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European General Practitioners perceptions on probiotics: Results of a multinational survey

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ABSTRACT

Public opinion and consumer adoption of probiotics is influenced by the perception and recommendations of General Practitioners (GPs), but the perceptions and recommendations of European GPs currently appear to be underreported. This paper therefore relates the perceptions of European GPs towards probiotics with their recommendations. **S**tandardized telephonic interviews were conducted with 1318 GPs to assess current perceptions. Fisher's exact tests were performed to quantify the relationship between perceptions and recommendation behavior. 80 % of GPs recommend probiotics in their practice at least sometimes, primarily for antibiotic associated diarrhoea, infectious diarrhea and abdominal pain. GPs that are familiar with the mode of action of probiotics, and/or who perceive them to be safe or efficacious, are more likely to recommend probiotics. The relation between non-recommending behavior and disagreeing on one of the statements seems to be weaker, suggesting that other factors such as culture/previous experiences could be responsible for their non-recommending behavior. Perceptions of European GPs towards probiotics are predominantly positive. Additional research is needed to identify whether and to what extent proximal factors, such as social norms and culture are of influence on the perceptions and recommendation behavior of currently non-recommending GPs to foster innovation in this domain.

1. Introduction

Probiotics, generally interpreted as microorganisms that are beneficial for health, have gained popularity over the years and have found applications in several general health and clinical scenarios [1]. Probiotics are defined by the World Health Organization (WHO) as "live microorganisms which when administered in adequate amounts confer a health benefit on the host" [2]. The relationship between probiotics and promotion of health has been studied by many researchers and it appears that the consumption of beneficial microorganisms may benefit patients with, for instance, Antibiotic Associated Diarrhoea (AAD) and Irritable Bowel Syndrome (IBS), but also indications related to the gut brain axis, such as anxiety and mental stress [3–6]. Despite this health promoting potential, survey reports show that consumers adoption of probiotics has not yet extended beyond the 50 % tipping point for adoption between early majority and late majority [9] as indicated by global usage rates, ranging from 5 % in the United States to 25 % in New Zealand [7,8]. Since business development and consumer adoption of probiotics is low it hampers the valorization cycle of probiotic in the market and society discourse [10].

Moreover, innovations in the probiotic domain are critically hampered by market challenges, such as difficulties obtaining regularity approval and competition with marketed probiotics with no evidence base [10,11]. So far, European Food and Safety Authority (EFSA) has rejected all submitted health claims for probiotics. The dissemination of knowledge on marketed products with beneficial microorganisms currently relies on the transmission of knowledge by medical professionals such as General Practitioners (GPs) and dieticians. Especially GPs, considering their role as gatekeeper to specialist care, could play a key role to foster probiotic innovations and consequently their perceptions influences the public opinion and adoption of probiotics [10,12]. Even though understanding the perceptions of GPs and their recommendation behavior is vital (because their perception on probiotics influences public opinion, including the potential consumers), their stance regarding probiotics currently seems to be underreported [10,12,13]. The present study therefore aims to provide an update on the current perceptions of European GPs towards probiotics. This article highlights the perceptions of GPs on the safety, efficacy and mode of action of probiotics and presents an overview of the indications for which GPs recommend probiotics. Furthermore, recommendation behavior of GPs

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will be reviewed and its implications for the adoption of probiotics are discussed.

2. Methodology

2.1. Data collection

A questionnaire was designed to review the perceptions and recommendation behavior of European General Practitioners (GPs) towards probiotics. The questionnaire comprised 10 closed questions. Demographics, frequency of nutritional- and probiotic advice, indications for advice (multiple answers were allowed), perceived familiarity with probiotics, attitudes towards probiotics and future preferred information types (multiple answers were allowed) were addressed. In order to assess the perceived familiarity of GPs with probiotics, GPs were asked to what extent they agreed with the following statements: "I am familiar with the mode of action of probiotics", "The use of probiotics is safe" and '"There is sufficient evidence regarding the efficacy of probiotics". One of the following choice options could be selected: "Disagree", "Slightly Disagree", "Slightly Agree" or "Agree". GPs that agreed or slightly agreed with these statements were considered to be familiar with the mode of action of probiotics, to perceive probiotics as safe or to perceive probiotics as efficacious, respectively. The survey questions were piloted before within the recent study of Flach et al. [14] in the Dutch context. Since this study was executed two years ago, also a comparison on recommendation behavior for this specific group was made. The interviews were exclusively performed by IQVIA, a data collection firm [15], according to current GDPR regulations. All raw results of the survey were double checked with IQVIA on validity and reliability, before they were analyzed and/or interpreted by the authors.

