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"Consensus on Placebo and Nocebo Effects Connects Science with Practice:" Reply to "Questioning the Consensus on Placebo and Nocebo Effects"

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We thank Drs. Hardman, Hutchinson and Ongaro for their thoughtful comments [1]. We provide consensus and recommendations in our paper on how to inform patients about placebo and nocebo effects in clinical practice, and how to train clinicians in disclosing that information, based upon previous consensus papers [2–4]. Hardman et al. claim that our recommendations are not in line with recent research that shows a disconnect between the modern scientific definition of placebo and nocebo effects and how patients and clinicians understand those effects [5]. However, it is precisely this disconnect that makes our consensus statement important. For example, while patients and clinicians tend to focus on "placebos" as inert sugar pills, *placebo effects* are defined broadly as "positive

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treatment outcomes that cannot be attributed to active treatment components, but are elicited by positive expectations and/or the psychosocial context in which treatment takes place" [2–4]. Thus, our definition and recommendations encompass an integrated approach to healthcare that includes biomedical, psychological, ethical, and philosophical perspectives. Moreover, our expert panel included a diverse group of scientists, medical ethicists, and clinicians from many disciplines.

Given the prominence of placebo and nocebo effects in healthcare, it is important to communicate about them with patients in an open and transparent manner [6]. However, Hardman et al. conclude that clinicians should usually disclose *nothing* about placebo or nocebo effects. Two randomised trials suggest that this recommendation might harm patients, for example, those taking statins or those suffering from wind turbine syndrome [7, 8]. Additionally, our consensus statement emphasized the need for guidance on tailoring information to a patient's specific needs and circumstances [3]. We also highlight the need to explain the mechanisms behind placebo effects, and to replace the term "placebo effect" with alternative terms (e.g., reflecting specific mechanisms) whenever it is deemed helpful. Nevertheless, attempts at crafting an alternative term that covers the *full* range of effects and mechanisms associated with "placebo effect" have so far been unsuccessful. To illustrate, the supplementary material of our paper provides many alternative terms, including several proposed by Hardman et al., that we considered, but were ultimately found unsatisfactory, as they failed to cover the entirety of that which modern science understands to be placebo and nocebo effects.

We should stress that the aim of clinician training would not be to provide practitioners with "ready-to-use" explanations of placebo and nocebo effects. Instead, training should always emphasize the need to take the context and needs of the *individual* patient into account. Ultimately, it is the clinician's decision whether to disclose information about placebo and nocebo effects to patients. To do so effectively, healthcare professionals need training and information about these effects [9]. Which types of training and information would be most effective for which types of patients needs to be investigated thoroughly. In particular, more research about the effects of disclosing information about placebo and nocebo effects to patients, the ways in which the information should be disclosed, and the impact of those disclosures on health outcomes is necessary.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

A.W.M.E. and S.H.M. prepared the first draft of the letter. All authors provided feedback and revised the letter.

References

1 Hardman D, Hutchinson P, Ongaro G. Questioning the consensus on placebo and nocebo effects. Psychother Psychosom. 2020 Dec;1–2.
2 Evers AWM, Colloca L, Blease C, Annoni M, Atlas LY, Benedetti F, et al. Implications of placebo and nocebo effects for clinical practice: expert consensus. Psychother Psychosom. 2018;87(4):204–10.
3 Evers AWM, Colloca L, Blease C, Gaab J, Jensen KB, Atlas LY, et al.; Consortium of Placebo Experts. What should clinicians tell patients about placebo and nocebo effects? Practical considerations based on expert consensus. Psychother Psychosom. 2021;90(1):49–56.
4 Mitsikostas DD, Blease C, Carlino E, Colloca L, Geers AL, Howick J, et al.; European Headache Federation. European Headache Federation recommendations for placebo and nocebo terminology. J Headache Pain. 2020 Sep;21(1):117.
5 Hardman DI, Geraghty AW, Lewith G, Lown M, Viecelli C, Bishop FL. From substance to process: A meta-ethnographic review of how healthcare professionals and patients understand placebos and their effects in primary care. Health (London). 2020 May;24(3):315–40.
6 Colloca L, Finniss D. Nocebo effects, patient-clinician communication, and therapeutic outcomes. JAMA. 2012 Feb;307(6):567–8.
7 Crichton F, Petrie KJ. Health complaints and wind turbines: the efficacy of explaining the nocebo response to reduce symptom reporting. Environ Res. 2015 Jul;140:449–55.
8 Wood FA, Howard JP, Finegold JA, Nowbar AN, Thompson DM, Arnold AD, et al. N-of-1 Trial of a statin, placebo, or no treatment to assess side effects. N Engl J Med. 2020 Nov;383(22):2182–4.
9 Bishop FL, Coghlan B, Geraghty AW, Everitt H, Little P, Holmes MM, et al. What techniques might be used to harness placebo effects in non-malignant pain? A literature review and survey to develop a taxonomy. BMJ Open. 2017 Jun;7(6):e015516.
10 Colloca L, Schenk LA, Nathan DE, Robinson OJ, Grillon C. When expectancies are violated: a functional magnetic resonance imaging study. Clin Pharmacol Ther. 2019 Dec;106(6):1246–52.