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A Case Study of Salami Slicing: Pooled Analyses of Duloxetine for Depression

Glen I. Spielmans Tracey L. Biehn Dustin L. Sawrey

Department of Psychology, Metropolitan State University, St. Paul, Minn., USA

Key Words

Duloxetine · Salami slicing, duplicate publication · Depression · Pooled analysis

Abstract

Background: Publishing separate, yet very similar pieces of a single dataset across multiple papers is known as 'salami slicing'. This practice may be motivated by researchers wishing to increase their publication counts and by the desire to increase exposure of their findings. 'Salami slicing' may also be used by the drug industry to help widely disseminate positive findings regarding its products. Journal editors across many scientific disciplines have bemoaned such duplicative publications on several occasions. However, little research has been conducted on the frequency of such publication practices, and findings have been inconsistent. No research has investigated whether 'salami slicing' may also occur in publications presenting results from pooled analyses of clinical trials. ***Methods:*** We examined the scientific literature on duloxetine as a treatment for depression, examining how data from clinical trials were reported across 43 pooled analyses. ***Results:*** The vast majority of pooled analyses (88%) had at least one author who was employed by the manufacturer of duloxetine. Several pooled analyses based on highly overlapping clinical trials presented efficacy and safety data that did not answer unique research questions, and thus appeared to qualify as salami publications. Six clinical trials had their data utilized as part of 20 or more separately published pooled analyses. ***Conclusions:*** Such redundant publications add little to scientific understanding and represent a poor use of peer reviewer and editorial resources.

When clinical trials are conducted, data are typically collected on several variables. Many times, a paper describing outcomes on some of these variables is published, followed by further publications which detail similar outcomes from the same trial. For instance, data on some efficacy measures from a given trial may be presented in one publication, followed by data from other efficacy measures in a separate publication. Data from a clinical trial's safety measures may likewise be divided into multiple overlapping publications. If a clinical trial of an antidepressant concludes that the drug is safe and efficacious, it makes little practical sense to publish separate, but highly similar pieces of the trial's results on multiple

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Glen I. Spielmans, PhD
Metropolitan State University, Department of Psychology
1450 Energy Park Drive
St. Paul, MN 55108 (USA)
Tel. +1 651 999 5826, Fax +1 651 999 5822, E-Mail glen.spielmans@metrostate.edu

occasions. Carving a study's data into multiple pieces and publishing these similar pieces individually is known as 'salami slicing' or as publishing 'least publishable units' [1–4].

'Salami slicing' may distort the medical literature, making a drug appear as if it has greater support than it has actually garnered from empirical investigations. A reader who does not look closely may not notice that multiple publications regarding a drug's efficacy and safety are actually based on the same underlying group of research participants. Salami manuscripts may waste the valuable time of peer reviewers. Journal editors from a variety of disciplines have bemoaned the practice of 'salami slicing' [1–6]. In general, salami publications have been linked to the 'publish or perish' environment of academia; however, salami publications are likely used for more than just advancing the careers of academics.

Drug marketers have noted that journal publications are an important factor in drug sales. Putting it bluntly, one memo from Pfizer asked 'What is the purpose of publication?' and replied, in part 'High quality and timely publications optimize our ability to sell Zoloft most effectively' [7, p. 18]. An internal Eli Lilly document listed 'new studies, publications, presentations …' under the heading of 'support the schizophrenia and bipolar franchises worldwide' for its antipsychotic drug olanzapine [8, p. 3]. PeerView is a company which provides a variety of services to the drug industry, including '… products that support publication strategy and other commercialization processes for our pharmaceutical and biotech clients …' [9]. PeerView's CEO, Timothy Bacon, stated that '… most pharma and biotech companies recognize the significant impact that the clear and consistent publication of results will have on subsequent commercialization efforts …' [10, p. 2].

Salami publications may be included as part of a pharmaceutical firm's publication plan. When supportive and highly similar points about a drug's efficacy and/or safety from a single clinical trial are published in a variety of journals, a wide audience of potential prescribers and key opinion leaders is reached. Thus, in addition to padding the curricula vitae of researchers, salami publications may lead to the results of a successful trial being disseminated across several publications, likely helping to boost product visibility and reinforcing the product's key marketing messages. Because various researchers and clinicians read differing journals, they may not notice that redundant findings are being presented in multiple publications. Empirical research on the prevalence of salami publications is relatively sparse and has found quite disparate results [11–14]. Most research on salami publications has focused on overlapping publications of individual clinical trials. Little attention has been placed on pooled analyses, publications in which data from several clinical trials are pooled into a single, larger dataset. However, pooled analyses also present the potential of salami publications, as similar variables from the same, or highly similar, set of clinical trials could be presented across several pooled analyses.

