Impact du visiteur médical indépendant sur la pratique des médecins de première ligne

KCE reports 125B

Federaal Kenniscentrum voor de Gezondheidszorg
Centre fédéral d'expertise des soins de santé
2010

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PREFACE

La démarche des « visiteurs médicaux indépendants » est partie d'un constat : les sommes importantes consacrées par les firmes pharmaceutiques aux démarches commerciales personnalisées auprès des médecins ne peuvent être justifiées que par un rendement subséquent en termes de changements de prescription. Dès lors, pourquoi ne pas reproduire cette initiative efficace avec un message porteur des meilleures données probantes ?

Tel était le raisonnement qui a conduit l'Agence Fédérale des Médicaments et Produits de Santé (AFMPS) à financer l'initiative « Farmaka » consistant à envoyer des visiteurs médicaux porteurs d'un message scientifique indépendant auprès des médecins généralistes.

Après cinq années d'expérience, l'AFMPS a souhaité connaître l'impact réel de ces visites et a demandé au KCE d'entamer une recherche à ce sujet. Certes, l'accueil semblait positif du côté des médecins généralistes, mais cet investissement annuel de plus d'un million d'euros atteint-il son objectif de modification des pratiques ?

Il est très difficile d'identifier de façon précise tous les tenants et aboutissants d'une pratique médicale. On ne trouvera donc pas dans le présent rapport d'analyses mathématiques avec des réponses tranchées. Néanmoins, la revue de littérature réalisée avec l'aide des chercheurs de Medstat (Leuven) et l'analyse qualitative pour laquelle le KCE s'est associé avec le centre de recherche Spiral de l'ULg, apportent des éclairages intéressants et des pistes utiles pour améliorer l'efficacité de la démarche.

Nous tenons à souligner le professionnalisme de nos partenaires scientifiques et à remercier tous les médecins qui ont accepté de collaborer à nos enquêtes.

Jean-Pierre CLOSON
Directeur général adjoint

Raf MERTENS
Directeur général

Résumé

CONTEXTE

La littérature définit les visiteurs médicaux indépendants ("academic detailers") et leur démarche de la manière suivante : "Approche pédagogique de type universitaire ou non commercial. La démarche implique une formation face-à-face des prescripteurs, dispensée par des professionnels de la santé formés à cette fin. L'objectif des visiteurs médicaux indépendants est de modifier le comportement professionnel de manière cohérente par rapport aux données probantes médicales, de renforcer la sécurité du patient et d'encourager des choix de médicaments avec un bon rapport coût-performance. Une facette essentielle des programmes de visiteurs médicaux indépendants universitaires ou non commerciaux est que ces visiteurs, les gestionnaires, le personnel et les initiateurs du programme n'ont aucun lien financier avec l'industrie pharmaceutique".

Depuis 2008, l'Agence Fédérale des Médicaments et Produits de Santé (AFMPS) soutient un programme de visiteurs médicaux indépendants qui se rendent chez des médecins généralistes (MG). L'organisation et la mise en œuvre de ce programme sont assurées par l'ASBL Farmaka. Le financement annuel par l'AFMPS a augmenté il y a peu pour passer de 503 960 euros (Oct 2006-Sept 2007) et 592 960 euros (Oct 2007-Déc 2008) à 1 121 193 euros pour 2009. En conséquence, la question du rapport coût-efficacité de cette initiative est dès lors primordiale.

OBJECTIF DU PROJET

L'objectif de ce présent projet est d'analyser l'impact des visiteurs médicaux indépendants sur la pratique des médecins généralistes (MG) en Belgique. Le rapport se fonde sur trois questions de recherche :

- Existe-t-il dans la littérature des preuves relatives au rapport coût-efficacité des visiteurs médicaux indépendants chez les médecins de première ligne ?
- Quelle est chez les MG en Belgique la perception des visiteurs médicaux indépendants ?
- L'entrevue avec un visiteur médical indépendant induit-elle un changement du comportement de prescription des MG belges ?

METHODES

Une revue de la littérature (chapitre deux) s'est déroulée en deux phases. Premièrement, une recherche dans la littérature grise a analysé l'organisation de huit programmes de visiteurs médicaux indépendants dans d'autres pays (notamment 3 aux États-Unis et 2 en Australie). Ensuite, une revue systématique de la littérature a été réalisée dans la littérature indexée (Medline, Embase, COCHRANE database of Systematic Reviews, Eric, Psychinfo et Econlit) dans le but d'identifier l'efficacité réelle et le rapport coût-efficacité des visiteurs médicaux indépendants. La recherche s'est concentrée sur les revues systématiques (n=16) et les études primaires de qualité élevée (87 études). Les résultats des deux analyses de la littérature sont fusionnés dans le chapitre « Résultats » ci-dessous.

Une étude qualitative a été réalisée auprès des MG qui ont reçu une offre d'entrevue avec un visiteur médical indépendant, en relation avec le sujet du diabète et/ou de la démence (chapitre 3). Farmaka a adressé 1498 courriers pour demander le consentement écrit de ces MG. Malheureusement, 19.8% seulement de cette population cible (n = 297) ont répondu positivement. Finalement, 126 MG, soit 8.4% de la population de départ, ont effectivement participé à l'enquête Delphi. Cette enquête a utilisé la méthode « Mesydel », à savoir une enquête Delphi en deux tours utilisant un outil Internet.

Une étude quantitative a analysé les prescriptions de ces mêmes MG afin de repérer un éventuel effet de l'entrevue avec un visiteur médical indépendant sur les prescriptions des médicaments pour le diabète ou la démence (chapitre 4). Les analyses ont utilisé les données Pharmanet de l'Agence Intermutualiste (AIM) (médicaments achetés par les patients). L'évolution de leurs prescriptions par semestre a été comparée à celle de la population des MG belges dans le but d'identifier les effets d'interventions concomitantes.

RESULTATS

ETUDE DE LA LITTÉRATURE RELATIVE AUX VISITEURS MÉDICAUX INDÉPENDANTS

Caractéristiques des interventions des visiteurs médicaux indépendants

Les interventions ont ciblé 44 populations de patients différentes, les pathologies cardiovasculaires arrivant en tête de liste (hypertension artérielle, insuffisance cardiaque). Un tiers des interventions étaient destinées à des patients souffrant de problèmes multiples. Les interventions ciblaient essentiellement le comportement en matière de prescription. Les autres comportements visés étaient, entre autres, la gestion de conditions/maladies conformément aux recommandations, le contrôle de paramètres cliniques, l'apprentissage de techniques spécifiques. Les professionnels qui ont assuré les visites étaient principalement des pharmaciens et des médecins. Les autres professions (notamment chercheurs et personnel infirmier) étant moins impliquées.

Dans l'ensemble, les précisions manquaient dans la description des interventions et il était malaisé de comprendre leur nature exacte (fréquence, teneur). D'ordinaire, l'intervention d'un visiteur médical indépendant prenait la forme de discussions interactives relatives aux guides de pratique clinique avec le support de matériel didactique. Dans les deux tiers des études, le programme comprenait plusieurs facettes et d'autres interventions que l'entrevue avec un visiteur médical indépendant, notamment un audit, un feedback, la fourniture de matériel d'information pour les patients.

Efficacité et rapport coût-efficacité

La majorité des études de la littérature indexée (77 sur 87) relataient l'efficacité des visiteurs médicaux indépendants en se basant essentiellement sur des indicateurs de processus (entre autres les prescriptions). La plupart de ces études (n=67) ont rapporté un effet positif de l'entrevue avec un visiteur médical indépendant pour certains résultats et 10 études n'ont rapporté aucun effet de la visite. Une revue systématique de littérature a estimé un effet limité de l'entrevue sur l'observance des messages avec une amélioration de seulement 5% environ vers la pratique souhaitée. Néanmoins, les revues systématiques concluent que les entrevues avec des visiteurs médicaux indépendants dans le cadre d'interventions comportant plusieurs facettes sont généralement efficaces pour améliorer les soins et la prescription.

Dix études ont également mentionné des résultats économiques. Sept d'entre elles étaient des évaluations économiques complètes, essentiellement des analyses de minimisation des coûts ou des analyses du rapport coût-efficacité. Toutefois, leurs résultats étaient contradictoires et n'autorisent pas de conclusion relative au rapport coût-efficacité des visiteurs médicaux indépendants.

L'examen des initiatives dans d'autres pays montre une carence en évaluations. Leurs dépenses annuelles sont comprises entre 50 000 $ (pour une intervention limitée) et 1 000 000 $. Ce dernier montant est similaire à l'investissement actuellement consenti en Belgique pour les visiteurs médicaux indépendants. Cependant, ces budgets ne sont en aucun cas comparables aux investissements énormes de l'industrie pharmaceutique dans les interventions de démarchage médical.

ETUDE QUALITATIVE AUPRES DES MG EN BELGIQUE

Les chercheurs ont identifié des biais dans l'échantillon ; A titre d'exemples, un nombre plus élevé de MG néerlandophones, une concentration dans des zones géographiques spécifiques, de nombreux MG manifestant un intérêt certain pour l'accessibilité et l'équité dans les soins de santé.

Perception de l'entrevue avec le visiteur médical indépendant

Le constat pose question : de nombreux MG ayant participé à cette enquête ne se souviennent pas de l'entrevue avec le visiteur médical indépendant ni de son contenu. Lorsqu'ils en avaient le souvenir, cette visite était perçue comme une entrevue à contenu scientifique, parfois trop dense. La qualité du visiteur (médecin ou pas) n'avait que peu d'impact sur la perception, à condition qu'il/elle possède les connaissances scientifiques nécessaires pour une discussion fructueuse. Le rôle de l'état dans l'apport d'informations aux médecins a suscité des réactions contradictoires : la plupart des MG interrogés ont reconnu que l'intervention de l'état était nécessaire et faisait contrepoids par rapport à l'industrie pharmaceutique.

Impact de la visite selon les MG

Les MG ont déclaré que les visiteurs avaient un message orienté vers un comportement plus conscient en matière de prescription, ce message portant également sur les traitements non médicamenteux. Les résultats indiquent que dans ce groupe de MG, l'effet consiste davantage en un renforcement positif de la pratique actuelle plutôt qu'en une volte-face radicale.

Les MG travaillant seuls dans leur cabinet ont particulièrement apprécié les entrevues avec les visiteurs médicaux indépendants car elles leur permettent d'échapper à leur isolement scientifique. Les MG en pratique de groupe ont plus d'occasions de partager des informations et des expériences.

Propositions des MG participants pour améliorer la démarche des visiteurs médicaux indépendants

Les MG qui ont participé à l'étude ont formulé certaines propositions intéressantes pour l'avenir:

- Élaborer un matériel didactique afin d'accroître la visibilité des visiteurs médicaux indépendants ;
- Mettre au point des systèmes en ligne pour partager et recevoir des informations ;
- Proposer un service complémentaire pour les patients ;
- Proposer une gamme de sujets pour la visite ;
- Offrir des visites plus fréquentes ;
- Cibler les cabinets de MG travaillant seuls ;
- Organiser des visites en groupe pour stimuler le débat ;
- Lier les visites aux crédits pour la procédure d'accréditation.

ANALYSE DES DONNÉES DE PRESCRIPTION

Le message clé de Farmaka par rapport aux médicaments pour le diabète était d'entamer le traitement en monothérapie (metformine en première intention ou une sulfonylurée en seconde intention). En cas d'échec de la monothérapie, Farmaka préconisait la prescription d'une bithérapie (metformine et sulfonylurées). En cas d'échec de cette bithérapie, ils proposaient d'ajouter de l'insuline et enfin, d'explorer d'autres possibilités.

S'agissant des médicaments de la démence (c-à-d les inhibiteurs de la cholinestérase, Mémantine ou Gingko Biloba), les messages clés de Farmaka étaient les suivants : l'absence de preuve de leur efficacité clinique (sauf chez un nombre limité de patients présentant des symptômes modérés) et leurs effets secondaires potentiels graves.

En raison de limitations importantes au niveau des données disponibles, très peu de conclusions cohérentes ont pu être formulées quant à l'impact des entrevues avec les visiteurs médicaux indépendants en Belgique dans le contexte de la prise en charge du diabète. Aucune conclusion n'a été tirée en ce qui concerne la démence.

La majorité des patients (81%) ayant entamé leur traitement pour le diabète après le passage d'un visiteur médical indépendant (« nouveaux patients ») ont reçu une monothérapie conforme aux recommandations de Farmaka. Cela étant, une proportion similaire (82%) des patients déjà sous traitement avant le passage d'un visiteur médical indépendant recevaient eux aussi une thérapie conforme à la liste Farmaka susmentionnée.

Parmi les patients sous traitement antidiabétique avant et après le passage du visiteur médical indépendant, un sur six (16.0%) dont la modalité de traitement n'était pas dans les recommandations, est passé au traitement préconisé. Par ailleurs, 5.2% de ceux qui suivaient un traitement inclus dans les recommandations sont passés à une modalité thérapeutique non incluse dans celles-ci.

Les limitations suivantes au niveau des données ont rendu impossible la formulation d'un plus grand nombre de conclusions relatives aux visiteurs médicaux indépendants en Belgique :

- L'échantillon de MG était fortement biaisé et, en conséquence, n'était pas représentatif ;
- Aucune information n'était disponible sur la maladie du patient ;
- Pas de caractéristiques relatives aux patients des pratiques de l'étude ;
- Conformité initiale très élevée des pratiques par rapport aux recommandations en matière de diabète ;
- Absence de données de prévalence sur les patients (non traités), pas de données sur la mortalité ;
- Lien imprécis entre les données de facturation disponibles pour les médicaments délivrés et la thérapie effective (calendrier, durée, observance thérapeutique…) ;
- Pas d'informations relatives aux prescriptions antérieures par des spécialistes (alors que l'instauration d'un traitement médicamenteux pour une démence est conditionnée par une consultation préalable de spécialiste).

CONCLUSION

La majorité des études de la littérature montrent un impact des visiteurs médicaux indépendants sur les procédures de prise en charge ciblées mais l'ampleur de cet impact est habituellement faible. Le rapport coût-efficacité n'est pas établi.

Les données de prescriptions disponibles pour la Belgique ont à peine permis de tirer une conclusion relative à l'effet de l'intervention des visiteurs médicaux indépendants sur les prescriptions d'un échantillon de MG. Les principales raisons sont les limitations de l'échantillon des MG et celles des données, ainsi que la conformité élevée des traitements par rapport aux recommandations de Farmaka avant le passage des visiteurs médicaux indépendants.

RECOMMANDATIONS

L'initiative actuelle des visiteurs médicaux indépendants reste isolée par rapport à l'ensemble des initiatives relatives à la qualité en Belgique. Une réorientation du programme s'impose afin de le replacer dans le cadre global des initiatives pour la qualité et en particulier celles qui visent à améliorer la qualité de la prescription. C'est dans ce contexte plus large qu'une attention particulière sera accordée aux points suivants :

Choix des sujets

- Le choix des sujets doit correspondre à des objectifs clairs en termes d'amélioration de la qualité et avoir été débattu au préalable avec les principales parties prenantes;
- Dans la sélection des sujets, les critères suivants devraient être pris en considération :
  - Importance du sujet (prévalence, gravité, coût…);
  - Marge/besoin d'amélioration et disponibilité de données probantes ;
  - Rôles respectifs des MG et des spécialistes;
  - Intérêts des MG;
- Les messages doivent être en adéquation avec les feedbacks du CNPQ-NRKP;
- Le visiteur médical indépendant pourrait offrir un choix entre plusieurs sujets pour correspondre au mieux à la pratique de chaque médecin généraliste.

Population cible

- Les ressources limitées en visiteurs médicaux indépendants devraient être utilisées de manière plus focalisée:
- Cibler les MG isolés qui n'ont pas l'occasion de partager leur expérience en pratique de groupe;
- NE PAS viser les MG ayant déjà une observance élevée des objectifs de qualité; le fait de cibler les médecins pourrait être réalisé sur la base des données disponibles au niveau des commissions de profils et du CNPQ (feedbacks);
- Cibler les leaders d'opinion parmi les MG afin d'accroître la diffusion du message;
- Cibler simultanément les spécialistes engagés dans le traitement des mêmes patients, dans le but de réaliser des synergies entre les niveaux de soins.

Diffusion du message

- La méthode face à face a ses limites en termes de rapport coût-efficacité : le recours à cette démarche devrait être limité et complété par d'autres outils de diffusion similaires à ceux qui sont utilisés par l'industrie pharmaceutique;
- En particulier, un renforcement des messages pourrait être proposé dans le contexte de discussions de groupes avec les GLEMs;
- Dans le même ordre d'idées, un système d'information pour le patient l'aiderait à comprendre le message et renforcerait les conseils du médecin (comme dans les campagnes de la BAPCOC contre les antibiotiques);
- Induire des changements de comportements requiert des compétences professionnelles spécifiques et un "know-how"; ceux-ci sont requis tant au niveau des visiteurs qu'au niveau du programme global.

Évaluation

- La poursuite éventuelle de cette initiative doit être subordonnée à un enregistrement des données et à une évaluation plus étayée.

Scientific summary

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1 BACKGROUND

1.1 ACADEMIC DETAILING

Marketing of high-priced drugs increasingly strains public and private health care budgets. As a consequence, interventions aim at optimizing the quality of care while controlling costs thus aligning the interests of physicians, payers and patients. Despite recent improvements in the dissemination of evidence into practice (e.g. through initiatives like the Cochrane Collaboration), there remains important variation in quality of clinical practice among medical practitioners[1-3].

Different interventions have been tested to improve optimal prescribing and medication management[4], provider diagnosis and treatment[5] and to engage physicians to change their practice[6]. Academic detailing (AD) is one such quality-driven endeavour that would contribute towards appropriate clinicians' decisions based on the best available safety, efficacy, and cost-effectiveness data.

1.2 DEFINITIONS

AD is intended to influence or change the physician's behaviour through the presentation of evidence-based information on a specific topic in a face-to-face encounter[7]. Common terms used in the literature are also "educational outreach", "university-based educational detailing" and "public interest detailing"[8].

For the purpose of this review, the following definition of Soumerai et al.[9] is used as it fits best to the system financed in Belgium:

"AD is university or non-commercial-based educational outreach. The process involves face-to-face education of prescribers by trained health care professionals. The goal of AD is to change professional behaviour consistent with medical evidence, support patient safety, and to foster cost-effective medication choices. A key component of non-commercial or university-based AD programs is that academic detailers, management, staff and program developers do not have any financial links to the pharmaceutical industry".

Key principles of AD are:

- To conduct interviews to investigate baseline knowledge and motivations for current prescribing patterns;
- To focus the AD programs on specific categories of physicians as well as on their opinion leaders;
- To define clear educational and behavioural objectives;
- To establish credibility by having a respected independent organizational identity, referencing authoritative and unbiased sources of information, and presenting both sides of controversial issues;
- To stimulate active physician participation in educational interactions;
- To use concise graphic educational materials highlighting and repeating the essential messages;
- To provide positive reinforcement of improved practices in follow-up visits.

AD has been used in primary care, teaching hospital settings and nursing homes to improve outcomes of care. This report focuses on primary care defined by the MESH thesaurus as "the care which provides integrated, accessible health care services by clinicians who are accountable for addressing a large majority of personal health care needs, developing a sustained partnership with patients, and practicing in the context of family and community".

In this project primary care refers to the care delivered by general practitioners and other specialists who work in the first line of care.

1.3 ACADEMIC DETAILING IN BELGIUM

The Federal Agency for Medicines and Health Products supports since 1998 an initiative of AD among general practitioners. The organization and implementation of AD is realized on the field by the "asbl-vzw" Farmaka[10]. Since 2006 the following themes have been presented to a growing number of GPs: dementia, allergy, anxiety, obesity, diabetes, angina pectoris, osteoporosis, gastroesophageal symptoms, atrial fibrillation and smoking cessation. GPs from a specific geographic area receive the offer of one visit about a given topic. The frequency of those visits each year varies according to the availability of the visitor.

The annual funding by the Agency recently increased from € 503 960 (October 2006-september 2007) and € 592 960 (October 2007-december 2008) to € 1 121 193 for the year 2009.

The question of effectiveness and cost-effectiveness of this investment has therefore been asked by the Ministers' Council in 2007.

1.4 OBJECTIVE OF THE PROJECT

The objective of this project is to analyze the effects of AD on the practice of the general practitioner. The report is based on three research questions:

- Is there evidence in the literature about the (cost) – effectiveness of academic detailing programmes for primary care physicians?
- What is the GP's perception of academic detailing visits in Belgium?
- Is there any noticeable change in the prescription behavior of Belgian GPs after the visit of an academic detailer?

The second chapter of the report answers to the first question by summarizing the existing evidence in the indexed literature. This chapter is completed by the analysis of the organization of AD in other countries. The third chapter of the report displays the results of a qualitative study among a selected sample of Belgian GPs who received the visit of academic detailers and accepted to take part to this study (survey and analysis of their prescriptions). The fourth chapter aims to detect changes in the prescription behaviour of those GPs after the visit of academic detailers. Finally, a chapter summarizes the findings, builds bridges between the chapters and draws possible avenues for the future.

2 LITERATURE REVIEW ON ACADEMIC DETAILING

2.1 AIM OF THE LITERATURE REVIEW

This literature review aims to assess the effectiveness and the cost-effectiveness of individual, face-to-face academic detailing among general practitioners and other physicians in primary care. A first part analyses the indexed literature. A second part identifies AD programmes in different countries through a search in the 'grey literature'. For these programmes limited or no publications are available in scientific peer reviewed national and international journals.

2.2 METHODOLOGY

2.2.1 Population – Intervention - Comparison – Outcomes (PICO)

The PICO has been defined as follows:

- Population: physicians in primary care
- Intervention: face-to-face individual AD
- Comparison: usual care or other independent (non commercial) educational techniques
- Outcome: physician's medical practice / patients outcomes / cost and cost-effectiveness

2.2.2 Search strategies

2.2.2.1 Systematic literature review

Research question

The research question was: "What is the (cost) effectiveness of face-to-face AD targeted at physicians in primary care?"

Since the trials are heterogeneous in their interventions, study populations and targets, the results are presented descriptively rather than combined as a meta-analysis.

Search strategy

Six databases (MEDLINE database of the National Library of Medicine, COCHRANE database of Systematic Reviews, Embase, Eric, Psychinfo and Econlit) were searched for English, French, Dutch and Spanish articles without any date limit. The last strategy has been performed in September 2009.

The search terms are in appendix 1.1 and the detailed strategies are available upon request. Three types of articles were selected:

- reviews of reviews including AD;
- systematic reviews including AD;
- trials on AD.

Exclusion criteria

The aim was to identify any study where AD was implemented in a primary care setting. Two reviewers (L.B and L.K) independently assessed the articles for eligibility.

Titles (of references) were rejected if:

- they did not deal with non commercial AD or continuing medical education;
- case reports, personal views, expert views, historical reviews, editorials, letters and duplicate entries;
- no abstract was available;

- articles other than English, French, Dutch and Spanish.

Abstracts were rejected if:

- studies were conducted in other settings than primary care.

Studies were rejected if:

- they did not report on AD according to the definition used in this review;
- if the study design was neither a trial nor an intervention study: (randomised) controlled trials (prospective or retrospective), before/after studies, retrospective studies and time series;
- if insufficient information was provided on relevant elements including:
  - type of AD,
  - health care providers providing the AD,
  - behaviour targeted,
  - setting,
  - measures of the effectiveness of the intervention.
- the full text article was not available;
- study conducted in non Western countries.

Quality appraisal of systematic reviews and individual studies

The methodological quality of the reviews was assessed using the items of the PRISMA statement[11]. PRISMA stands for Preferred Reporting Items for Systematic Reviews and Meta-Analyses. It is an evidence-based minimum set of items for reporting in systematic reviews and meta-analyses. The PRISMA Statement consists of a 27-items checklist and a four-phase flow diagram. It describes the preferred way to present the abstract, introduction, methods, results and discussion sections of systematic reviews/meta-analysis. This checklist has been created for evaluating reviews of RCT's but it is also a valuable instrument to assess the quality of systematic reviews that include other types of studies. The result of the quality appraisal is in appendix 3.

A quality appraisal of the individual studies was performed using the 14 items used in the KCE report 118. The items give a score to the presence of a clear research question, study population, intervention, comparison, outcomes, design, statistics, possibility to generalize, addressed confounders, randomization, blinding, clustering effect and data endpoints. The detailed results of the quality appraisal of the individual studies are in appendix 1.2 and 1.3. Studies with a score lower than 7 on 14 were not included.

Table 1. Quality appraisal of individual studies.

QUALITY APPRAISAL SCORE	NUMBER OF STUDIES (%)
14/14	6 (7%)
13/14	29 (33%)
12/14	11 (14%)
11/14	11 (13%)
10/14	7 (8%)
9/14	13 (15%)
8/14	4 (4%)
7/14	3 (3%)
Not applicable (e.g. modelling studies)	3 (3%)
Total	87 (100%)

Data analysis

The standardized extraction form (see appendix 1.3) was based on the form developed by the Effective Practice and Organization of Care Group [a] :

- Country of the study,
- Initiator of the programme,
- Type of research design,
- Objectives,
- Setting,
- Profile of caregivers targeted,
- Type and number of behaviours targeted,
- Type and number of patient populations targeted,
- Professionals providing AD,
- Type, number and intensity of interventions for AD,
- Effectiveness and cost-effectiveness.

2.2.2.2 *Grey literature: analysis of AD programmes in other countries*

Research question

The research question of this grey literature analysis is: *"What programmes do exist on face-to-face AD targeting physicians in primary care settings that have not been published in national/international peer reviewed journals?"*

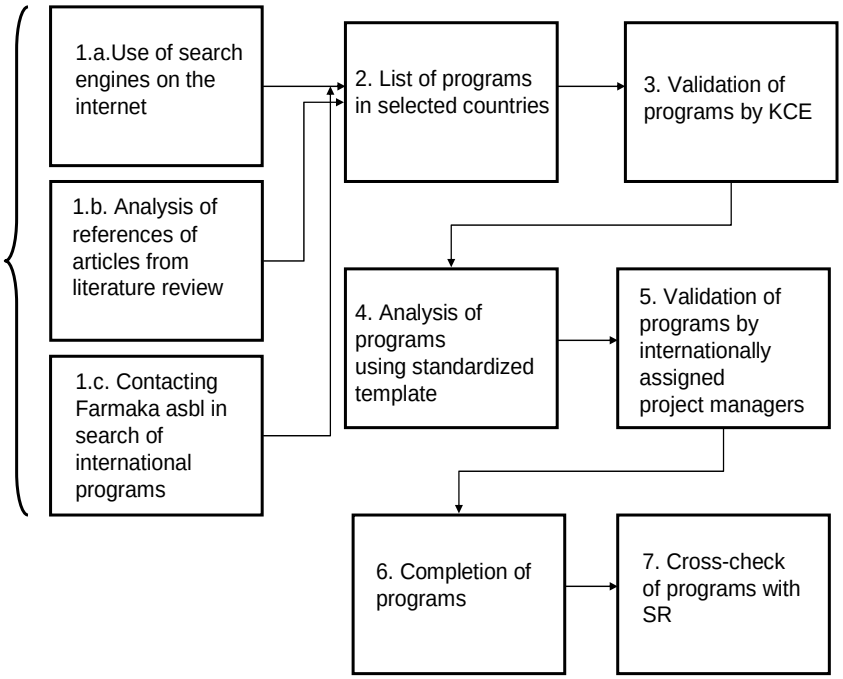
Search strategy

The search used a stepwise approach in 7 steps for the identification and validation of international programmes on AD:

- Step 1a, 1b and 1c: Use of different search engines on the internet, search in reference lists of articles from literature review, and contacting Farmaka asbl and the Federal Agency for Medicines and Health Products to identify potential programmes in other countries.
- Step 2: Overview of programmes in different countries
- Step 3: Validation of overview of programmes by KCE
- Step 4: Analysis of the programmes using a standardized template similar to the template used for the other studies;
- Step 5: Validation of programmes by identified contact persons;
- Step 6: Completion of the information;
- Step 7: Cross-check with the results of the systematic review and integration of the findings in the common discussion.

[a] Cochrane Effective Practice and Organization of Care Group (EPOC). Data abstraction template. http://www.epoc.cochrane.org/files/website/ Reviewer%20Resources/data%20Abstraction20%Form

Figure 1. Step-wise approach for the identification and validation of international programs on academic detailing



Exclusion criteria

Programmes were excluded from the analysis if :

- results on the programme are already published in international (peer reviewed) journals and analysed in the systematic literature review;
- health care systems with little relevance to the Belgian one;
- programmes conducted in other settings than primary care;
- no available formal description for the content of the programme.

