**SUPPLEMENTARY MATERIALS**

# Application of ChatGPT as a content generation tool in continuing medical education: acne as a test topic

Luigi Naldi,[1,2] Vincenzo Bettoli,[2,3] Eugenio Santoro,[4] Maria Rosa Valetto,[5] Anna Bolzon,[1,6] Fortunato Cassalia,[1,6] Simone Cazzaniga,[2,7] Sergio Cima,[5] Andrea Danese,[8] Silvia Emendi,[5] Monica Ponzano,[6] Nicoletta Scarpa,[5] Pietro Dri[5]

[1]Dermatology Unit, Ospedale San Bortolo, Vicenza; [2]Centre of the Italian Group for Epidemiological Research in Dermatology (GISED), Bergamo; [3]Section of Dermatology and Infectious Diseases, Department of Medical Sciences, University of Ferrara; [4]Unit of Research in digital health and digital therapeutics, Department of Clinical Oncology, Mario Negri Institute for Pharmacological Research, Milan; [5]Zadig ltd Benefit Company, CME national provider, Milan; [6]Unit of Dermatology, Department of Medicine, University of Padua, Italy; [7]Department of Dermatology, Inselspital University Hospital of Bern, Switzerland; [8]Unit of Dermatology, Department of Integrated Medical and General Activity, University of Verona, Italy

**Corresponding author:** Luigi Naldi, Dermatology Unit, Ospedale San Bortolo, Vicenza, Italy; Study Centre of the Italian Group for Epidemiological Research in Dermatology (GISED), Bergamo, Italy.
E-mail: luiginaldibg@gmail.com

**Key words:** acne; Artificial Intelligence; ChatGPT; medical information; medical education; large language models (LLMs).

**Author Contributions:** PD, LN, ES, MRV, study design; SCi, SE, NS, query sessions and data collection; AB, VB, FC, AD, MP, analysis of contents; SE, NS, analysis of reproducibility; SCa, statistical analysis and preparation of figures and tables; VB, LN, ES, MRV, manuscript drafting; PD, ES, critical revision of the manuscript; PD, supervision of each phase of manuscript preparation. All authors read and approved the final version to be published.

**Conflict of interest**: the authors declare that they have no competing interests.

**Ethics approval and consent to participate**: not applicable due to the methodologic nature of the study and because the study did not involve human or animal subjects nor implied access to identifiable personal information.

**Availability of data and materials**: the data supporting the findings of this study are available in the supplementary file of this article or from the corresponding author upon reasonable request.

**Funding**: this research received no grant from any funding agency in the public, commercial, or not-for-profit sectors.

**Supplementary Table 1.** Qualitative judgements of evaluators for all answers of the questionnaire.

| Questions | Evaluators | | | | |
|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 4 |
| Q1 Can the use of cosmetics influence the appearance of acne? | The information provided in this paragraph is too detailed for general practitioners | | Chat GPT could be more precise and give more examples of products to avoid. Differently to the NICE guidelines, it does not specify the type of cleansing products to be used, such as synthetic, syndet, or non-alkaline (neutral or slightly acidic to match the skin's pH). | | Occlusive agents: petrolatum instead of petroleum |
| Q2 Can diet influence the appearance and severity of acne? | | It is important to emphasize in the conclusions that currently diet does not represent a disease-modifying factor for acne, as highlighted by the NICE guidelines. | Chat GPT's response on dietary advice is better developed than the guidelines, which instead give only general advice | | One of the most frequently reported key word is "potential". It is important to limit the idea that some foods are a major player in acne development. Interestingly, the fact that dietary interventions can be beneficial for some patients and not universally effective is reported |
| Q3 When and how to start an acne treatment? | | | The NICE guidelines are more comprehensive in | | The topical retinoid trifarotene is not mentioned. |

