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THE ROLE OF INDUSTRY FUNDING IN RANDOMIZED CONTROLLED TRIALS OF ANTIMUSCARINIC MEDICATIONS FOR OVERACTIVE BLADDER

Hypothesis / aims of study
To examine the funding characteristics of randomized controlled trials (RCTs) of antimuscarinic medications for adult overactive bladder (OAB).

Study design, materials and methods
A Medline search was performed for the period from 1988 to 2008 with the keywords “anticholinergic” OR “antimuscarinic” OR “oxybutynin” OR “tolterodine” OR “darifenacin” OR “trospium” OR “solifenacin” OR “fesoterodine”. Studies were limited to English language publications with the following type: “clinical trial, all” OR “clinical trial, phase I” OR “clinical trial, phase II” OR “clinical trial, phase III” OR “clinical trial, phase IV” OR “clinical trial” OR “controlled clinical trial” OR “randomized controlled trial”. Manual review of all abstracts was performed to identify RCTs that were performed for the treatment of OAB in adults. Studies were categorized by the type of intervention and funding source. A trial was considered to be industry sponsored if industry support was acknowledged in the body of the paper, or if one of the authors was listed as employed by industry.

Results
A total of 1272 publications were identified with the initial Medline search. Manual review identified 269 relevant publications related to OAB. Of these, 191 were excluded for the following reasons: pediatric trial (n=34), neurogenic bladder trial (n=30), pharmacokinetic/ bioavailability study (n=35), trial limited to men (n=12), safety/tolerability study (n=17), cohort study (n=18), open-label extension (n=12), review article (n=3), pooled analysis (n=10), and post hoc analysis (n=20). This resulted in 78 RCTs that were eligible for analysis. In these 78 RCTs, the vast majority of funding was provided by industry sources (58 trials with 25,850 participants). Government funding accounted for 4 trials (596 participants), while 16 trials (1922 participants) were performed with institutional/ internal funding. Therefore, industry sponsored trials accounted for 74% of OAB medication RCTs, incorporating 91% of trial participants. Eleven of the 78 RCTs were performed using anticholinergic medications that are not FDA-approved for overactive bladder (propiverine, propantheline, imipramine, penthienate bromide, terodiline). Study designs for the remaining 67 trials are presented in the Table.

Study Design
Drug vs placebo n=28 - Oxybutynin IR (n=4) - Contemporary drug (n=24)
Drug and other treatments n=12 - Behavioral therapy (n=9) - Electrical stim (n=1) - TENS (n=1) - Salivary pastilles (n=1)
Various doses of the same drug n=2
Drug A vs drug B (vs placebo) n=25 - Contemporary drug vs oxybutynin IR (n=16) - Contemporary drug vs tamsulosin (n=1) - Tolterodine ER vs tolterodine IR (n=1) - Contemporary drug A vs contemporary drug B (n=7) ▪ Oxybutynin ER vs tolterodine IR ▪ Oxybutynin ER vs tolterodine ER ▪ Oxybutynin transdermal vs tolterodine ER vs placebo ▪ Solifenacin vs tolterodine IR vs placebo ▪ Solifenacin vs tolterodine IR vs placebo ▪ Solifenacin vs tolterodine ER ▪ Fesoterodine vs tolterodine ER vs placebo

All 7 trials which compared two ‘contemporary’ antimuscarinics were industry-funded, and each of these concluded that the sponsor’s drug was superior to its competitor.

Interpretation of results
Not unexpectedly, the vast majority of RCTs addressing the use of antimuscarinic agents for OAB have been supported to some extent by industry. Notably, all head-to-head comparative effectiveness trials of contemporary medications have been funded by industry. This is unusual, as head-to-head studies for other medical conditions have generally been funded by government sources. It is well documented that pharmaceutical company support is strongly associated with results that favor sponsors’ interests. Therefore, the potential exists for systematic bias in the literature in favor of antimuscarinic efficacy.

Concluding message
There is a need for comparative effectiveness research related to antimuscarinic therapy for OAB that is free from potential industry bias.

Specify source of funding or grant	**None.**
Is this a clinical trial?	**No**
What were the subjects in the study?	**NONE**