Data analysis

The analysis of all programmes relied on similar items as for the articles in the indexed literature (see items above and details in appendix 1.3).

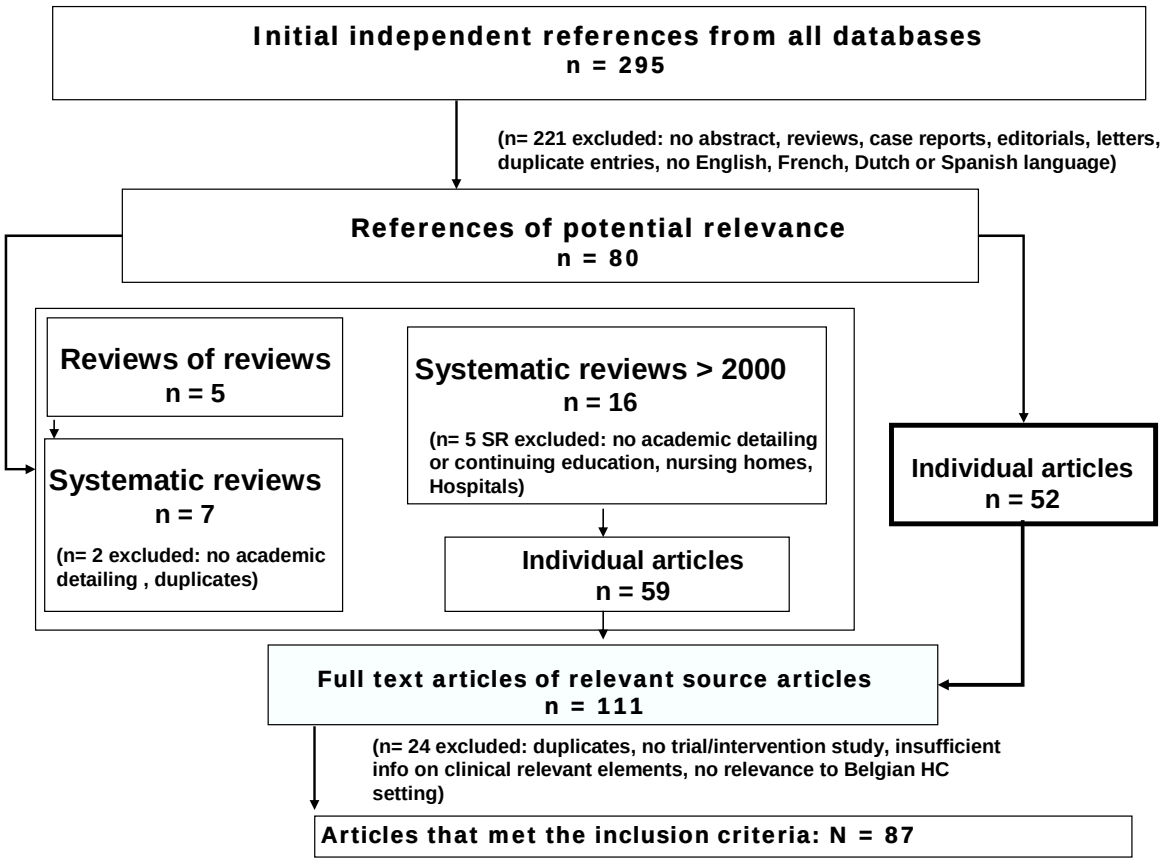
2.3 RESULTS

2.3.1 Systematic literature review

2.3.1.1 Quorom statement flow diagram

The initial search identified a total of 295 citations from all databases. After scanning titles of the citations and abstracts, 5 reviews of reviews, 16 systematic reviews published after 2000 and 52 individual articles were selected for further screening and full text articles were retrieved. The combination of the 52 articles with the relevant source articles of the 16 systematic reviews represented 111 relevant individual articles. Twenty-four (n=24) articles were not included: the reasons for rejection are in appendix 1.3.

Figure 2. Quorom statement flow diagram: selection and inclusion of studies in the review



2.3.1.2 *Reviews of reviews and systematic reviews*

The 5 reviews of reviews and the systematic reviews are presented in the tables in appendix 1.2. The reviews of reviews were used to identify systematic reviews within the scope of this review. The systematic reviews were used to select source articles if they answered to the inclusion criteria for the analysis: (randomised) controlled trials, before and after studies, retrospective studies and time series studies within the scope of this research.

The tables in appendix 1.4 summarise the main research question, the databases consulted, in and exclusion criteria in the review and the source articles that were selected for this literature review.

2.3.1.3 *Source articles*

A total of 87 relevant source articles were finally included in the study. The summary tables are presented in appendix 1.4, including a detailed description of the AD interventions in the 87 articles.

Countries where the studies were conducted

A large number of countries were presented in the different studies (Table 2). Most studies were conducted in the United States (38%) and Australia (18%). A substantial number of studies however were conducted in different countries in Europe (40%), including Belgium, The Netherlands, UK, Sweden, Norway, Denmark, Finland, France, Spain, Portugal, Switzerland, Germany and Ireland. Three studies were conducted in Canada and one study in Malaysia.

Table 2. Countries of the studies

Countries	Number (%)
US	33 (38%)
Australia	16 (18%)
UK	13 (15%)
The Netherlands	7 (8%)
Canada	3 (3%)
Sweden	2 (2%)
Norway	2 (2%)
Belgium	2 (2%)
Others	9 (10%)
Total	87 (100%)

Initiator of the programme

All studies were research studies with either public or private funding and only very few of them mentioned the initiator of the program. When this initiator was mentioned, it was a Health Maintenance Organisation (4 studies with one study within Kaiser Permanente), a medical association (1 study) and a consortium of State's medical societies (1 study).

Research design

Most studies (68%) used a (cluster) randomized controlled trial design. Controlled, but non-randomized designs were used in 9% of the studies. Before-after designs were applied in 13% of the studies and time series designs were used in 6% of the studies. Studies using a modelling approach (3%) often focused on cost-effectiveness of AD. A retrospective study design was used in only one study.

Table 3. Research designs

TYPE OF RESEARCH DESIGN	NUMBER OF STUDIES (%)
(Cluster) Randomized Controlled Trials	59 (68%)
Before/after	11 (13%)
Controlled trial	8 (9%)
Time series	5 (6%)
Modelling approach	3 (3%)
Retrospective study design	1 (1%)
Total	87 (100%)

Objectives of the interventions

The studies targeted mostly the effectiveness of AD and sometimes its cost-effectiveness. Studies on feasibility and acceptability of AD were excluded.

Primary care settings

In most studies AD services were provided in the physician's office. A few studies also mentioned primary care clinics or non-commercial settings.

Table 4. Settings

TYPE OF SETTING	NUMBER OF STUDIES (%)
Physician's office	84 (97%)
Primary care clinic	2 (2%)
Other	1 (1%)
Total	87 (100 %)

Target population of caregivers

Nearly all studies primarily targeted general practitioners. One study targeted psychiatrists and a last one targeted both primary care physicians and specialists. The vast majority of studies targeted one profile of caregiver, except in one study.

Targeted behaviours

A large number of behaviours were targeted in the different studies. This review classified them into seven categories:

- Prescribing;
- Comprehensive management of conditions/diseases in accordance with guidelines;
- Clinical control of specific conditions;
- Clinical techniques;
- Reporting;
- Screening/preventive actions;
- Detection skills.

PRESCRIBING

Nearly half of the studies (n=40) targeted the prescription of drugs (agents) only. Examples include the adequate prescription of antibiotics, antihypertensive drugs, NSAIDs, antidepressants (SSRIs), angiotensine receptor 2 antagonists and gastroprotective agents.

COMPREHENSIVE MANAGEMENT OF CONDITIONS/DISEASES

The comprehensive management of conditions/diseases is a second type of behaviour often targeted in 16 studies. It includes a broad range of actions beyond the prescription of drugs e.g. clinical examination, follow-up, screening, referral and patient education. Clinical conditions or diseases most often mentioned as the subject of comprehensive management are depression, shoulder pain, heart failure and hazardous alcohol consumption.

CONTROL OF SPECIFIC CLINICAL PARAMETERS

Six studies targeted the control of specific clinical parameters, mostly blood pressure and glycemia.

TECHNIQUES

Four studies targeted improvements in the knowledge or skills of physicians for specific techniques. Examples include diagnostic imaging, inhaler technique, spirometry and feet examination.

SCREENING AND PREVENTIVE ACTIONS

A fifth category includes 18 studies that targeted screening and preventive actions. Preventive/screening actions included e.g. immunization, folic acid supplementation, smoking cessation advice and mammography prescription.

REPORTING OF ADVERSE DRUG EVENTS AND DETECTION

Finally, one study addressed the reporting of adverse drug events and another one addressed lump detection skills.

Table 5. Behaviours targeted

1. Drug prescription (40 studies, 46%)
Antibiotics (for acute cough)
Antibiotics (for tonsillitis)
Antibiotics (uncomplicated acute bronchitis)
Antibiotics (otitis media)
Antibiotics (upper / lower respiratory tract infections)
Antibiotics (urinary tract infections)
Asthma medication
Benzodiazepines in patients with anxiety
Antipsychotic drugs
Antidepressants (SSRIs)
Antitrombotics (Warfarin) in atrial fibrillation
NSAIDs
ACE inhibitors
Antihypertensive drugs
Angiotensin 2 receptor antagonists
Cyclooxygenase-2 inhibitors
Gastroprotective agents
CVD preventive therapies
Anti-ulcer agents
Riperidone long-action injection (RLAI)
2. Comprehensive management of conditions/diseases in accordance with the guidelines (16 studies, 18%)
Shoulder pain
Depression
High serum cholesterol levels
Systolic hypertension in elderly patients
Low back pain in adult patients
Attention deficit/hyperactivity disorder
Smoking
Hypertension
Hypercholesterolemia
Angina pectoris
Heart failure
Hazardous alcohol consumption
Asthma
Helicobacter pylori
Chronic pain
Obesity
Acute maxillary sinusitis
3. Control of clinical parameters (6 studies, 7%)
Blood pressure control
Control of glycemia
Weight
Hyperlipidemia
Hypertension
Acid-related disorders
4. Techniques (4 studies, 5%)
Diagnostic imaging
Inhaler technique (asthma)
Spirometry
Funduscopy
Feet examination
Use of structured consultation 'prompts'
5. Preventive actions – screening (18 studies, 21%)

Mammography
Immunization (influenza, pneumococcus)
Folic acid supplementation
Smoking cessation advice
Mammography (breast cancer)
Occult blood (cancer detection)
PSA screening
Prevention of stroke
Alcohol abuse
Hypertension management
6. Reporting (one study)
Adverse drug events
7. Detection skills (one study)
CBE (clinical breast examination) - lump detection

Type and number of patient populations targeted

A broad range of patient populations were targeted in the different studies, including 44 different patient categories. An overview of these patient categories is provided in table 5. Patient populations for which quality improvements through AD were most often targeted were patients with hypertension (13%), heart failure (9%) and cancer (7%). Patient populations were mentioned referring to their disease (e.g. patients with asthma), the medications they used (e.g. patients who need antibiotics) or their demand/need for health care (e.g. patients who need clinical breast examination or preventive services).

Some studies targeted the whole patient population. Other ones focused on age groups: elderly people, children, healthy woman age > 45 years.

Sixteen studies targeted multiple populations at the same time, ranging from two to six different patient populations.

Table6. Patient populations

TYPE OF POPULATIONS	N STUDIES (%)
Patients with hypertension	11 (13%)
Patients with heart failure	8 (10%)
Patients with cancer	6 (7%)
Patients with depression	5 (6%)
Patients who need antibiotics	4 (5%)
Patients with diabetes	4 (5%)
Patients with upper and lower respiratory tract infect	3 (3%)
Patients with osteoarthritis	2 (2%)
Patients needing immunization	2 (2%)
Patients with hazardous alcohol consumption	2 (2%)
Patients with new dyspepsia and chronic users of antisecretory drugs	2 (2%)
Patients with high serum cholesterol levels	2 (2%)
Patients who smoke	2 (2%)
Patients needing benzodiazepine anxiolytic drugs	2 (2%)
Patients who need NSAID medications	2 (2%)
Patients needing cardiovascular preventive care	2 (2%)
Patients needing ACE inhibitors	1 (1%)
Patients with shoulder pain	1 (1%)
Patients with low back pain	1 (1%)
Patients with rheumatic disorders	1 (1%)
Patients with helicobacter pylori	1 (1%)
Patients with anxiety	1 (1%)
Patients with schizophrenia	1 (1%)
Patients with attention deficit/hyperactivity disorder	1 (1%)
Patients with uncomplicated acute bronchitis	1 (1%)
Patients with otitis media	1 (1%)
Patients with urinary tract infections	1 (1%)
Patients with asthma	1 (1%)
Patients with risk for CV disease or CVDisease	2 (2%)
Patients at risk for cancer	1 (1%)
Patients taking Warfarin	1 (1%)
Patients needing cerebral and peripheral vasodilatators	1 (1%)
Children needing immunization	1 (1%)
Children needing antibiotics	1 (1%)
Children with respiratory diseases	1 (1%)
Patients with obesity	1 (1%)
Healthy woman (age > 50)	1 (1%)
Elderly patients needing benzodiazepines	1 (1%)
Patients needing preventive actions (folic acid supplementation,…)	1 (1%)
Patients with abnormal screening result for faecal occult blood	1 (1%)
Elderly patients	1 (1%)
Patients not specified	1 (1%)
General population	1 (1%)

Table 7: Studies targeting multiple patient populations for quality improvement through academic detailing

Avorn, 1983[12]	Patients needing cerebral and peripheral vasodilatators, oral cephalosporin and propoxyphene
Feder, 1995[13]	Patients (adults) with asthma and/or diabetes
Freemantle, 2002[14]	Patients needing ACE inhibitors, raised cardiovascular risk patients needing aspirin, NSAIDs needing patients with joint pain, patients needing antidepressants
Frijling, 2003[15]	Patient with heart failure, hypertension, hypercholesterolemia and angina pectoris
Goldberg, 1998[16]	Patients with hypertension and depression
Ilett, 2000[17]	Patients with upper and lower respiratory tract infections, otitis media and urinary tract infections.
Jackson, 2004[18]	Patients with atrial fibrillation and an elevated risk to develop stroke
Kim, 1999[19]	Patients needing immunization, mammography and clinical breast screening
McDonald, 2003[20]	Elderly patients with heart failure and chronic pain associated with osteoarthritis
Mold, 2008[21]	Patients needing selected immunizations and preventive services
Naughton, 2007[22]	Patients with CVD or diabetes
Nilsson, 2001[23]	Patients with hypertension, peptic ulcer/dyspepsia and depression
Pit,2007[24]	Elderly patients taking benzodiazepines, NSAIDs/COX-2 inhibitors and antihypertensive agents
Siegel, 2003[25]	Patients with hypertension, diabetes mellitus and heart failure
Sheinfeld, 2000 [26]	Patients with cancer: colon, rectum, cervix, prostate, breast and lung
Williams, 1994[27]	Patients with cancer: colon, rectum, prostate and breast

Professionals providing academic detailing

In the majority of studies pharmacists provide AD services (32%) followed by physicians (16% of the studies). One fifth of the studies (21%) did not specify the profession of the detailers. Other professionals who are responsible for providing these services are nurses (8%), specialists (2%) and researchers (11%). In a few studies professionals with different backgrounds are involved in the provision of AD services. Six studies (7%) used both pharmacists and physicians, whereas other studies used combinations of pharmacists, physicians and nurses.

Only a few studies provide additional information on the professional background of the detailers, the training they received in the context of the AD program or other relevant characteristics including age, gender and years of professional experience.

Table 8: Professionals providing academic detailing

Professionals who provide the information	**NUMBER OF STUDIES (%)**
Pharmacists	28 (32%)
Detailers not specified	18 (21%)
Physicians	14 (16%)
Researchers	10 (11%)
Nurses	7 (8%)
Pharmacist and physician combined	6 (7%)
Specialists	2 (2%)
Pharmacist and nurse combined	1 (1%)
Physician and nurse combined	1 (1%)
Total	87 (100%)

Interventions

The different studies offer a broad range of AD interventions. Hardly any study provided a theoretical background for the intervention, such as the Diagnostic Evaluation Model (DEM)[28], based on socio-cognitive theories and theories of Reasoned Action. Overall the description of the interventions often lack sufficient detail to understand the exact nature of the intervention.

Information on the duration of each AD session and the number of sessions is provided in some studies. Most sessions lasted 15 to 45 minutes and the number of consecutive sessions ranged from 1 to 7. The most frequent models for one-to-one visits were interactive discussions on scientific guidelines combined with educational materials.

A substantial number of studies consisted of multifaceted programs that included other interventions besides AD such as e.g. audit, feedback and the provision of educational materials to patients. Two thirds (67%) of the studies were multifaceted programs including AD services, whereas 33% provided only AD.

Table 9. Interventions for academic detailing

One-to-one academic detailing services	Discussing of evidence based guidelines
	Provision of educational materials
	Provision of medical journal articles
	Empowerment of physicians
	Knowledge enhancement
	Teaching of techniques
	Provision of technical tools (e.g. automatic blood pressure devices)
	Provision of practice prescribing workbooks
Academic detailing related services	Provision of educational materials for patients
	Audit
	Reminders
	Feedback
	Information technology support
	Credits for continuing medical education
	Mailings

Effectiveness and cost-effectiveness of the interventions

INDICATORS OF EFFECTIVENESS

The effectiveness of the interventions is mostly assessed by process indicators (effect on medical practice): few studies provide measures at the patient level.

The different measures used in the studies are grouped into five categories:

- Process indicators: e.g. prescription indicators, number of lump detections, percent of patients with target values, requests for examinations, knowledge levels of specific clinical problems;
- Economic outcomes: e.g. cost reductions, cost of prescription, hospital admissions;
- Patient biological outcomes such as immunization rates, levels of total cholesterol, symptom resolution;
- Psychosocial outcomes: e.g. quality of life, scores on SF-36;
- Other indicators: e.g. availability of materials and instruments.

COMBINATIONS OF MEASURES

A total of 14 different combinations of measures have been identified in the 87 studies (see table 10).

Most studies used a single group of measures. More than half of them (n=52) analysed process indicators only, including prescription indicators.

Ten studies included economic outcomes (alone or besides other measures). Eight of them focused on costs (and potential savings) of prescribing. The two last ones targeted immunization and prevention strategies.

The other studies provided a combination of different groups of outcome measures.

Table 10. Measures of effectiveness

N of studies providing different types of measures (N=87)		
1.	Only process indicators	52 (60%)
2.	Only economic measures	6 (7%)
3.	Patient biological outcomes and process indicators	6 (7%)
4.	Psycho-social and process indicators	5 (6%)
5.	Process indicators and other outcomes	4 (5%)
6.	Process and economic outcomes	4 (5%)
7.	Biological, process and economic measures	2 (2%)
8.	Other measures	2 (2%)
9.	Biological, psycho-social and process measures	1 (1%)
10.	Biological and psycho-social measures	1 (1%)
11.	Biological, process and other measures	1 (1%)
12.	Biological, psycho-social, process and other measures	1 (1%)
13.	Biological and other measures	1 (1%)
14.	Psycho-social and other measures	1 (1%)

ECONOMIC STUDIES

Most studies (n=77) solely reported on the effectiveness of AD . Ten studies also reported economic outcomes. The table below summarizes the classification of these last studies after thorough full-text evaluation.

Table 11. Classification of economic studies

<table>
<tr><th colspan="4">Are both costs (inputs) and consequences (outputs) of the alternatives examined?</th></tr>
<tr><th colspan="2" rowspan="2"></th><th colspan="2">No</th><th rowspan="2">Yes</th></tr>
<tr><th>Examines consequences only</th><th>Examines costs only</th></tr>
<tr><th rowspan="4">Is there a comparison of at least two alternatives?</th><th rowspan="2">No</th><td colspan="2">Partial evaluation</td><td>Partial evaluation</td></tr>
<tr><td>Outcome description</td><td>Cost description</td><td>Cost-outcome description</td></tr>
<tr><th rowspan="2">Yes</th><td colspan="2">Partial evaluation</td><td>Full economic evaluation</td></tr>
<tr><td>Efficacy or effectiveness evaluation</td><td>Cost comparison
Braybrook et al., 1996
Newton-Syms et al., 1992</td><td><u>PRESCRIPTION</u>
Fretheim et al., 2006 (CBA & CEA)
Grandjour et al., 2005 (CEA)
Mason et al., 2001 (CEA)
Simon et al., 2007 (CBA)
Watson et al., 2001 (CBA)
<u>PREVENTION</u>
Franzini et al., 2007 (CEA)
Stone et al., 2004 (CEA)
<u>EXCLUDED (scope)</u>
Gomel et al., 1998 (CEA)</td></tr>
</table>

Adapted from Drummond M, O'Brien B, Stoddart G, Torrance G. Methods for the economic evaluation of health care programmes. Oxford: Oxford University Press; 3d edition; 2005.

Seven studies compared both the costs and outcomes of AD interventions versus their comparator. These studies were thus full economic evaluations, mostly cost-minimisation or cost-effectiveness analyses[29-35].

Another study was also a full economic evaluation but it did not measure any relevant outcome for the purpose of the current study[36];

Two studies estimated the potential savings associated with prescription changes, without considering the cost of the AD intervention. These studies are thus rather (partial) cost-comparisons rather than full economic evaluations[37, 38].

Table 12. Effectiveness of academic detailing

Number of studies providing results on effectiveness of academic detailing (N= 77) without monetary outcome	
Only positive effects	42 (55%)
No effect	10 (13%)
Mixed results	25 (32%)
Negative effect	0
Number of studies providing results on (cost-)effectiveness of academic detailing (N=10)	
Positive effect on effectiveness only	2 (20%)
Not cost-effective	2 (20%)
Inconclusive (mixed effects on effectiveness or cost-effectiveness)	3 (30%)
Cost-effective	2 (20%)
Not relevant outcome	1 (10%)

EFFECTS OF ACADEMIC DETAILING ON CLINICAL OUTCOME MEASURES (77 STUDIES)

Most studies reported a positive effect of AD on the outcomes under study: more than half of the 77 studies (n=42, 55%) showed only positive effects and one third of the studies (n=25, 32%) showed mixed results including both positive as well as no effect for the measures under study. These studies used combined outcome categories. Ten out of the 77 studies (13%) reported no effect of the intervention.

The positive changes are listed below:

Positive effects of academic detailing demonstrated for (prescription data first):
Number of cerebral and peripheral vasodilators, and oral cephalosporin and propoxyphene
Number of benzodiazepines units prescribed (n=3)
Number of antibiotic units prescribing (n=8)
Number of antidepressants units prescribed (n=3)
Number of co prescriptions of warfare-interacting medications
Number of prescribed units of NSAID (n=4)
Number of ACE inhibitors units prescribed
Number of thiazides units prescribed
Number of depressives first-generation tricyclics units prescribed
Number of omeprazole and metronidazole units prescribed
Number of low-dose thiazide and beta-blocker prescribed
Number of Warfarin and aspirin units prescribed
Number of medium-and long-acting benzodiazepines and total benzodiazepines units prescribed
Number of agents acting on the renin-angiotensin system
Number of risperidone long-acting injection (RLAI) units prescribed
Number of total DDDs dispensed for the recommended first-line agents (amoxicillin-potassium clavulanate, cephalexin and trimethoprim)
Number of thiazide diuretics units prescribed
Number of anti-ulcer agents (cimetidine, ranitidine and sucralfate) units prescribed
Number of contra-indicated antibiotics (chloramphenicol, clindamycin, tetracycline for children younger than 8 years) and cephalosporins.
Number of diazepam units prescribed
Number of calcium antagonists, beta-blockers, thiazide diuretics units prescribed (n=2)
Number of angiotensine converting enzyme inhibitor or angiotensin receptor blocker units prescribed
COX-2 utilization rates
Knowledge about identifying and managing shoulder problems

Management of systolic hypertension
Referral to physiotherapists or the back pain unit
Use of guidelines for the assessment and treatment of ADHD
Use of computer-tailored smoking cessation programmes
Proportion of patients who received the advice to quit smoking
Recording of review of inhaler technique, smoking habit, and review of asthma symptoms, quality of prescribing in asthma.
Reporting of ADR (adverse drug reactions)
Self-reported provider behaviour
Assessment of risk factors in patients with hypercholesterolemia, angina pectoris, hypertension and heart failure
Advice to patients with hypercholesterolemia and hypertension
Checking for clinical signs of deterioration in patients with heart failure
Number of practices adhering to the guidelines for cardiovascular disease
Number of influenza, pneumococcal, and tetanus immunization
Folic acid supplementation, smoking cessation and hypertension treatment
Deficiency score (the difference between ideal and actual practice)
Organizing preventive care.
Proportion of patients with a chart-documented mammogram, clinical breast examination, Papanicolaou smear and occult blood slide test
Number of practices who implemented one or more of the evidence-based processes (selected immunizations and preventive services)
CDE (complete diagnostic evaluation)rates for FOBT
Satisfaction in GPs
Helicobacter pylori testing, use of recommended helicobacter pylori treatment regimens, and discontinuation rates of proton pump therapy after treatment
Number of falls and injury requiring medical attention
Number of HbA1c tests (increase) and blood glucose measurements and urine microalbumin
Number of physicians that discussed obesity with their patients, reference to obesity management increased, BMI and cardio-vascular co-morbidities improved
Number of standards drinks consumed by risky drinkers
Number of pneumoccocal vaccinations
Number of identified barriers to practice
Quality of practice management.
Quantity of cholesterol testing
Rates of screening SIG (flexible sigmoidoscopy)
Number of correct responses to questions about prostate cancer treatment effectiveness and endorsement of PSA testing for prostate cancer by professional bodies
Compliance rates + increased awareness of resources of ACS and in prompting physicians to adopt cancer prevention and screening procedures
Geriatric knowledge scores
Recall of GPs advice about nicotine replacement patches and gum
Rates of mammography prescription
Requests for ultrasound imaging,
Number of correct lump detections

The authors analysed more closely the effectiveness of studies which targeted diabetes mellitus and dementia to make the link between this literature review and the analysis of IMA data (see chapter 4). There were four studies targeting diabetes, but no single study targeted dementia (see appendix 1.4). Two studies were positive. The study of Feder and Ricordeau showed positive effects of AD on process outcomes e.g. the number of HbA1c tests, blood glucose and microalbuminurin measurements. The study of Naughton demonstrated positive effects on the satisfaction of the GPs, but no effect was shown on the prescription data of statins and antiplatelet medications. The study of New did not yield any positive effects on the biological or process outcomes measured.

Effects of academic detailing on cost measures (10 studies)

Of the ten studies reporting economic outcomes, one study was excluded from this review as it did not analyze the impact of AD on the clinical practice but rather on the uptake of an intervention to follow support sessions related to hazardous alcohol use[36].

Two studies measured the potential savings of prescription behaviour modification and the 7 last ones were full economic evaluations.

Effect of AD on the cost of prescriptions only

Braybrook et al[37] found positive changes in some antibiotic prescribing indicators following one AD visit. The change was mainly a move to generic prescription and lasted for about one year. It should be noted that the control group was the population who refused the intervention. The authors also found a reduction in the costs associated with antibiotics prescription. This reduction was more obvious in the intervention than in the control areas where similar trends were also noted, probably due to concurrent interventions.

Newton-Syms et al.[38] reported a switch of NSAIDs drugs toward the first choice agent after an AD intervention. AD also produced a lower prescribing cost per month for the intervention group compared with the reference group (5 months after the intervention).

Again, although the impact of AD on the overall cost of prescriptions appears to be favourable according to both studies, formal conclusions cannot be derived since the incremental cost of implementing AD was not accounted for.

Cost-effectiveness studies of AD

Of the 7 full economic evaluations identified, 5 assessed the impact of AD on prescribing behaviours and 2 on immunisation and screening programmes.

Modification of prescription behaviour

Fretheim et al.[30] reported that AD produced a significant shift in the prescription of hypertensive drugs towards the use of thiazides. In their cost-minimisation analysis, modest savings were expected over a modelled two-year period with this multifaceted intervention. This positive net benefit is linked with the promotion of a low cost albeit EBM drug.