| | | | | | |
|---|---|---|---|---|---|
| | | | terms of information regarding therapy | | The systemic tetracycline lymecycline is not mentioned. It is not available all over the world (no US)<br>Patient education - side effects:<br>1) ...photosensitivity with (add "some") tetracyclines - Lymecycline is not photosensitizing<br>2) ...topical retinoids (add "and benzoyl peroxide"). Avoidance of known exacerbating factors: stress is not mentioned |
| Q4 Is it always necessary to start an acne treatment? | | | | | Acne-Induced Erythema is not mentioned |
| Q5 In mild-to-moderate acne which treatment regimen to adopt? | | | | | Acne-Induced Erythema is not mentioned.<br>Avoiding antibiotics as monotherapy is not sufficiently underlined.<br>Systemic therapies: used for a limited duration - the correct duration is not reported |
| Q6 In moderate-severe acne which treatment regimen to adopt? | | | | | Oral antibiotics: mode of action - the anti-inflammatory effect |

| | | | | | |
|---|---|---|---|---|---|
| Q7 Are there gender aspects to consider in managing acne? If yes, which ones? | | | | | doesn't depend necessarily on the reduction of *C. acnes*, it can be direct.<br>Hormonal therapy - mode of action: androgens are active also on keratinocytes<br>Oral retinoids - isotretinoin: iPLEDGE program is active only in North America. Mucocutaneous dryness is dose-dependent (to be underlined). The causative role of isotretinoin in inducing mood alterations is not demonstrated<br>Procedures: light and laser - the reduction of sebum production is not fully demonstrated.<br>Chemical peels may partially remove only the very small and superficial open comedones. The closed ones do not respond at all. (to be specified)" |

| | | | | | |
|---|---|---|---|---|---|
| Q8 Are there physical acne therapies? If so, how should they be included in the therapeutic program? | | According to the NICE guidelines, the only physical therapies proposed for acne are photodynamic therapy and intralesional corticosteroid injections. The other approaches suggested in Chat GPT's response are not incorrect, but it would be useful to establish an evidence-based hierarchy. | | | Cryotherapy - almost never used in clinical practice - never mentioned in guidelines. It doesn't deserve mentioning |
| Q9 Does photodynamic therapy have an indication? If so, how should it be used (times and ways)? | | | | | Side effects such as erythema, burning and inflammation are dose dependent and not sufficiently described |
| Q10 Is exposure to blue light helpful? | | | | | Clinical application - mild-to-moderate acne: BPO reduces *C. acnes* more easily. Procedure protocol: too frequent sessions - difficult to follow. Efficacy and limitations: 50% reduction is not enough considering the complexity of the procedure |
| Q11 How to deal with sun exposure in case of acne? | | | Oral retinoids are missing among the medications | | Exacerbation potential: overproduction of sebum by prolonged |

| | | | | | |
|---|---|---|---|---|---|
| | | | | | UV exposure is not demonstrated |
| Q12 Is professional extraction of comedones useful? | | | | | |
| Q13 What about the role of hormonal therapies? | | | | | COCs: Cyproterone acetate and dienogest are missing |
| Q14 What about the use of systemic and intralesional steroids? | | | | | The modalities of use are quite far from real-life use |
| Q15 Can psychological support be useful in patients with acne? If yes, in which cases? | | | | | |
| Q16 How to evaluate the response to acne treatment? | | | The guidelines and GPT diverge in that the guidelines focus on drug therapy management | | Some details regarding the global assessment scores and the need of a combined physician and patient assessment are not sufficiently specified |
| Q17 How long should acne treatment be continued? | | | Chat GPT covered this paragraph more thoroughly than the guidelines, however lacking the management of long-term antibiotic therapy | | Six months duration of systemic antibiotics is a UK position – the European position is 3 months isotretinoin duration; 5-9 months is strange. Data to be checked.<br>The concept of cumulative dose is not supported anymore (Ref: J. Tan).<br>Definition and duration of maintenance therapy are not fully defined - There are some data |