2.2. Study population

Standardized telephonic interviews were conducted with GPs who were working in: Belgium, Germany, Finland, France, Italy, Netherlands, Sweden and UK, representing Western-Europe. The contact information list was composed by IQVIA.

2.3. Statistical analysis

Statistical analysis was performed using R Statistical Software. Two-tailed Fisher's exact tests were used to analyse differences between groups. A p-value of < 0.05 was considered to be statistically significant

3. Results

3.1. Survey respondents' characteristics

For this study 5600 GPs were contacted (700 per country) and a total of 1349 respondents completed the survey between July 2018 and February 2019; the response rate was 24 %. There was no financial compensation for their time. A total of 31 respondents did not meet the inclusion criteria and were excluded from data-analysis as they were either still in training (n = 1) or were from another specialization than the intended study population (n = 25). Hence, 1318 GPs were included in the data-analysis of the present study. Each country included in this study was represented by at least 95 GPs. The demographics of survey participants are presented in Table 1.

Table 1
Survey Participants Characteristics.

	N = 1318 (100 %)
Country	
Belgium	210 (16 %)
Germany	204 (15 %)
Finland	95 (7 %)
France	202 (15 %)
Italy	207 (16 %)
Netherlands	99 (8 %)
Sweden	112 (8 %)
UK	189 (14 %)
Age	
< 30 years	98 (7 %)
31–50 years	671 (51 %)
51–64 years	352 (27 %)
> 65 years	183 (14 %)
Didn't want to answer	14 (1 %)
Sex	
Male	673 (51 %)
Female	645 (49 %)

3.2. Nutritional and probiotic advice

86 % of the GPs indicated to provide nutritional advice sometimes, regularly or often (Fig. 1A). Similarly, probiotic advice was given to patients by 80 % of GPs at least sometimes (Fig. 1B). GPs that recommended probiotics in their practices sometimes, regularly or often/always are referred as 'advisors' and GPs that do not advice probiotics are referred as 'non-advisors'. When GPs indicate to recommend probiotics in their practice, this is true for the patients who visit the GP with one of the indications that were mentioned by the GPs in Fig. 2. GPs who indicated to often/always give nutritional advice were more likely to indicate that they also often/always gave probiotic advice (45 %) than regularly, sometimes or never/seldom (27 %, 17 %, 11 %). The same held true for GPs who regularly give nutritional advice were also more likely to regularly advise probiotics (47 %) rather than often/always, sometimes or never/seldom (23 %, 18 %, 12 %). In the current study 84 % of the Dutch GPs recommend probiotics in their practices.

3.3. Indications for probiotic advice

The primary indications for which probiotics were recommended were Antibiotic Associated Diarrhea (AAD) (64 %), infectious diarrhea (63 %), abdominal pain/belly ache (60 %), Inflammatory Bowel Syndrome (IBS)/pouchitis (56 %), and bloating (55 %). A complete overview of indications is displayed in Fig. 2.

3.4. Perceived knowledge, safety and efficacy

Fig. 3 shows the perceived knowledge, safety and efficacy of GPs towards probiotics. The advisors significantly more often *''Agreed''* with the statement "*I am familiar with the mode of action of probiotics*" as compared to non-advisors (38 % vs. 27 %, Fisher's exact, $p < 0.005$), whereas the non-advisors significantly more often stated they "Disagreed" compared to advisors (25 % vs. 19 %, Fisher's exact, $p < 0.05$). The advisors significantly more often "*Agreed*" (40 % vs. 26 %, Fisher's exact, $p < 0.0005$ or "*Slightly Agreed*" (27 % vs. 21 %, Fisher's exact, $p < 0.05$) with the statement "*The usage of probiotics is safe*" as compared to non-advisors, whereas the non-advisors significantly more often "*Slightly Disagreed*" (26 % vs. 19 %, Fisher's exact, $p < 0.05$) as compared to advisors. The advisors significantly more often "*Agreed*" (43 % vs. 32 %, Fisher's exact, $p < 0.005$) with the statement "*There is sufficient evidence regarding the efficacy of probiotics for the treatment of specific disorders*" as compared to non-advisors, whereas non-advisors significantly more often "*Slightly Disagreed* "(25 % vs. 18 %, Fisher's exact, $p < 0.05$) as compared to advisors. * $p < 0.05$, ** $p < 0.005$, *** $p < 0.0005$.

