

Effectiveness of Academic Detailing to Optimize Medication Prescribing Behaviour of Family Physicians

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ABSTRACT – PURPOSE. To synthesize current knowledge about the effectiveness and the magnitude of the effect, of Academic Detailing (AD), as a stand-alone intervention, at modifying drug prescription behavior of Family Physicians (FPs) in primary care settings. **METHODS.** A search of MEDLINE, EMBASE, CENTRAL, and Web of Science databases of all English language articles between January 1983 and July 2010 was conducted. We hand-searched the bibliographies of articles retrieved from the electronic search to identify additional studies. Inclusion criteria were: full-length articles describing original research; randomized controlled trial (RCT), or observational study design with a control group; studies of AD delivered to FPs; AD as a stand-alone intervention; drug prescription as the target behavior. Data extraction was done independently by two reviewers. Outcomes evaluated were: the difference in relative change in prescription rate between the intervention and control groups; the difference in absolute change in prescription rate between the intervention and control groups; and effect size, calculated as the standardized mean difference. **RESULTS.** 11 RCTs and 4 observational studies were included. Five RCTs described results showing effectiveness, while 2 RCTs reported a positive effect on some of the target drugs. Two observational studies found AD to be effective, while 2 did not. The median difference in relative change among the studies reviewed was 21% (interquartile range 43.75%) for RCTs, and 9% (interquartile range 8.5%) for observational studies. The median effect size among the studies reviewed was - 0.09 (interquartile range 2.73). **CONCLUSION.** This systematic review demonstrates that AD can be effective at optimizing prescription of medications by FPs. Although variable, the magnitude of the effect is moderate in the majority of studies. This systematic review also provides evidence supportive of the use of AD as a strategy to promote evidence based prescription of medications or incorporation of clinical guidelines into clinical practice.

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INTRODUCTION

Gaps between research, policy and practice have been identified globally, with attention focused on making research-based evidence easily available so that it can facilitate change in the behaviours of health practitioners. Clinicians and family physicians (FPs) in particular, are faced with burgeoning scientific literature on a variety of topics, making it difficult to stay up to date. Current evidence suggests that dissemination of research results through peer-reviewed publications alone and conventional continuing medical education (CME) techniques have little effect[1, 2] while interactive techniques, such as

audit/feedback, academic detailing and reminders, have been shown to be effective for changing physician behaviour or healthcare outcomes[3].

Academic detailing (AD), or educational outreach visits, is a form of CME in which a trained health care professional, such as a physician or pharmacist, visits physicians in their offices to provide evidence-based information on a selected topic [4-6]. Some of the important elements of AD are: a) identifying and defining the problem and specific behaviours to be promoted or discouraged;

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b) examining baseline knowledge and motivations for current practice patterns; c) defining clear objectives for behaviour change; d) establishing credibility of the information provided by referencing unbiased information sources; e) providing interactive and short sessions with opportunity for discussion; f) highlighting and reinforcing key messages with concise graphic information; and g) providing positive reinforcement through follow-up visits [4].

Despite originating in 1983 [7], adoption of AD by health policy planners as a health service intervention is fairly new. In Canada, AD was first systematically introduced in Nova Scotia in 2001 [5] and is now implemented in six provinces [8, 9]. Although the effectiveness of AD to influence the knowledge and practice of various health care professionals has been demonstrated in previous reviews [2, 3, 10, 11], its effectiveness as a stand-alone intervention targeted at family physicians (FP) to optimize their medication prescribing behaviour has not been previously evaluated, as far as we know, in a systematic review. Focusing on medication prescription by FPs is particularly important because they are responsible for most medication prescriptions. In Canada, FPs prescribe drugs at about 50% of office visits and are accountable for the majority of the prescriptions dispensed annually [12]. Given rising health care costs, with drugs (prescription and non-prescription) ranking as the second major contributor to healthcare spending [13, 14], facilitating and supporting evidence-based prescribing patterns is very important. To provide a

more focused evaluation of the effectiveness of AD among a select group of professionals, this systematic review aims to synthesise current knowledge about the effectiveness, and the magnitude of the effect of AD as a stand-alone intervention at modifying drug prescription behaviour of FPs.

METHODS

Literature Search Strategy: We conducted a search of MEDLINE, EMBASE, CENTRAL, and Web of Science databases of all English language articles between January 1983 and July 2010. We used terms that mapped to Medical Subject Headings (MeSH) in combination with keyword terms as described in Table 1. We also hand-searched the bibliographies of articles retrieved from the electronic search to identify additional studies.