Gandjour et al.[31] developed a German model assessing the impact of AD on the primary prevention of stroke (treatment of hypertension) and on the secondary prevention of coronary heart disease (CHD, prescription of lipid-lowering drugs). From their model, they computed an incremental implementation cost per patient over a lifetime and an incremental cost per QALY gained. The QALY (Quality Adjusted Life Year) is a measure of disease burden, including both quality and the quantity of life. The QALY is based on the number of years of life that would be added by the intervention. Each year in perfect health is assigned the value of 1.0 down to a value of O.O of death. If the extra years would not be lived in full health, for example, if the patient would lose a limb, or have to use a wheelchair, then the extra life years are given a value between 0 and 1 to account for this.

The incremental cost-effectiveness ratio, expressed as the lifetime incremental cost per QALY gained was €3407 and €5653 for stroke and CHD, respectively. Grandjour et al. report that AD may then well be considered cost-effective but the authors further estimated that if outreach educators visited all primary care physicians to improve the prescription of hypertensive (or lipid-lowering) drugs, the annual implementation cost would amount to € 238 (€ 215) million i.e., 0,2% of the health insurance total budget, a substantial budget impact.

Mason et al.[32] modelled the cost-effectiveness of AD interventions following the publication of guidelines. The first guideline promoted the use of ACE inhibitors (angiotensin-converting enzyme) for patients with heart failure. The second guideline focused on the care of depressive patients. The authors concluded that AD is cost-effective for the implementation of ACE inhibitors prescription ($ 2602 per life-year gained) considering an effect of the AD visit lasting for one year. By contrast, AD for reducing the use of SSRIs in favour of tricyclic antidepressants was not estimated to be cost-effective: the cost per patient outreach exceeding the potential savings of behavioural change.

Simon et al.[33] assessed the impact of mailed guideline, AD and group detailing. None of the intervention had an effect on the prevalent cases, i.e. on patients already receiving a treatment. For incident cases, the authors reported that individual AD resulted in a (non significant) net decrease in average daily drug cost per patient during the first year of follow-up. The differences with the mailed guideline group were not significant during the second year of follow-up. A previous publication on the same intervention did not record any effect on the blood pressure level[39].

Finally, Watson et al.[35] compared AD with the effectiveness of mailed guidelines for the prescription of NSAIDs. They concluded that there is no evidence for the effectiveness or cost-effectiveness of AD in comparison with the mailing of guidelines one year after the intervention.

Immunization and cancer prevention

Franzini et al.[29] reported no favourable cost-effectiveness ratio to improve immunization coverage in children by means of AD with one year follow-up. They concluded that the costs for one child with up-to-date immunization status are higher than potential societal savings.

Stone et al.[34] estimated the effect of a national programme that would reduce the number of screening tests by 19.1 % among patients older than 70 years. In the most plausible scenario, the total burden of prostate cancer disease expressed in Disability Adjusted Life Year (DALYs) would decrease by 4.7% in those aged 70 and over, with no loss of life. The incremental cost-effectiveness ratios were 16.000/DALY (gross) and 8.500/DALY (net).

Effectiveness of academic detailing compared to other educational strategies

The effectiveness of AD services compared to other educational strategies was measured in 34% of the studies. AD compared with other specified intervention is generally effective for improving appropriate care and prescribing.

Effectiveness of multifaceted versus single intervention programs

A single AD service was defined as providing one or two services (usually interactive face-to-face visits and educational materials). A multifaceted program was defined as providing 3 or more interventions (most often single AD + audit, feedback, phone services, follow-up or educational materials for patients).

The multifaceted programs produced positive effects in 86% of the studies, including 38% of the studies that reported no effect for some measures (besides the positive results noted). Most single intervention programs (93%) also produced some positive results, including 17% of the studies with mixed results.

Table 13. Multifaceted versus single intervention studies: outcomes

Multifaceted studies : results on (cost)effectiveness (N= 58)	
Only positive effects	28 (48%)
No effect	8 (14%)
Mixed results	22 (38%)
Negative effect	0
Single intervention studies: results on (cost)effectiveness (N=29)	
Only positive effect	22 (76%)
No effect	2 (7%)
Mixed results	5 (17%)
Negative effect	0

Professional background of the detailer

The professional background of the background detailer did not influence the success of AD (pharmacists: 64%; physicians: 64%; nurses: 57%; pharmacists and physicians combined: 67%). Less positive results were noted (40%) only when researchers were involved.

Table 14. Outcomes of studies related to the professional background of the detailer

Professionals who provide the information	**Number of studies**	**Positive outcomes**	**No outcomes**	**Mixed results**
Pharmacists	28	18 (64%)	3 (11%)	7 (25%)
Detailers not specified	18	11 (61%)	4 (22%)	3 (17%)
Physicians	14	9 (64%)	1 (7%)	4 (29%)
Researchers	10	4 (40%)	0	6 (60%)
Nurses	7	4 (57%)	1 (14%)	2 (29%)
Pharmacist and physician	6	4 (67%)	0	2 (33%)
Specialists	2	2	0	0
Pharmacist and nurse	1	0	0	1
Physician and nurse	1	1	0	0

2.3.2 Academic Detailing programmes in other countries

Nine programmes have been identified and were sufficiently detailed in the grey literature to allow a comprehensive description:

	Programmes	**Country**
1.	**The Independent Drug Information Service (IDIS)**	US
2.	**The South Carolina Medicaid Academic Detailing Programme (SCORxE)**	US
3.	**The Vermont Academic Detailing Programme**	US
4.	**The Canadian academic Detailing Collaboration (CADC)**	Canada
5.	**The National Heartwatch programme**	Ireland
6.	**The Infoproximed programme**	France
7.	**FARMAKA vzw**	Belgium
8.	**The Promoting and Supporting Evidence Based Medicine through Divisions of General Practice Project**	Australia
9.	**The Drug and Therapeutics Information Service (DATIS) programme**	Australia

2.3.2.1 Programme 1: The Independent Drug Information Service (IDIS)

1. The Independent Drug Information Service	**Content**
Country	**US**
Initiator	The Independent Drug Information Service is sponsored by the PACE Programme of the Pennsylvania Department of Aging and has no ties to any pharmaceutical company. Its clinical content is created by an independent group of physicians and researchers on the faculty of Harvard Medical School. .
Initiated since	2005
Annual budget	$1 million
Objectives	To discuss clinically appropriate therapeutic choices and patient care practices. An independent group of physicians and drug researchers on the faculty of Harvard Medical School comprehensively evaluate medical journals and other data sources to pull together the best available, objective information about drugs used commonly in primary care practice. They then synthesize it into concise, clinically relevant summary documents, decision-making tools, and patient education materials
Setting	Primary care
Population	See behaviour targeted
Caregivers targeted	Physicians
Behaviour targeted	Prescription of NSAIDs and cox-2 inhibitors, Upper G.I. symptoms, Anti-platelet therapy, Lipid-lowering therapy, Antihypertensive therapy, Type 2 Diabetes management, Depression management, Falls and mobility, Cognitive impairment, Chronic Obstructive Pulmonary Disease.
AD professionals	Trained pharmacists, nurses, and other health professionals visit with physicians in their offices to discuss clinically appropriate therapeutic choices and patient care practices. Rather than promote particular products, academic detailers provide summaries of the evidence to help physicians prescribe the safest, most effective medications for their patients.
Interventions	Academic detailers provide summaries of the evidence to help physicians prescribe the safest, most effective medications for their patients. In many cases, the most appropriate therapeutic options are tried and true drugs with safety-risk profiles that demonstrate benefit at relatively lower risk, and because they have been on the market longer, they are often available as affordable generics. This is particularly true in the case of heavily marketed drug classes such as acid-suppressing therapy. But AD is not simply about prescribing generics.
Results	2,400 AD sessions over last 2 years. No information on outcomes.
Contact person	**Independent Drug Information Service** PO Box 990041, Boston, MA 02199 Toll free: 1-877-410-5750 / info@RxFacts.org
References	www.rxfacts.org

2.3.2.2 Programme 2: The South Carolina Medicaid Academic Detailing Programme (SCORxE)

2. The South Carolina Medicaid Academic Detailing Programme (SCORxE)	**Content**
Country	**US**
Initiator	This programme is a collaborative effort between the South Carolina College of Pharmacy (SCCP) and the South Carolina Department of Health and Human Services (SCDHHS). SCDHSS provided $1.98 million to the College to provide AD services to physicians who serve Medicaid patients with mental health disorders, HIV/AIDs or cancer.
Initiated since	2007
Annual budget	$1.9 million over two years (2007-2009)
Objectives	The programme is officially identified as SCORxE which stands for *South Carolina Offering Prescribing Excellence*. The objective of the programme is to improve the quality of care for South Carolina Medicaid patients in the most cost effective manner by promoting quality, evidence-based drug therapy and best practices through face-to-face communication with providers.
Setting	Primary care
Population	Medicaid patients with mental health disorders, HIV/AIDs or cancer.
Caregivers targeted	Physicians
Behaviour targeted	Mainly prescription behaviour
AD professionals	Physicians, clinical pharmacists
Interventions	Clinical consultants meet face-to-face with providers to offer them unbiased, evidence-based clinical information about drug therapy and best-practices that will assist with making best prescription decisions.
Results	No information on outcomes.
Contact person	office@sccp.sc.edu
References	SC College of Pharmacy, SC Department of HHS www.sccp.sc.edu/SCORxE

2.3.2.3 Programme 3: The Vermont Academic Detailing Programme

3. The Vermont Academic Detailing Programme	Content
Country	**US**
Initiator	The Vermont AD Programme is sponsored by the UVM College of Medicine Office of Primary Care with funding and other support from Blue Cross Blue Shield of Vermont/Vermont Health Plan, the Fletcher Allen Community Health Foundation, the Vermont Department of Health, and the University of Vermont. There is no drug company sponsorship associated with the Vermont AD Programme nor do the programme faculty have any ties to the pharmaceutical industry. Thus, they are able to objectively review clinical topics, covering the latest evidence for lifestyle changes and generic medications in addition to the latest in medication releases.
Initiated since	1999: Established by a PharmD-MD team Began as a formulary management tool for BlueCross BlueShield Additional support from UVM AHEC, Community Health Foundation • 2004: Amanda Kennedy and Rich Pinckney hired to co-direct programme • 2007: Vermont Legislature supports expansion Charles MacLean, MD Act 80: Increasing Transparency of Prescription Drug Pricing and Information www.leg.state.vt.us
Annual budget	$ 50.000
Objectives	Refining Medication Prescribing Practices.This programme presents an objective overview of evidence from studies about the various drugs used to treat a specific medical condition.
Setting	Sessions are delivered at Vermont practices.
Population	Patients with migraines, insomnia and depression
Caregivers targeted	Primary care physicians
Behaviour targeted	Management of migraines, insomnia and depression. One new module a year (100 hours development per year)
AD professionals	One medical doctor and one pharmacist
Interventions	The programme consists of one-hour, case-based interactive sessions geared to practitioners who prescribe drugs. Sessions are delivered at Vermont practices by UVM's AD team—physicians. Noontime sessions, group AD sessions including physicians, nurses.
Results	Average of 25 visits a year. No information on outcomes.
Contact person	Laurie McLean. Administrative Assistant to the Vermont AD Programme (802) 656-2179 or lmclean@uvm.edu
References	http://www.med.uvm.edu/ahec/downloads/ADoverview2008.03.13.pdf

2.3.2.4 Programme 4: The Canadian academic Detailing Collaboration (CADC)

4. The Canadian academic Detailing Collaboration (CADC).	**Content**
Country	**Canada**
Initiator	The Canadian AD Collaboration (CADC) is a group of programmes and services which provide AD (or educational outreach) to physicians and other health care providers in Canada. Member groups include the following: 1) British Columbia Provincial AD Service (expanded from the original North Shore CDUP) 2) AD - Alberta Health Services 3) RxFiles AD Programme - Saskatchewan 4) Prescription Information Service of Manitoba (PRISM) 5) Dalhousie AD Service (Nova Scotia). These groups from the Canadian AD Collaboration (CADC).
Initiated since	British Columbia - 1993 Saskatchewan - 1997 Nova Scotia & Alberta -2001 Manitoba- 2003
Annual budget	$ 2 million
Objectives	The goal of the CADC is to prepare AD topics more accurately and efficiently and to disseminate evidence more effectively
Setting	Primary care
Population	Primarily patients with heart failure
Caregivers targeted	British Columbia: 50-60 physicians in North/West Vancouver Alberta: 100 rural and 150 urban physicians Saskatchewan: 400 physicians Manitoba: 120 physicians Nova Scotia: 350 physicians
Behaviour targeted	Primarily heart failure
AD professionals	Pharmacists
Interventions	Shares expertise and content material, organizes training and development workshops for academic detailers, publishes commentaries, and makes presentations at academic meetings. Half-an hour face-to-face visits+ decision aids + educational materials
Results	Preliminary data show changes in prescribing of heart failure medications in intervention group receiving AD.
Contact person	ann.nguygen@vch.ca
References	Maclure M, Allen M, Bacovsky R et al. Show me the evidence: best practices for using educational visits to promote evidence-based prescribing. Victoria, BC: Drug Policy Futures, 2006 Bacovsky R, Maclure M, Nguyen A, et al. Canadian AD Collaboration : evaluating processes and outcomes of AD. CPJ 2006; 139(Mar/Apr): 54-7.

2.3.2.5 Programme 5: The National Heartwatch programme

5. The National Heartwatch programme	Content
Country	**Ireland**
Initiator	Department of Health and Children, the former health boards, Irish College of General Practitioners and Irish Heart Foundation.
Initiated since	2003
Annual budget	Not available
Objectives	Aims at secondary prevention of CVD and involves 20% of GPs practices in Ireland and has enrolled over 7000 patients. Based on the second European Joint Task Force recommendations for secondary prevention of coronary heart disease (CHD).
Setting	Primary care
Population	High risk population, those with history of myocardial infarction, coronary artery bypass surgery or percutaneous transluminal coronary angioplasty and a small number of diabetic patients.
Caregivers targeted	Primary care physicians
Behaviour targeted	Prevention of CVD
AD professionals	Physicians
Interventions	Heartwatch sets out to provide infrastructure and a framework for the development of services for patients with heart disease within primary care. Patients are seen on a quarterly basis and care is implemented according to defined clinical protocols.
Results	The aim was to examine the effect of the first 2 years of the Heartwatch programme on cardiovascular risk factors and treatments. Prospective cohort study of patients with established CHD enrolled into the Heartwatch programme. Four hundred and seventy (20%) general practitioners nationwide participated in the programme, recruiting 11,542 patients with established CHD (earlier myocardial infarction, coronary intervention or coronary artery bypass surgery). Clinical data were electronically transferred by each general practitioner to a central database. Comparison of changes in risk factors and treatments at 1-year and 2-year follow-up from baseline were made using paired t-test for continuous and McNemar's test for categorical data. Statistically significant changes in systolic blood pressure, diastolic blood pressure, total and low-density lipoprotein cholesterol and smoking status at 1 and 2 years (P <0.0001) were observed. Little or no improvements were shown for exercise, BMI or waist circumference. Increases in the prescribing of statins, angiotensin-converting enzyme inhibitors and beta-blockers over the course of the study were observed. The Heartwatch programme has demonstrated significant improvements in the main risk factors and treatments for CHD. More effective interventions are required to reduce BMI, waist circumference and physical inactivity in this population. The increases in treatment uptake are approaching the optimal levels in this population.
Contact person	Not identified
Reference	National Heart Watch programme. Heartwatch Clinical Report, March 2003-December 2005. http:/www.icgp.ie. Bennett K, Jennings S, Collins C, M, Leahy J, Bedford D, Shelley E. Heartwatch: A secondary prevention programme in primary care in Ireland. Eur J Cardiovasc Prev Rehabil. 2008 dec;15(6):651-6.

2.3.2.6 Programme 6: The Infoproximed programme

6. The Infoproximed programme	**Content**
Country	**France**
Initiator(s)	URCAM (Union régionale des caisses d'assurance maladie); URLM (Union Régionale des Médecins Libéraux); CRIM (Centre Régional d'Information sur le Médicament (CHU de Rennes) ; Société ICONES (Interventions Conseils Etudes Santé SA Piloted by : APIMED : Association Loi 1901 ; FAQSV (Fonds d'aide à la qualité des soins de ville)
Initiated since	2003
Annual budget	Not available
Objectives	To evaluate the effectiveness of AD
Setting	Primary care
Population	Otitis media in children, folic acid/immunization, cardiovascular risk (cholesterol and statins), prevention of digestive impact of NSAIDs, clearance and functioning of kidneys and headache
Caregivers targeted	General practitioners: 152, of which 15 GPs that took part in Quality Circles
Behaviour targeted	Prescription behaviour
AD professionals	Pharmacist or physician
Interventions	Every 2 months visit a half an hour visit by detailer of the general practitioner + overview of key messages + electronic reminders + interactive group discussions + role play
Results	Outcome measures: knowledge on key messages, satisfaction with programme, quality outcome indicators and cost of the programme. A total of 613 visits were performed on 6 themes. 95% of GPS expressed to be very satisfied with programme Results on quality indicators not documented.
Contact person	urml@urml-bretagne.com
Reference	Bataillon R, Locquet C, Leneel C, Leneel H, Humbert C, Hascoët JY. Visite médicale académique. LE Programme Infoproximed de la région Bretagne. La revue du Practicien. Médecine générale. Tome 19, Novembre 2005.

2.3.2.7 *Programme 7: FARMAKA vzw*

7. FARMAKA vzw	Content
Country	**Belgium**
Initiator(s)	Physicians, and financially supported by Federal Agency for Drugs and Health Products
Initiated since	1998 (pilotstudy)
Annual budget	Budget oct 2006-sept 2007 (12m): 503.960,31 Budget oct 2007-dec 2008 (15m): 592.960,04
Objectives	To promote rational use of medications and health care services in professionals, patients and governments through research and projects. Farmaka uses evidence-based methodologies to select medicines for which a rational use is desired.
Setting	Primary care
Population	Patients who smoke, who have digestive problems, osteoporosis, type 2 diabetes mellitus, obesity, anxiety, allergies, dementia, migraine, who use NSAIDs, anti-hypertensive drugs, oral diabetes drugs, who have dyspepsia, GERD and cystitis.
Caregivers targeted	Only physicians
Behaviour targeted	Prescription behaviour and use of health care services: smoking cessation, digestive complaints, osteoporosis, type 2 diabetes mellitus, obesity, anxiety, allergies, dementia, migraine, NSAIDs, anti-hypertensive drugs, oral diabetes drugs, dyspepsia, GERD, cystitis.
AD professionals	Physicians, pharmacists
Interventions	Individual face-to-face AD (15 minutes visits), educational materials
Results	Feasibility and acceptability evaluated: positive results (see study Habraken)
Contact person	vzw Farmaka asbl Maatschappelijke zetel: Coudenberg 70/1 - 1000 Brussel. Administratieve zetel Kleindokkaai 3-5 / 6de verdieping - 9000 Gent - Tel + 32 (0)9 265 76 40 Fax +32 (0)9 265 76 49 - info@farmaka.be
Reference	Habraken H, Janssens I, Soenen K, van Driel M, Lannoy J, Bogaert M. Pilot study on the feasibility and acceptability of academic detailing in general practice. Eur J Clin Pharmacol (2003), 59: 253-266.

2.3.2.8 Programme 8: The Promoting and Supporting Evidence Based Medicine through Divisions of General Practice Project

8. The Promoting and Supporting Evidence Based Medicine through Divisions of General Practice Project	**Content**
Country	**Australia**
Initiator(s)	Australian Commonwealth Department of Health and Aged Care
Initiated since	Requested
Annual budget	Requested
Objectives	To evaluate the effectiveness of AD on prescription behaviour
Setting	Primary care
Population	Not specified
Caregivers targeted	Primary care physicians
Behaviour targeted	EBM
AD professionals	Researchers
Interventions	Practice visits (30-45 minutes) by researchers to promote evidence based medicine.
Results	AD has led to significant improvement in knowledge scores and self-perceived understanding of EBM. No information on changes in clinical behaviour.
Contact person	Peter Schatnner. Monash Division of General Practice and Monash University Department of General Practice, East Bentleigh, Victoria, Australia.
Reference	Markey P, Schattner P. Promoting evidence-based medicine in general practice-the impact of academic detailing. Family Practice 2001; vol. 18, No 4, 364-366.

2.3.2.9 Programme 9: Drug and Therapeutics Information Service (DATIS) programme

9. The Drug and Therapeutics Information Service (DATIS) programme	**Content**
Country	**Australia**
Initiator	DATIS is a continuing medical education initiative of the Pharmacy Department of the Repatriation General Hospital, Daw Park, South Australia.
Initiated since	1996
Annual budget	$1.048284
Objectives	This programme seeks to: 1) enhance the opportunities for GPs in Adelaide's Southern Western and Central and Eastern Divisional areas to maintain and improve the quality of care for patients; 2) maintain and further develop the Drug and Therapeutics Information Service (DATIS) presently established for GPs at the Repatriation General Hospital - Daw Park; and 3) develop opportunities for Australia-wide expansion of DATIS services, and to extend DATIS services to an additional two hundred GPs in metropolitan Adelaide.
Setting	A drug and therapeutics information service for more than 200 community medical practitioners has been established by the Repatriation General Hospital - Daw Park using 'academic detailing' principles.
Population	Not specified
Caregivers targeted	Serves 1000+ primary care practitioners in South Australia
Behaviour targeted	Prescribing practice
AD professionals	Clinical pharmacists
Interventions	Face-to-face visits + telephone service + educational materials + laboratory therapeutic drug monitoring
Results	Use of process indicators (percent of the total possible medical practitioners in the defined area continuing to receive the service; percent of medical practitioners who's DATIS manual is found on the desk at the time of interviews), impact indicators (changes in dispensing patterns within the geographic area where targeted prescribing practice are occurring; quantity of drugs delivered into pharmacies geographically located near prescribers receiving the service), and outcome indicators (indicators that reveal direct evidence of the quality use of medicines in the health of patients as a result of the service provisions—lower levels of hospital admission for targeted iatrogenic conditions)) Improved patient outcomes have been demonstrated as a result of better quality use of medicines.
Contact person	Dr David Tye, Dr Frank May. Pharmacy Department, Repatriation General Hospital, Daws Road, DAW PARK, SA, 5041
References	DATIS : drug & therapeutics information service / principal author: Jody Braddon ; contributing author: Kylies Foot. 2006

2.4 DISCUSSION: RESULTS FROM THE INDEXED AND GREY LITERATURE

This part discusses the common findings from the systematic literature review and the grey literature. When there are differences between findings from the systematic review and findings from the grey literature, they will explicitly be mentioned.

Overall the quality of the papers was very high as illustrated by the results of the quality appraisal scores. This allows for reliable conclusions at different levels, but caution is warranted given the important heterogeneity in the funding, study populations, interventions and outcomes under study.

2.4.1 Widespread use of academic detailing

The US pioneering trial of Avorn and Soumerai in 1983[12] first demonstrated a 14% reduction in prescribing of target overused medications with long-lasting intervention effect. Other AD initiatives have been launched afterwards in many countries. This review and the analysis of the grey literature identified a total of 17 countries where AD programs are deployed. In some countries AD became part of the routine health service as in the UK, Australia and the US.

In parallel, detailing organised by pharmaceutical companies is widely used and structurally embedded in virtually all healthcare systems[40]. An evaluation of this type of detailing was beyond the scope of this literature review but it is important to mention that the budgets invested in those initiatives are out of proportion ($4.8 billion dollars in the US in 2000) with the budgets invested in the initiatives of AD. The effectiveness of AD detailing is therefore not comparable to the effectiveness of the commercial one. It also depends on many factors as the characteristics of the drug to be promoted (e.g. being the first alternative on the market).

2.4.2 Rationale of academic detailing

Main reasons for AD were the over use, under use and misuse of medications, clinical examinations and the related quality and cost implications. Particular reasons put forward to try to change the physician behaviour by means of AD were for example the resistance to antibiotics, the use of contraindicated antibiotics and the potential for harm of new drugs. Especially programs that were identified in the 'grey literature' emphasized the need for the cost-effective use of medications.

Some authors highlight the fact that all doctors do not regularly attend continuing medical education sessions to keep up to date with advances in medicine. This explains the need for bringing the scientific information into their practice. On the other hand, the success of the marketing strategy of the industry justifies the application of similar principles to foster the use of EBM among physicians.

2.4.3 The concept and content of academic detailing

2.4.3.1 Concept

The concept of AD covers different interventions but the basic constituents defined by Soumerai et al.[9] were described in most interventions described in this systematic literature review. These basic constituents include:

- To conduct interviews to investigate baseline knowledge and motivations for current prescribing patterns;
- To focus the AD programs on specific categories of physicians as well as on their opinion leaders;
- To define clear educational and behavioral objectives;
- To establish credibility by having a respected independent organizational identity, referencing authoritative and unbiased sources of information, presenting both sides of controversial issues;
- To stimulate active physician participation in educational interactions;

- To use concise graphic educational materials highlighting and repeating the essential messages;
- To provide positive reinforcement in follow-up visits.

The description of the Belgian project of AD visits also shows the respect of those principles except the focus on opinion leaders and the reinforcement in follow-up visits.

A few programmes only mentioned underlying theoretical concepts such as the Diagnostic Evaluation Model (DEM)[28] and lessons from complexity theory, such as disease management[41].

2.4.3.2 Description of the AD interventions

An overall finding is that interventions described in AD programmes often lack sufficient detail to fully understand and replicate the intervention in other settings (e.g. the content of education). This finding is in line with those of the literature review of Richens et al[42] who stated that questions about the nature of the AD intervention need further studies. If AD remains a 'black box' because of the heterogeneity of the AD programmes, its effectiveness is still documented in a substantial amount of individual studies.

2.4.4 Target population of caregivers

The populations of the studies were mostly general practitioners. Soumarai et al.[9] suggested to target specific populations and to include explicitly their opinion leaders. Other populations to consider are the providers who have knowledge deficits and/or a practice that deviates from the expected one[5]. Interventions would be expected to have a greater impact on the practice of those care providers. Hardly any study and no programme abroad defined its target population based on those providers' characteristics.

2.4.5 Professionals who provide academic detailing

A variety of professionals are responsible for the provision of AD services (both in individual studies and structural programs). Whereas a decade ago physicians most often provided AD services, recent studies mostly apply (clinical) pharmacists to fulfil this role with also positive results[43]. Results of this review show that there is no relation between the professional background of the detailer and the effectiveness of the intervention.

An interesting finding is that the combination of professionals with different backgrounds (e.g. nurses and physicians, pharmacists and physicians) also become more common. This finding is of relevance for the Belgian experience. The Belgian AD project began with GPs detailers but currently employs academic detailers with other scientific backgrounds. The qualitative study below shows that the new profile of AD visitors in Belgium does not hamper the impact if other conditions for the quality of AD are fulfilled (e.g., the scientific background).

2.4.6 Behaviour targeted by academic detailing programs

The prescription behaviour is mostly targeted in the studies and programmes, as in the current Belgian initiative. However, there is a growing interest AD for other evidence based processes. One illustration is the management of chronic diseases including diabetes and heart failure.

Programmes identified in the grey literature most often targeted multiple behaviours but the publications in the literature mostly reported the effect on a single behaviour. A publication bias might not be excluded as simple interventions are easier to describe, to assess and to publish.

2.4.7 Conditions and diseases targeted by academic detailing programmes

Chronic conditions are more frequently targeted as compared to acute conditions: in particular topics related to cardiovascular diseases were mentioned in a quarter of the studies from the indexed literature. The rationale for the choice of topics is not clear, even if the topics relate to the prevalence of diseases in primary care. Other factors might play a role either isolated or in combination: the growing number of evidence-based guidelines with a need to promote their message, public health concerns (e.g. antibiotics resistance, diabetes epidemics), heterogeneity in practices of clinicians, the development of new and expensive medications (e.g. in cardiology). It is important to note that preventive services are less frequently targeted, which might be the witness of a focus on "curative"-oriented interventions together with less available evidence and less challenges from a cost-containment perspective.

Interestingly, the topics presented by academic detailers in Belgium (see introduction) only partly cover the topics described in the literature. The groups of conditions are comparable to the topics in the international literature i.e. mostly chronic conditions and curative treatments. However, apart from diabetes, the Belgian topics are the focus of one or two foreign studies only (e.g. smoking, gastroesophageal symptoms, obesity). Other topics are never presented in foreign studies (e.g. atrial fibrillation, dementia) whilst they are a concern to the Belgian public health system (quality and costs). On the opposite, hypertension, heart failure and cancer, the three top conditions selected by foreign programs, have not yet been selected by the Belgian programme.

The rationale for choosing a topic in Belgium is mainly the existence of EBM educational material for GPs, also linked to the prevalence in primary care. However, the choice of AD topics has also to consider other criteria: one of them is the potential to change the prescription behaviour. When specialists play a major role in the initiation of the prescription (as for dementia) the absence of change is to be expected.