In the sub-analysis we merged "*Disagree*" with "*Slightly Disagree*". Also, we merged "*Slightly Agree*" with "*Agree*". The merged groups were labeled *''not familiar''* and *''familiar''*, respectively. The advisors were significantly more often familiar with all three statements, the mode of

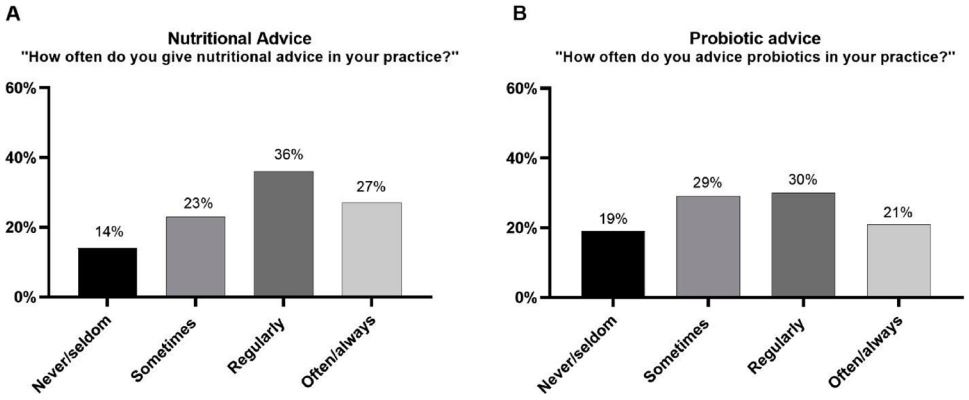

Fig. 1. Advise rates were very similar between nutritional and probiotic advice, respectively 86 % and 80 %.

action and/or safety and/or efficacy of probiotics (60 % vs. 53 %, Fisher's exact, $p < 0.05$), whereas the non-advisors significantly more often stated they were not familiar with all three statements compared to advisors (47 % vs. 40 %, Fisher's exact, $p < 0.05$).

3.5. Future information types

Advisors were statistically more interested in data on efficacy (41 % vs. 52 %, resp. $p < 0.005$), mode of action (48 % vs. 38 %, resp. $p < 0.0005$) and colleague experiences (43 % vs. 38 %, resp. $p < 0.005$), see Fig. 4. Out of all types of information advisors and non-advisors showed the highest preference for more efficacy data.

3.6. Differences between countries`

Clustering GPs by country or age did not provide further information (similarities) for further sub classification. Country or age as a variable was not of significant influence on the recommendation behavior of GPs.

4. Discussion and conclusion

This study reports the perceptions of GPs on probiotics in relation with their recommendation behavior. We show that both nutritional and probiotic advice is provided by over 80 % of GPs in their practice at least sometimes. The most common indications for probiotic advice are indications related to the bowel, such as AAD, infectious diarrhea and abdominal pain. GPs that are familiar with the mode of action of probiotics, who perceive them to be safe or to be efficacious, are more likely to recommend probiotics than GPs who disagree on one of these statements.

In comparison with the earlier study by Flach et al. [14], were only 53 % of the Dutch GPs recommended probiotics (at least sometimes) in their practice, the present study found that the vast majority of Dutch GPs (84 %) recommends probiotics. A possible explanation for probiotics becoming more mainstream could be the wide (and growing) range of potential indications for which probiotics might be beneficial as well as the extensive and increasing variety of strains, shapes and types of probiotic products available on the market [2,17]. The current findings are in line with previous studies indicating that probiotics are recommend by around 80 % of GPs in Europe [7,16].

In recent years, the list of indications for which probiotics are considered potentially beneficial, expanded [17]. Current scientific literature shows that the efficacy of probiotics depends on several parameters, including carrier matrices and doses. Hence, GPs should be reluctant to make generalizations on probiotics [17,18]. Although most health effects can not be extrapolated from one strain to another, the term ''probiotics'' seems to be generalized to one mechanism in communication towards consumers and health care professionals [19]. Therefore, GPs should carefully make a consideration based on, among others, scientific literature. Nevertheless, it appears that GPs have insufficient information and at times adhere to the erroneous notion that one strain could benefit all indications [10]. In addition, the extensive variety of probiotic products, which are available as food, food supplement or drug, makes it challenging for consumers and GPs to choose the right product for the right indication [19]. Moreover, the EFSA has to date not awarded any probiotic with the right to place health claims on products labelling, leaving consumers and GPs faced with strain names (i.g. *Lactobacillus rhamnosus* GG) on the packaging rather than the intended indication, creating confusion rather than clarity [20]. In this regard, guidance documents that summarize and categorize