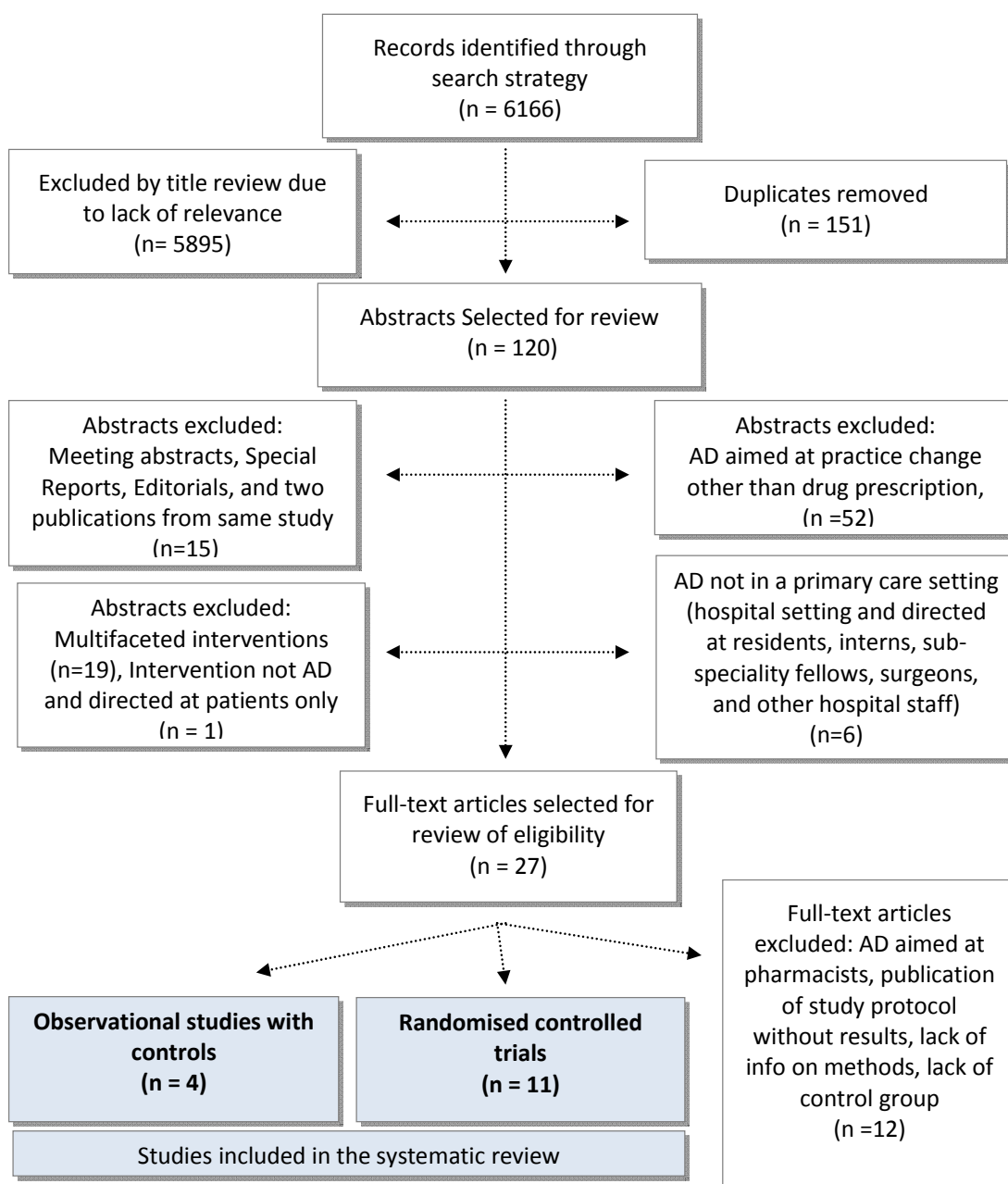
Selection of Studies: Two authors (HC and VB) reviewed all titles and abstracts identified to select studies which met the following inclusion criteria: 1) Full-length articles describing original research; 2) Randomized controlled trial (RCT), or observational studies with a control group; 3) Studies of AD delivered to FPs; 4) AD as the sole intervention; 5) Drug prescription as the target behaviour of AD (Table 2). Figure 1 illustrates the flow of study inclusions/exclusions. The two reviewers also independently reviewed the selected studies for quality assessment and data abstraction. Any discrepancies were discussed and resolved by consensus.

Table 1. Medical Subject Headings (MeSH) terms and keywords used in electronic search strategy

Concept	MeSH Terms	Keywords
Academic Detailing	Education, Medical, Continuing	Academic detailing, academically based detailing, continuing medical education, public interest detailing, educational outreach
Family Physicians	Physician	Physicians, general practitioner, family practice, family doctor, primary health care provider, general practice, primary Health Care
Practice Patterns	Physician practice patterns	Practice pattern, drug prescription, antibiotic prescribing, drug dose calculation

Table 2. Inclusion and exclusion criteria for study selection

	Inclusion Criteria	Exclusion Criteria
Study design	RCT, observational study with control group	Observational study without a control group
Participants	FPs in primary care setting	specialist physicians, other healthcare professionals
Intervention	AD as a single intervention (not as part of a multifaceted intervention)	other CME , educational intervention, multifaceted interventions
Target behavior	Drug prescription	other physician practice pattern

**Figure 1.** Flow Diagram of Studies identified in Systematic Review

Quality Assessment of Studies: Standardized quality assessment forms were developed for the purpose of our study, using the CONSORT (Consolidated Standards of Reporting Trials) statement[15] and EPOC (Cochrane Effective Practice and Organisation of Care group) guidelines for RCTs; and the STROBE (Strengthening the Reporting of Observational studies in Epidemiology) guidelines[16] and Newcastle Ottawa Scale for observational studies[17]. In general, studies were assessed for the quality of the study design, conduct and reporting, using the scoring criteria of: 0 = not done or not reported, 1 = partially done or reported, 2 = well done and clearly reported (Appendix I).

Data Extraction: Descriptive information extracted from each study included: year of publication; country ; study design; objectives; target FP population and sample size, source and period of prescription data (e.g. administrative health data including electronic pharmacy records, survey data); information about the AD visits (type, number, place and whether AD principles were followed); control group description and whether controls received any intervention; profession and training of academic detailer; target drugs; study outcomes assessed, length of follow-up; and effect of the intervention.

Outcome Measurement: The primary outcome, evaluating the magnitude of the effect of AD, was

the difference in relative change in prescription rate between the intervention and control groups (Table 3).

Secondary outcomes included the difference in absolute change in prescription rate between the intervention and control groups. Relative or absolute changes with a positive sign imply that the prescription rate increased following the intervention; whereas a negative sign implies that the prescription rates decreased.

Standardised mean differences (SMD) were also calculated to estimate the effect size, as the difference between group means for the outcome measure divided by the standard deviation of the outcome measure for the study group [18]. A Poisson distribution was assumed in studies where data were not normally distributed or where the outcome was measured as number of events. In studies where data were normally distributed and confidence intervals or Z-values were provided, we used the available p values, Z- values or confidence intervals to calculate the standard deviations for the computation of SMD. An effect size with a negative sign implies a lower prescription rate in the intervention group compared to the control group, which would be a desirable effect in a study trying to decrease prescription rates, and an undesirable effect in a study trying to increase prescription rates.

