Reviewer’s report

Title: Evaluation of real-world evidence for the effectiveness of academic detailing on appropriate prescribing of pain relief medication in Belgian general practices: a cluster randomized trial

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Reviewer: Mario Bracco

Reviewer's report:

Congratulations to the authors for this worthy effort in conducting a pragmatic approach to studying effectiveness of the Academic Detailing Service (ADS), in Belgium. This paper stimulates important reflections on relevant issues about sustainability of the health systems as well as pharmaceutical industry, based on rational use of drug resources and balancing between commercial and marketing purposes. Assessing the effectiveness of ADS on the application of the recommended protocol for pain relief in osteoarthritis, throughout the reimbursements of analgesics and NSAID prescriptions, the paper provides relevant information that support a successful public policy in the best interest of the population who is covered by that, in Belgium, and other countries that have similar ADS.

Abstract

The main scientific purpose is not stated, instead only that it was ordered by the Federal Agency for Medicine and Health Products (FAMHP) to Farmaka ADS. This alone is not enough to justify the study.

The method is quite complex related the sampling process, types of eligible practices, and GP coding. There are too many details that are difficult to understand. I suggest making the methods more intelligible for the readers with a more comprehensive and synthesized description.

The results also have too many details about the randomization process and the final analyzed sample. I suggest reporting the main results about the effectiveness and impact of the academic detailers.

Introduction

The first part raises the problem comparing published data on the effectiveness of Continuing Medical Education (CME) and ADS. The authors cite a Cochrane's review that attributes small
improvements in drug prescribing related to ADS. A recent synthesis of systematic reviews about CME impact published by Cervero & Gaines, has shown significant but small effects on physician performance and patient health outcomes, of 6% and 3%, respectively (Cervero RM, Gaines JK. The impact of CME on physician performance and patient health outcomes: an updated synthesis of systematic reviews. J Contin Educ Health Prof. 2015;35:131-8.) I think that this information can be relevant to the readers make judgments about the effectiveness of both different strategies.

The second paragraph promotes awareness about the FAMPH request of this effectiveness trial based on insufficient evidences published in two previous small RCT studies, although they have shown effectiveness in antibiotic and benzodiazipines prescribing. Thus, I wonder that if this request is an updating research process or it was triggered by any other reason. Moreover, as I mentioned in the Abstract's comments, would be helpful to know why the authors chose the appropriate use of pain relief drugs for chronic pain in osteoarthritis (OA), to be evidenced.

In the third paragraph, it is stated that OA is a common condition that NSAIDs are often prescribed increasing risks of gastrointestinal complications. The references list brings 7 articles about OA and NSAID use bleeding complications, but just one is cited in the introduction (#10). As a reader, I think there is a need for a more detailed approach of this issue in Belgium, handled by health authorities and Farmaka, in my opinion.

Methods

It is useful that this section comes splitted in sub-sections. It is understandable that the randomization was performed over the practices instead of individuals GPs to minimize contamination bias between GPs, in group or duo practices. I cannot understand what mean these different practices and how it improves the data reliability. The authors explain that the practices were performed in permuted blocks of two (exposed x control group, I suppose), and stratified according detailer, visits, and type of practice as well as they were sorted by GP's descending code. This explanation needs more clarification to whom is not familiarized with these practices and GPs, in Belgium context. It is not a technical questioning about the method used, but what are the practices and their types, and how GP's codes identify practices. There is no mention about them in the whole paper. On the other hand, the intervention is well described as well as the Key Messages (KM).

The data characteristics sub-section provides the information that the practices, GPs, and Academic Detailers data, were provided by Farmaka, and the additional important data were provided by the Intermutualistic Agency. There is no mention about the reliability of this dataset, although the authors remark that all data had a unique identification code. Thus, how these datasets were built or joined, seems important to be mentioned.
The primary and secondary outcomes are well explained and the complex process of intention-to-treat analyses in different scenarios are well described and depicted in figure 3, as well as the statistical modeling.

Results are well described and depicted in the tables and figures. It is not so easy to understand them in function of the multiple scenarios modeled for ITT and per protocol analyses.

Discussion

The discussion misses important issues that could be related to these results. There is no mention about the main problem raised by the study question, which is the effectiveness of ADS on chronic pain relief drug prescribing by GPs. Although the authors reinforce their findings agreeing with the former RCTs about effectiveness of antibiotics and benzodiazepines, in Belgium, would be interesting to have more information about similar studies of other countries about this issue, mainly when they pointed out that the impact of ADS might be very condition and outcome specific. Is there any information in the literature reinforcing or not this hypothesis? The Borgermans et al. paper cited is written in Flemish that restricts this knowledge to non-Flemish speakers. I think that it needs stronger evidences to support this statement.

The other significant findings related to Academic Detailer profile is low explored by the authors, as well. There are no information about them, who could appear in the Introduction. It is no possible to wonder why being older or physician could promote higher impact in drug prescription.

The sub-section "On the use of reimbursement data" pointing out missed information about Paracetamol, seems to me one major study limitation that was neither mentioned at the Methods, nor as a limitation. The author's strategy to analyse these data only in patients 60 and older, and that they get paracetamol reimbursement only by prescription, could improve the reliability about the significant small impact on paracetamol dosage finding. Moreover, the lack of consensus on the paracetamol recommendation in OA, is stated by the authors as a major study limitation. I do not agree, since the main result was related to the recommended NSAID adequacy prescription, although it can be a really limitation. The other limitations, i.e., missing by almost a quarter of eligible practices and short-term effects should be more clarified to give the readers the dimension of how these limitations could impact the conclusions.

Finally, the pragmatic cluster RCT design has brought robustness to the findings, aside the large sample of practices analysed.
Conclusions

The authors conclude that only impact of the study was the improvement in NSAID adequacy prescription, but there were other impacts related to detailers and paracetamol prescribing that could be added.

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