One prior investigation examined the publications associated with 42 clinical trials which examined antidepressants submitted to the Swedish drug regulatory authority [15]. The authors found 11 pooled analyses in which the trials' data were utilized; in some instances, individual trials contributed data to multiple such pooled analyses. However, their sample of pooled analyses was relatively small and the topics of the pooled analyses were not mentioned, making it difficult to know to what extent the pooled analyses contained redundant data. The present study examined the prevalence of salami publications across pooled analyses in the case of the antidepressant duloxetine for depression, focusing on studies that discussed the safety and efficacy of the drug.

Method

Search Strategy

We searched Medline and the Cochrane Registry of Controlled Clinical Trials on October 9, 2007 using the search term 'duloxetine'. Duloxetine was selected as the drug of choice because a literature search for a prior meta-analysis [16] revealed the existence of several pooled analyses regarding the drug's safety and efficacy in depression which seemed to present quite similar data. As our analysis was intended to solely investigate studies which examined the efficacy and safety of duloxetine in the treatment of depression, we excluded papers that did not focus directly on these outcomes. Our search yielded 520 articles, of which 401 were eliminated for the following reasons: studied animals (n = 49); primarily described the biological effects (i.e., pharmacokinetics or pharmacodynamics) of duloxetine (n = 44); were not relevant to depression (n = 253); were not published in English (n = 23); were case studies (n = 25) or letters to the editor (n = 7).

Analysis

Two reviewers (G.I.S., T.L.B., or D.L.S.) independently categorized each publication into one of three categories: clinical trial, pooled analysis (or post hoc analysis of a single trial), or narrative review article. All disagreements were resolved through consensus. If a publication reported data from a single study in which depressed participants received duloxetine, it was classified as a clinical trial. A placebo or active medication control was not necessary for inclusion as a clinical trial. Pooled analyses combined

data from two or more clinical trials and must have reported original statistical analyses. We also categorized articles reporting post hoc analyses from a single trial as pooled analyses. Papers which discussed findings of duloxetine research but conducted no original statistical analyses were considered narrative reviews. As our interest was on the literature that primarily concerned duloxetine, we did not include papers which focused on duloxetine as but one of many treatments. For example, a meta-analysis that examined outcomes of all second-generation antidepressants was not included, as its overall focus was on second-generation antidepressants as a whole, not duloxetine in isolation [17]. However, papers which focused on how duloxetine compared to other treatments were included. In each pooled analysis, we examined which clinical trials contributed data for analysis. Whether each publication had at least one author who was an employee of Eli Lilly (manufacturer of duloxetine) was also tabulated.

Labeling an individual paper as a salami publication is at least somewhat subjective in several aspects. For example, if 7 pooled analyses exist regarding a drug's safety for a particular condition, then various reviewers may differ regarding whether each slice of data merited publication as a stand-alone paper. One reviewer may conclude that the data contained across the 7 publications could have been more efficiently presented in 1 or 2 publications, but another reviewer may differ entirely in his or her assessment. Given the inexact nature of assessing overlapping publications, we opted not to label each included pooled analysis as either a salami publication or as sufficiently original. Rather, we examined the general conclusions of each pooled analysis and noted which underlying clinical trials contributed data to each pooled publication. We then noted areas in which data and conclusions appeared to be redundant.

Results

We found 30 papers which utilized duloxetine in a clinical trial for the treatment of major depression. In addition, our literature search netted 43 pooled analyses (2 of which were post hoc analyses of a single trial) and 46 review articles. Of the clinical trials, 25 (83%) had at least one author who was employed by Eli Lilly. Of the 43 pooled analyses, 38 (88%) had at least 1 Eli Lilly-affiliated author, while 8 (17%) of the narrative review articles had at least one Eli Lilly author.

While reviewing the clinical trials, we found one instance of duplicate publication. A trial compared the outcomes of untreated depressed patients who initiated duloxetine to depressed patients who switched from their current antidepressant to duloxetine. One paper reported outcomes after 8 weeks of the 12-week trial [18], while a second paper reported outcomes at study endpoint without referencing the other publication [19].