Table 3. Formulas

	Formula
Relative Change (%)	$\frac{\text{Rate of prescription post intervention} - \text{Rate of prescription pre intervention}}{\text{Rate of prescription pre intervention}} \times 100$
Difference in Relative Change	$\text{Relative Change}_{\text{AD}} - \text{Relative Change}_{\text{Control}}$
Absolute Change	$\text{Rate of prescription post intervention} - \text{Rate of prescription pre intervention}$
Difference in Absolute Change	$\text{Absolute Change}_{\text{AD}} - \text{Absolute Change}_{\text{Control}}$
Standardised Mean Difference	$\frac{\text{Difference between group means for outcome measure}}{\text{Standard deviation of outcome measure for study group}}$

Due to heterogeneous and limited data availability, effect size could not be calculated in a homogenous way across studies; hence, a meta-analysis could not be performed.

RESULTS

Study Selection: The literature search yielded 6,166 citations, of which 120 were retained for abstract reviews, and 27 full article reviews (Figure 1). Twelve studies were excluded for the following reasons: intervention targeted at pharmacists, study protocol without results or incomplete methods description, or observational study design without a control group. The systematic review includes 15 studies: 11 RCTs and 4 observational studies [7, 19-32].

Description of Studies: Randomized controlled trials (RCTs): The RCTs were generally of high quality, with quality assessment scores varying from 38 to 51 out of maximum possible score of 53 (median = 48). Five of the 11 RCTs described results showing effectiveness, i.e. achieving a change in the direction recommended by the AD intervention. Two RCTs reported a positive effect on some but not all the target drugs, while 4 RCTs reported no effect from the AD intervention (Tables 4 and 6). Two RCTs evaluated AD aimed at increasing prescription of the target medication.

Neither study reported a statistically significant effect for the intervention[25, 33]. Five RCTs aimed at decreasing medication prescription. Of these, two studies showed a statistically significant effect for all[7, 34], and one study for some [29], of the target medications. Four studies evaluated AD aimed at increasing the prescription of some medications while decreasing others. Of these, two showed statistically significant effects for all [26, 35] and one study for some of the target medications[24].

Avorn et al. assessed the effectiveness of AD at decreasing the use of cerebral and peripheral vasodilators, an oral cephalosporin (Cephalexin) and propoxyphene [7]. They compared the mean number of drug units prescribed per physician over a one year period before and after the intervention in groups who received AD and controls receiving no intervention. AD was effective at reducing prescription of all target drug types (the authors report a between group mean difference of 782 units for all three drugs combined, $p < 0.0001$). We

calculated a difference of -14% in relative change between AD and controls; and an effect size of -7.8.

De Burgh et al. evaluated the effect of AD on reducing benzodiazepines (BDZ) prescriptions for insomnia and anxiety[22] by comparing the rate of BDZ prescriptions per 100 patient encounters with diagnoses of anxiety or insomnia. The overall rate of BDZ prescriptions decreased by 23.7% between pre and post- intervention surveys ($p < 0.001$) in the entire study sample, but no statistically significant differences were observed between AD and controls ($p = 0.2$) in overall BDZ prescription rates or in prescription of BDZ for either anxiety or insomnia. We calculated a difference in relative change of -7% and -3%, respectively, for anxiety and insomnia. Effect size could not be calculated.

Zwar et al. [23] evaluated the effectiveness of AD at decreasing repeat prescriptions of BDZ. They measured BDZ prescriptions per 100 patient encounters, for all indications, sleep problems and anxiety in the intervention group and a control group receiving AD on an unrelated topic. A decrease in BDZ prescription rates post intervention was observed in both groups, for all indications [$p = 0.042$]; but no statistically significant differences were detected between groups for sleep problems or anxiety. We calculated a difference in relative change between AD and control groups of +10%, -2% and -22%; and effect sizes of +0.42, -0.08 and -0.529, for BDZ prescriptions for all indications, sleep problems, and anxiety, respectively.

Ilett et al. [24] evaluated the effectiveness of AD at modifying antibiotic prescriptions for upper and lower respiratory tract infections, otitis media, and urinary infections. They compared the total number of prescriptions in the AD and control groups over a three month period pre and post intervention. An overall increase in all antibiotic prescriptions was observed from pre to post intervention. However, the increase in prescription of two of the recommended drugs, doxycycline and amoxicillin 250 mg, was greater in the AD than control group (median number of prescriptions per FP increasing from 1 to 6 in AD vs. 1 to 2 in controls for doxycycline, $p = 0.001$; and from 3 to 6 in AD vs. 4.5 to 7.5 in controls for amoxicillin, $p = 0.03$ respectively. Furthermore, the increase in non-recommended drugs, Cefaclor and Roxithromycin, was less in the AD than control group (from 5.5 to 7.5 in AD vs. 5.5 to 10 in controls, $p = 0.03$ for Cefaclor, from 8.5 to 11.5 in AD vs. 12 to 18.5 in controls, $p = 0.03$ for Roxithromycin). We

calculated a difference in relative change of +59% and -74%; and a combined effect size of -0.51 and +2.02, for the eight recommended and two non-recommended antibiotics, respectively.

Ray et al. [34] evaluated the effectiveness of AD at decreasing the use of NSAIDs for osteoarthritis in elderly patients. The estimated intervention effect was an absolute reduction in mean duration of NSAID use of 21.3 days (95% CI, 10.2 to 32.4) and a relative reduction of 7% (95% CI, 3% to 11%). We calculated an effect size of -3.76.