2.4.8 Patients targeted by AD programmes: specific populations

Different patient populations are targeted through AD. However, some patient populations included hinder the possibility to generalize the results as they were highly selected (e.g. urban regions) or self-selected (patient registries from individual practices).

2.4.9 Effectiveness of academic detailing on clinical outcomes

Many authors are positive about the effect of the AD intervention on prescription behaviour. This outcome is indeed the major target of many AD interventions and in the same time an outcome easier to measure than outcomes at the level of the patient. Hardly any study analysed the impact of the interventions on the patients' outcomes and those studies usually failed to show any significant effect for example on blood pressure, quality of life, falls and admissions for gastric ulcer.

The positive findings on the effectiveness of AD on process measures presented in this review are in line with results from previous reviews of reviews[44-48] and systematic reviews[5, 6, 49-58]. Those authors showed that (especially multifaceted) AD interventions have a consistent positive effect for improving physicians' prescribing (process indicators) but a moderate positive effect on other measures[4, 8]. A recent Cochrane Collaborative Review on AD[8] involving 69 studies and 15,000 providers concluded that AD is effective for improving the prescription of targeted medications with an effect about 5% from baseline (median 4.8%, interquartile range 3.0% to 6.5%).

Existing programmes identified through the grey literature lack an evaluation; when present, this one included most often intermediary outcomes.

Literature provides no conclusive evidence on the link between the intensity of the intervention and the magnitude of the effectiveness. Moreover, this particular link has not been studied so far.

2.4.10 Cost-effectiveness of academic detailing

A second major objective of AD is frequently a cost-saving effect. AD is a complex and expensive method of continuing medical education. The review of initiatives in other countries indicates that their annual costs range from 50 000 $ (for a limited intervention) to 1 000 000 $. The logical question is the cost-effectiveness of these investments.

Only 7 studies assessed the cost-effectiveness of AD interventions, five of them targeted the prescription of medications. The result section details the 7 studies: most of them showed the effectiveness of the intervention e.g. a positive effect on the prescription behaviour. However, there is insufficient evidence to generalise about the cost-effectiveness. Two studies were positive: one promoted the use of a low cost agent (thiazide) and the other one reduced the number of PSA screening tests and subsequent procedures [30, 34]. Three other studies were inconclusive and reported mixed effects on the outcomes [31-33]. The two last studies on the promotion of immunization and change in NSAIDs prescription were not found to be cost-effective[29, 35].

More robust evidence is needed from large-scale randomised controlled trials to confirm whether AD is cost-effective. Further studies should also show specific classes of medications for which the interventions are cost-effective.

2.4.11 Effectiveness of AD programmes compared to other interventions

Recent reviews have confirmed that traditional forms of education such as conferences or printed educational materials produce little or no change in behaviour for a variety of areas of patient care[8]. O'Brien et al. reported that multifaceted educational outreach visit interventions compared with other specified intervention or no intervention were generally effective for improving appropriate care and prescribing. Multifaceted interventions (that include educational outreach) compared to a control group and multifaceted interventions (that include educational outreach) compared to distribution of educational materials were also found to be generally effective interventions for appropriate care. This finding is interesting because the Belgian initiative also combines outreach visits with other interventions (educational material previously sent by mail).

Other combinations could also be envisaged, as for example a combination with the guidelines published by the Belgian "BAPCOC" on antibiotics prescription or those published by the Belgian scientific GP societies.

Key points systematic literature review

- **Academic detailing has been implemented since decades in many countries, sometimes in a structural way**
- **Initiators (when mentioned) are scientific organisations, governmental bodies, university departments, either alone or in combination**
- **The most frequent behaviour targeted is the evidence-based prescription of medications (40 out of 87 studies)**
- **The most frequent topics are chronic conditions (one quarter of the studies on cardiovascular conditions): their spectrum illustrates avenues for topics not yet explored in Belgium**
- **Unfortunately, the content of the interventions usually remains a black box, as well as the frequency needed to achieve an optimal effect**
- **The effect of AD does not change according to the professional background of the professionals who provide it (pharmacists and/or physicians in more than half of the studies)**
- **More than half of the studies reported an impact on the process measures and one third had mixed results on the outcomes under study; the change in compliance with desired behaviour has been estimated about 5% only in a systematic review**
- **There is limited evaluation of the cost-effectiveness (7 full economic evaluations) and evaluation based on patients' outcomes: when available, the results are contradictory**
- **AD seems to have more impact when combined with other educational interventions**

3 QUALITATIVE STUDY AMONG GENERAL PRACTITIONERS

3.1 OBJECTIVE OF THIS PART

The objective of this part is the analysis of qualitative data about the perception of the Farmaka visits by the GPs and its impact on their prescription habits using the methodology described in the section below.

3.2 METHODOLOGY

3.2.1 Tools for data collection: interviews and Mesydel methods

SPIRAL (ULg) was in charge of conducting the qualitative aspects of the research with the use of two qualitative tools in parallel:

3.2.1.1 Semi-directive interviews

A semi-directive interview is a technique where only a few questions are scripted, used as a guide. The interviewer has a grid – usually mentally – identifying the various topics to explore. This method has the advantage over a directive interview (with fully scripted questions) in that it allows interesting topics to emerge, which were not present in the original grid. The interviewer gets insight on new observations or ideas.

3.2.1.2 Delphi method: Mesydel

Goals

The Mesydel session had two major goals in this research:

- to control that the answers were consistent with the answers given during the face-to-face interviews;
- to complete them with more sensitive questions, that would be difficult to ask face-to-face.

Online Delphi method

The goal of a Mesydel session is to collect and analyze stakes and to see if carefully chosen questions aim at a consensus or at a disensus. Mesydel is a computer implementation of the *Delphi* method. The Mesydel software formalizes the consecutive steps of a Delphi survey. The online aspect of the method allows the busiest experts to answer key questions, even if they do not have the time to be interviewed face-to-face. Moreover, it allows the researchers to submit the questionnaire to the complete sample, provided they have an e-mail address. The confidentiality of the answers can also reassure an audience which could be reluctant to confess sensitive information in a face-to-face interview.

Sequence with two rounds

Three months of research were needed to carry out a two rounds survey. Each round spanned two or three weeks. The analysis of the answers of the first round helped to write the second round of questions, to clarify positions and make emerge material that did not emerge during the first round. The questionnaire for the second round is based on the information that was lacking or inaccurate in the answers of the first round. At the end of the second round, a second synthesis is written. This synthesis, the answers to the interviews and the clear answers from the first round are used in the analysis.

Interpretation using "tagging" and "facets"

A system of annotation, "tagging" and "facetization" allows the researchers to exploit thoroughly the answers in a systematic way (see examples in appendix J). "Tags" are labels that are systematically put by researchers on answers that discuss the same idea (for instance "pro-EBM" where the participant has a pro-EBM discourse or "state trust" when the discourse shows that the participant has trust in the State).

"Facets", on the other hand, are categories of tags, where tags are grouped according to their context in the study.

For instance, the tags "statetrust" and "statedistrust" were used each time a participant stated in an answer that (s)he had either trust or distrust in the State. In the tag cloud (see Appendix J for an example), the tag "statetrust" was written in a bigger font than "statedistrust", which gives the information that there were more GPs who answered that they trusted the State than GPs who answered that they distrusted it.

3.2.1.3 Analysis of Interviews and Mesydel

Both the interviews and the Mesydel answers were analysed by means of the same set of tools: Mesydel has an analysis framework in its mediator module, while the interviews are encoded in our Mosaïqs software, a *CAQDAS* (Computer Assisted Qualitative Data Analysis Software) using the same analysis framework as Mesydel. *Grounded theory* methodology allows, among other things, researchers to analyze text corpuses by annotating them heavily, in our case thanks to the use of "tags" and "facets". Tags are keywords that are systematically associated when a topic or idea emerges from the text, while facets can be seen as directories of tags.

3.2.1.4 Important notice about qualitative methods and their interpretation

Qualitative methods are very good at showing tendencies and making notions emerge. However they cannot be used to quantify opinions. The results are never expressed in figures and percentages but in words like "a lot", "a vast majority", "few", "a minority". These expressions depend on the context where they appear. An illustration of a rough scale, in ascending order, of the most often used expressions is the following: none, very few, few, some, half of, a lot of, many, most (of), a vast majority and all. For example, "very few" means a marginal part of the sample (or of the subsample, depending of the context) and "a vast majority" means that there was almost consensus about a given topic. Due to the very nature of qualitative methods, this scale is imperfect and depends greatly on the context.

3.2.2 Methodological background: Grounded Theory

Grounded Theory is a research method for collecting and analysing research data[59]. Grounded theory specifically attempts to investigate the real world, usually through interview data collected from persons in real-world environment. The Grounded Theory approach has the huge advantage of using information directly given by field actors. This approach is particularly important when studying emerging phenomena, in the most concrete possible contexts, because the problematic borders or its internal features are particularly fuzzy or indeterminate[60, 61].

Strauss & Corbin[62] recommend to transcribe the interview in full, word by word or expression by expression. The goal is to make emerge sufficiently precise codes to identify contained information from interviews. The codes are then analysed and those that relate to a common theme are grouped together, under a "concept". Merging the codes to discover emerging concepts is a central part of the Grounded Theory method. This derivation of codes, concepts and categories is a fundamental part of the analysis method in Grounded Theory. The data are analysed in a systematic and rigorous manner to discover the concepts leading to the categories. This iterative process requires time, patience and analytic skills. The Mesydel and Mosaïqs software contribute to support the researchers in their analysis of the interviews transcripts.

During the interviews, it is useful for the interviewer to be opened for emerging positions, to new codes that can help him to reframe his/her approach. The framework presented by the interviewer to justify the interview will be general and neutral. The first questions must be as loose and open as possible in order to limit biases. The researcher sets up a creation/conception dynamic by doing round-trips between data and the conceptual framework in construction[63].

3.2.3 Population

The population was composed of all GPs who were contacted to receive the visitor on two topics *i.e.*, Alzheimer disease and diabetes (n=1498). The choice of those topics relied on the initial objective to link the answers of the respondents with data on their prescription (see chapter 4). However, this link could not be confirmed, as explained further.

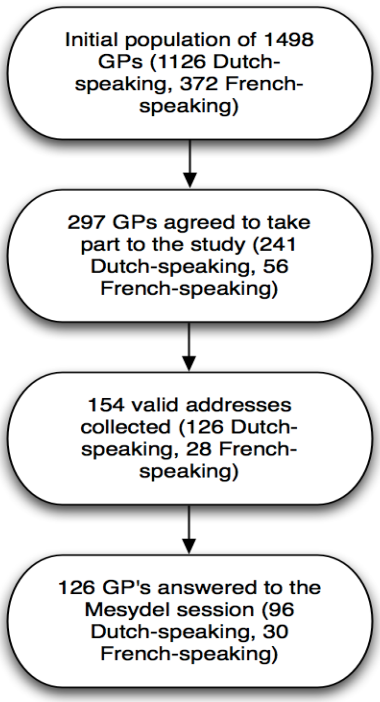
3.2.3.1 Sample

Farmaka insisted on contacting themselves the GPs to ask their agreement for taking part to the KCE study. Only one fifth of the initial population (19.8%) did agree i.e., 297 out of 1498 letters sent to all GPs who were contacted to receive a visit on dementia or diabetes. The proportions were 241/1126 Dutch-speaking (21.4%) and 56/372 (15%) French-speaking GPs.

The French-speaking GPs received a visit on diabetes. 122 Dutch-speaking GPs also received a visit on diabetes and 150 Dutch-speaking had a visit on Alzheimer disease. Only a few of them refused to receive the visit of the visitor (6 out of 297).

The sample was composed of 65 women and 232 men (approximation based on the first names listed). Two GPs were from the region of Brussels-Capital, 22 from the province of Flemish Brabant, 19 from the province of Walloon Brabant, 64 from the province of Antwerp, 15 from the province of Limburg, 3 from the province of Liège, 17 from the province of Namur, 15 from the province of Hainaut, 48 from the province of Occidental Flanders and 92 from the province of Oriental Flanders.

Figure 3. Flow chart of selection for GPs



3.2.3.2 Biases

As stated above, a major bias is linked to the acceptance of the GPs to participate to this study i.e. only one fifth (19.8%) of the initial Farmaka population who were eligible for the visit (and mostly had it).

Furthermore, we noted at least four major biases in the list of potential participants:

- The **first bias** is that the list was compiled by Farmaka i.e. a list where most GPs had accepted to receive Farmaka visitors, GPs who are probably more favourable to AD than the average GP.
- The **second bias** is that the list is highly asymmetric from a language community point of view: there are 4.3 times more Dutch-speaking GPs than French-speaking ones. One potential explanation is that the topic Alzheimer had only been presented in Flanders and the initial Farmaka population had therefore 241 Dutch-speaking GPs and 56 French-speaking GPs. Moreover, Farmaka has been first implemented in Flanders and might have a greater renown among GPs.
- The **third bias** is a geographic one: there were strong geographical concentrations: usually the Farmaka visitor seems to have "his/her area". In some areas, we have a strong concentration of GPs whereas in some big cities (Liège, Mons, Kortrijk and Hasselt, for instance), we did not have any GP in our sample. Especially with French-speaking GPs, we noticed during the interviews that the Farmaka visitor was an acquaintance of the GP.
- An example of this concentric effect is that one fifth of the Dutch-speaking GPs sample is situated in the city of Ghent (25 GPs) or its area (29 GPs) the city of Ghent (cradle city of the Farmaka initiative).
- The **fourth bias** emerged from the interviews with French-speaking GPs. Their characteristics indicated towards a selection bias *i.e.*, GPs with a specific interest for affordability/equity in health care or working in medical houses.

These biases are important to be mentioned as it would be dangerous to extrapolate the results to the whole population of Belgian GPs.

3.2.4 Protocols

3.2.4.1 Interview Protocol

The researchers interviewed forty GPs face-to-face and asked them questions allowing starting a discussion or conversation (see Appendix A, B, D). The general framework of these interviews was based on the two main questions submitted by KCE in this research:

- What is the impact of academic detailing on the GPs practice?
- How do the GPs who have been visited by an independent medical representative perceive the impact and the usefulness of this visit regarding their therapeutic behaviour?

However, since the quality of information was very dependent on the quality of the contact between the GPs and the interviewers, we enlarged the strict *academic detailing* theme to satellite questions, in order to understand the dynamics of medical information from a more global point of view:

- the privileged sources of information of the GPs and the criticism they have about some of them;
- the distinction between public information and the one given by pharmaceutical firms;
- the medical publications they usually read;
- their opinion about the system of continued training;

- their way of getting information in case of problem or new therapies.

Practically, a typical interview was divided in two parts. The first part presents the interviewer and details the objectives of the interview. The second part is the semi-directive interview itself, as we described it earlier.

3.2.4.2 Mesydel session

A Mesydel session consisting of two rounds was conducted after the interviews. All GPs have been invited to join the Mesydel session (see invitation letters in appendix E). They had to send back a voucher to the KCE, with their e-mail address and agreement to be contacted by SPIRAL researchers to participate to the session. Confidentiality was guaranteed to participants.

The first round ran from September 21 to October 4 and the second round ran from October 16 to November 8. This schedule was slightly modified to allow a three weeks second round, to take the recent news events (A/H1N1 pandemic) into account. The pandemic augmented the work charge of GPs and giving them one more week to answer helped us obtain better results.

3.2.5 Sampling

3.2.5.1 Face-to face interviews with GPs

Given the important size difference between the French-speaking subset and the Dutch-speaking subset, the researchers opted for a one third/two thirds split between French- and Dutch-speaking GPs, since there were far more (4.3 fold) Dutch-speaking in the sample of this study. The (qualitative) saturation was estimated to be around a bit less than 40 GPs. The researchers conduct face-to-face interviews with 13 with French-speaking GPs and 27 Dutch-speaking GPs (see the characteristics in appendix C).

3.2.5.2 Characteristics of the Mesydel participants

All GPs who accepted to participate by letter (297 GPs) received a voucher. By sending back this voucher to KCE, they gave Spiral their e-mail address and agreed to participate to the study. A total of 126 GPs participated to the Mesydel survey: the details of these participants and their participation are described in appendix G and summarised here.

Most participants were men (100 out of 126). This imbalance was more pronounced for the Dutch-speaking group (16 women and 80 men) than for the French-speaking one (10 women and 20 men).

The age of the French-speaking participants ranged from 33 to 61 years, with a mean age of 49 years (sd = 9.76). Dutch-speaking participants had a similar mean age (51, sd = 9.78): the youngest participant was 30 years old and the oldest one was 72 years old.

Overall, 56 GPs worked in single handed practices (44.4%), 50 in association (39.7%, with 7 GPs in medical houses) and 20 unspecified (15.9%). Nine French-speaking participants (n=9, 30%) worked in single handed practices, 15 in association (50 %) (including 7 in medical houses) and 6 unspecified (20 %). Nearly half of the Dutch-speaking participants worked in single handed practices (n=47, 48.9 %), one third in association (36.5 %, n=35) and 14 unspecified (14.6 %). It should be noticed that no Dutch-speaking participant worked in a medical house.

3.2.5.3 Characteristics of the face-to-face sample and the Mesydel sample

A. French-speaking GPs

The most important criterion for choosing among the 56 GPs was to be geographically representative (while keeping in mind that the third bias of the list made a strictly geographically representative list impossible). It allowed us to visit GPs who had seen different Farmaka visitors and lived in different kinds of neighbourhoods. There was no indication on the age of the GPs. Since the French-speaking list is better balanced between male and female than the Dutch-speaking one, we decided to make a sample made of approximately half male GPs and half female GPs.

We contacted 23 of the 56 GPs. Four of them were not available, four other ones were not interested by the study, one was very interested but was on sick leave.

B. Dutch-speaking GPs

The most important criterion for choosing among the 241 GPs was also to be as geographically representative as possible. Without any indication on the age of the GPs and in presence of much more (three fold) of men than women we interviewed 5 female GPs and 22 male GPs.

We contacted 40 of the 241 GPs. Five of them were not available, one was retired, one had forgotten his meeting with the Farmaka visitor and a last one just did not want to participate to a study.

The large number of interviews, as well as the large number of Mesydel answers allowed us to reach the saturation point, *i.e.* doing more interviews or obtaining more answers would no longer have an impact on our research.

3.2.6 Development of the Mesydel questions

3.2.6.1 Writing of the questions

Fifteen questions were drafted based on the scientific literature and on the first interviews. Some questions were amended after discussion with the KCE to fit their own analysis method (based on the *behaviour change theory*). As noted before, the analysis of the Mesydel heavily relies on the *grounded theory*. The final questions of the first round are in appendix H.

Second round questions were written after the analysis of the first round (questions 1, 2 and 3) and of the interviews (questions 4, 5 and 7). Question 6 was initially proposed for the first round but was finally kept for the second round, while question 8 just asked if all went well with the Mesydel session. The final questions for the second round are in appendix I.

3.2.6.2 Mesydel first round pre-test

A pre-test of the final nine questions, taking into account the changes made by the KCE, was conducted on paper at the KCE with three physicians. The pre-test green lighted the questionnaire, with only a semantic detail that had to be changed in the identification questions.

3.2.6.3 Mesydel second round pre-test

We did a pre-test of the eight questions of the second round by phone with KCE members. The eight questions were green lighted by the KCE with no major change during that phone call.

3.2.7 Summary of the methodology

In summary, the methodology involved two steps:

- At first, face-to-face semi-directive interviews have both an exploratory and informative roles. Concomitantly, the first Mesydel round is conducted, which is both exploratory and informative.
- In the second step, the Mesydel (second round) digs the topics further, to get insight on unclear positions, to search consensuses and disensuses and to make emerge new positions. The questions of the second round are based on the information collected in the first step.

GPs proved to be an excellent audience for Mesydel: both rounds received answers from more than 70% of invited GPs, one of the best answer rates the Spiral team ever had in their researches using the tool Mesydel.

Key points methodology qualitative study

- **Combination of two methods i.e., semi-directive interviews and Mesydel (Delphi method online)**
- **The analysis relied on the Grounded theory and CAQDAS**
- **Biases were identified in the sample: only one fifth of the GPs contacted by Farmaka took part to this study, the list was compiled from a subset of GP who were on the list for an AD visit, uneven distribution between language communities, geographical concentrations, special interest for affordability/equity**
- **Sample: 40 interviews, 111 answers at the first Mesydel round, 108 at the second one i.e., a very high response rate to this online survey**

3.3 ANALYSIS

This part of the study focuses on four themes:

1. changing relationship between the patient and his/her GP;
2. perception of the Farmaka visit and visitor by the GPs;
3. impact of the visit on the GPs: what works and what does not work;
4. wishes expressed by the GPs for enhancing Farmaka's efficiency.

This analysis only provides the raw material (what emerged in the interviews and in the Mesydel session), truthfully to what the GPs actually said or wrote: the suggestions will further appear in a dedicated chapter.

The word "interviewees" refers both to the face-to-face interviewees and the Mesydel answerers.

3.3.1 The GPs and their context

3.3.1.1 From a paternalistic approach to a dialog approach

"*I think that many GPs – especially the oldest ones – still present themselves as all-powerful holders of knowledge, and the patient has only to "obey*".

It appeared very clearly that, for the interviewees, **the relationship between the patient and the GP has been profoundly reshaped in the last few years**. According to the interviewees, the GP was previously seen as an authority, a paternalistic figure, who did not have to explain his/her decision (e.g. diagnosis, treatment). Nowadays the patient has more and more to say about his/her health, the responsibility is shared. Over time, the GP lost his prestige. **The old image of *the Priest, the Teacher and the Doctor* faded out and the GP as authority withers more and more.**

"*The time of the house GP has come to an end. Now we don't have complicity with our GP anymore. You go to see a GP, then after six hours, you have another.*"

"*The patient is the only one to decide if he wants to be cured, if he wishes to change his habits, if he wants to take a medical treatment.*"

The interviewees often declared that the profile of GP is not the only one to have changed: the patient sees himself as an expert, "*an expert on him/herself*": (s)he argues that nobody knows him/her more than (s)he does, that (s)he educated her/himself on her/his illness, on the health system. Many interviewees told that nowadays, the patient chooses his GP after what looks like a casting procedure. (S)he searches a GP who agrees with his/her ideas, who thinks like (s)he thinks. This behaviour seems to be quite recent: before this shift, a patient had a GP and kept him for life.

"*The GPs are not prescriptors, we are actually educators. We often receive people in first line. While I think that prevention is fundamental, it's something people are not interested enough.*"

"*I work a lot with my patients. Someone who has too much cholesterol, we will work throughout his lifestyle; I will not only give him medications to lose weight. That doesn't interest me at all. It's everything around.*"

Many interviewees told that at the slightest discrepancy, the patient just changes his/her GP just as (s)he would go to another store if the first one disappointed him/her. If this GPs panel often refuse the idea of a patient-merchandise, patients in turn are increasingly seeing their GP as a service provider (see 3.3.1.6). **This reshaping of the profession led some GPs to change their practice and to communicate more**. Those who do so extend the duration of their visits: for them, a patient is no longer equal to this illness, but is a whole person. As a consequence these GPs see themselves as guarantors of the good physical and psychological health of the patient.

"*I think that patients must make important decisions knowingly. It is therefore essential to give them accurate and scientifically correct information. Then, we must respect their decisions, especially in case of a heavy therapy (chemotherapy, open heart surgery...).*"

"*[My job] is to explain to the patient what he suffers from and to explain him the tools he has at his disposal and that he can implement himself. People, they want to take themselves in charge, they are searching.*"

"*When a patient comes back all the time for a sore back, we try to find out why. He is not forced to see a physiotherapist for life: it costs! Now, with ten minutes of stretching every day, he will have a healthier back. I try to make my patients take themselves in hand.*"

Some interviewees told that their treatment would be less efficient if they would ignore what the patient has to say. For that matter, ***patient value* is one of the three pillars of EBM** (alongside *best evidence* and *clinical expertise*). According to interviewees, another good reason to enhance the information given to patients, to give them voice, is that **the patient himself is a valuable source of feedback about his/her own health and health history**.

3.3.1.2 How the GPs get information for their practice

"I use the Internet extensively. Especially for drug names, I use the CBIP/BCFI online."

Most of the interviewees cite **the Internet as their main source of information**. They value the CBIP/BCFI and CEBAM websites, as well as various other sites (each GP has its own website portfolio).

"How do I get my information? Well, for a large part through my colleague who floods me with e-mails."

Another often cited information source, deemed very efficient, is the **discussion with peers** (not only in the frame of quality circles (GLEMs/LOKs), but also with associated GPs e.g. in medical houses).

"It is comfortable to lean on the advice of a specialist. It's easy, fast and lessens my responsibility..."

About half of them, when uncertain about a treatment, **ask a specialist physician, usually by phone**. It is to be noticed that most of them, by specialty, refer to a specialist physician they know and trust, not an "opinion leader" specialist physician.

"[Talking about firms] One must be able to put things into perspective and take the useful information, but try to put aside all that feels a bit too commercial."

A significantly less important part of the interviewees use the information given by pharmaceutical firms (through their delegates). When asked about the commercial bias, they answer that they know enough to be able to sort and fairly synthesize the information.

"*[About information provided by Farmaka:] This info is always well-documented and most often comparable to what the independent literature tells us ("Prescrire", for example).*"

Most of them recognize that some journals (in French-speaking interviews "Prescrire" is often cited) contain a lot of valuable information. They deplore their lack of time to read them thoroughly and understand them enough to use them as a prescription guide.

Very few interviewees cite Folia Pharmaceutica, Transparency Fiches, or, in a more general way scientific **publications**.

"Farmaka's advantage is mostly that they do the groundwork and see all recent studies on a given subject. And so, if I've read one of these studies, I can discuss about them without necessarily having read them all. There is a kind of pre-digestion and pre-chewing of information that is interesting."

"This is all the more interesting that one finds almost with the same medical visions that one can be found in a medical journal."

The vast majority of interviewees appreciate Farmaka and Farmaka-like initiatives. They like to be able to **exchange information from knowledgeable person to knowledgeable person, and value the pre-chewed, synthesized, information**. They reckon that with a very short time for reading reviews, such contacts are really useful.

A lot of them complain that, **for schedule reasons, GLEMs/LOKs and similar meetings are a burden.** They see in the information from Farmaka an alternative to meetings that is more compatible with their busy agenda.

3.3.1.3 Information sources of the GPs and the criteria of validity of these sources

"*Access to databases with more background information is certainly useful, but only when we are being adequately educated to work with them.*"

All interviewees use online resources, but the older ones (50+ years old) admit they sometimes find with difficulty their way in this ever-growing mass of information. They ask either easier websites, either training for using the existing sites in an optimal way.

A small but nonetheless significant part of the interviewees would like to have an access to the complete Cochrane Library, but most of them are satisfied with the content of the CEBAM website and think that the complete Cochrane would be too hard to fathom.

3.3.1.4 Validity criteria of these data according to the GPs

"*I do not have time to read studies. In general medicine, you can see ten different diseases on the same day. Therefore, you can't ask us to know everyone of them in depth; this is not our role in general. In any event, we do not have time!*"

A lot of the interviewees cite the **scientific nature of the given information**. "Prescrire"-like journals are often cited as a reference. Some cite the Cochrane Library too. However, **as discussed above, most GPs who cite these sources as references also deplore their lack of time to consult them**.

"*I am not sure that specialists are more critical than we are. In the long run, given my age, I still feel that some specialists are guided by firms as well. There are relative truths and then, you can feel fashions, etc.*"

Most GPS are extremely critical and sceptical regarding the information coming from the pharmaceutical firms (for instance, they easily identify contradictory discourses between competing firms). A lot of them are puzzled by conferences given by specialist physicians (opinion leaders) who are sponsored by these firms.

Interviewed GPs often use analogies, such as car analogies: for them competing car companies are allowed to lie a bit, to enhance the truth, because cars are just objects. But GPs "core business" is not selling drugs; it is all about the wellness of their patients.

A lot of them express their disgust to see the same marketing techniques being used for the wellness of human beings as those being used for selling goods.

3.3.1.5 The relationship between the GP and online information

> "*The Internet is a very useful tool to be informed. Of course you have to separate the wheat from the chaff.*"
>
> "*When I go on the Internet or on a university website, I find the information I want, updated to the last minute. In a paper publication, you can read about many subjects, but which don't interest us at this time and therefore we forget them.*"

All interviewees had access to a computer with Internet access (it was noted during the interviews and Mesydel participants would not have been able to participate without any computer). All of them used one in their practice in one way or another. **It is to be noted that virtually no interviewee had anything bad to say about online sources**, which tends to prove they have a great interest in them.