| | | | | | |
|---|---|---|---|---|---|
| | | | | | on duration of maintenance - available references |
| Q18 Are there reasons to propose long-term maintenance treatment once a satisfactory therapeutic response has been obtained? | | | Chat GPT addressed this topic differently to the guidelines as it does not discusses abundantly skin care and pharmacological management | | |
| Q19 What are the main side effects of topical acne treatments? | | Some topical treatments mentioned by Chat GPT are not included in the NICE guidelines | | | Azelaic acid skin irritation: itching is not a typical symptom |
| Q20 What are the main side effects of systemic acne treatments? | | | | | Lymecycline is never mentioned.<br>Clinical relevance and incidence of side effect is not mentioned, though clinically relevant.<br>Details on side effects, for instance regarding corticosteroids would be useful |
| Q21 Are there permanent sequelae of acne? If yes, which ones? If yes, how to prevent them? | | | GPT discusses the topic in greater depth than the guidelines | | PIH/AIH can't be pink to red! |
| Q22 Is there a role for lasers in the management of acne and its outcomes? | | In the NICE guidelines, the only mention of laser use is related to post-acne scars, not to active lesions | | | The role of laser on the active phase of acne is really controversial |

| | | | | | |
|---|---|---|---|---|---|
| Q23 Is there a role for peels in the management of acne and its outcomes? | The information provided in this paragraph is too detailed for general practitioners | In the NICE guidelines, the only mention of chemical peels use is related to post-acne scars, not to active lesions | Chat GPT discusses the topic in greater depth than the guidelines | | CROSS technique is not mentioned |

**Supplementary Table 2.** Qualitative judgements of evaluators for each reference.

| Questions | Evaluators | | | | |
|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 |
| Q1 Can the use of cosmetics influence the appearance of acne? | | | | There are better references available; these are not updated enough | Reference 1 is very old |
| Q2 Can diet influence the appearance and severity of acne? | | | | | Some recent references are missing |
| Q3 When and how to start an acne treatment? | | | | | |
| Q4 Is it always necessary to start an acne treatment? | | | Reference 1 is not so accurate about the necessity of initiating Acne Treatment | | More recent and relevant references are available |
| Q5 In mild-to-moderate acne which treatment regimen to adopt? | | | | | |
| Q6 In moderate-severe acne which treatment regimen to adopt? | | | | | Updated references are needed |
| Q7 Are there gender aspects to consider in managing acne? If yes, which ones? | | | | | |
| Q8 Are there physical acne therapies? If so, how should they be included in the therapeutic program? | | | References 2 and 3 do not provide detailed information about physical acne treatments | | |
| Q9 Does photodynamic therapy have an indication? If so, how should it be used (times and ways)? | | | | | Updated references are needed |
| Q10 Is exposure to blue light helpful? | | | In reference 1, the topic is only briefly covered and is not the main focus of the article | | Updated references are needed |
| Q11 How to deal with sun exposure in case of acne? | | | | | |

| | | | | | |
|---|---|---|---|---|---|
| Q12 Is professional extraction of comedones useful? | | | | | Updated references are needed |
| Q13 What about the role of hormonal therapies? | | | | | Updated references are needed |
| Q14 What about the use of systemic and intralesional steroids? | | | | | |
| Q15 Can psychological support be useful in patients with acne? If yes, in which cases? | | | | | |
| Q16 How to evaluate the response to acne treatment? | | | Reference 3 is not so pertinent | | All the references are old but refer to specific methods set up at that time |
| Q17 How long should acne treatment be continued? | | | | | Pertinent and relevant references are missing |
| Q18 Are there reasons to propose long-term maintenance treatment once a satisfactory therapeutic response has been obtained? | | | | | |
| Q19 What are the main side effects of topical acne treatments? | | | Reference 2 does not sufficiently address adverse reactions to topical treatments | | "The European Guidelines on acne treatment - 2016 - EADV - EDF have never been mentioned! Updated references are needed" |
| Q20 What are the main side effects of systemic acne treatments? | | | | | Updated references are needed |
| Q21 Are there permanent sequelae of acne? If yes, which ones? If yes, how to prevent them? | | | References 2 and 3 do not sufficiently address the topic | | Updated references are needed |
| Q22 Is there a role for lasers in the management of acne and its outcomes? | | | | | Updated references are needed |
| Q23 Is there a role for peels in the management of acne and its outcomes? | | | | | |