Hall et al. [25] evaluated the effectiveness of AD at increasing the use of omeprazole and metronidazole for the management of *H. pylori*. There was a non-significant change in prescribing of -0.02 (95% CI: -0.12 to +0.08) for Omeprazole and -0.005 (95% CI: -0.025 to 0.015) for Metronidazole. We calculated a difference in relative change of -9% and -5%, and effect sizes of -0.4 and -0.5, for omeprazole and metronidazole, respectively.

Van Eijk et al. [26] evaluated the effectiveness of AD at reducing the prescription of highly anticholinergic antidepressants for elderly people. Intent to treat analysis revealed a reduction in the rate of highly anticholinergic antidepressants in elderly people of 26% (95% CI: -4 to 48%) in the individual AD arm and of 45% (95% CI: 8 to 67%) in the group AD arm, compared with controls. The use of less anticholinergic antidepressants increased by 40% (95% CI: 6 to 83 %) in the individual AD and by 29% (95% CI: -7 to 79 %) in the group AD, compared to controls. We calculated a difference in relative change of -47% and +68%, for highly anticholinergic and less anticholinergic antidepressants, respectively, with individual AD of -59% and +39%, respectively, with group AD.

Bernal-Delgado et al. [35] evaluated the effect of AD on increasing prescriptions of Diclofenac and Piroxicam, while decreasing prescriptions of Aceclofenac, Meloxicam, and Tenoxicam for osteoarthritis. The intervention led to reduced use of non-recommended drugs. Relative reductions of 25.5% in AD vs. 1.2% in controls were observed for Meloxicam; and relative reductions of 22.6% in AD vs. 14.4% in controls for Tenoxicam. We calculated a difference in relative change of +7.49% and +9.71%; and effect sizes of +1.97 and +2.01 for the two recommended NSAIDs, and differences in relative changes of -6.49%, -24.31% and

-37.03%; and effect sizes of -1.28, -2.63 and -8.25 for the three non-recommended NSAIDs.

Witt et al. [28] examined the effect of AD on increasing prescription of inhaled steroids and decreasing inhaled beta-2-agonists in children, as recommended in clinical guidelines for asthma. No significant short term ($p = 0.10$) or long term ($p = 0.72$) effects of the intervention were detected for either medication. We calculated a difference in relative change of +7% and -2%; and effect sizes of -0.09 and +0.18 for inhaled steroids and beta-agonists, respectively.

Midlov et al. [29] evaluated the effect of AD on reducing prescription of BDZ and antipsychotic drugs in the elderly. They measured daily defined doses (DDD) dispensed over three month periods for one year after the intervention, and calculated the percent difference in the geometric mean at one year compared to baseline. There was a statistically significant reduction in prescription of medium and long acting BDZs, with a difference in relative change of -26.63% (95% CI: -0.03 to -46.15, $p < 0.05$) and total BDZs (-25.8%, 95% CI to -1.32; -44.20, $p < 0.05$). No statistically significant difference was observed for antipsychotic drugs.

Simon et al. [30] evaluated the effectiveness of group and individual AD compared to a control group receiving printed guidelines by mail at increasing use of diuretics and beta blockers for hypertension, to improve adherence to hypertension guidelines. The percentage of new hypertension patients receiving a diuretic or beta-blocker in the first year after the intervention increased by 13% in group AD practices, 12.5% in individual detailing practices and 6.2% in controls. Two years following the intervention, a persistent effect of individual AD was seen, although it was not statistically significant (OR, 1.22; 95% CI, 0.92 to 1.62) but there was no longer any effect for group detailing (OR, 1.06; 95% CI, 0.80 to 1.39). We calculated a difference in relative change of +10.9% between the individual AD and control group, and a difference of +14.7% between the group AD and control group.

Observational studies: Four observational studies were included (Table 5). All evaluated AD aimed at decreasing prescription of a target drug [20, 21, 31, 32]. Of these, 2 found AD to be effective [20, 21], while 2 did not [31, 32]. Quality assessment scores varied from 36 to 44 out of a possible maximum score of 47 (median score = 41.5).

Atkin et al. [31] studied the effect of AD on reducing the number of concurrent medications taken by the elderly patients. No differences were found between the groups ($p = 0.19$); a reduction in concurrent medication prescriptions was observed in the entire sample over the study period ($p < 0.02$), perhaps due to the introduction of copayment as a new health policy over the same period. We calculated a difference in relative change of -9% and an effect size of -0.81.

Peterson et al. [21] examined the effectiveness of AD at encouraging the use of Paracetamol (PCM) instead of NSAIDs as first line treatment for rheumatic diseases in elderly patients. Changes in daily defined doses of NSAIDs relative to PCM were evaluated. A reduction was observed in both control and intervention regions, with a significantly greater reduction within the intervention than the control region ($p < 0.0001$). We calculated a difference in relative change of -6% and an effect size of -5.24.

Tomson et al. [32] assessed the effect of AD on reducing inhaled beta agonists and increasing inhaled steroids for asthma. The ratio of prescribed daily defined doses of inhaled beta agonists to inhaled steroids decreased significantly after the intervention in the AD area ($p = 0.001$) while there was no significant change in the control area ($p = 0.1$), but the difference between the two areas was not statistically significant (p value not provided), possibly due to lack of power (number of health centers in the control area = 26).

Graham et al. [20] evaluated the effect of AD on reducing the prescription of selective cyclooxygenase-2 inhibitors (COX-2) anti-inflammatory medications in patients with osteoarthritis. The decrease in COX-2 prescriptions over the first 3 months post intervention was greater in the AD than in the control group ($p = 0.04$). The effect was not sustained at 12 months ($p = 0.398$), however 3 months was the primary end point of the study. We calculated a difference in relative change of -23% and an effect size of -0.09.