3.3.1.6 The relationship between the GP and "online" self-diagnosing patients

> "*I see many patients who actually go online and come with impossible diseases and ludicrous tales (*"histoires abracadabrantes"*). The diagnosis is known and they dye. It's hard to compete with the power of the Internet today and certainly with the power of Internet in the future.*"

A lot of GPs were extremely concerned by the recent rise of Internet websites and forums, which are directed to patients and sometimes contain dubious information. Interviewees complained that more and more patients come to their office with a pre-established diagnostic they made according to what they read on these websites. Sometimes, patients go as far as printing a webpage and just ask for a specific prescription, totally bypassing the GPs usual work routine. Most of the time, it appears that **the self-diagnostic is erroneous**, but it becomes **harder and harder to refute it**, especially when patients come with an "authority" website print, for instance, the website of a pharmaceutical firm on a specific medicine.

3.3.1.7 The role of the State: trust and distrust

> "*[The State] should highlight the independent sources and require the identification of conflicts of interest in advertising and media for pharmaceutical companies.*"
>
> "*In my opinion, the State has a role in our prescribing habits, it pushes us to think more when prescribing and to prescribe in the most appropriate way possible, I do not think the ultimate goal is to reduce expenditure but to achieve a better care quality.*"

The relationship between the State and the GPs and the "ideal" role that the State should play is one of the themes that provoked a strong disensus amongst interviewees. This topic made emerge various views of what the State is and what it should be.

> "*I think it is the doctors and especially the GPs who must make savings. But these benefits are redistributed to mutual companies, which are in fact politized. There, I begin to see a little red.*"
>
> "*But with public money, I think we must be accountable. That's my point of view. With money you do what you want, but money from INAMI/RIZIV is public money: it's normal to be accountable.*"
>
> "*GPs are no longer pure independent workers, evolving in a purely liberal system: health is largely a public service (or at least a sector regulated by the State), therefore we are partly "public service agents". Whether we like it or not.*"

First, there were three views of the State: some viewed it as a *political* power, some as an *economical* power. Only a few GPs from the sample saw the State as *both a political **and** economical* power. For instance, a "red flag" was brandished by some when the topic of the State intervention was put on the table: they assimilated State and INAMI/RIZIV, which was seen as an over controlling organism, preventing them to do their work in the best possible way.

However, this stance was from a minority: **most interviewees acknowledged that the State's intervention was necessary and useful**.

> "*Farmaka helps for a positive, more conscious prescribing behaviour. Contrary to the State who likes reprimanding.*"
>
> "*I understand that it is necessary to save money. The State still requires savings and it is often GPs who are affected. Should we not save money in hospitals too, where our patients benefit every day from unnecessary blood tests...*"

Secondly, for many GPs, **the responsibility of the State is to vouch for reliable information, scientifically neutral and independent of economical interests**. Others manifested the fear of the State coercing them to prescribe cheaper (in a pejorative sense), acting like a "Big Brother".

> "*When there is so much money going to a firm, there is a part that is returned to the State also, therefore, it is quite an ambiguous situation...*"

A minority of the interviewees thought that the State was corrupted or manipulated by the pharmaceutical industry just as anybody else and so developed a strong distrust against it.

3.3.1.8 The relationship between GPs and specialist physicians

> "*Those experts who lecture at continuing training and such? From the firms? Ah, but that's also coloured, isn't it. I don't even attend. No way. Sometimes I attend to meet colleagues, but I don't listen to what the experts say. That's not information.*"

A lot of GPs used **very tainted, vindictive, scowling terms when talking about specialist physicians** during interviews and in the Mesydel session. They often accused them of being in the pay of pharmaceutical companies. Many noted that it is **impossible in practice to go against the advice of a specialist physician** because in the eyes of the patient, a specialist physician is exactly what his name indicates: a specialist, an expert. They particularly deplore this point of view when the specialist physician clearly works on "ABM" principles. "ABM", "*Authority-Based Medicine*", is the practice of medicine based on what *opinion leaders* (well-known specialist physicians, professors) say and publish, regardless of the science behind their discourse. The term is often used as an antonym for EBM, which integrates *best evidence*, *clinical expertise* and *patient value*.

> "*Specialists certainly do have more know-how. It's necessary to consult them, and their advice strongly determines the way I start treatment, especially when they point out scientific evidence.*"

Quite a small minority of interviewees (usually older GPs) have the exact opposite opinions: they **would never go against the advice of a specialist physician** that they see as an authority figure that cannot (and *should* not) be challenged.

> "*I'm not sure they [specialist physician] are so permeable [to EBM], they are closer to emerging publications. Therefore, they already have their opinion a bit or even they participate themselves in the preparation of certain studies. So they are more in tune with these things.*"

For that matter, a lot of interviewed GPs explained that an initiative such as Farmaka has few to no chance to work with specialists, who are "*living in their own world*". When asked if one Farmaka's role could be (or become) a facilitator between GPs and specialist physicians, those who had a distrust discourse against specialist physicians answered in a pessimistic way, arguing that specialist physicians would not change anything in their practice, whatever the method used.

> "*Specialists are even more manipulated than GPs. I have never seen a patient get out of a specialist consultation with a generic.*"

Many interviewed GPs would like to be able to play to role of **counterweight**, and, thanks to their privileged relationship with the patient go beyond the authority of the specialist physician in helping the patient to make a choice knowingly.

3.3.1.9 Life-long learning

> "*I am a young GP. In my medical training, we talked a lot of EBM. And therefore, I always wait for medicines to prove their worth. I learned that way.*"
>
> *"No further suggestions, except maybe to send independent visitors more regularly to older GPs.*"

As we hinted before (see 3.3.1.1), **the relation between the age (more exactly seniority) of the GP and his type of practice is very strong**. **More recently graduated GPs were pro-EBM**, which can be in part explained that they have been in contact with EBM principles during their training, whereas older GPs who are pro-EBM became aware of it thanks to continuing education or personal curiosity and their own research to do their practice the best they can.

3.3.2 Perception of the Farmaka visit and visitor by the GPs

3.3.2.1 The AD visitor as perceived by the GP: scientific, economical or political role?

> "*Scientific! I don't notice anything political into it, the man speaks very neutral and objective.*"
>
> "*Farmaka visitors are certainly well trained scientifically. They know the studies but they often have an economic aspect which is probably politically tainted.*"
>
> "*They are almost not political, very scientific but with a science focused on EBM, a* "political" *science which is sometimes questionable in our reality.*"
>
> "*[Farmaka visitors] are politically tainted. I don't need people to teach me science under an ideological umbrella – it's a bit what they do.*"
>
> [Answer to the second question of the second round of the Mesydel:] "*This is a politically coloured stance. We know we may doubt politics and justice sometimes – this is clear by now. But I don't follow the paranoid aspect of the second stance.*"

Most interviewees perceived the AD visit as a strictly scientific meeting. A **minority of them perceived it as political**, in the pejorative sense of the term. The economical goal, which was never mentioned in the questions, emerged often and should be mentioned: it was generally used as a positive version of "political" and was usually talked about by GPs who saw Farmaka as "rather scientific". The reasoning was that a **good scientific overview of the available medicine led to cost savings** (by helping GPs not to fall into the "traps" of pharmaceutical firms).

> "*I haven't perceived any ideological message in the discourse of independent medical visitors: their approach was based purely on evidence-based medicine and was only scientific!*"

It should be noticed that a few French-speaking GPs were clearly offended by the mere fact that we suggested that Farmaka had a political role. It was clear in their discourse that they had a very pejorative understanding of the word "political".

3.3.2.2 Background of the AD visitor, according to the GPs

> "*I really think this would be good if they would remain field people who talk about things we actually use.*"
>
> "*Someone who understands the trade. Not some manager.*"

The vast majority of interviewees usually expect an AD visitor to **be able to have a good, scientific conversation about the selected topic**. They reckon the visitors must have an **excellent knowledge of EBM and a scientific training**.

> "*It can also be someone else (than a GP) but who worked in the field, who functioned, who understands and will perhaps also have an interesting view, because we come from different horizons.*"

When asked, **very few of them wanted the visitor to be a GP himself**. The vast majority of them reckon that the minimum training is a bachelor's degree in science (chemistry, biology, pharmacy, paramedical profession – nurse or physiotherapist, for instance) or a master's degree in the same topic. In fact, it appears that the initial training of the visitor does not matter much: **what matters for the interviewees is that the visitor has received a good training in EBM and can discuss his topic, in a scientific way, without hitting a wall at a certain point of the conversation**.

"*We have the same training, we have the same vision. We do not defend a product or a point of view. We're here to discuss the well-being of the patient.*"

Nonetheless, in the interviews of French-speaking GPs (where the visitors are all GPs), **a lot of them were delighted to have received the visit of a fellow doctor**, because it allowed them to **discuss concrete clinical cases, based on their own practice, between peers**. However, this last finding is to be interpreted with caution: we noticed a strong *network effect* with the French-speaking GPs, who personally knew "their" Farmaka visitor. The network effect allows a better flux of information.

"*Contrary to commercial delegates, [the independent visitors use] good sources, objective comparison between alternative treatments.*"

A lot of the interviewees added that "their" Farmaka visitor looked far more knowledgeable than the average pharmaceutical delegate. More than half of the GPs made a clear distinction between an AD visitor and a pharmaceutical delegate: **they saw their jobs as two completely different jobs**. A few of them were extremely bothered when AD visitors were referred as "delegates", because it insinuates a parallel that has no *raison d'être*.

It is interesting to note that most interviewees never ask pharmaceutical delegates what formal training they got.

3.3.2.3 Expectations of GPs regarding a Farmaka visitor meeting

"*I think that instead of these approaches being done individually, it would be better if they were collective. We should mobilize ourselves for a round table or a question and answer session, to save time. This would be more productive because there are always more in ten heads than in one. So, if there is one who has not understood something, another one is there to reiterate it.*"

As for the expectation of GPs regarding a Farmaka visitor meeting, the majority of the interviewees wanted them to **be able to have a frank, open conversation, without ever hitting a wall**. They want to be able to **push the conversation to the extreme**. Some suggested that, **to enhance the level of the conversation, it would be interesting to make group visits**, in the form of meetings of two or three GPs and a Farmaka visitor. This would lead to a good discussion between peers and on real cases.

Interviewees were usually delighted about the Farmaka visit but many also had f**aded memories** of **the** visit. This *recall bias* is mentioned in section 3.3.4. The research team did not anticipate this bias when designing the questions/Mesydel. No systematic question was asked about the topic[b] but the bias emerged from the analysis of interviews and Mesydel session. The researchers are therefore not able to give numbers – or even estimations – about how many did remind the visitor or the topic of the visit. The analysis shows that a few GPs did not remember the visitor at all and a sizable number declared that they had forgotten either the topic or the content of the visit.

"*I would like to be visited by Farmaka more often in the future, at least concerning relevant topics. We have a campus practice, so topics such as dementia and diabetics aren't useful.*"

[b] The closest question to this topic was the fifth question of the first Mesydel round, which did not give us enough information to translate them into numbers – Mesydel being a qualitative tool, participants were able to chose to answer or not to the relevant part of the question.

A common request from the interviewees about Farmaka's visits would be the selection of the topic by the GP. In fact, several GPs had young patients (on university campuses for instance). They did not really see the point of a visit about elderly dementia. **Better-targeted topics are a recurring demand** when it comes to the expectations of GPs about Farmaka visitors.

> "*For products that are more controversial, I think Farmaka is a little more low profile. There are probably other molecules for which they would have things to say, or molecules that have more important stakes.*"
>
> "*Themes must be diversified in order to give an opening to everyone. In our case, diabetes fell well because we have a lot of diabetic patients. But (during our studies) we were taught so much about diabetes that when she arrived, we already knew about all.*"

A lot of the interviewees (especially face-to-face interviewees) noted that Farmaka chooses easy, consensual themes. For instance, diabetes and obesity are themes already well known by the GPs, who already feel knowledgeable about these themes. **Interviewees demand more marginal themes, polemic or actuality themes**.

3.3.3 Impact of the Farmaka visit: what works

3.3.3.1 More conscious prescribing behaviour and non-drug treatments

> "*Farmaka helps for a positive, more conscious prescribing behaviour. Contrary to the State who likes reprimanding.*"
>
> "*There is really a vision that is truly medical and non-economically interested: what are the drug treatments, but also what are non-drug treatments?*"
>
> "*Well, this kind of visit breaks certainties. So they are quite critical of the arguments, evidence, compared to what firms often talk about. Firms often tell part of the truth: what they say is not false, but is only half true.*"

Interviewed GPs who said their prescribing habit was changed by Farmaka's visit stressed the fact that

- **Farmaka is not intrusive**, as some GPs think the State or the INAMI/RIZIV is;
- Farmaka has a broader speech than drug treatments, they also inform about **non-drug treatments**;
- Farmaka does not necessarily tell GPs to prescribe cheaper. It does tell it when it is the better treatment, but **if there is a really more effective drug, they recommend it, regardless of it cost**.

3.3.3.2 Counterweight to pharmaceutical firms

> "*Farmaka is relevant, if only to remember us that there are other schools of thought than taught by pharmaceutical companies*"
>
> "*It is important to counterweight the biased messages of firms.*"
>
> "*[Farmaka should extend to more GPs] to counter the weight of the firms. They provide objective and validated information.*"

A lot of the interviewees stressed the fact that Farmaka is a necessary **counterweight** to the pharmaceutical industry in that it helps them to remain unbiased towards the "*continuous propaganda*" of the industry. We emphasize the word "counterweight" because, of all words and metaphors that interviewees used to describe Farmaka, this one was the more reoccurring.

Interviewees told that Farmaka visitors help them to understand why a new medicine can or cannot be better than an old one: Farmaka visitors go against the discourse of "newer is better", without having any prejudice against newer, when it is in fact better.

3.3.3.3 Positive reinforcement

> "*In the prescribing habits of some colleagues, I can see things that are anchored. Then themselves, when we talk, recognize these influences that have been implemented. We are easily influenced, there's no denying about it.*"

According to interviewees, it looks like one Farmaka visit a year is the norm, while a GP can receive up to twenty pharmaceutical delegates a day if (s)he wants: the Farmaka message is lost in the mass. A lot of interviewees recognized that the pharmaceutical industry uses "brainwashing" techniques and they are influenced against their will by this well-oiled mechanic.

> "*Yes we receive them, but it has been a very long time. I actually thought the project had been cancelled.*"
>
> "*I had one in three years. Then you have the feeling it contributes little.*"

A lot of GPs were unable to remember the topic(s) they were visited for by Farmaka and a few of them did not even remember Farmaka's visit at all. A lot of them complain about the "anecdotic" character of the Farmaka visit.

> "*With time, the message does not necessarily remain. So there are things that they might need to activate more often.*"

It is to be noted that when we talk about the weak impact of the Farmaka visit, we do not talk about the obsolescence of the message, which is usually said by the interviewees to be up-to-date, but the impact is weak because "*it was so long since I have seen them that I can't remember anything about the meeting*".

> "*In any case, for me, it reassures my prescription which is, I think, a fairly rational prescribing. I prefer not to prescribe the novelties. I prefer to wait a bit to see them proving their worth. I stay with a fairly narrow prescription, and medication that I'm getting to know well and that have become familiar to me.*"
>
> "*We find ourselves saying:* "Yeah, it's consistent with my scope. And I'm not far from the truth even if I did not prescribe anything that's new and much better."."
>
> "*It has reinforced my way of working that was: few drugs, many dietary supplements, and a healthy lifestyle, reduce stress. All this is for me as important as medicine at the end of the day. It reassured me somewhere. I was disappointed for the drugs themselves, but not disappointed for my practice.*"

A lot of the interviewees told us that Farmaka reinforced them in their practice and their conviction. **For them, we cannot speak of a *behaviour change*, but we can certainly talk about *positive reinforcement*.**

3.3.3.4 Comparison of perception between single handed practices, group practices and medical houses

> "*You know, you're very alone in a practice... having the opportunity to discuss subjects on which we have no time to read is exciting indeed. And we need it!*"
>
> "*I think that ultimately, the GP who works in association, when he has a problem, he has a colleague who is nearby, if I can say so. Me, I must take the time to make a phone call, at the risk of disturbing a colleague.*"

The Farmaka initiative is especially appreciated by interviewees who work in single-handed practice. When the visit was held with GPs working either in collaboration, either in a medical house, we noticed less impact according to the interviewees, because, since they work in groups, they already have plenty of opportunity to discuss practical cases together, they already have been *reinforced* (see 1.3.3.3). Solo GPs, by contrast, had the feeling of being *decompartmentalized*.

3.3.4 Impact of the Farmaka visit: what does not work

As discussed in the previous section, the Farmaka visit has an "anecdotic" character: a lot of interviewees confessed to have faded memories of their Farmaka visit. Some even forgot the visit itself: this **introduces a new bias in our study, i.e. a *recall bias***. That means that a lot of interviewees had faded memories of their Farmaka visit and therefore were **unable to give a valid feedback**.

Moreover, as mentioned in the analysis of the sample (3.2.3.2), we have mostly opinions of pro-Farmaka people (see also bias 1, section 3.4.1).

With these two facts in mind, we can hypothesize that a sample with a better recall of the visit and less biased in favour of Farmaka, would make emerge more critical opinions about the visit of Farmaka.

3.3.4.1 Imperfect target audience

> "*This would become much more interesting if it were extended to all GPs. Otherwise the visitors are likely to "preach to the choir.*"

Farmaka visits in medical houses have little impact. Interviewed GPs who worked in medical houses were committed to EBM principles and seemed well trained in this field. So, in an apparently paradoxical way, the Farmaka visit is less useful for them. Even the *positive reinforcement* we discussed earlier was not noticeable here, since their way of practice is already supporting this reinforcement.

Because of this apparent paradox, we can hypothesize that Farmaka visits **miss their ideal target audience**, which should ideally count less GPs working in medical houses and GPs practicing in association who have the opportunity to share their experiences and knowledge.

> "*It is true that there are more poor patients who come to the medical house. There are situations where there are more intellectual challenges, more implementation challenges and more human challenges in order to help those people.*"
>
> "*I work in a medical house, in a multidisciplinary team. We pay attention to concepts of accessibility, comprehensiveness, much more than other GPs. I don't work in "liberal" way.*"

Especially in the South of the country, the fourth bias is particularly strong (see 3.2.3.2.) *i.e.* GPs have a particular interest for social aspects of their practice. **Social matters were a major concern amongst interviewees**, who rarely confined their activity to the simple practice of medicine, some of them even routinely performing tasks usually assigned to social workers.

However, there was a link between the social character of a physician and his appreciation of Farmaka: **the higher a GPs social orientation, the higher the chance he is pro-Farmaka**.

3.3.4.2 Lack of accreditation advantage linked to the visit

> "*Accreditation is in my view not necessary but would help greatly."*
>
> "*I think that objective information "out-firm" is interesting. It is our role to remain attentive enough that it is not only geared towards the economic side. If in addition, it can be part of the accreditation is even better...*"
>
> "*The training process is a good thing to take because the questioning is necessary and medicine is changing every day. If the visit is long, why not offer accreditation points?*"

Most interviewees were enthusiastic about accreditation points for AD visits;. However, a few interviewed GPs were offended by this idea as they considered this activity as a part of their activity.

> *"I am myself certainly willing to adjust my prescribing behaviour, should this be necessary. A clear reason should be stated for this. I don't need anything for myself in return. I would do it for State or the patient, in which the interest of the patient is more important to me than firms."*
>
> "*I do not see why you even talk about a return, I am not a dealer, and I treat human beings in distress who trust me.*"

Even if accreditation is, by far, the most often cited incentive for practice change by interviewees, it is hard to extrapolate more from the answers because, especially in the French-speaking group, **the vast majority of the GPs was already sold to the idea that changing their prescribing behaviour was necessary** (in fact most of them had already changed their prescribing behaviour – and the younger GPs never practiced the "old-school" behaviour).

3.3.4.3 Continuing education role of Farmaka: towards an official recognition?

> "*What I find unfortunate is that it is not recognized as continuing education. Because it's really about spending an intense enough half hour where we are really focused on a given subject.*"
>
> "*The independent delegates aren't qualified to teach us, GPs, any lessons on clinical-medical grounds.*"

Most of the interviewed GPs see Farmaka as a form of **continuing education**, accreditation being its corollary. It is interesting that the continuing education aspect of Farmaka though rarely emerged when the topic was not about accreditation.

A few adverse reactions came from interviewed GPs who did not believe in the educative role of Farmaka: most of these ones did not like the idea of being schooled by anyone. A part of them did not like the system of accreditation at all, because they favoured their own experience and their own self-learning above the State-provided education ("*We are able to think by ourselves*").

3.3.4.4 "Granularity" of Farmaka's information

> "*It is very strongly mathematical and technical. When you read a little fast, you do not remember much. What would be interesting, pedagogically, is that after she does her stuff, she would summarize it in three or four lines.*"
>
> "*I would like less detail and more general directing lines. Even more schematic if I can say so. I know there are things I will not remember or will not use in my practice.*"

Several interviewees insisted on the fact that Farmaka's information was very dense, in its contents as well as in its in scientific richness. To overcome this complexity, a lot of them demanded a **less detailed presentation.** When the presentation is too detailed, a lot of interviewed GPs confessed that they are not able to use it in real clinical cases. They also asked a physical support where the addressed topic would be both synthesized and explained in greater lengths than during the visit.

3.3.5 Wishes of interviewed GPs

3.3.5.1 Online presence of Farmaka

> "*What would be interesting on the other hand, is a website where you could find the information. Often, during continuing education sessions, we take some notes and then we just lose them somewhere.*"
>
> "*Farmaka could make such summaries in French. If possible, summaries of recent studies relevant to our practice. These summaries should be available to physicians on a website.*"
>
> "*I think it would be interesting to have a website where we could find the information that was presented. Pieces of paper? We can't keep them all!*"

A lot of the interviewees are **very favourable to a stronger online presence**, a few of them even suggesting that Farmaka would be more efficient if it were an **online information provider**, complementing what already exists (CBIP/BCFI and CEBAM, particularly), by offering more scientific, EBM documents, readily usable in their practice. A few of them mentioned the possibility of a Farmaka hotline.

Regarding the hotline, the idea was developed by interviewees in two distinct ways:

- either a hotline strictly for GPs who need a quick scientific answer to help them on a specific case, to help them to better manage an uncertainty;

"*A hotline is a good idea [especially for rare infections], analogous with the anti poison centre.*"

- either a mixed hotline, for GPs and patients, that would work like the anti poison unit line, where patient would be able to freely ask simple questions or advices on simple subjects. The service would give the same kind of information as what was suggested as an online "Farmaka for patients".

However, especially for younger GPs, a fair amount of interviewees **thought of the hotline as an anachronism and suggested to put all the effort in an online system**.

3.3.5.2 Farmaka for all Belgian GPs

When asked if Farmaka should **extend their services to all Belgian GPs**:

- slightly more than half of the interviewees said that it would be a good thing, mostly because they think their colleagues' knowledge about EBM is often lacking;

"*I would not be against it being a paid service or subject to a contribution. Why not? This would seem logical, I mean.*"

- slightly less than half of the interviewees said that Farmaka should only visit on a **voluntary basis, because if it was mandatory, not interested GPs would only pretend to listen**, just to obey the rules. It would be a waste of resources, human as well as monetary;
- some interviewees did not know that Farmaka was not offered to all Belgian GPs.

At this stage, the reader should remind the first bias of the study (sample bias): interviewees had a tendency to be supporters of Farmaka. A less biased sample would probably have given significantly different answers.

3.3.5.3 More frequent Farmaka visits and choice of topic

"*I mean, when it is a large firm, there is a delegate every week. An independent delegate visits us only once every six months. There is really a negative balance.*"

How Farmaka could enhance its services? The first answer was almost always the same: by visiting the GPs more often, once every month being often considered ideal by the interviewees. As we said before, by **extending their topic portfolio** and – even better – by **giving the choice of the topic of a visit**.

3.3.5.4 *Farmaka for patients*

> "*If Farmaka was aimed at patients too, it would facilitate my work, because there would be many details that I would not have to give myself anymore.*"

About a half of the interviewees think that Farmaka should open up to patients through a website. Please note that **none of them demanded that the online resources for the GPs become available to the general public**: when discussing "Farmaka for patients", there was a consensus that this service would be a **very different service**, helping the general public to have access to quality resources: scientific and didactic vulgarized information based on EBM principles and adapted to the level of the layman. For instance, information about allergies, explanation of why "antibiotics should not be automatic": beyond the slogan, the public does not really know why antibiotics are useless for certain illnesses. **Since GPs repeat the reasons patient after patient, interviewees think that this kind of online services for patients would help a lot.**

> "*[Independent medical information] must extend not only to the GP, it must extend to the patient. If (s)he goes on the web, nine times out of ten, he finds something which is funded by the pharmaceutical industry. Even the websites of some patient associations, for certain diseases.*"

Interviewees stressed that such a resource for the patients would also act as a **counterweight for the erroneous or biased information they can find online**: it would be an official website, with unbiased information, that people could trust. And it would help GPs facing an erroneously self-diagnosed patient: (s)he would just have to give him the website URL or even to print a folder.

> "*Patients seeking information often do it on an issue that concerns them personally and they'll already find an answer on patient association websites, for example. More general information will be more credible if it passes through the patient's GP.*"

It is interesting to note that **interviewees who did not want Farmaka to extend their services to patients were, for the major part of them, those who understood that the "Farmaka for patients" would mean that patients would have access to the same website as the GPs**.

3.3.5.5 *Demand for more reference sources*

> "*The Cochrane Library is too broad and does not respond to specific clinical questions for the prescription, I'd rather be interested by websites of quaternary independent literature that make a relevant summary of recent data on the clinical question asked.*"

A lot of interviewed GPs asked more summaries, simplifications, unbiased and hardly scientific, EBM, "quaternaries sources" based on these source references.

Key points : analysis of the qualitative study

GPs and the information sources:

- **the GPs say they use mostly information from the internet and from peers**
- **they state that they select the information based on a scientific ground**
- **they express doubt about the independency of specialist physicians from the pharmaceutical industry**
- **The role of the State gives rise to a variety of reactions but most interviewees acknowledge that the State's intervention is necessary and useful**
- **recently graduated GPs of our sample were pro-EBM.**

Perception of the academic detailing visit:

- **some GPs did not recall the visit and/or its content of it**
- **the AD visit is mostly considered as scientific, sometimes too dense**
- **the visitor's background has little influence if scientific background**

Impact of the visit according to the GPs:

- **AD visitors advice a more conscious prescribing behaviour, also non-drug treatments**
- **AD is a counterweight to pharmaceutical firms**
- **The effect is more a positive reinforcement rather than a real behaviour change**
- **GPs in single-handed practices in particular appreciate AD (help to feel decompartmentalized) – less impact for group practices**

3.4 CRITICAL DISCUSSION OF RESULTS AND ENHANCEMENT LINES

This analysis gives the raw material, truthfully to what the GPs actually said or wrote. However, it suffers from the four biases discussed in section 3.2.3.2.

In this chapter, it is verified whether the biases were confirmed or not by the interviews and the Mesydel and, if it was possible to fix them. A methodology is proposed for the further enhancement of the results.

3.4.1 Biases

3.4.1.1 First bias: sample bias

The extent of this bias was impossible to fix, since the parent population was known and biased from the start (acceptance by letter). The hypothesis was that by exploring a sample being compiled from GPs who had almost all accepted Farmaka's visit (and the study), we would have an overrepresentation of GPs who are very favourable to Farmaka and pro-EBM. The interviews and Mesydel tended to confirm it, with the vast majority of interviewees being very favourable to Farmaka and few interviewees who were unfavourable to Farmaka. This bias could also explain the paucity of statements regarding the concrete impact of AD on the prescription behaviour.

This absence of expected changes probably contributes to the lack of results in the analysis of the prescriptions (see chapter 4).

During the interviews and Mesydel session, we also noted an overrepresentation of GPs in their fifties in the Flemish community. The age curve was better balanced (but still not representative) in the French community. No other biases emerged during our study (except for the *recall bias*, which is of a different nature). **A more representative sample of Belgian GPs would give a more nuanced view on the Farmaka initiative**.

3.4.1.2 Second bias: unequal distribution between language communities

The sample was highly unevenly distributed regarding language communities, with 4.3 times more GPs practicing in the Flemish community than in the French community. The researchers were able to fix this bias partially. Firstly the huge number of answers to the Mesydel session allowed securing the qualitative saturation point in both communities. Secondly, a first separate analysis of both communities before merging the results allowed making a comparison. We can posit the hypothesis that this bias was fixed.