Table 1 shows the authors' conclusions from each pooled analysis along with the topic of analysis. Several pooled analyses authored by Eli Lilly scientists appeared to demonstrate 'salami slicing'. For example, one study [20] compared the safety and efficacy of duloxetine in the treatment of African-Americans to Caucasians. Using data from the same underlying clinical trials, another publication compared duloxetine's efficacy and safety between Hispanics and Caucasians [21]. In both cases, the authors concluded that the racial groups did not differ in a meaningful way in their response to duloxetine. Another pooled analysis compared males and females in terms of safety outcomes [22], and another analysis based on the same underlying patients [23] compared genders in terms of efficacy, with neither analysis finding any notable differences along gender lines. One pooled analysis examined the cardiovascular effects of duloxetine in depressed patients [24] while another such analysis reported on the cardiovascular profile of the drug across various conditions [25]; both concluded that the drug possesses a benign cardiovascular safety profile. Other safety or tolerability concerns were examined in several pooled analyses, many of which were based on a very similar set of underlying trials: body weight [26]; suicidal behaviors and ideation [27]; discontinuation symptoms [28]; treatment-emergent hypomania [29]; sexual functioning [30]; urinary side effects [31], and nausea [32]. Other pooled analyses provided analyses of duloxetine's safety and efficacy in patients aged 55 and over [33] and women aged 40–55 [34]; neither analysis concluded that age moderated the drug's efficacy. Several pooled analyses also examined other factors that may moderate the impact of duloxetine: dose-response relationship [35–37]; level of depression severity as a moderator of efficacy [38, 39]; characteristics of depressive episode [40], and the presence of melancholic features [41]. These analyses concluded that none of the aforementioned traits, with the exception of drug dosage, influenced patient outcome. Other pooled datasets yielded reports of duloxetine's effects in: treating milder depression [42]; treating depression using number needed to treat as the outcome variable [43]; time course to improvement [44]; onset of action [45], and treating depression with comorbid anxiety symptoms [46]. The analyses examining time course to improvement and onset of action were based on the same 2 underlying clinical trials. In addition, 6 pooled analyses reported analyses based solely on data from 2 clinical trials.

Double-blind clinical trials were easily the most commonly included sources of data in pooled analyses. Table 2 displays the number of occasions in which the 8 most frequently cited clinical trials, all of which were double-blind, were included as part of a pooled analysis. Six trials were included in 20 or more pooled analyses.

Table 1. Pooled analyses focusing on duloxetine as a treatment for depression

Study	Focus	Lilly authors?	Trials included	Conclusion
Acharya et al. [27]	Suicidal behaviors and ideation	Yes	Does not cite trials individually; claims all 27 phase II and III trials were included	'We found no evidence of an increased risk of suicidal behaviors or ideation during treatment with duloxetine compared with placebo in MDD patients. HAMD item-3 suicidality scores had more improvement and less worsening of suicidal ideation with duloxetine than placebo.' (p. 587)
Bailey et al. [20]	Efficacy and tolerability: African-American vs. White	Yes	[50–54, 80, 81]	'… no convincing evidence was found to suggest that the overall safety and tolerability profile or the efficacy profile for duloxetine in this cohort of African-American patients differed from that observed in a comparator group of Caucasian patients.' (p. 437)
Ballesteros et al. [55]	Response, remission	No	[50, 51, 53, 56, 57] additional trial not cited	'At the moment, we sincerely think more research is needed to clarify the current evidence regarding the comparative efficacy of duloxetine across different dose ranges.' (p. 221)
Bech et al. [35]	Dose-response relationship	Yes	[50, 51, 53, 56, 57, 81]	'Findings support that duloxetine 60 mg daily is the best effective dose.' (p. 273)
Brannan et al. [45]	Onset of action	Yes	[51, 53]	'In this study, duloxetine-treated patients demonstrated clinically meaningful improvements within the first weeks of treatment. Approximately 35% of the total baseline-to-endpoint improvement for duloxetine-treated patients occurred in the first week of treatment, while approximately 50% of the total improvement had been achieved following 2 weeks of therapy.' (p. 171)
Burt et al. [34]	Women aged 40–55	Yes	[51, 53]	'The magnitude of duloxetine's treatment effect in women ages 40–55 was similar to that observed in younger (age <40 years) and older (age >55 years) female patients.' (p. 345)
Cookson et al. [43]	Efficacy with number needed to treat as DV	Yes	[50, 51, 53, 54, 56–58, 80, 81]	'The [number needed to treat] for several measures of efficacy including remission consistently demonstrated the treatments benefits of duloxetine as well as of fluoxetine and paroxetine compared to placebo.' (p. 267)
Delgado et al. [30]	Sexual functioning compared to paroxetine and placebo	Yes	[50, 56, 57, 81]	'… patients receiving duloxetine (40–120 mg/day) or paroxetine (20 mg/day) had a significantly higher incidence of acute treatment-emergent sexual dysfunction when compared with placebo patients. However, the incidence of acute treatment-emergent dysfunction for duloxetine was significantly lower than that observed for paroxetine.' (p. 686)
Dunner et al., 2003 [46]	Treatment of anxiety symptoms in depression	Yes	[50, 51, 53, 54]	'In these studies, duloxetine provided rapid relief of anxiety symptoms associated with depression that lasted throughout the acute treatment period.' (p. 61)
Dunner et al. [29]	Treatment-emergent hypomania	Yes	Eight trials; no individual trials cited	'Duloxetine was associated with a low incidence of treatment-emergent hypomania, mania, of hypomanic-like symptoms in patients with major depressive disorder.' (p. 115)
Eckert and Lançon [59]	Duloxetine compared to venlafaxine and fluoxetine	No	22 fluoxetine trials 9 duloxetine trials 8 venlafaxine trials [50–54, 57, 80, 81] one trial not in our database	'Fluoxetine was not significantly different in either tolerability or efficacy when compared with duloxetine. Venlafaxine was significantly superior to duloxetine in all analyses except dropout rate. In the absence of relevant data from head-to-head comparison trials, results suggest that venlafaxine is superior compared with duloxetine and that duloxetine does not differentiate from fluoxetine.' (p. 1)
Fava et al. [60]	Efficacy for painful physical symptoms in depression	Yes	[51, 53]	'Treatment with duloxetine, 60 mg q.d., significantly reduced pain compared with placebo. Improvements in pain severity were attributable equally to the direct effect of duloxetine and to associated changes in depression severity.' (p. 521)
Fava et al. [61]	Anxious vs. non-anxious depression	Yes	[19]	'Duloxetine's efficacy in anxious depression was somewhat superior to non-anxious depression; tolerability was comparable between groups.' (p. 187)
Gahimer et al. [62]	Safety analysis across various indications	Yes	64 trials; no individual trials cited	'The safety profile for the molecule from the overall duloxetine exposures integrated safety database suggests that benign and common pharmacologic side effects occur with duloxetine treatment.' (p. 175)