DISCUSSION

To our knowledge, this is the first systematic review specifically examining the effectiveness of AD as a stand-alone intervention to optimize the prescription behaviour of FPs. This systematic review confirmed the effectiveness of AD, with 60% of the studies reviewed showing a statistically

significant change and in the desired direction in the prescription behaviour of FPs. Our study results support the use of AD as a strategy to promote incorporation of research findings into clinical practice or to improve compliance with clinical guidelines.

The magnitude of the effectiveness of AD varied widely across studies. Lack of relevant data prohibited calculation of measures of variability associated with the difference in relative change. Thus we could not calculate a pooled estimate of the difference in relative change from the individual studies. The median between group differences in relative change among the studies reviewed was 21% (interquartile range 43.75%) for RCTs, and 9% (interquartile range 8.5%) for observational studies (Table 4).

The heterogeneity in method used to calculate effect sizes made it impossible to perform a meta-analysis and pool the effect size results across the studies and limited our ability to compare individual effect sizes across studies. Nonetheless, the median effect size among the studies reviewed was - 0.09 (interquartile range 2.73) (Table 6), which represents a substantive effect size. Using Cohen's criteria for effect sizes [18] in the 7 studies evaluating 11 medications where effect sizes were calculated and were positive (i.e. in the direction of the recommended change), 8 effect sizes were large, 1 was medium, and 2 were small. There are limitations to the interpretation of the effect sizes we calculated. Cohen's rule is a general rule that is used in the event of unavailability of specific criteria for clinical relevance in research results [18, 36]. We used a Poisson assumption to calculate effect size, when data were not normally distributed, which can lead to overestimation, especially when large effect sizes are found. However, even small effects on inappropriate prescribing may be clinically important when they affect a large number of patients or a clinically important health outcome [37]. Finally it was difficult for us to compare effect sizes based on normal and non-normal distributions [38].

Our systematic review supports the use of AD as a strategy to optimize prescribing behaviour in a variety of contexts. Specifically, AD has been effective at reducing or increasing prescription of medications according to recommendations. The most frequent rationale for the recommended prescription change was to reduce the risk of side-effects (67% of the studies), followed by improving

cost-effectiveness (20% of the studies). Less frequently, AD was used to promote implementation of clinical guidelines (13% of studies). The rationale for the prescription change advocated in the AD intervention did not appear to influence the results of the studies, although the small number of studies evaluated did not allow this to be evaluated formally with regression analysis.

Our results complement information from other reviews [2, 3, 10, 11] that have synthesized data on the effectiveness of AD in different clinical contexts, including a previous Cochrane review [11]. The Cochrane review, published in 2007 [11] included RCTs evaluating the effect of AD aimed at improving clinical behaviours of a range of health care professionals (GPs, pharmacists, counter attendants, nurses, residents, dentists, etc). The authors found that AD, with or without the addition of other interventions, can be effective at improving the practice of health care professionals, but the effect is variable. For studies where the health care outcome was measured as a dichotomous variable representing compliance with a recommended behaviour, effect was measured as the between-group difference in improvement in compliance with the desired behaviour [11]. They found greater improvement in compliance in the AD than control groups receiving no intervention, with a median difference of 5.0% (inter-quartile range 3.2%) between groups. For studies where the health care outcome was a continuous variable, the relative percentage change attributable to the intervention was measured, and found a median value of 23% (inter-quartile range 27%). The effect specifically on prescribing behaviour was only evaluated in studies looking at multifaceted interventions, of which AD was one component; therefore, the effect attributable to AD could not be evaluated. They found that the improvement in compliance with desired prescription behaviour was superior in the intervention groups with a median between group difference of 4.8% (inter-quartile range 3.5%).

Another systematic review by Grimshaw et al. [10] evaluated various guideline dissemination and implementation strategies, including the use of AD as part of multifaceted educational interventions. This review, similar to the Cochrane review [11] did not focus specifically on FPs and does not provide evidence about the effectiveness of AD as a stand-alone intervention. For studies measuring the process of care using a dichotomous outcome measure, the performance of care (measured as the

proportion of people who received appropriate treatment) post intervention was better in the intervention group, with a median absolute difference between intervention and control group of 6% (minimum to maximum: -4.0 to +17.4 %) for RCTs and 7.3 % for observational studies (minimum to maximum: -5.6 to 16.4 %). For studies measuring the process of care using a continuous outcome variable, the median relative difference between groups in post intervention performance was 15% (minimum to maximum: 1.7% to 24%) for RCTs and 11.3% for the single observational study. Although direct comparison of our results with those of previous systematic reviews is not possible due to differences in the interventions compared and in the outcomes used to measure effectiveness, results are consistent in confirming the effectiveness of using AD for health care practitioners, with effects of at least moderate magnitude.

To evaluate the magnitude of the effect of the AD interventions, we chose to calculate and report between-group differences in relative change from baseline as the primary outcome, and between-group differences in absolute change from baseline and effect size (SMD) as secondary outcomes. Changes were calculated from baseline, rather than comparing uniquely the post intervention rates in both groups, because despite the randomization, baseline rates of prescriptions differed between groups in many of the studies. Relative change was selected rather than absolute change due to the heterogeneity in the outcome measures of the individual studies, which prevented meaningful comparison of absolute rates across studies. Calculation of effect size is preferable in this circumstance; however, available data only allowed calculation in 10 of the 15 studies and the results could not be pooled in a meta-analysis because of heterogeneity in the data available for calculating effect sizes. Nevertheless, our choice of primary outcome has some disadvantages. Expressing effects as relative changes can be difficult to interpret, or even misleading, especially when baseline rates are small. In such situations, small absolute changes can lead to large relative changes. Conversely, when baseline rates are fairly large, clinically meaningful absolute changes can appear as small relative changes. Therefore, we suggest relative changes need to be interpreted in the context of the actual baseline rates. It is statistically more challenging to demonstrate effectiveness

when comparing changes from baseline between two groups, than when comparing differences in post intervention rates[39]. We may have underestimated or overestimated the effect of AD reported in terms of difference in relative change in this systematic review. Regrettably, due to the nature of the studies and the availability of data, this was the only consistent and meaningful outcome measure that could be calculated across studies.