3.4.1.3 Third bias: geographical bias

The third bias was that the sample had strong concentration effect: some major cities (e.g. no GPs in the Mons or Hasselt) and important areas (only three GPs for the entire province of Liège) were absent from the sample. The researchers were able to adjust this bias, only in part, thanks to Mesydel, which allowed contacting members of all covered areas. However, the areas not represented in the original sample were still lacking. Therefore, we were partly able to fix this bias, but could not avoid that the rural, semi-rural and urban distribution as well as the socio-economic distribution were not representative. We can posit the hypothesis that a more balanced sample with regard to socio-economic and environmental criteria could have highlighted additional aspects of the issue.

3.4.1.4 Fourth bias: social bias

The fourth bias was an overrepresentation of GPs either showing a specific interest for social aspects of the medical practice or already working in medical houses. After the interviews and Mesydel session, this bias was confirmed with certainty for the French speaking community and in a less significant way, for the Flemish speaking community (the social aspect was less prominent, although not completely absent). Therefore, this bias still exists for the Flemish community, but to a lesser extent than for the French community. We can posit the hypothesis that an investigation based on the Belgian Order of Physicians listing, adjusted according to socio-political positions would have given significantly different results.

3.4.1.5 Recall bias

A last bias has been added during the analysis of the results i.e. a recall bias linked to the fade memory of the visit and its content; This bias means that the global results of the Mesydel have to be interpreted with caution given the lack of precision from a proportion of respondents.

3.4.2 Discussion of some seemingly contradictory opinions in the analysis

The analysis provided raw, untreated material. It made emerge some seemingly contradictory opinions. This section discusses and clarifies these unclear opinions.

3.4.2.1 GPs want more exchanges, but do not like GLEMs/LOKs

- A lot of GPs feel that going to meetings after hours is a burden. Some are not bothered at all and think they are very useful. We present the results in an aggregated form, but each GP answered on his/her own, without communication with his/her peers.
- Some GPs do not like GLEMs/LOKs because they feel they waste their time, listening to a very polarized discussion. Asking a "mediator" (a Farmaka member in our case) is very coherent with this opinion.
- A lot of GPs insist on the possibility to have access to interactive online meetings, which would be a bit like a GLEM/LOK at home. This position is also very coherent with the "GLEM/LOKs are a burden" opinion.

3.4.2.2 GPs ask for information on a website

Most GPs who ask a follow-up of Farmaka's visit on a website are just not aware that the information is already provided by Farmaka on a website. In fact, many GPs are unaware of the online scientific sources directed to them (Farmaka, CEBAM, CBIP/ BCFI).

3.4.2.3 Other aspects of the Farmaka visit

In the analysis, little is said about the perception of the visitor himself and his human qualities (or the lack of them), such as their sympathy, empathy, the quality of the exchange from a more human than scientific point of view. It can be explained at least by two factors:

- The absence of direct questions about this aspect of the Farmaka visit;
- A possible GPs reserve on this topic during the interviews as well as during the Mesydel session.

3.4.3 Further research

Considering the biases discussed in 3.4.1, it should be clear that the results would have been significantly different with a more representative sample of the population of the Belgian GPs. Further research could be carried out, using the same methodology with a more representative group of GPs than a sample of voluntary GPs contacted by Farmaka and who gave their agreement for this study.

We could obtain decisive clarifications about Belgian GPs regarding:

- how they deal with scientific sources;
- how they deal with scientific uncertainty;
- their opinion on EBM *vs.* ABM;
- their opinion on academic detailing;
- their awareness of Farmaka (do they know it exists, do they know what it does) as well as their interest in being visited by Farmaka visitors;
- their willingness to change their prescription behaviour and the conditions at which they would accept such a change.

A good way to avoid most biases discussed in 1.4.1 would be to start from a population sample based on a representative sample of clinicians.

Special attention would be given to a set of identification variables that we identified as possible determinants in the attitude towards academic detailing:

- the socio-economical status of patients;
- the environmental (rural, semi-rural, urban) setting of the GPs offices;
- the geographical setting of the GPs office;
- the kind of medical practice (GPs type of practice)
- the socio-political affinities of the GPs;
- the age group of the GPs.

The sample should also include a weighting of French and Dutch speaking communities, as well as a proper weighting of Belgium's major cities.

3.5 IMPROVEMENT PATHS: SUGGESTIONS FOR IMPLEMENTATION

3.5.1 EBM for specialist physicians

(*see analysis, section 3.3.1.8*)

According to the interviewees, the impact of EBM is limited in practice when the GP is faced with a specialist physician. Moreover, if a treatment is initiated by a specialist physician, the GP has to follow it. The interviewees have been extremely sceptical about an extension of Farmaka (or any form of academic detailing) to specialist physicians.

However, we cannot extrapolate the opinion of specialist physicians from what our research, because we had no specialist physician in the sample.

3.5.2 Support of the medical information

(*see analysis, section 3.3.5.1*)

The analysis has shown that all interviewees are equipped with an online computer. Internet became the first source of information for the vast majority of them, making printed publications obsolete.

With that in mind, the development of various information materials based on new technologies could enhance Farmaka's visibility. The question is to know the awareness of GPs of Farmaka's material online.

3.5.3 Online forum and focus groups for GPs

(*see analysis, section 3.3.5.1*)

Especially GPs working in single-handed practices feel compartmentalized in their practice. Online services could therefore go further than "read-only" website and offer enhanced interactivity, in the form of traditional Internet forums, or of a tailor-made *focus group* system.

This idea of a tailor-made *focus group* system did not emerge directly from the interviews themselves, but from the unexpected huge participation rate to the online questionnaire (Mesydel), whose operating principle is very near of what an online focus group would be.

This finding combined with the fact that the Internet has become the first information source for GPs tend to prove that GPs are very open to – and even demanding – online, non-intrusive participative tools. The online aspect allows them to be freed from temporal and spatial constraints: participants can answer at any hour of the day (or night), from any computer connected to the Internet, without leaving their home or practice. This positive aspect contrasts with complaints that meetings and GLEMs/LOKs are a burden because of their heavily busy schedule.

The interactivity could be both between peers (GPs) and between GPs and Farmaka, to discuss Farmaka topics or even to suggest topics or request visits.

3.5.4 Emerging problem: patients who misuse the Internet for self-diagnosis

(see *analysis, section 3.3.1.6*)

A lot of GPs are very concerned by the fact that patients are more and more using the Internet to create a self-diagnostic. The problem is that they take the information they find at face value, without a critical mind. The problem is that this information suffers from at least three severe biases:

- anybody can participate in forum discussions, but a layman who can write convincingly is not more knowledgeable about scientific topics just because he can be convincing;
- most of the forum sites (not only medical forums) suffer from what is known in the community forums as "*astroturfing*", *i.e.* people with an agenda posing as laymen, disguising themselves as sick people and influencing the opinion of other members by taking part on the discussion and praise a treatment while discrediting another;
- some informative sites (for instance http://www.monasthme.be/ or http://www.astrazeneca.be/info-sante/bpco/) belong to pharmaceutical firms (sometimes this belonging is clearly mentioned, sometimes it is well hidden) and give biased information.

This research shows that this growing trend complicates the discussion between GPs and patients, especially on EBM matters. A future idea could be creating an online service for patients that would parallel sites as, for instance, the CBIP/BCFI, with a more ergonomic interface and didactic content, to be understood by any patient.

3.5.5 Farmaka's visitor profile

(see *analysis, section 3.3.2.2*)

The professional background of the visitor does not matter much even if a GP would be better to discuss cases between peers. What matters for GPs is that the visitor has received a good training in EBM and can discuss his topic, in a scientific way, without hitting a wall at a certain point in the conversation.

3.5.6 Choice of the topic of the visit by the GP

(see *analysis, section 3.3.5.3*)

A recurring demand about the visits from Farmaka would be to let the GP chose the topic of the visit, to better fit their own practice. Farmaka could propose a portfolio of topics that can be chosen by the GPs before the visit. This portfolio should be expanded to include actuality themes and more controversial topics.

3.5.7 Better target group for the AD visits

(see *analysis, section 1.3.5.2 and 3.3.3.4*)

The analysis showed divergent opinions on the eventuality of enlarging Farmaka's visits to all Belgian GPs. Some interviewees said that it would be a waste of money, as non-interested GPs would just "pretend" to listen to the visitor. However, it is more useful to enhance the awareness of EBM to GPs who were less (or not) exposed to it, than to GPs who are already pro-EBM. As stated before, for the later ones a Farmaka visit is only *positive reinforcement*.

In the same way, GPs in single handed practices could be the target of Farmaka's visit as they are more eager to learn from Farmaka than GPs in group practices. Those last ones have more opportunity to share EBM practice with peers.

3.5.8 Accreditation procedure linked to the Farmaka visit

(see *analysis, section 3.3.4.2*)

Many interviewees are favourable to include the Farmaka visit in the accreditation scheme even if they never refused the visit because of the lack of accreditation. However, the sample bias (see section 1.4.1) suggests that the participants were pro-Farmaka. Therefore a further study would be useful to test the impact of accreditation points on the acceptance and impact of the visit.

3.5.9 Enhancing awareness of Farmaka amongst GPs

(see *analysis, section 3.3.5.3*)

Many GPs had trouble remembering the content of the last visit of even its existence. Some GPs proposed more frequent visits to overcome this failure. Some of them proposed one visit a month: one visit every other month looks more realistic and less intrusive. Another way to enhance academic detailing awareness should be to organize discussion groups involving a Farmaka visitor and GPs. That proposal could be materialised through the invitation within a GLEM/LOK group.

3.5.10 Life-long learning

(see *analysis, section 1.3.1.9*)

The youngest GPs in this sample were more favourable to EBM than the older ones. This finding validates the fact that EBM is indeed future-proof.

Key points : suggestions of GPs about new developments

- **to develop didactic material to enhance the AD visibility**
- **to develop an online system**
- **to propose an AD service for the patients**
- **to offer the freedom of choice to GPs to choose a topic**
- **to have better target groups for the visits (single handed practices)**
- **to link the visit to an accreditation procedure**
- **to offer more frequent visits and/or group visits**

4 PRESCRIPTION DATA OF A SELECTED SAMPLE OF BELGIAN GPS

The objective of this project is to assess the impact of the Academic Detailing (AD) visit on the practice of the GP. The specific objective of this part is to assess the possible impact of the AD visit on the prescription of Belgian GPs by an analysis of their prescription data before and after the AD visit.

4.1 BACKGROUND

4.1.1 Choice of the topics

The analyses focused on two themes i.e., diabetes and dementia, for two reasons:

- Farmaka's messages partly in relation with the prescription of medications;
- Most medications registered in the IMA/AIM database (versus other themes as allergy);
- The prescriptions can be attributed to the treatment of a specific disease (versus other non specific medications e.g. cardiovascular medications).

The themes were identical to the ones chosen to select the population interviewed in the qualitative study.

4.1.2 Key messages of Farmaka AD visitors

During the visit of the AD, key points are made by topic. The analysis of change in prescription was therefore based on the adherence to these key messages.

4.1.2.1 Diabetes

The visits on the diabetes topic were conducted between February 2008 and June 2008. The key messages were those of the website of Farmaka[10]:

1. Begin with a monotherapy:
   - Metformin (first choice)
   - Sulfonylurea compounds (second choice)
2. In case of failure of the monotherapy, give a bitherapy: metformin and sulfonylurea compounds as a first choice;
3. In case of failure of the bitherapy, add insulin;
4. In case of failure, refer to the specialist.

4.1.2.2 Dementia

The visits on the dementia topic were conducted between October 2006 and February 2007, only in the Dutch-speaking part of the country.

The main message for dementia was based on the website of Farmaka[10] i.e. the absence of evidence for a clear effect of the medications on the symptoms (except for a limited percentage of patients with moderate symptoms). The major suggestions were to reduce the medications related to that specific pathology (cholinesterase inhibitors, Memantine, Ginkgo Biloba) and to take care with associations with other medications for behavioral problems (e.g. neuroleptics).

4.2 METHODOLOGY

4.2.1 Data source

Farmaka provided KCE with a list of GP's who were contacted and visited along with date and topic of the visit. Moreover, these GPs were GPs who gave their written consent to Farmaka to have their prescriptions analysed.

The extraction of the data from the 2006 – 2008 datasets of IMA/AIM database, the Belgian Agency of Health Insurance Funds was based on the following criteria:

- Prescriptions from the visited GPs
- Medications included in the following list by topic:

For the topic Diabetes:

- A10A – Insulin and analogues
- A10B – Blood Glucose Lowering Medications, Excluding insulin
- A10X – Other Medications used in Diabetes

For the topic Dementia:

- C04A – Peripheral Vasodilatators
- N03A – Antiepileptics
- N05A – Antipsychotics
- N05B – Anxiolytics
- N05C – Hypnotics and sedatives
- N06A – Antidepressants
- N06B – Psychostimulants, agents used for ADHD and nootropil
- N06C – Psycholeptics and psychoanaleptics in combination
- N06D – Medications for dementia

The information contained in the IMA/AIM database include all the data concerning the delivery of medications in pharmacies, i.e. the reimbursed cost, the cost/part of the patient, the amount of packages delivered and date of delivery by medication purchase.

4.2.2 Planned Analyses

In order to answer the research question the following analyses were planned to be performed by topic (Diabetes or Dementia):

- Age distribution of the patients included in the analysis, by topic.
- Number of GPs included in the analyses, by topic.
- Mean number of patients included in the analyses by GP and topics.
- Number of subjects by active substance, as defined by the level 5 of the Anatomical Therapeutical Chemical classification system (ATC system), before the visit and after the AD visit
- Changes in type of therapy before and after the AD visit, by topic.
- Changes on the cost of the therapy before and after the AD visit, by topics
- Comparison of the sample of GPs and all the GPs in term of prescriptions behaviour.

4.2.3 Statistics

Continuous variables were analysed by descriptive statistics including the mean, standard deviation (sd), median, interquartiles (Q1 and Q3), and, minimum and maximum.

Categorical variables were analysed by a frequency distribution table (number and percentage of cases).

It was decided not to perform formal testing due to the sampling bias, systematic bias, omitted variables bias and limitations of the data. In fact, those biases are external biases that may affect the accuracy of the statistical measurements. Therefore, it makes the estimation of population parameters impossible and any statistics computed from that sample has the potential to be consistently erroneous.

4.2.4 Rules

In order to analyse the data, several manipulations of the data sources and rules were applied by topics and are described here below.

4.2.4.1 General

Assumption was made that the therapy could be determined based on the medications delivered in the pharmacy and therefore part of the IMA/AIM database.

For analyzing the data and the impact the AD visit on the practice of the GPs, the following general rules were applied:

- Selection of Adults: ≥ 18 years,
- If the patient had a contact with several GPs visited by an Academic Detailer for the any of the Topics, assumption was made that the effect of the AD would be more reflected in the prescriptions data of the first GP visited. Therefore, all the prescriptions linked to the first GP visited were taken into account for the analyses for that specific patient,
- Selection of the data within a 6-months period before and after the AD visit to the GP was made. This period corresponds, in general, to the maximal period for medication renewal (taking into account a possible lack of compliance),
- In case the purchase of a differed medication was given on the delivery date selected for the analysis (following the rule of the preceding point), this medication was not taken into account for the determination of the therapy given to the patient.

4.2.4.2 Diabetes

The following rules were applied for analyzing the data on diabetes:

- Assumption was made that the therapy given to a patient could be determined based on the prescription and therefore on the purchase of the medications. The medications delivered on the closest date before and the closest date after (or on) the AD visit date were taken into consideration for the determination of, respectively, the therapy given before and the therapy given after the AD visit,
- Exclusion of the patients with Diabetes type I was made, i.e.
  - The patient considered as under monotherapy of insulin before the AD visit,
  - Patient without prescriptions data available in the 6-months preceding the AD visit and under monotherapy of insulin after the AD.

In order to determine the therapy given to the patients, a first classification of the medications was done as follows:

- Group 1 = Insulins and Analogues → ATC level 3 = A10A
- Group 2 = Metformin → ATC level 5= A10BA02

- Group 3 = Metformin and sulfonylurea compounds → ATC level 5 = A10BD02
- Group 4 = Metformin and rosiglitazone → ATC level 5= A10BD03
- Group 5 = Sulfonylurea compounds (=GLY) → ATC level 4 = A10BB
- Group 6 = Others - Glitazones → ATC level 4 = A10BG
- Group 7 = Others - Glinides - Exenatide → ATC level 4 = A10BX
- Group 8 = Others - Sitapliptines → ATC level 4 = A10BH
- Group 9 = Others → ATC level 3 = A10X

Based on the groups of medications defined above, the type of therapies was determined as follows:

- **Monotherapy**: if the patient took only medications of one of any groups (except of Group 3 and Group 4).
- **Bitherapy**: If the patient took a combination of medications from 2 different groups (except of Group 3 and Group 4) or only medications in Group 3 or only in Group 4.
- **Tritherapy**: if the patient took a combination of medications from 3 different groups (or 2 different groups in case one of the group is Group 3 or Group 4).
- **Others** combinations of more than 3 groups

If several medications of a similar group were given to a patient, these medications were comptabilised as one for the determination of the therapy (e.g: patient taking rosiglitazone and pioglitazone was considered as a patient under a **monotherapy** of "other – Glitazone").

4.2.4.3 Dementia

The following specific rules were decided to analyze the data on dementia topic

- In order to analyse the behaviour of the GP before and after the AD visit on this specific topic Dementia, the selection of the patients taking at least one Alzheimer medication (defined as a medication with the level 3 of the ATC system = N06D) during the 6-months before or after the visit, was made,
- Assumption was made that the therapy given to a patient could be determined based on the purchase of the medications.
- The medication(s) of interest for this topic were the Alzheimer medication(s). Therefore, for the determination of the therapy given before and/or after the AD visit, focus was made firstly on the purchases including an Alzheimer medication(s) and, in case of none, on the purchases including other medications in the list of medications under investigation for Dementia (sees section 4.2.1).
- The medication(s) delivered on the closest date before and the closest date after (or on) the AD visit date were taken into consideration for the determination of, respectively, the therapy given before and the therapy given after the AD visit.

A first classification of the medications included in the therapy given to the patient was done as follows:

- Alzheimer N05C – Hypnotics and sedatives
  - N06A – Antidepressants
  - N06B – Psychostimulants, agents used for ADHD and nootropil
  - N06C – Psycholeptics and psychoanaleptics in combination

In light of the key message of Farmaka, the following types of therapies were further analyzed:

- Monotherapy of Alzheimer medications:

- Monotherapy of Cholinesterase inhibitor (Monotherapy of Donepezil , Monotherapy of Rivastigmine or Monotherapy of Galantamine);
- Monotherapy of Other medications for dementia (Monotherapy of Memantine – Monotherapy of Ginkgo Biloba);

- Monotherapy of an Alzheimer medication in association with other medication(s) (medications included in the group "Other") ;
- Other (patient taking medication(s) included in the group "Other" and no Alzheimer medication)

4.3 RESULTS

All analyses were performed with SAS Entreprise Guide 4. The detailed results are available in appendix.

4.3.1 Diabetes

As stated above the AD visits for Diabetes started in March 2008 and ended in June 2008. The analyses described here below included all the data from IMA/AIM database following the rules described in section 4.2.4.

4.3.1.1 Population description

A total of 6 584 patients for 156 GPs visited by the AD from Farmaka were considered for the analyses on the prescription data for the Diabetes topic.

The mean age of the patients was of 68 years (sd =13). The number of patients included in the analyses by GP was in median of 41 patients (Q1 = 25 patients and Q3 = 55 patients).

Table 15. Number (%) of patients by available 6-month period information – Population of patients who received diabetes medications

	6-months **After** the AD visit		
6-months **Before** the AD visit	No data	Data available	**Total**
No data	0 (0.0%)	1 193 (18.1%)	1 193 (18.1%)
Data available	894 (13.6%)	4 497 (68.3%)	5 391 (81.9%)
Total	894 (13.6%)	5 690 (86.4%)	6 584

Percentage are computed based on the total number of patients included in the Overall Population (N = 6 584)

Table 15 describes the number of patients with available data on the prescriptions within the 6-months before and/or after the AD visits. Available data means that there were purchased of medications included in the list of medications under investigation for Diabetes (see section 4.2.1).

On the 6 584 patients analysed:

- a total of 4 497 (68.3%) patients had data available on both periods of interest (within the 6-months period before and 6-months period after the AD visit to the GPs) (considered as prevalent cases);
- a total of 894 (13.6%) patients had available data only within the 6-months period before the AD visits (i.e. either false diagnosis or they did stop the treatment);

- a total of 1 193 (18.1%) patients had data concerning the purchase of medications for diabetes only after the AD visit (considered as incident cases);

4.3.1.2 Analyses of the therapies

Overview

The results are presented for the following (sub)populations:

1. Overall population (N = 6 584 patients) is the population of patients who received diabetes medications within the studied timeframe;
2. Subgroup of patients from the overall population with no data available on medications for diabetes within the 6-months preceding the AD visit but with medications for diabetes delivered after the AD visit - "New" Cases Subgroup (N = 1 193 patients);
3. Subgroup of patients from the overall population with data available on medications for diabetes on both periods – "Complete" Cases Subgroup (N = 4 497 patients).

The subgroup of patients with data on medications for diabetes available only within the 6-months period before the AD visit will not be analysed. Those cases are part of the limitations of the data and are discussed in section 4.4.

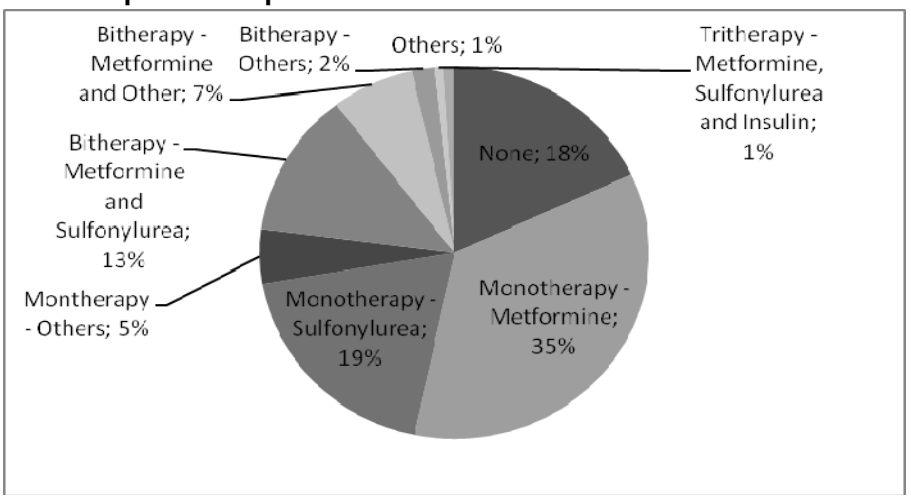
The evaluation of the impact of the AD visits on the practice of the GPs considers the classification of therapies in light with the key messages of Farmaka[10]:

- Monotherapy of Metformin (recommended by Farmaka as first choice of Monotherapy);
- Monotherapy with Sulfonylurea compound (recommended by Farmaka as second choice of Monotherapy);
- Monotherapy of Insulin;
- Monotherapy of Others;
- Bitherapy of Metformin and Sulfonylurea compound (recommended by Farmaka in case of failure with the monotherapy);
- Bitherapy of Metformin and other than Sulfonylurea compounds;
- Bitherapy of others combinations;
- Tritherapy of Metformin, Sulfonylurea compound and Insulin (recommended by Farmaka in case of failure with the bitherapy);
- Others.

Overall population with diabetes medications

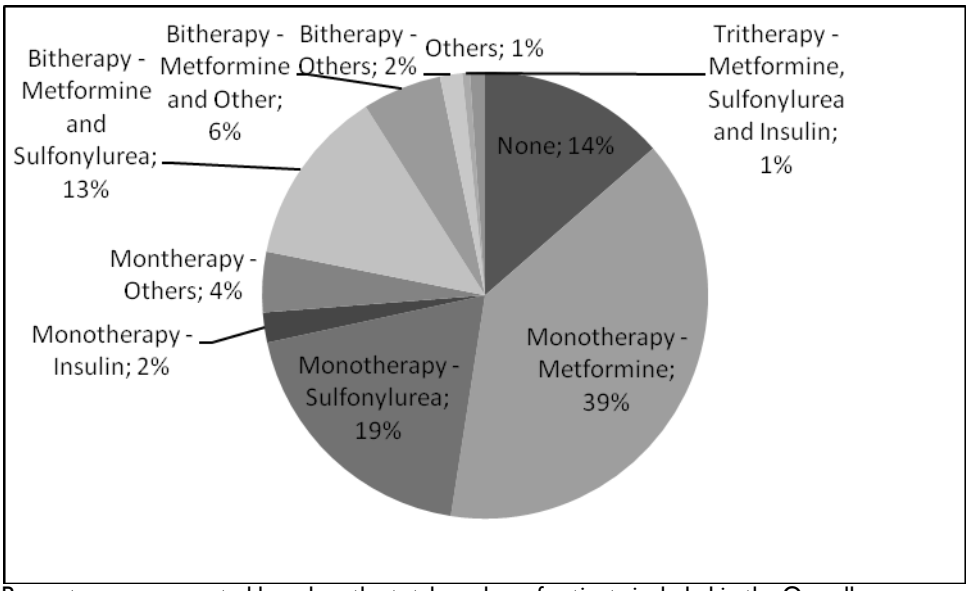
The total of 6 584 patients were included in the population with diabetes medications.

Figure 4. Percentage of patients by type of therapy given before the AD visits – Population of patients who received diabetes medications



Percentage are computed based on the total number of patients included in the Overall Population
(N = 6 584 patients)

Figure 5. Percentage of patients by type of therapy given after the AD visits – Population of patients who received diabetes medications



Percentage are computed based on the total number of patients included in the Overall Population (N = 6 584 patients)

Figure 4 and 5 show the frequency distributions of the different types of therapies delivered, respectively, before and after the AD visits.

Within the period before the AD visit, the majority of the patients had:

- Monotherapy of Metformin (35%)
- Monotherapy of Sufonylurea (19%)
- Bitherapy of Metformin and Sulfonylurea compound (13%)
- Bitherapy of Metformin and Others (7%)
- Monotherapy of Others (5%)

One fifth (18%) of the patients had no data on medications for diabetes available within the 6-months before the AD visits.

There were few changes in the frequency distribution of the type of therapy between before and after the visit of the AD visit. After the AD visit, those proportions were:

- Monotherapy of Metformin (39%)
- Monotherapy of Sufonylurea (19%)
- Bitherapy of Metformin and Sulfonylurea (13%)
- Bitherapy of Metformin and Others (6%)
- Monotherapy of Others (4%)

A proportion of patients (14%) had no data on diabetes medications within the 6-months after the AD visit.

Table16. Number (%) of patient by Active Substance and Period

Level 5 of ATC System (Active Substance)	Before AD Visit N=6 584 n (%)	After AD Visit N=6 584 n (%)
exenatide	1 (0.0%)	5 (0.1%)
glibenclamide	122 (1.9%)	120 (1.8%)
gliclazide	1 158 (17.6%)	1 177 (17.9%)
glimepiride	341 (5.2%)	336 (5.1%)
glipizide	54 (0.8%)	54 (0.8%)
gliquidone	389 (5.9%)	378 (5.7%)
insulin aspart	80 (1.2%)	96 (1.5%)
insulin detemir	1 (0.0%)	4 (0.1%)
insulin glargine	44 (0.7%)	49 (0.7%)
insulin glulisine	1 (0.0%)	5 (0.1%)
insulin lispro	7 (0.1%)	9 (0.1%)
insulin(human)	252 (3.8%)	303 (4.6%)
metformin	3 507 (53.3%)	3 696 (56.1%)
metformin and rosaglitazone	6 (0.1%)	7 (0.1%)
metformin and sulfonamides	217 (3.3%)	227 (3.4%)
pioglitazone	15 (0.2%)	13 (0.2%)
repaglinide	523 (7.9%)	481 (7.3%)
rosiglitazone	192 (2.9%)	185 (2.8%)
sitagliptin	12 (0.2%)	11 (0.2%)
None	1 193 (18.1%)	894 (13.6%)

% are based on the total number of patients (N) included in the Overall Population (N = 6 584 patients)

Table 16 reports the medications included in the therapy considered for the analyses and the number (%) of patients taking at least this active substance (identified as the level 5 of the ATC system) and period. Patients with a combination of several medications referenced under the same active substance (i.e. same level 5 in the ATC system) are counted, in the table, as one patient taking at least this active substance but patients taking a combination of several medications with different active substances are counted as one patient in each of the different active substances group.