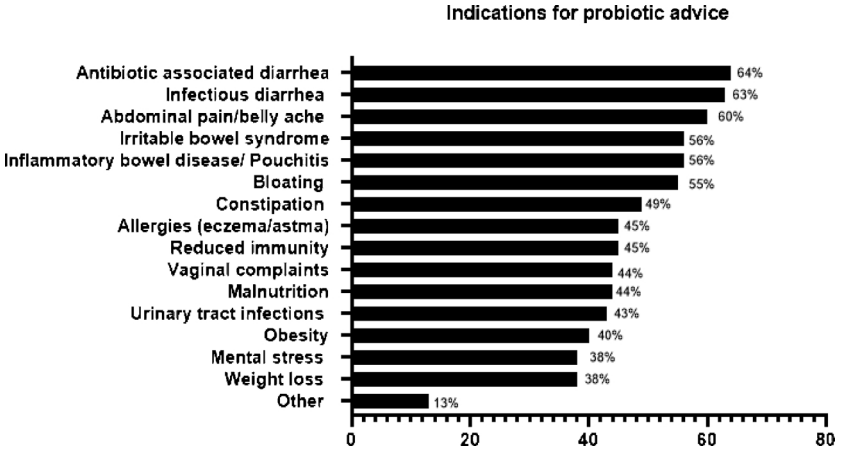

Fig. 2. Probiotics are predominantly recommended for indications related to the intestines.

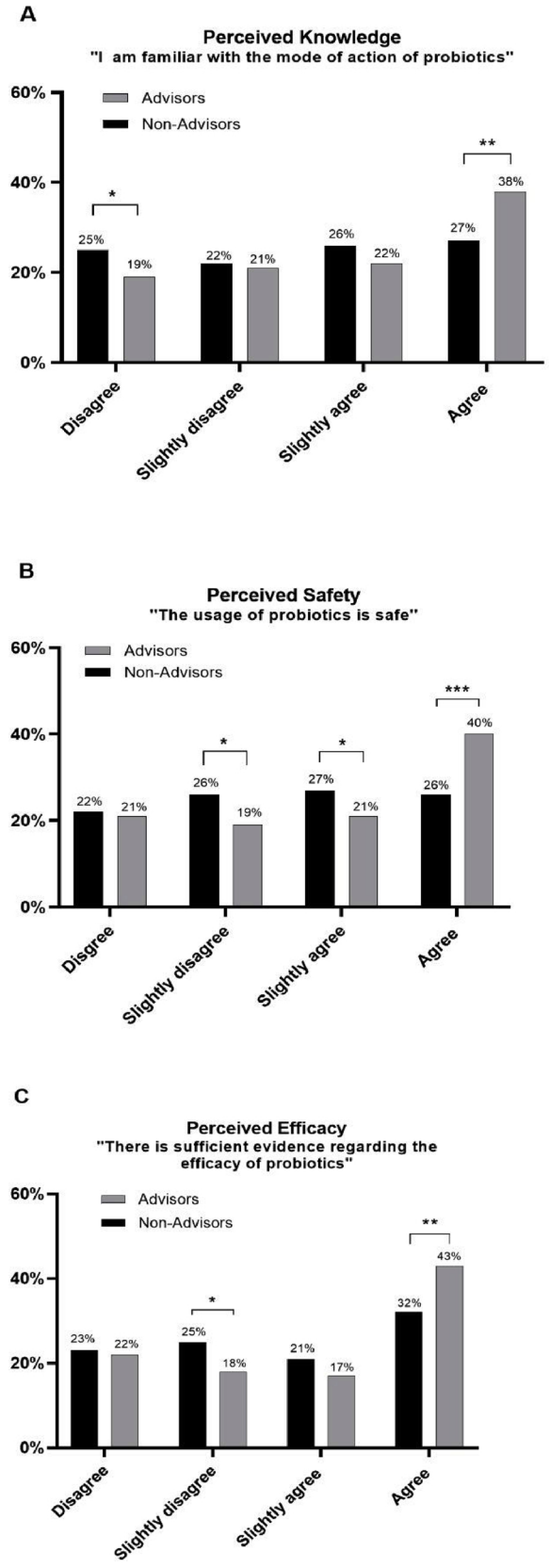

Fig. 3. Safety (A), efficacy (B) and mode of action (C) of probiotics are less established according to non-advisors as compared to advisors (* $p < 0.05$, ** $p < 0.005$, *** $p < 0.0005$).