Our systematic review has provided an overview of different clinical contexts in which AD has been used to optimize prescription of medications by FPs and synthesized current evidence about its effectiveness and the magnitude of the effect. This information is of interest to health policy planners implementing or considering the implementation of AD programs, to medical educators and health care professionals designing AD interventions, as well as to researchers, professional bodies and other organizations looking for effective ways to disseminate research evidence or to incorporate clinical guidelines. Our results support the increased use of AD programs aimed specifically at FPs seen over the last decade in Canada and elsewhere. Such programs offer a practical alternative for FPs to stay up to date with rapidly evolving new research evidence. They provide physicians with evidence based non-biased information about incorporating research evidence in their practice based on a synthesis of the current literature.

In conclusion, AD has been used, as a stand-alone intervention to alter the prescription behaviour of FPs. This systematic review demonstrates that AD can be effective at optimizing prescription of medications by FPs, and that, although variable effect magnitudes were moderate in the majority of studies. This systematic review provides evidence supporting the use of AD as a strategy to promote evidence-based prescription of medications or incorporation of clinical guidelines into clinical practice [4].

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Table 4. Descriptive Table Randomised Control Trials

Author Year Country	Target prescription change	Rationale for target prescription change	Type of AD visits	No. of AD visits	Sample size*	Academic detailer	Intervention for control group	Primary outcome	Analysis	Quality score (0- 53)
Avorn 1983 USA	Reduce use of: 1) Propoxyphene 2) Cerebral & peripheral vasodilators 3) Cephalexin	Lack of evidence for efficacy (1&2); To reduce side effects (1&2); To improve cost effectiveness (3)	Individual	2	281	Pharmacist	None	change in mean number of drug units prescribed per physician over 1 yr before and after intervention	Multi-variable regression model controlling for pre intervention Rx rate among individual physicians and prescribing trends in control group.	48
De Burgh 1995 Australia	Reduce BDZ Rx for anxiety and insomnia	To reduce risk of side-effects	Individual	1	286	Three medical staff & pharmacist	None	Rx rate per 100 pt encounters with diagnoses of anxiety or insomnia	Encounter based analysis controlling for patient, doctor and practice characteristics.	46
Zwar 2000 Australia	Reduce repeat Rx of BDZ for anxiety, insomnia and all indications	To reduce risk of side-effects and dependence	Individual	1	157	FP	AD on unrelated topic	Mean rate of BDZ Rx per 100encounters with diagnoses of anxiety, sleep disorders and all indications	Repeated measure ANOVA comparing results of pre AD survey with surveys at 6 and 12 months post AD.	40
Author Year Country	Target prescription change	Rationale for target prescription change	Type of AD visits	No. of AD visits	Sample size*	Academic detailer	Intervention for control group	Primary outcome	Analysis	Quality score (0- 53)
Ilett 2000 Australia	Increase Rx of: Amoxycillin with or without clavulinic acid,	To Reduce risk-of side effects and improve cost effectiveness	Individual	1	112	Pharmacist	None	Total number of Rx per FP over a 3 month period	Wilcoxon's 2- sided rank sum test for between and within group	38

	Cephalexin, Doxycycline, Erythromycin, Penicillin, Trimethoprim; Decrease Rx of: Cefaclor, Roxithromycin								comparisons	
Ray 2001 USA	Reduce Rx NSAIDS for osteoarthritis in elderly population.	To reduce risk of side-effects, esp. GI complications	Individual	1	220	Physician educator	None	Mean no. of days of prescription NSAIDS dispensed over 1 yr period per NSAID user	Relative and absolute change in NSAID use over one year period before and after intervention. Difference in change between AD & control groups.	49
Author Year Country	Target prescription change	Rationale for target prescription change	Type of AD visits	No. of AD visits	Sample size*	Academic detailer	Intervention for control group	Primary outcome	Analysis	Quality score (0- 53)
Hall 2001 UK	Increase Rx of Metronidazole & Omeprazole for H. pylori	To improve quality of care and health outcomes (by reducing risk of peptic ulcers) and cost savings	Individual	1	76♦	Pharmacist	None	Mean dose units prescribed, per quarter, per patient	Analysis of overall usage of drugs over 12 month periods before and after intervention, using multilevel mixed modelling taking into account repeated measures.	51

Van Eijk 2001 Netherlands	Reduce Rx of highly anticholinergic; Increase Rx of less anticholinergic antidepressants in elderly people (age ≥ 60)	To reduce risk of side effects	2 arms: 1) Individual AD 2) Group AD	2	1) 138 (indiv.) 2) 120 (group)	FP	None	Rate of incident Rx of highly or less anticholinergic antidepressants per 1000 person years in people aged ≥ 60 yrs	Poisson regression model to estimate rate ratio of starting highly and less anticholinergic antidepressants in each AD group compared to control group	49
Author Year Country	Target prescription change	Rationale for target prescription change	Type of AD visits	No. of AD visits	Sample size*	Academic detailer	Intervention for control group	Primary outcome	Analysis	Quality score (0- 53)
Bernal Delgado 2001 Spain	NSAIDs for OA. Increase Rx of: Diclofenac, Piroxicam; Decrease Rx of: Aceclofenac, Meloxicam, Tenoxicam	To improve cost effectiveness	Group	1	104	Pharmacist	None	Number of prescriptions of each type of NSAID per FP during 6 month period before and after intervention	Relative change (and 95% CI) in rate of Rx of each NSAID over 6 months before and after intervention, in AD and control groups.	49
Witt 2004 Denmark	Increase Rx of inhaled steroids and decrease Rx of Beta-agonists for asthma in children < 16 years.	To improve compliance with clinical guidelines for asthma medication	Individual	1	185	FP	Postal distribution of asthma medication guidelines	Number of DDD _i of steroids or beta-agonists per child per practice	Mixed model adjusted for seasonal variation and general trends	48