As examples:

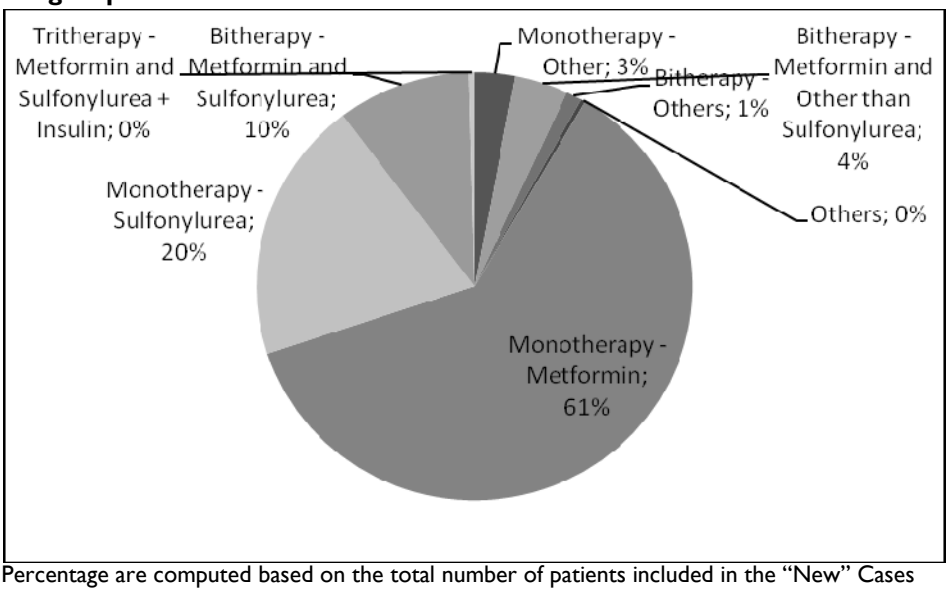
- Case 1: Patient taking Metformin TEVA (active substance – Metformin) and Metformax Forte (active substance – Metformin) is counted as a patient taking at least one medication of Metformin, as both medications have the same active substance – the Metformin.
- Case 2: Patient taking Metformin TEVA (active substance – Metformin) and Diamicron (active substance – Gliclazide) in his therapy is counted once under the active substance Metfomine and once under the active substance Gliclazide.

The majority of the patients had a therapy including at least Metformin (before and after the AD visit) and around one fifth of the patients had a therapy including at least one medication with gliclazide (before and after the AD visit).

"New" Cases Subgroup

A total of 1 193 patients had no data on delivery of any medication from the list (see section 4.2.1) within the 6-months period before the AD visit but had data available on medications for diabetes after the AD visit. Those patients are included in the "New" Cases Subgroup i.e. incident cases. The "New" cases do not only include newly diagnosed diabetic patients, this population might also include some diabetic patients without available pharmacy data in the 6-months period before the AD visit or other special cases that will be described in the discussion.

Figure 6: Percentage of Patients by Type of Therapy – "New" Cases Subgroup



Percentage are computed based on the total number of patients included in the "New" Cases subgroup (N = 1 193 patients)

Figure 6 presents the frequency distribution of the patients in the different types of therapies.

- Monotherapy of metformin (61% of patients);
- Monotherapy of sulfonylurea compound (20%);
- Bitherapy of metformin and sulfonylurea compound (10%);
- Other types of therapies were taken by less than 4% of patients.

Table 17. Number (%) of Patients by Type of Therapy After the AD Visit and recommendation of AD visitor – "New" Cases Subgroup

Recommended by Farmaka	Type of Therapy after the AD Visit	N = 1 193 n (%)
Yes	Monotherapy - Metformin	733 (61.4%)
	Monotherapy - Sulfonylurea compound	236 (19.8%)
	Bitherapy - Metformin and Sulfonylurea compound	118 (9.9%)
	Tritherapy - Metformin and Sulfonylurea compound + Insulin	5 (0.4%)
No	Monotherapy - Other	36 (3.0%)
	Bitherapy - Metformin and Other than Sulfonylurea compound	47 (3.9%)
	Bitherapy - Others	14 (1.2%)
	Others	4 (0.3%)

Percentage are computed on the total number of patients included in the "New" Cases Subgroup (N = 1 193 patients)

Table 17 presents the number (%) of patients included in each therapy according to the recommendations of Farmaka (see section 4.1.2.1). The recommended monotherapies were prescribed to 969 (81%) patients included in the "New" Cases Subgroup. This figure is similar to the prevalence of "recommended treatments" before the AD visit in the group of "completed" cases who already have a medication before the visit (see below).

"Complete" Cases Subgroup

A total of 4 497 patients with data on medications for diabetes available within the 6-months before and within the 6-months after the AD visit are included in the "Complete" Cases Subgroup, i.e. prevalent cases.

Table18. Number (%) of Patients by Type of Therapy Before and After the AD Visit – "Complete" Cases Subgroup

	After AD visit							
Before AD Visit	**Monotherapy Metformin**	**Monotherapy Sulfonylurea compound**	**Monotherapy (insulin and Other)**	**Bitherapy Metformin Sulfonylurea compound**	**Bitherapy including the Metformin**	**Metformin, Sulfonylurea and Insulin**	**Others**	**Total**
Monotherapy - Metformin	1614	45	53	76	60	2	9	1859
	(35.9%)	(1.0%)	(1.2%)	(1.7%)	(1.3%)	(0.0%)	(0.2%)	(41.3%)
Monotherapy - Sulfonylurea	49	818	20	140	2	2	14	1045
	(1.1%)	(18.2%)	(0.4%)	(3.1%)	(0.0%)	(0.0%)	(0.3%)	(23.2%)
Monotherapy - "Others"	17	3	168	3	39	0	19	249
	(0.4%)	(0.1%)	(3.7%)	(0.1%)	(0.9%)	(0.0%)	(0.4%)	(5.5%)
Bitherapy - Metformin and Sulfonylurea	73	135	6	492	6	11	10	733
	(1.6%)	(3.0%)	(0.1%)	(10.9%)	(0.1%)	(0.2%)	(0.2%)	(16.3%)
Bitherapy including the Metformin	70	2	107	0	207	1	14	401
	(1.6%)	(0.0%)	(2.4%)	(0.0%)	(4.6%)	(0.0%)	(0.3%)	(8.9%)
Metformin, Sulfonylurea compound and Insulin	2	2	7	7	1	11	6	36
	(0.0%)	(0.0%)	(0.2%)	(0.2%)	(0.0%)	(0.2%)	(0.1%)	(0.8%)
Others	2	19	34	11	16	4	88	174
	(0.0%)	(0.4%)	(0.8%)	(0.2%)	(0.4%)	(0.1%)	(2.0%)	(3.9%)
Total	1827	1024	395	729	331	31	160	4497
	(40.6%)	(22.8%)	(8.8%)	(16.2%)	(7.4%)	(0.7%)	(3.6%)	

Table 18 is a cross-table between the type of therapy taken before and the type of therapy taken after the AD visit for this subgroup of patients (N=4 497 patients). The results are:

- For 3 379 (75.1%) patients, there was no change of therapy after the AD visit (see figures on the diagonal of table 18);
- For the other patients, most marked changes are:
  - 107 (2.4%) patients changed from a bitherapy including the metformin to a monotherapy of metformin;
  - 140 (3.1%) patients changed from a monotherapy of sulfonylurea compound to a bitherapy of metformin and sulfonylurea compound;
- Other changes occurred for less than 2% of the patients.

The recommendations of Farmaka[10] were mainly :

- **Monotherapy**: either Metformin or Sulfonylurea compound;
- **Bitherapy**: Metformin and Sulfonylurea compound;
- **Tritherapy**: add insulin to Metformin and Sulfonylurea compound.

Table 19 groups the data from table 18 to present the number of patients with therapies in line (or not) with the recommendations of Farmaka.

Table 19. Number (%) of patients by therapy (not) recommended by Farmaka – "Complete" Cases Subgroup

		After AD visit				
Before AD Visit	**Therapy not in recommendations done by Farmaka**		**Therapy recommended by Farmaka**		**Total**	
Therapy not in recommendations by Farmaka	692	(15.4%)	132	(2.9%)	824	(18.3%)
Therapy recommended by Farmaka	194	(4.3%)	3 479	(77.4%)	3 673	(81.7%)
Total	886	(19.7%)	3 611	(80.3%)	4 497	

Percentage are computed on the total number of patients included in the "Complete" Cases Subgroup (N = 4 497 patients)

The majority of the patients (92.8%) did not switch from one group of therapy to another one.

The main results are:

- **Before the AD visits**:
  - a total of 3 673 (82%) patients were already under a therapy included **in the Farmaka recommendations**
  - a total of 824 (18%) patients were under a therapy **not included in the Farmaka recommendations**
- **After the AD visits:**

  Among the patients already under a therapy included **in the Farmaka recommendations** (i.e. 82% of the overall population):
  - 95% of them did not switch of therapy type (i.e. 77% of the overall population);
  - 5% of them switched for a therapy not included in the Farmaka recommendations (i.e. 4% of the overall population).

Among the patients not under a therapy included **in the Farmaka recommendations** (18% of the overall population):

- 84% of them did not switch of therapy type (i.e. 15% of the overall population) ;
- 16% of them switched for a therapy included in the Farmaka recommendations (i.e. 3% of the overall population).

4.3.1.3 Analyses of the Costs

In view of the results on the therapies, most patients did not change the therapy after the AD visit. Therefore, the analyses on the costs were not performed.

4.3.1.4 Comparison with the population of general practitioners in Belgium

The groups of medications investigated in this section were only diabetes medications classified under the Chemical Substance "Blood glucose lowering drugs, excluding insulins" (ATC level 3 = A10B). These groups were defined as follows:

- Metformin → ATC level 4= A10BA
- Sulfonylurea compounds → ATC level 4= A10BB
- Metformin and Sulfonylurea compound → ATC level 5 = A10BD02
- Glitazones → ATC level 4 = A10BG
- Others → ATC level 4 = A10BX or A10BH or Metformin and Rosiglitazone (ATC level 5 = A10BD03)

The following paragraphs compare the prescriptions of the GPs who had an AD visit with the prescriptions of GPs in Belgium; the comparison has been performed on:

- Volume expressed in number of Defined Daily Doses (DDDs) by group of medication(s) and semester over the period 2006 – 2008 (calculated for each GP),
- Proportion (expressed in %) of the prescription volume amongst the total prescription volume of medications classified under Blood glucose lowering drugs, excluding insulins (calculated for each GP). The proportion (in %) of prescriptions of the group of medications is calculated, by GP, as followed:
  - (Volume, in number of DDDs, for the group of medication) divided by (Volume, in number of DDDs, of all medications under the ATC level 3 = A10B) expressed in %.

The tables with all results are presented in Appendix.

Metformin

Overall, from the 1st semester 2006 to the 2nd semester 2008, 17 094 to 17 995 GPs prescribed metformin. The sub-population of GPs visited for diabetes topic was represented by 148 to 155 GPs from 1st semester 2006 to 2nd semester 2008, respectively. It means that the sample of visited GPs represent around 1% of the Overall GPs population

Figure 7 shows the evolution by semester (from 1st semester 2006 to 2nd semester 2008) of the volumes (in terms of number of DDDs) of Metformin. The volumes follow slightly the same evolution over the time in both populations (visited GPs and Overall GPs population).

The "visited" GPs prescribed, in median, more than the overall GPs population. As shown in figure 7, they prescribed, in median, a volume of Metformin of 1992 DDDs over the 1st semester 2006 to 2675 DDDs over the 2nd semester 2008. In the overall GPs group, the GPs prescribed, in median, a volume of Metformin of 915 DDDs over the 1st semester 2006 to a volume of 1065 DDDs over the 2nd semester 2008. Therefore, the "visited" GPs are not representative of the overall GPs population in terms of the volume of prescriptions of Metformin.

Two hypotheses are that

- the overall GPs population includes a heterogeneous population in terms of size of the practice;
- the group of visited GPs agreed about receiving an AD visit that relates to a topic that concerns many of their patients.

Figure 7. Volume (in number of DDDs per GP) of Meformin by semester for the visited GPs and for the overall GPs Population

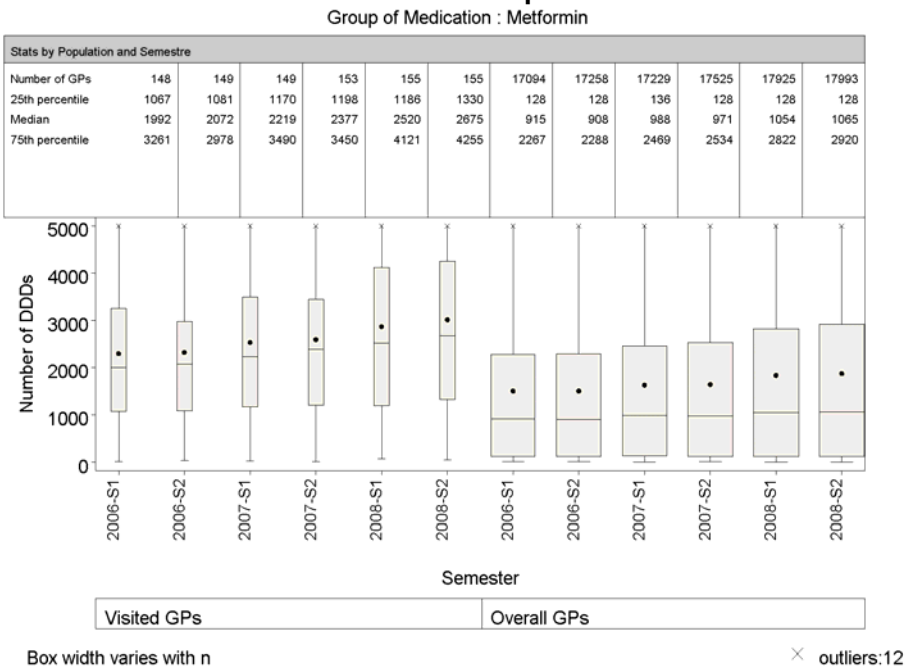
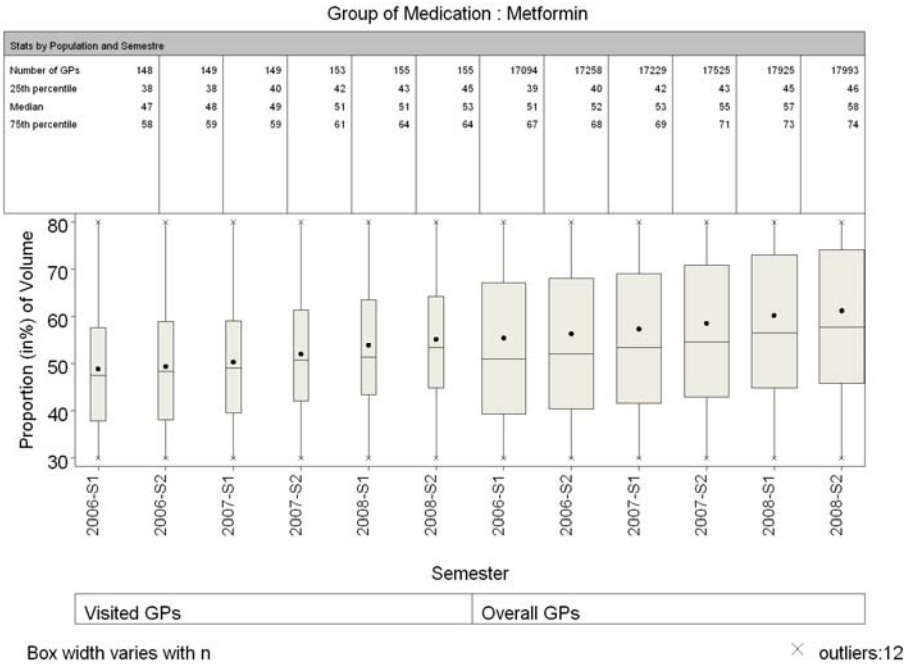


Figure 8 shows the evolution by semester (from 1st semester 2006 to 2nd semester 2008) of the proportion of Metformin over the total volume of diabetes medications, by GP (in DDD). The median volume of Metformin as a % of the total prescription of diabetes medications (excluding insulins) was around 50% for both populations with a slight increase along the time in both groups of GPs. Therefore, the part of the volume of Metformin within the total volume of diabetes medications was similar between the "visited" GPs population and the overall GPs population: that means that the "visited" GPs had similar prescription habits.

The visits of Farmaka visitors occurred between March 2008 and June 2008. Looking specifically at the semester before and after the visit, there was an increase in the median from 50.7% (in 2nd semester 2007) to 53.3% in the 2nd semester 2008 for the "visited" GPs. However, the same trend was observed in the overall GPs population where this median percentage increases from 54.6% to 57.7%.

Figure 8. Proportion (in %) of Meformin prescriptions by semester and Population



Sulfonylurea compounds

Overall, 15 648 to 15 721 GPs prescribed sulfonylurea compounds from 1st semester 2006 to 2nd semester 2008, respectively. The sub-population of "visited" GPs was represented by 144 to 150 GPs prescribing sulfonylurea compounds from 1st semester 2006 to 2nd semester 2008, respectively.

Figure 9 shows the evolution by semester of the volumes (in terms of number of DDDs per GP) of Sulfonylurea compounds. These volumes slightly follow the same evolution over time in both populations ("visited" GPs and Overall population of GPs).

The "visited" GPs prescribed, in median, more than the overall GPs population (for the 1st semester 2006, the median number of DDDs per GP was of 1423 DDDs for the group of visited GPs and 723 DDDs for the overall GPs population). As previously discussed for the Metformin, the GPs visited by Farmaka visitors are not representative of the overall GPs population for the volume of prescriptions.

Figure 9. Volume (in number of DDDs per GP) of Sulfonylurea compounds by semester and for both GP populations ("visited" and "overall")

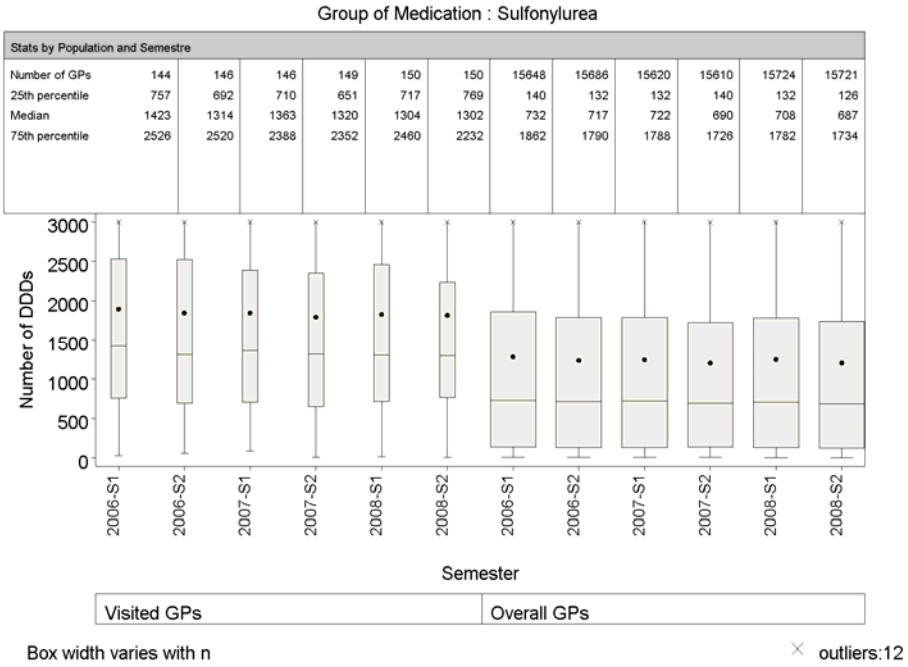
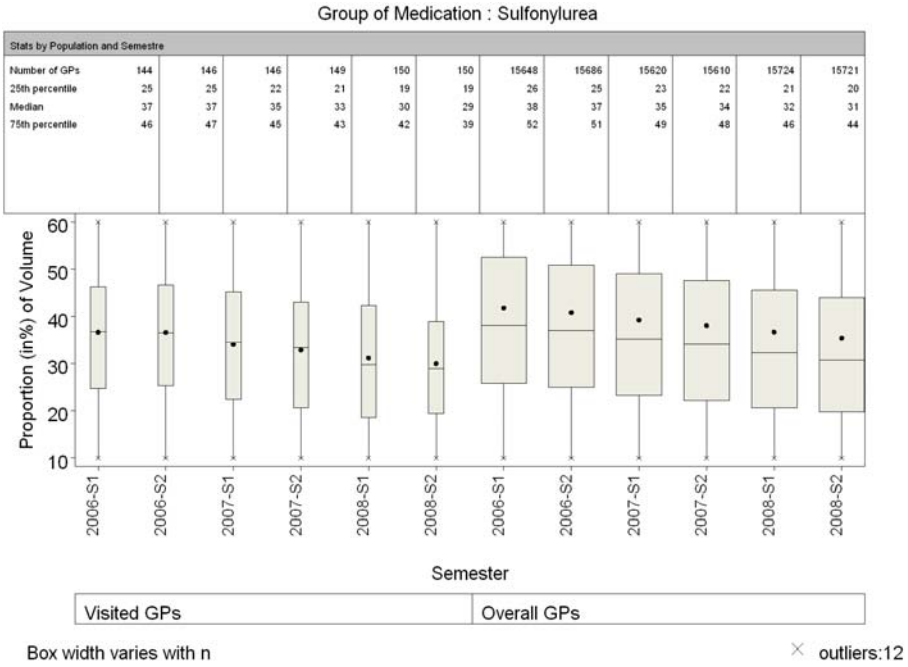


Figure 10 shows the evolution by semester of the proportion of Sulfonylurea compounds among the total volume of diabetes medications, by GP. The median volume of Sulfonylurea compounds as a % of total prescription of diabetes medications (excluding insulins) was around 37% for both populations with a slight decrease over time in both groups of GPs. Therefore, the repartition of the volume of sulfonylurea compounds among the total volume of anti-diabetic medication was similar between the "visited" GPs population and the overall GPs population meaning that the "visited" GPs had similar behaviour of prescriptions

The visits of Farmaka visitors were performed between March 2008 and June 2008. Therefore, looking specifically at the semester before and after the visit, there was a decrease in the median from 33.4% (in 2nd semester 2007) to 28.9% in the 2nd semester 2008. However, the same trend was also observed in the overall GPs population where this median percentage decreases from 34.0% to 30.6%.

Figure 10. Proportion (in %) of Sulfonylurea compounds prescriptions by semester and for both GP populations ("visited" and "overall")



Combination of Metformin & Sulfonylurea compounds

Overall, 5 189 to 5 357 GPs prescribed medications combining Metformin and Sulfonylurea compounds from 1st semester 2006 to 2nd semester 2008, respectively. The sub-population of "visited" GPs was represented by 64 to 80 GPs prescribing medications of Metformin and Sulfonylurea compounds from 1st semester 2006 to 2nd semester 2008, respectively.

Figure 11 shows the evolution by semester (from 1st semester 2006 to 2nd semester 2008) of the volumes (in terms of number of DDDs per GP) of medications of Metformin and Sulfonylurea compounds. The volumes follow slightly the same evolution over the time in both Population (Visited GPs and Overall GPs). The GPs included in the group of GPs visited by a Farmaka visitor prescribed, in median, the same volumes than the overall GPs population.

Figure 11. Volume (in number of DDDs per GP) of medications of Metformin and Sulfonylurea compounds by semester and for both GP populations ("visited" and "overall")

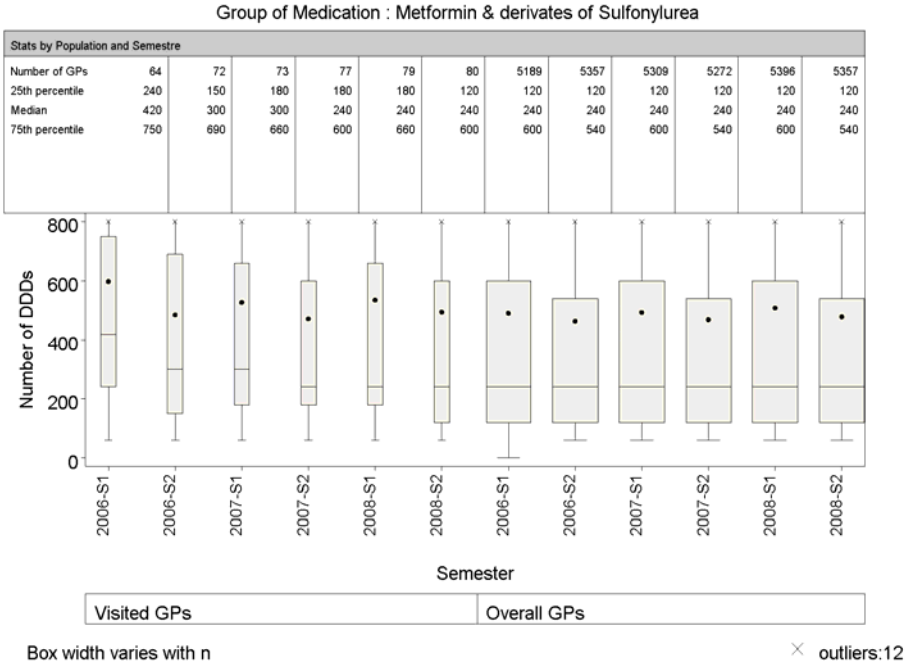
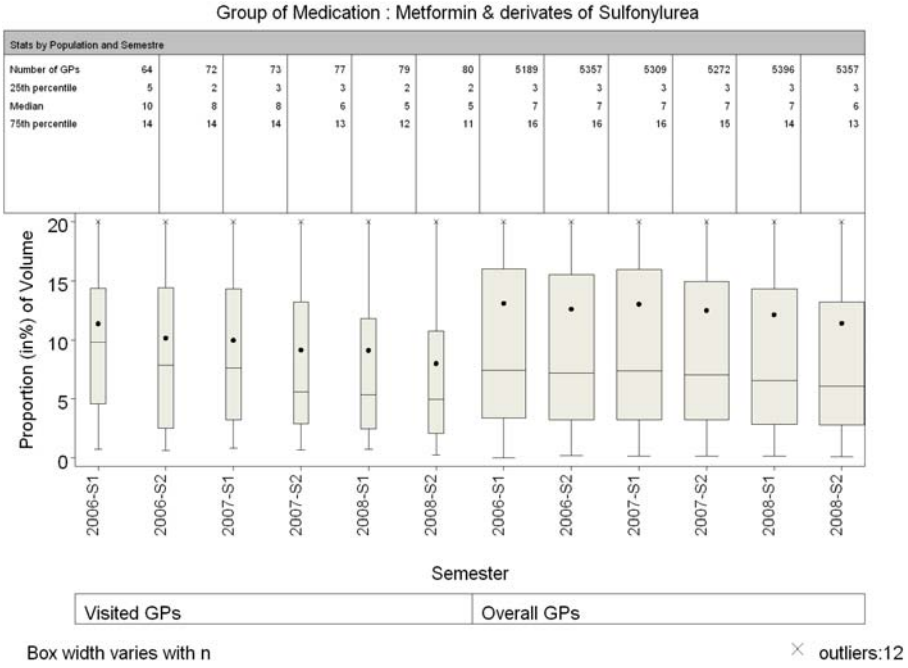


Figure 12 shows the evolution by semester (from 1st semester 2006 to 2nd semester 2008) of the proportion of medications with Metformin & Sulfonylurea compounds within the total volume of diabetes medications, by GP. The median volume of these drugs as a % of total prescription of diabetes medications (excluding insulins) was around 7% for both populations with a slight decrease over time in both groups of GPs.

The visits of Farmaka visitors were performed between March 2008 and June 2008. Therefore, looking specifically at the semester before and after the visit, there was a decrease in the median from 5.6% (in 2nd semester 2007) to 5.0% in the 2nd semester 2008. However, the same trend was also observed in the overall GPs population where this median percentage decreases from 7.0% to 6.1%.

