 Migacz-Gruszka K, Branicki W, Obtulowicz A, Pirowska M, Gruszka K, Wojas-Pelc A. What's new in the pathophysiology of alopecia areata? The possible contribution of skin and gut microbiome in the pathogenesis of alopecia - big opportunities, big challenges, and novel perspectives. *Int J Trichology* 2019; **11**: 185–188.
- 62 Lewis DJ, Chan WH, Hinojosa T, Hsu S, Feldman SR. Mechanisms of microbial pathogenesis and the role of the skin microbiome in psoriasis: A review. *Clin Dermatol* 2019; **37**: 160–166.
- 63 Tett A, Pasolli E, Farina S et al. Unexplored diversity and strain-level structure of the skin microbiome associated with psoriasis. *NPJ biofilms and microbiomes* 2017; **3**: 14.
- 64 Shin W, Rosin NL, Sparks H et al. Dysfunction of hair follicle mesenchymal progenitors contributes to age-associated hair loss. *Dev Cell* 2020; **53**: 185–98.e7.
- 65 Matsumura H, Mohri Y, Binh NT et al. Hair follicle aging is driven by transepidermal elimination of stem cells via COL17A1 proteolysis. *Science* 2016; **351**(6273): aad4395.
- 66 Cao W, Li L, Kajiura S et al. Aging hair follicles rejuvenated by transplantation to a young subcutaneous environment. *Cell Cycle* 2016; **15**: 1093–1098.
- 67 Williams R, Westgate GE, Pawlus AD, Sikkink SK, Thornton MJ. Age-related changes in female scalp dermal sheath and dermal fibroblasts: how the hair follicle environment impacts hair aging. *J Invest Dermatol* 2021; **141**: 1041–1051.
- 68 Takahashi T, Mamada A, Breakspear S, Itou T, Tanji N. Age-dependent changes in damage processes of hair cuticle. *J Cosmet Dermatol* 2015; **14**: 2–8.
- 69 Madaan A, Verma R, Singh AT, Jaggi M. Review of hair follicle dermal papilla cells as in vitro screening model for hair growth. *Int J Cosmet Sci* 2018; **40**: 429–450.

- 70 Philpott MP. Culture of the human pilosebaceous unit, hair follicle and sebaceous gland. *Exp Dermatol* 2018; **27**: 571–577.
- 71 Castro AR, Logarinho E. Tissue engineering strategies for human hair follicle regeneration: how far from a hairy goal? *Stem Cells Transl Med* 2020; **9**: 342–350.
- 72 Abaci HE, Coffman A, Doucet Y *et al*. Tissue engineering of human hair follicles using a biomimetic developmental approach. *Nat Commun* 2018; **9**: 5301.
- 73 Lee J, Rabbani CC, Gao H *et al*. Hair-bearing human skin generated entirely from pluripotent stem cells. *Nature* 2020; **582**: 399–404.
- 74 Bassino E, Antoniotti S, Gasparri F, Munaron L. Effects of flavonoid derivatives on human microvascular endothelial cells. *Nat Prod Res* 2016; **30**: 2831–2834.
- 75 Völker JM, Koch N, Becker M, Klenk A. Caffeine and its pharmacological benefits in the management of androgenetic alopecia: a review. *Skin Pharmacol Physiol* 2020; **33**: 93–109.
- 76 Daniels G, Akram S, Westgate GE, Tamburic S. Can plant-derived phytochemicals provide symptom relief for hair loss? A critical review. *Int J Cosmet Sci* 2019; **41**: 332–345.
- 77 Kil MS, Kim CW, Kim SS. Analysis of serum zinc and copper concentrations in hair loss. *Ann Dermatol* 2013; **25**: 405–409.
- 78 Abdel Aziz AM, Sh Hamed S, Gaballah MA. Possible relationship between chronic telogen effluvium and changes in lead, cadmium, zinc, and iron total blood levels in females: a case-control study. *Int J Trichology* 2015; **7**: 100–106.
- 79 Deo K, Sharma YK, Wadhokar M, Tyagi N. Clinicoepidemiological observational study of acquired alopecias in females correlating with anemia and thyroid function. *Dermatol Res Pract* 2016; **2016**: 1–5.

Appendix 1

List of panellists (Trichology Experts Network)

Name	Last name	Country
Antonio José	Alcaide Martin	Spain
Manuel	Almagro Sánchez	Spain
Rubina	Alves	Portugal
Jose	Castiñeiras González	Spain
Andrea	Combalia Escudero	Spain
Cristina	De hoyos Alonso	Spain
María Elena	De las Heras Alonso	Spain
Rachita	Dhurat	India
Andrei	Doroshkevich	Russia
Nkechi	Enechukwu	Nigeria

Appendix 1 Continued

Name	Last name	Country
Beatriz	Fernández Jorge	Spain
Javier	Forteza	Spain
Manuel	Galán Guitérrez	Spain
Cristina	Garciandía	Spain
Alba	Gómez Zubiaur	Spain
Dimitar	Gospodinov	Bulgaria
Angela	Hermosa Gelbard	Spain
María	Herrero Moyano	Spain
Maribel	Iglesias Sancho	Spain
Alejandro	Lobato Berezo	Spain
Nino	Lortkipanidze	Georgia
Olszewska	Malgorzata	Poland
Nuria	Martí Fajardo	Spain
Alejandro	Martin Gorgojo	Spain
Constanza	Martínez Mera	Spain
Grisha	Mateev	Bulgaria
Joan Francesc	Mir Bonafé	Spain
José María	Mir Bonafé	Spain
Iria	Montero Perez	Spain
María	Moreira Fonseca	Portugal
Antonio	Morillo-Velarde Chiclana	Spain
Ana María	Mota Burgos	Spain
Yuliya	Ovcharenko	Ukraine
Cristina	Paradelo García	Spain
Carmen	Peña Penabad	Spain
Javier	Pedraz Muñoz	Spain
Juan	Peris Martí	Spain
Ramon	Pigem Gasos	Spain
Ana Rita	Rodrigues Barata	Spain
Lisset	Sarda Perez	Spain
Tatiana	Silyuk	Russia
Filipa	Ventura	Portugal
Francisco	Vílchez-Márquez	Spain
Anja	Vujovic	Belgium
Anna	Waśkiel-Burnat	Poland