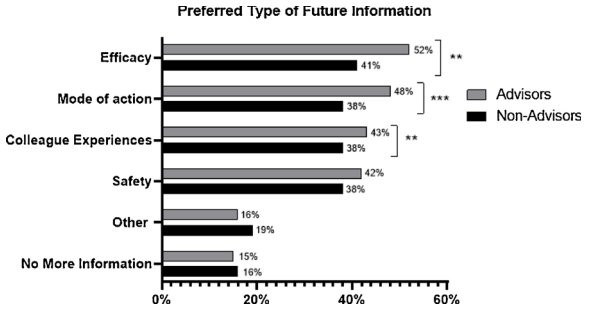

Fig. 4. The advisors, significantly more often than the non-advisors, stated they prefer to obtain information on the efficacy of probiotics, mode of action, and colleague experiences (* $p < 0.05$, ** $p < 0.005$, *** $p < 0.0005$).

available probiotic products per indication, as provided by Agamennone and colleagues (2018), can be of great assistance to foster adoption [21,22]. The safety profile of orally consumed probiotics is excellent [23–26], and probiotics seem to be effective in use, as they contribute to a decrease in symptoms of several indications. Yet, 40 % of the advisors indicated that they disagreed or slightly disagreed with the safety or efficacy statements of probiotics. Even more remarkable are the 10 % of the GPs who recommend the use of probiotics to their patients, despite their concerns on both safety and efficacy. A possible explanation for these findings could be the application of cost-benefit analysis for individual cases. Regarding safety concerns, GPs might thus be willing to recommend alternative medication that might have side effects but still could be beneficial to their patients. Hence, despite the fact that these clinicians doubt the safety of probiotics and are aware of the potential side effects for their patients, they are willing to recommend them for among others their perceived efficacy. At the same time, when a GP considers the efficacy of probiotics per single case, the efficacy will in all likelihood be estimated low, since probiotics will not be effective for every individual. For instance, earlier research on the efficacy of probiotics for AAD showed that the number needed to treat for an additional beneficial outcome (NNTB) is 6, which justifies the decision of GPs to recommend probiotics despite their doubt concerning the efficacy of probiotics per individual [27]. More education and training are needed to make sure GPs are knowledgeable enough to assess the safety and efficacy of probiotics.

The results of this study indicate a significant link between the perceptions of GPs towards probiotics, and whether they advise probiotics or not (Fig. 3A–C). However, there is also variation in advising behavior which cannot be significantly linked to GPs' perception towards probiotics. Although earlier research shows that patient and provider characteristics are critical for explaining variation in health care and clinical decision making, our study didn't show any significant relations between provider characteristics (i.e. age, gender, and/or country) and their recommendation behavior [30]. This could indicate that recommendation behavior is also influenced by factors beyond provider characteristics on probiotics. In addition, GPs – whether advisor or non-advisor did not give an unambiguous answer to what information they would like to receive (Fig. 4). This could indicate that something other than distal information drives their recommendation behavior. In a previous study on attitudes of Dutch GPs [14], it was shown that the primary use of conventional media (such as TV and Radio) is associated with negative perceptions and lowered recommendation rates among physicians [14]. Other studies indicate that also cultural and individual factors, such as social team dynamics, hierarchy, time pressure, personal norms, prior experiences, culture and religion, are factors that, positively or negatively, influencer-ecommendation behavior [28]. In this regard, the fact that probiotics

are rarely adopted in guidelines for physicians [29] (and recommendation of probiotics would therefore go against the norm), could be another prominent barrier to innovation [10]. Further research is needed to indicate whether and to what extent these proximal factors are of influence on the perceptions and recommendation behavior of GPs to foster innovation in this domain.

5. Limitations

The findings of this study should be interpreted in the light of several limitations. Even though the term 'probiotics' unites, or covers, a plethora of products, we didn't focus on specific strain/matrix (product) combinations because the aim of this study was to obtain a general overview on the perceptions of GPs towards probiotics. Since our study shows that GPs recommend probiotics for a variety of indications we would advise follow-up studies to make a clear distinction between the different types of probiotics and the corresponding perceptions. This will provide better insight into which products, strains and indications are the main cause of GPs being hesitant to recommend probiotics.

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Declaration of Competing Interest

O.F.A Larsen is also Senior Manager Science at Yakult Nederland B.V., J. Flach is also Clinical Research Scientist at CR2O and Director of Clinical Affairs at Triall, E. Claassen is also CEO at Vironovative BV and Linda van de Burgwal is also Managing Partner at FFUND.

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