Midlov 2005 Sweden	Decrease Rx of BDZ and antipsychotic drugs to elderly people ≥ 65 years	To reduce risk of side effects	Group	2	54	FP & pharmacist	None	Mean number of DDD _j of BDZ or Antipsychotic drugs	Differences in geometric mean between active and control groups were calculated using a mixed model (group by period interaction, fixed effects; and practices as random effects).	43
Author Year Country	Target prescription change	Rationale for target prescription change	Type of AD visits	No. of AD visits	Sample size*	Academic detailer	Intervention for control group	Primary outcome	Analysis	Quality score (0- 53)
Simon 2005 USA	Increase Rx of diuretic or beta- blocker for hypertension in adults	To improve compliance with guidelines and improve cost- effectiveness	2 arms: 1) Individual AD 2) Group AD	1	367	FP	Mailed printed guidelines	% of newly diagnosed hypertension patients treated with Diuretics or β -blockers over 1 year	Logistic regression with GEE estimating effect of intervention and controlling for clustering (FP level) and for patient characteristics	49
Abbreviations: Rx - prescription, NA - not available, FP - Family Physician; BDZ - Benzodiazepines, NSAIDS - Non Steroidal Anti-inflammatory Drugs, PCM - Paracetamol, COX-2 - Cyclooxygenase, GEE - Generalised Estimating Equations										
* sample size of physicians in both control and AD group, ♦No. of GP practices (no. of patients not provided), jDaily defined doses.										

Table 5. Descriptive Table Observational Studies

Author Year Country	Target prescription change	Rationale for target behaviour	Type of AD visits	Number of visits	Sample size	Academic detailer	Description of control group's characteristics and intervention	Primary Outcome	Analysis	Effectiveness of AD, as reported in publication	Quality score 0- 47
Atkin 1996 Australia	To reduce number of concurrent medications for elderly	Reduce risk of adverse drug reactions	Individual	2	59 AD 47 Control	Pharmacist	Geographically distinct area with similar demographic characteristics; no intervention received	Mean no. of medications prescribed concurrently per elderly patient who visited FP in 12 months post intervention.	Repeated measure ANOVA evaluating differences in mean per-doctor prescribing between the groups; differences in prescribing over time; and group/time interaction.	No significant difference between the two groups at any data collection point (df=1,F=1.72,p=0.19); Significant reduction(df=3,F=3.78,p<0.02)in prescribing in both groups probably due to introduction of co-payment.	42
Peterson 1996 Australia	To reduce Rx of NSAIDs and increase Rx of PCM for rheumatic diseases in elderly	Reduce risk of side-effects (gastric bleeding)	Individual	1	250 AD control group sample size NA	Pharmacist	Geographically distinct area with similar demographic characteristics; no intervention received.	Ratio of NSAID to PCM in DDD units	Change over time within and between study areas were compared using a normal approximation to binomial distribution.	Statistically significant effect Reduction post intervention observed in control (Z = 7.78, p < 0.0001) and intervention (Z = 14.42, p < 0.0001), with a significant between group difference (Z = 5.22, p < 0.0001).	36
Tomson 1997 Sweden	To decrease Rx of inhaled β- agonists; and increase inhaled steroids for asthma	Improve compliance with asthma guidelines	Group	2	70 AD 26 Control	Pharmacologist and pharmacist	No intervention received	Ratio of inhaled β- agonists to inhaled steroids in DDD units	Mann-Whitney's U test to analyse difference in changes between groups & Wilcoxon signed-rank test for changes within groups	No statistically significant between group difference. Within group change observed in AD but not control group.	41
Graham 2008 Canada	To reduce Rx of COX-2 for OA in elderly patients	Improve Cost effectiveness	Individual	1	231 AD 265 Control	Pharmacist (n=2) or nurse (n=1)	Differences in FP and patients characteristics adjusted for in analysis. No intervention received.	Rate of COX-2 Rx in DDD per elderly pt in each FP practice over 3 months (Primary endpoint), follow-up until 12 months (Secondary endpoint) post intervention	GEE model accounting for repeated measures over time, and propensity score to adjust for differences in FP and patient characteristics	Yes (first 3 months post intervention only) Greater decrease in AD group over first 3 months [between group difference (95% CI) of 0.76 (0.037;1.48) DDD/pt; Z = 2.06; p = 0.04]. No significant difference at 12 months.	44

Abbreviations: AD= Academic Detailing, Rx = prescription, NA = not available, FP = Family Physician, BDZ –Benzodiazepines, NSAIDS – Non Steroidal Anti-inflammatory Drugs, PCM – Paracetamol
COX-2 – Cyclooxygenase, DDD=Daily Defined Doses, GEE= Generalised estimating equation