**Supplementary Table 3.** Recurrence of the references.

| Reference | N (%) |
|---|---|
| Zaenglein AL, Pathy AL, Schlosser BJ, et al. Guidelines of care for the management of acne vulgaris. J Am Acad Dermatol 2016;74:945-73.e33. DOI: 10.1016/j.jaad.2015.12.037. | 10 (14.5%) |
| Fabbrocini G, Annunziata MC, D'Arco V, et al. Acne scars: pathogenesis, classification and treatment. Dermatol Res Pract 2010;2010:893080. DOI: 10.1155/2010/893080. | 3 (4.3%) |
| Thiboutot DM, Dréno B, Abanmi A, et al. Practical management of acne for clinicians: An international consensus from the Global Alliance to Improve Outcomes in Acne. J Am Acad Dermatol 2018;78(2 Suppl 1):S1-S23.e1. DOI: 10.1016/j.jaad.2017.09.078. | 3 (4.3%) |
| Bhate K, Williams HC. Epidemiology of acne vulgaris. Br J Dermatol 2013;168:474–85. DOI: 10.1111/bjd.12149. | 2 (2.9%) |
| Eichenfield LF, Krakowski AC, Piggott C, et al; American Acne and Rosacea Society. Evidence-based recommendations for the diagnosis and treatment of pediatric acne. Pediatrics 2013;131 (Suppl 3):S163-86. DOI: 10.1542/peds.2013-0490B. | 2 (2.9%) |
| Tan JK, Bhate K. A global perspective on the epidemiology of acne. Br J Dermatol 2015;172 (Suppl 1):3-12. DOI: 10.1111/bjd.13462. | 2 (2.9%) |
| Walsh TR, Efthimiou J, Dréno B. Systematic review of antibiotic resistance in acne: an increasing topical and oral threat. Lancet Infect Dis 2016;16:e23-33. DOI: 10.1016/S1473-3099(15)00527-7. | 2 (2.9%) |
| Yentzer BA, Hick J, Reese EL, Uhas A, Feldman SR, Balkrishnan R. Acne vulgaris in the United States: a descriptive epidemiology. Cutis 2010;86:94-9. | 2 (2.9%) |

**Supplementary Table 4.** Internal reproducibility of the references.

| | | Answers | References* | Matching (references *vs* answers) |
|---|---|---|---|---|
| | | N (%) | N (%) | N (%) |
| Sessions 1-2 (N=23) | CO | 2 (8.7%) | 1 (4.3%) | 1 (50.0%) |
| | PO | 19 (82.6%) | 15 (65.2%) | 13 (68.4%) |
| | NO | 2 (8.7%) | 7 (30.4%) | 0 (0.0%) |
| Sessions 1-3 (N=23) | CO | 10 (43.5%) | 1 (4.3%) | 0 (0.0%) |
| | PO | 12 (52.2%) | 14 (60.9%) | 6 (50.0%) |
| | NO | 1 (4.3%) | 8 (34.8%) | 0 (0.0%) |
| Total 1-2-3 (N=46) | CO | 12 (26.1%) | 2 (4.3%) | 1 (8.3%) |
| | PO | 31 (67.4%) | 29 (63.0%) | 19 (61.3%) |
| | NO | 3 (6.5%) | 15 (32.6%) | 0 (0.0%) |

CO: complete overlap, NO: no overlap, PO: partial overlap

* For references: AO, PO and NO mean respectively 3, 1-2 and 0 references reproduced over a total of 3 references per question. Hallucinations were included in this analysis.

**Supplementary Table 5.** Unexpected or unpredictable events during query sessions.

| Question | | Unexpected or unpredictable events |
|---|---|---|
| 11 | How to deal with sun exposure in case of acne? | Session 3: line interruption and prompt for bibliographic records immediately resubmitted |
| 18 | Are there reasons to propose long-term maintenance treatment once a satisfactory therapeutic response has been obtained? | Session 1: when asked to indicate 3 bibliographic references referring to this question ChatGPT independently drafted two versions of bibliography, each with 3 entries, asking the operator to choose one among the two proposed versions. The operator chose the first one in order to proceed with the query |
| The majority of questions (N = 52) in all query sessions | | ChatGPT provided 3-4 bibliographic references already at the end of each answer, before they were explicitly requested. However, ChatGPT was asked to provide 3 references separately following the predefined methodology. The references indicated by ChatGPT at the end of the answers were not considered for the bibliographic analyses |