Figure 12. Proportion (in %) of medications of Metformin and Sulfonylurea compounds prescriptions by semester and for both GP populations ("visited" and "overall")

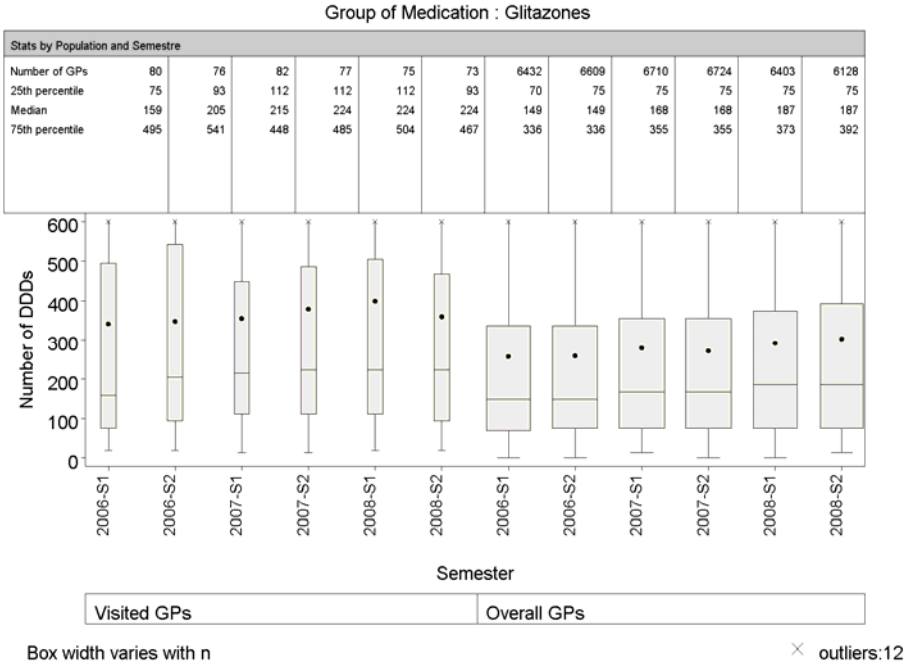


Glitazones

Overall, 6 432 to 6 128 GPs prescribed medications of Glitazones from 1st semester 2006 to 2nd semester 2008, respectively. The sub-population of "visited" GPs was represented by 80 to 73 GPs prescribing medications of Metformin and Sulfonylurea compounds from 1st semester 2006 to 2nd semester 2008, respectively. It means that the sample of visited GPs represent around 1% of the Overall GPs population.

The volumes of Glitazones prescribed by GP were very low in both populations. The median volume per GP was around 150 DDDs as presented in figure 13.

Figure 13. Volume (in number of DDDs per GP) of medications of Glitazones by semester and for both GP populations ("visited" and "overall")



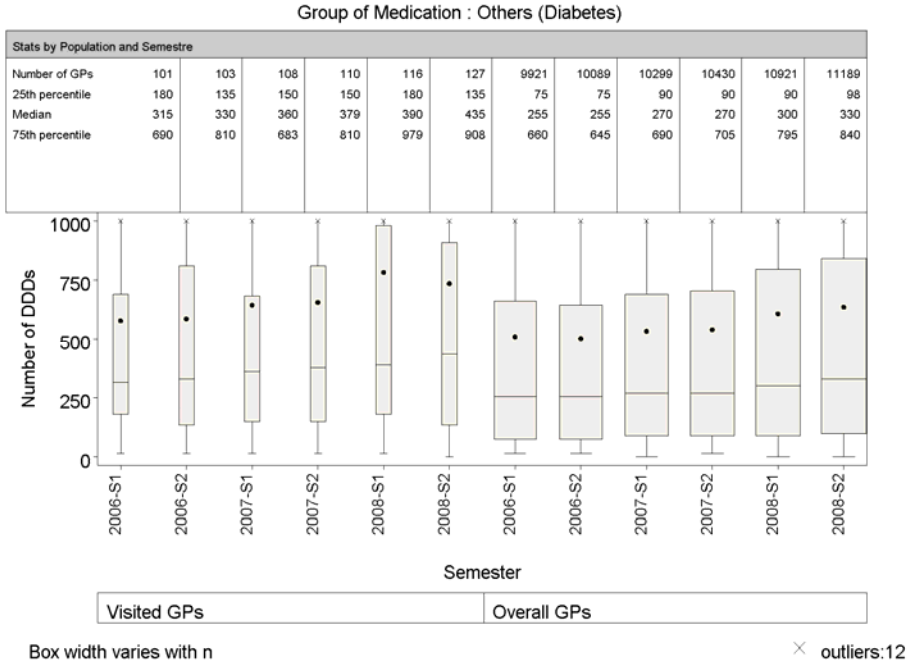
The proportion (in %) of the prescriptions of Glitazones was, in median, around 4% of the total volume of medications classified under the Chemical Substance "Blood glucose lowering drugs, excluding insulins" (see appendix for more details).

Other Medications

The group of other medications contains the medications of Metformin & Rosiglitazones and the medications classified under the ATC level 3 = A10BX or A10BH. Overall, 9921 to 11 189 GPs prescribed these medications from 1st semester 2006 to 2nd semester 2008, respectively. The sub-population of "visited" GPs was represented by 101 to 127 GPs prescribing these medications from 1st semester 2006 to 2nd semester 2008, respectively.

The evolution of the Volume of those medications per GP is shown in figure 14. As described for the other group of medications, the "visited" GPs population are, in median, slowly above the overall GP population in term of Volume of prescriptions per GP.

Figure 14. Volume (in number of DDDs per GP) of Other medications by semester and for both GP populations ("visited" and "overall")



4.3.2 Dementia

The AD visits for Dementia started in October 2006 and ended in February 2007. The analyses below included all the data from IMA/AIM database following the rules described in section 4.2.4.

An important limitation was here that no mortality data was available and therefore all results should be taken with caution.

4.3.2.1 Population

The 117 GPs who received an AD visit had a total of 543 patients considered for the analyses of dementia therapy. Only patients using at least one medication in the class of dementia medications (level 3 of ATC system = N06D) were selected for the analyses (as mentioned in section 4.2.4.3).

The mean age of the patients was of 82 years (sd =7). The median number of patients by GP (i.e. patients with Alzheimer medications prescribed within the 6-months before or after the AD visit) was 4 patients (Q1 = 2 patients and Q3 = 6 patients).

Table 20. Number (%) of patients who (do not) use Alzheimer therapy and Period – All patients with dementia medications

		After the AD visit	
Before the AD visit	**Use of Alzheimer Therapy**	**No Use of Alzheimer Therapy**	**Total**
Use of Alzheimer Therapy	319 (59%)	97 (18%)	416 (77%)
No Use of Alzheimer Therapy	127 (23%)	0 (0%)	127 (23%)
Total	446 (82%)	97 (18%)	543

Percentage are computed based on the total number of patients included in the Overall Population (N = 543 patients).

Table 20 reports the number of patients by type of therapy (Alzheimer therapy versus No use of Alzheimer therapy (including other therapies or no therapy) by period (N=543).

- a total of 319 (58.7%) patients were under an Alzheimer therapy in both periods;
- a total of 97 (17.9%) patients were under a Alzheimer therapy before the AD visit but not anymore within the 6-months period after the AD visit;
- a total of 127 (23.4%) patients were not under an Alzheimer therapy during the 6-months period before the AD visit but were under an Alzheimer therapy after the AD visit.

4.3.2.2 *Analyses of the therapies*

Overview

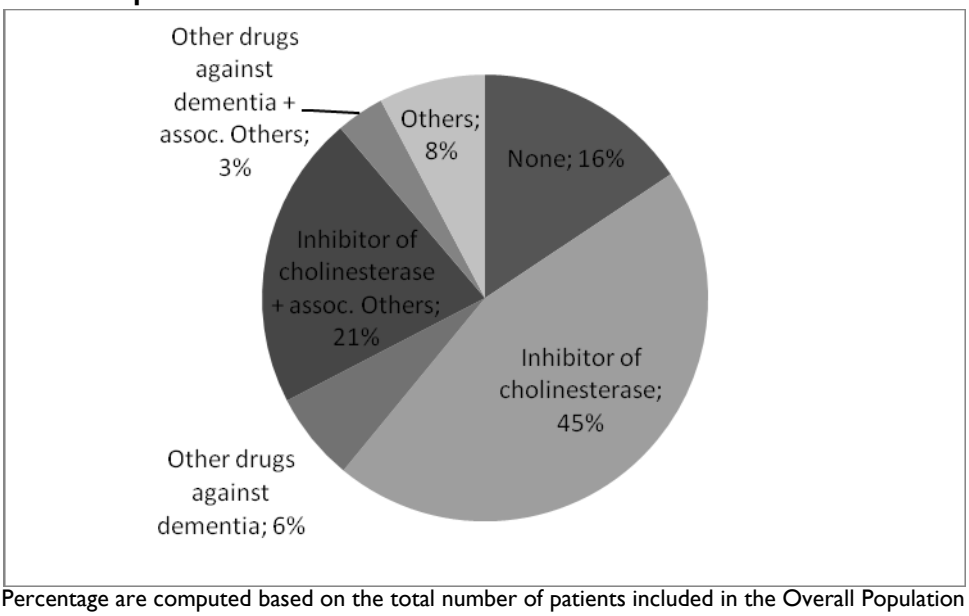
The classification of therapies was done in light with the key message of Farmaka in order to evaluate the impact of the AD visits on the prescription of the GPs:

- Monotherapy of medications in the class of cholinesterase inhibitors (level 4 of ATC system = N06DA);
- Montherapy of medications in the class of other medications for dementia (level 4 of ATC system = N06DX: memantine and Ginkgo Biloba);
- Medications in level 4 of ATC system other than N06DA and N06DX;
- Monotherapy of medications in the class of cholinesterase inhibitors in association with other medications (but not in N06DX);
- Montherapy of medications in the class of other medications for dementia in association with other medications (but not in N06DA).

Overall population of patients with dementia medications

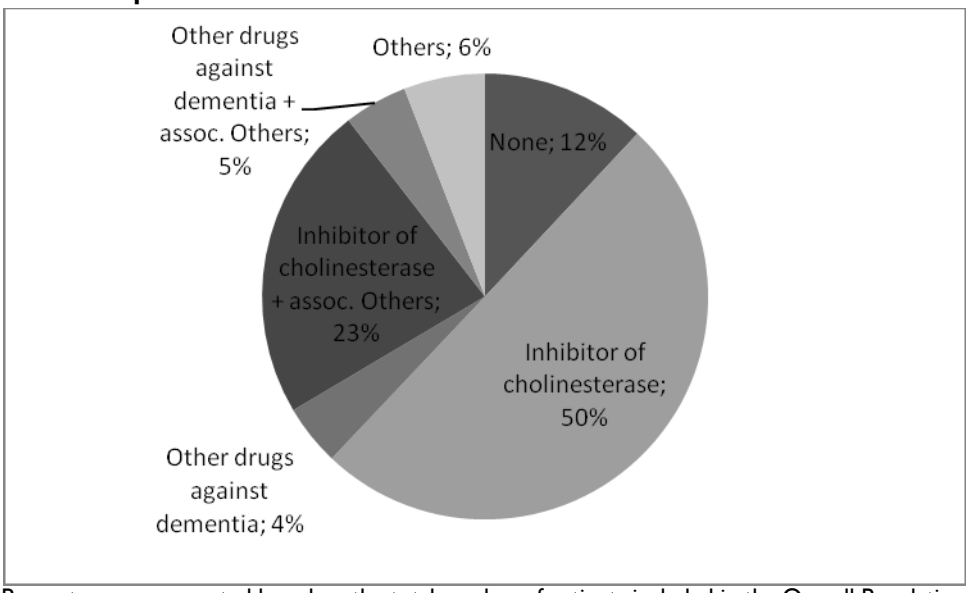
Figures 15 and 16 show the frequency distribution of the different types of therapies delivered respectively just before and just after the AD visit to the GP.

Figure 15. Percentage of patients by type of therapy given before the AD visits – All patients with dementia medications



Percentage are computed based on the total number of patients included in the Overall Population (N = 543 patients).

Figure 16. Percentage of Patients by Type of Therapy given after the AD visits – All patients with dementia medications



Percentage are computed based on the total number of patients included in the Overall Population (N = 543 patients).

The most common therapies were:

- Monotherapy of cholinesterase inhibitor (45% before the AD visit and 50% after the AD visit);
- Association of cholinesterase inhibitor with "other medications" (21% before the AD visit and 23% after the AD visit : "Other medications" refer to the medication(s) included in the list presented in section 4.2.1 except the Alzheimer medications).

Table 21: Number (%) of patients by type of therapy and period – All patients with dementia medications

	Therapy After						
Therapy Before	**None**	**Cholinesterase inhibitor**	**Other medications for dementia**	**Cholinesterase inhibitor + assoc. Others**	**Other medications for dementia + assoc. Others**	**Others**	**Total**
None	0 (0%)	65 (12%)	2 (0%)	16 (3%)	2 (0%)	0 (0%)	85 (16%)
Cholinesterase inhibitor	43 (8%)	158 (29%)	2 (0%)	32 (6%)	0 (0%)	11 (2%)	246 (45%)
Other medications for dementia	8 (1%)	0 (0%)	17 (3%)	0 (0%)	8 (1%)	2 (0%)	35 (6%)
Cholinesterase inhibitor + assoc. Others	11 (2%)	27 (5%)	0 (0%)	61 (11%)	0 (0%)	17 (3%)	116 (21%)
Other medications for dementia + assoc. Others	3 (1%)	0 (0%)	1 (0%)	0 (0%)	13 (2%)	2 (0%)	19 (3%)
Others	0 (0%)	22 (4%)	2 (0%)	16 (3%)	2 (0%)	0 (0%)	42 (8%)
Total	65 (12%)	272 (50%)	24 (4%)	125 (23%)	25 (5%)	32 (6%)	543

Percentage are computed based on the total number of patients included in the Overall Population (N = 543 patients)

Table 21 is a cross-table between the type of therapy taken before and the type of therapy taken after the AD visit (N=543 patients).

The main results are:

- A majority of patients with no change in their therapy (45% of patients);
- 16% of the patients had a "New" dementia therapy after the visit, most of them (12%) received a cholinesterase inhibitor;
- 12% of the patients did not have anymore prescription for dementia medication after the visit;
- Withdrawal of other associated type of medication(s) than Alzheimer medications after the AD visit (6% of patients);
- Addition of Other medication(s) after the AD visit to the cholinesterase inhibitor (6% of patients).

4.3.2.3 *Analyses of the Costs*

In view of the results on the therapies, most of the patients did not change the therapy after the AD visit. Therefore, the analyses on the costs were not performed.

4.3.2.4 *Comparison with all general practitioners*

The groups of medications investigated in this section were all dementia medications classified under the Chemical Substance "Drugs for dementia" (ATC level 3 = N06D) . The different groups were defined as followed:

- Cholinesterase inhibitors → ATC level 4= N06DA
- Memantine and Gingko Biloba → ATC level 4= N06DX

The populations analyzed in this section were:

- "Visited" GPs population = population of GPs with AD visit for Dementia
- Overall GPs population = population of All GPs prescribing in Belgium (including the "visited" GPs)

The comparison between samples was done on:

- Volume expressed in number of Defined Daily Doses (DDDs) by group of medication(s) and semester over the period 2006 – 2008 (calculated for each GP),
- Proportion (expressed in %) of the prescription volume with respect to the total prescription volume of medications classified under Anti-dementia Drugs (calculated for each GP). The proportion (in %) of prescription of the group of medication was calculated, by GP as follows:
  - (Volume, in number of DDDs, for the group of medication) divided by (Volume, in number of DDDs, of all medications under the ATC level 3 = N06D) expressed in %

The tables with all results are in Appendix.

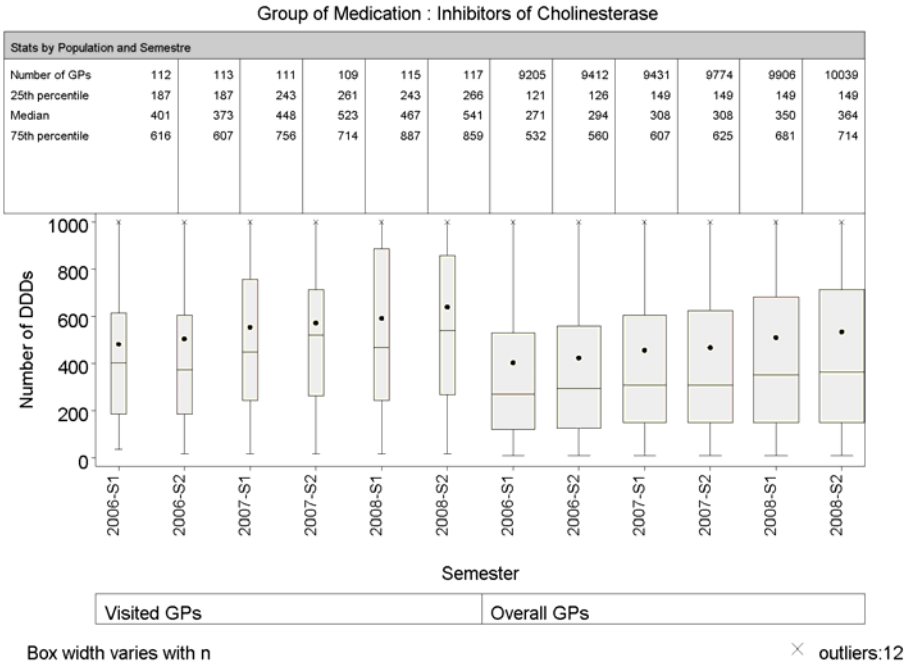
Cholinesterase inhibitors

Overall, 9 205 to 10 039 GPs prescribed Cholinesterase inhibitors from 1st semester 2006 to 2nd semester 2008, respectively. The sub-population of "visited" GPs was represented by 112 to 117 GPs prescribing cholinesterase inhibitors from 1st semester 2006 to 2nd semester 2008, respectively. It means that the sample of visited GPs represent around 1% of the Overall GPs population

Figure 17 shows the evolution by semester (from 1st semester 2006 to 2nd semester 2008) of the volumes (in terms of number of DDDs per GP) of the Cholinesterase inhibitors.

The "visited" GPs prescribed, in median, more than the overall GPs population. As shown in figure 17, this group prescribed, in median, a volume of Cholinesterase inhibitors of 401 DDDs over the 1st semester 2006 to 541 DDDs over the 2nd semester 2008. In the overall GPs group, the GPs prescribed, in median, a volume of Cholinesterase inhibitors of 271 DDDs over the 1st semester 2006 to a volume of 655 DDDs over the 2nd semester 2008. Therefore, the GPs are not representative of the overall GPs population. The hypotheses for explaining this higher prescription volumes are similar to those detailed above i.e., a selection bias towards larger practices with more patients who suffer from the disease presented by the AD visitor.

Figure 17. Volume (in number of DDDs per GP) of Cholinesterase inhibitors by semester and for both GP populations ("visited" and "overall")



The group of cholinesterase inhibitors represented nearly all prescriptions of the medications for dementia. The visits about dementia were performed on the 2nd semester 2006 in Flanders. However, there was no important change and not in the expected direction. The volumes increased in the populations of "visited" GPs and in the overall GP population between the 1st semester 2006 and 1st semester 2007. These analyses can not provide evidence of the impact of AD visit on the prescription.

Memantine and Ginkgo Biloba

The number of GPs prescribing Memantine or Ginkgo Biloba is very small (around 40 GPs in the group of visited GPs and around 3 100 in the overall GPs group). The median volume by GP was around 112 DDDs for both population and each semester. The details are in appendix.

4.4 DISCUSSION: ANALYSIS OF THE GPS' PRESCRIPTIONS

The results do not reflect on the quality of care of this patients' population. They just analysed the concordance between the messages spread by the Farmaka visitors and the prescriptions of the GPs after the visits. These analyses could not demonstrate a clear effect of the AD visit on the prescription behaviour of the GPs for any of the topic under consideration (diabetes and dementia).

There are major limitations in the interpretation of the analyses due to the available data and assumptions.

- Only one fifth of the GPs who received the AD visit gave their consent for this study. The GP sample was heavily biased and, hence, lacked representativity,
- An assumption was that the therapy could be determined based on the medication(s) delivered in the pharmacy on a date which was the closest to the AD visit,
- No diagnostic information available,
- An assumption was that the period considered for the analyses (6-months period) were long enough to capture the required information. There might be cases where the prescription could cover a longer period than the 6-months treatment but this information could not be taken into account in the analyses performed. On the other hand, extending the

study period after 6 months had few chance to capture the real effect of one AD visit,

- The impact of the other pharmaceutical delegates' visit or other sources of information (e.g. guidelines dissemination) could not be quantified and put in perspective with the AD visits,
- Prescriptions might include medications for other persons than the patient him/herself.
- Lack of precision in the link between the available invoice data and dispensed drugs and actual therapeutic regimens (timing, compliance, duration…),
- The compliance (or not) with the recommendations can not be linked with the quality of care as there is no data on the patient's health status.

Specific points linked to the diseases and intervention under study might also induce biases in the interpretation of the results:

- Both diseases under study can also be diagnosed and treated by specialists. In particular, the authorization for the prescription of an Alzheimer medication has to be initiated by a specialist. The GP follows usually the therapy initially prescribed by the specialist. The expected changes after the AD visit on the GP's prescriptions might therefore be very limited.
- In particular, Alzheimer medications might be difficult to stop for the patients and his/her caregivers as they might represent a hope.
- There was no mortality data, a limitation for the interpretation of discontinuing the dementia therapy.
- Recommendations from Farmaka are usually in line with other communication channels, in particular the Folia Farmacotherapeutica. The respective impact of the interventions is not measurable.
- For both topics, the new prescriptions after the AD visit might be for patients who did not need any refill of the medication(s) within the 6-months before the AD visit but needed a refill after the AD visit. This explanation could also explain "new" cases of diabetes taking directly a bitherapy or tritherapy.
- Diabetic patients usually do not stop their treatment. Therefore the patients with no information available after the AD visit are either patients who had enough refill for 6 months or patients who had requested a prescription for another person or patients who did not need any further treatment (e.g. diet).

As stated above, the results of the quantitative analyses could not show any clear evidence of an impact of the AD visit on the prescription.

The comparison with the overall GPs population shows that the group of GPs who accepted the AD visit and gave their consent for this study data was not a sample representative of the overall GPs population. The volumes were in general higher in the population visited. Probably the GPs who gave their consent have more patients with the disease of interest. However, the proportion (in %) of the prescriptions within the class of medications of interest was similar in both populations (visited and overall GP population) and the evolution along the semesters was similar.

5 CONCLUSIONS

This project aimed to analyse the effects of AD on the GPs' practice using three approaches i.e. an analysis of the international literature, interviews of GPs who were contacted to receive an AD visit and an analysis of their prescriptions in the IMA/AIM database. The data do not allow drawing firm conclusions for AD in Belgium but the results give avenues for the future of this initiative.

5.1 LITERATURE FINDINGS: MODERATE EFFECTIVENESS ON THE PRACTICE

The global effect of AD on the practice has been shown in some systematic reviews and in some studies selected for this literature review. A recent Cochrane Collaborative Review on AD[8] estimated a limited effect on the compliance with desired practice of about 5% only with possible publication bias. Some studies analyzed outcomes at the patient level but the results are contradictory. In the same way, the cost-effectiveness of AD interventions is not demonstrated.

The paucity of evidence contrasts with the cost-effectiveness of the commercial detailing financed by the pharmaceutical industry. The most likely hypothesis is the size of the budget invested by private companies in comparison with the budgets mentioned in the Belgian and foreign AD initiatives. Moreover, commercial initiatives that promote new promising molecules are much more attractive than AD messages: these last ones focus on old-fashioned treatments and/or advocate a decrease in the prescriptions.

5.2 EFFECTIVENESS NOT DEMONSTRATED IN THIS STUDY

One objective of this report was to analyse the effect of one AD visit on the prescription behaviour of a sample of GPs in Belgium. The results do not reflect on the quality of care of this patients' population. They just analysed the concordance between the messages spread by the AD visitors and the prescriptions of the GPs after the visits.

This part of the study had serious limitations. First two themes only (out of ten) could be studied i.e. diabetes and dementia, as the related prescriptions were specific and recorded in the IMA/AIM database. The prescriptions for these topics are often (always for dementia) initiated and/or modified during the follow-up by specialist physicians. Secondly, the sample did not allow performing formal testing due to several biases (sample bias, systematic bias, and omitted variable bias) and limitations of the data. The group in charge of AD in Belgium (Farmaka) had a confidential list of all GPs contacted for an AD visit. They contacted themselves the GPs to receive their written consent for this study. Unfortunately, only one fifth of the initial sample of GPs gave their consent to participate. Finally, other limitations were linked to the available data as discussed in the fourth chapter.

In this sample of highly motivated GPs (and for the visit and for this research), for the diabetes topic, most of the patients (81%) who started their diabetes therapy after the AD visit received a monotherapy in accordance with the recommendations of Farmaka. Yet, before the AD visit, a similar proportion (82%) of the patients with therapy before and after the AD visit had a therapy in accordance with the Farmaka recommendation list. Among the patients with a therapy before the AD visit not included in the Farmaka's list of recommended therapies (i.e. 18% of the population), one in six of those patients switched to a therapy within the list (i.e. 3% of the population with therapy before and after the AD visit). On the other hand, among the patients under a recommended regimen before the AD visit, 5% of those patients switched to a therapy not included in the list (i.e. 4% of the total population with therapy before and after the AD visit).

The comparison with the prescriptions of all GPs in Belgium show similar patterns of prescriptions i.e. similar proportions of medications within a group. The GPs who had an AD visit and the overall GP population had a similar evolution of the volumes prescribed across the semesters, independently of the AD intervention (e.g. increase of cholinesterase inhibitors volumes).

These results can be compared with the studies on the same topics in the international literature. None study focused on the prescription of dementia medications. Four studies analysed AD interventions for diabetes. Two of them showed positive results on the process outcomes under study. The two other ones could not demonstrate any affect of AD (except on the satisfaction of the GP) as in this research.

5.3 ACADEMIC DETAILING IN BELGIUM: WHICH WAY FORWARD?

The GPs who accepted to participate to the qualitative study were positive about AD in Belgium, although a proportion of them did not remind its content. They considered that the AD visits had a scientific added value linked to the scientific background of the visitor (even non GP).

The literature and the suggestions of the GPs highlight interesting avenues for the future. They relate e.g. to the choice of the topic, the target population, the way to spread academic detailing.

5.3.1 Choice of topic

The choice of the topics raises the question of the impact of AD among GPs only whilst the decision on treatment might be (for diabetes) or has to be (for dementia) initiated by the specialist. One study showed indeed a difference between the effect of AD on the prescriptions for newly diagnosed patients and the absence of impact for patients who already received medications[33]. The difficulty to convince specialists for EBM oriented treatments is underlined by the GPs in the qualitative study. The effect of AD might be seriously enhanced if the specialists were involved in the same intervention.

The GPs also suggest tailoring the messages according to the GP's preferences: the question is to know if the impact will be greater by answering to the GPs' demands.

5.3.2 Target population of physicians

The literature suggests that AD should specifically target opinion leaders to enhance the dissemination of the key messages. The effect of AD is also more patent when it targets GPs whose knowledge could be best improved.

On the contrary, AD visitors in Belgium focus their efforts towards GPs who live nearby. Moreover, the interviews highlighted a selection bias towards GPs who are already convinced by EBM. They also showed a particular interest from the single handed GPs who appreciate this scientific contact that breaks their isolation. A way forward is certainly to target this population and to decrease efforts towards groups of GPs who have more opportunities to share their experience and knowledge.

5.3.3 Face-to-face or ... ?

The Belgian AD system only relies on face-to-face AD, the most energy consuming method. GPs suggested in the interviews to integrate AD in existing activities i.e. GLEMs/LOKs meetings. In the same way, the GPs suggested online AD. However, AD for groups and on the internet were not included in the literature review and no conclusion can be drawn about their effectiveness. These proposals could be a complementary approach and act as a reinforcement of individual AD.

5.3.4 Background of the visitor

The Belgian initiative began with GP visitors but is moving towards professionals with other academic backgrounds (mostly pharmacists). The international literature shows that visitors are frequently non physicians without any impact on the effectiveness. Moreover, the GPs themselves find that the background of the visitor has little importance if this person thoroughly knows the topic.

5.3.5 Other suggestions from GPs in Belgium

Other suggestions to improve AD in Belgium included the use of other tools to spread the information: however the GPs did not know about the existence of the AD Belgian website.

They also suggested more frequent visits: the AD programme inn Belgium has currently "one shot" visits about one topic and the frequencies vary between GPs.

Finally, they suggested to couple the AD visits with information for patients.

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