Table 6. Results of studies included in the systematic review

Author	Medications evaluated	Target change in Prescription	Outcome Measured	Pre Intervention Prescription rate		Post Intervention Prescription rate		Reported effectiveness of AD (yes/no)	Difference in Relative Change	Difference in absolute change	Effect Size calculated
				Control	AD	Control	AD				
Avorn	Propoxyphene, Cerebral and peripheral vasodilators cephalixin BDZ For Anxiety	-	Mean number of drug units prescribed per FP over one year period	5415	5439	4921	4174	yes	-14%	-771	-7.8
			Rx rate per /100 pt encounters with	59.9	56.1	53.8	46.6		-7%	-3.4	
De Burgh	BDZ For Insomnia	-	diagnoses of anxiety or insomnia	92.4	94.5	88.5	87.4	No	-3%	-3.2	NA
Zwar	BDZ (All indications)	-	Mean Rx rate per	2.2	2.3	1.5	1.8	No	10%	0.2	0.42
	BDZ Sleep problems		100 encounters with	77.2	70.5	73.5	66		-2%	-0.8	-0.08
	BDZ Anxiety		diagnosis specified	25.7	35.7	27	29.7		-22%	-7.3	-0.53
	Amoxicillin 500 mg			721	308	993	604		58%	24	
	Amoxicillin 250 mg			652	293	825	594		76%	128	
	Amoxicillin 500 mg with clavunic acid			229	221	333	249		-33%	-76	
	Cephalexin			219	217	255	242		-5%	-11	
	Doxycycline	+		296	235	400	865		233%	526	-0.51 i
	Erythromycin			69	42	75	56		25%	8	
	Penicillin		Total number of Rx by all FPs in AD and control groups over a 3 month period	93	76	83	82	yes for some but not all drugs	19%	16	
Iiett	Trimethoprim			296	197	291	261		34%	69	
	All rec. drugs combined			2575	1589	3255	2953		59%	364	
	Cefaclor			623	829	1218	975		- 78%	-449	
	Roxithromycin			987	874	1875	1039		-71%	-723	-2.02 i
	All non rec drugs combined	-		1610	1703	3093	2014		-74%	-1172	

Author	Medications evaluated	Target change in Prescription	Outcome	Pre Intervention Prescription rate		Post Intervention Prescription rate		Reported effectiveness of AD, yes/no	Difference in Relative Change	Difference in Absolute change	Effect Size calculated
				Control	AD	Control	AD				
Ray	NSAID	-	Mean number of days of Rx NSAIDS dispensed over 1 yr period per NSAID user	284.9	287.2	238.39	219	yes	-7%	-21.3	-3.76
Hall	Omeprazole	+	Mean dose units prescribed per quarter, per patient	2.95	3.66	3.53	4.05	No	-9%	-0.19	-0.4
	Metronidazole			0.29	0.27	0.37	0.33		-5%	-0.02	-0.5
Van Eijk	Highly anti-cholinergic antidepressants	-	Rate of incident Rx of highly or less anticholinergic antidepressants per 1000 person years in people aged ≥ 60 yrs	5.82	8.02	8.2	7.5	Yes	-47%	-2.9	**
Individual AD	Less anti- cholinergic antidepressants	+		10.32	11.8	7.9	17		68%	+7.62	
Group AD	Highly anti-cholinergic antidepressants	-		5.82	6.36	8.2	5.2	Yes	-59%	-3.54	**
	Less anti- cholinergic antidepressants	+		10.32	12.72	7.9	14.72		+39%	+4.42	
Bernal-Delgado	Diclofenac	+	Relative change in number of Rx of each type of NSAID per FP during six months pre and post intervention	-16.55% (-26, -6.82)•		-9.06 % (-17.18, -0.94)β			+7.49%		+1.97
	Piroxicam			-28.23% (-40.02, 16.44)		-18.52% (-29.51, -7.53)			+9.71%		+2.01
	Aceclofenac			-22.85% (-33.84, 11.86)		-29.34% (-42.22, -16.46)		Yes	-6.49%		-1.28
	Meloxicam	-		-1.17% (-3.99, 1.65)		-25.48% (-37.81, 13.15)			-24.31%		-2.63
	Tenoxicam			14.44% (5.22, 23.66)		-22.59% (-34.42, 10.76)			-37.03%		-8.25
Witt	Inhaled Steroids	+	Number of DDD steroids or beta-agonists/ child/practice	0.23	0.21	0.235	0.23	No	+7%	+0.015	-0.09
	Beta-agonist	-		0.2	0.22	0.25	0.27		-2%	0	+0.18

Author	Medications evaluated	Target change in Prescription	Outcome	Pre Intervention Prescription rate		Post Intervention Prescription rate		Reported effectiveness of AD, yes/no)	Difference in Relative Change	Difference in Absolute change	Effect Size calculated
				Control	AD	Control	AD				
Midlov	BDZ	-	Prescribed DDD of BDZ or		**			Yes	-25.8%¶		**
	Antipsychotic drugs		Antipsychotic drugs for elderly patients					No	+1.13%¶		**
Simon	Diuretics, β- blockers	+	% of newly diagnosed hypertension patients treated with Diuretics or β-blockers over 1 year	57.6	57.6	63.8	70.1	No	+10.96%	6.3¥	**
			Mean number of medications prescribed concurrently per elderly patient	57.6	59.1	63.8	72.3	No	+14.75%	8.5 €	**
Atkin	Concurrently prescribed medications	—	Ratio NSAIDs: PCM, in DDD	4.53	5.44	4.41	4.81	No	-9%	-0.51	0.808
Peterson	NSAIDS, PCM	—	Ratio inhaled β - agonists: steroids, in DDD	3.16♦	3♦	2.92	2.59	Yes	-6%	-0.17	-5.24
Tomson	Inhaled β - adrenoceptor agonists, inhaled corticosteroids	—	Rate of COX-2 Rx, in DDD per patient	3.91♦	3.23♦	2.57	1.89	No	**	**	**
Graham	COX-2 inhibitors	—		3.6	3.98	NA	NA	Yes	-23%	-0.87	-0.09

Abbreviations: Rx = prescription, NA = not available, FP = Family Physician, BDZ –Benzodiazepines, NSAIDS – Non Steroidal Anti-inflammatory Drugs, PCM – Paracetamol
COX-2 – Cyclooxygenase

* + indicates AD intervention aimed at increasing Rx rate and - indicates AD intervention aimed at decreasing Rx rate, ¶combined effect size of 8 recommended drugs and combined effect size of 2 non-recommended drugs, ** Insufficient data for calculations,¶ Difference in relative change in geometric mean of daily defined doses of BDZ and Antipsychotic drugs as provided in the publication, ¥ Individual AD versus control, € Group AD versus control, ♦ Ratio , •Relative change and 95% CI in controls, βrelative change and 95% CI in AD group