Table 1 (continued)

Study	Focus	Lilly authors?	Trials included	Conclusion
Goldstein et al. [63]	Effect of duloxetine on painful physical symptoms	Yes	[51, 53, 54]	'The authors concluded that duloxetine reduces the painful physical symptoms of depression.' (p. 17)
Greist et al. [32]	Incidence and onset of nausea	Yes	[50, 51, 53, 54, 56, 57, 80, 81]	'Duloxetine induced mild to moderate nausea in a subset of patients with MDD during treatment initiation. Nausea resolved rapidly with continued treatment. The incidence of duloxetine-induced nausea resembled that produced by paroxetine and fluoxetine.' (p. 1446)
Hirschfeld et al. [44]	Time course to improvement	Yes	[51, 53]	'Clinically meaningful response to duloxetine therapy was most rapid for some of the emotional and painful physical symptoms of depression (week 1), with symptoms of retardation and hypochondriasis responding within 2 to 3 weeks, respectively. Slower responses (5–9 weeks) were achieved for sleep, genital, and nonpainful somatic symptoms.' (p. 176)
Hudson et al. [64]	Safety and tolerability	Yes	[50, 51, 53, 54, 56, 57, 80, 81]	'The results are consistent with those obtained previously from smaller pooled data sets, and suggest that duloxetine is safe and well tolerated in patients with MDD.' (p. 327)
Khan and Schwartz [65]	Efficacy and suicidality	No	Six duloxetine Four escitalopram Unclear which trials were included	'Suicide and suicide attempt risk varied considerably … We also noted similar magnitude of response to placebo and antidepressants among the three studies [referencing two prior publications and the current analysis].' (p. 31)
Kornstein et al. [23]	Male vs. female: efficacy	Yes	[50–54, 80, 81]	'In this analysis of pooled data, the efficacy of duloxetine did not differ significantly in male and female patients.' (p. 761)
Lewis-Fernandez et al. [21]	Hispanic vs. Caucasian	Yes	[50–54, 80, 81]	'In this analysis of pooled data, no evidence for a differential effect of duloxetine in Hispanic and majority Caucasian patients was found in efficacy or safety outcomes.' (p. 1379)
Mallinckrodt et al. [66]	Efficacy and safety	Yes	[50, 51, 53, 54, 80, 81]	'In these studies, duloxetine was safe and effective in the treatment of both emotional and physical symptoms of MDD. Based on dose assessments, 60 mg q.d. appears to be the optimum starting and therapeutic dose.' (p. 19)
Mallinckrodt et al. [67]	Assessment of efficacy using MMRM vs. LOCF methods	Yes	[50, 51, 53, 54, 56, 57, 80, 81]	'Empirical research has clearly demonstrated the theoretical advantages of MMRM over LOCF-ANOVA. However, interpretations regarding the efficacy of duloxetine in MDD were unaffected by the choice of analytic technique.' (p. 1)
Mallinckrodt et al. [41]	Depression with and without melancholic features	Yes	[50, 51, 53, 54, 56, 57, 80, 81] Two others referenced as part of New Drug Application reviewed by FDA for depression	'In the analysis of pooled data, the efficacy of duloxetine in patients with melancholic features did not differ significantly from that observed in non-melancholic patients.' (p. 1)
Mallinckrodt et al. [37]	Efficacy and safety of 40 mg and 60 mg doses	Yes	[50, 51, 53, 81]	'Duloxetine provides safe and effective acute phase treatment of MDD at doses of 40 mg–60 mg/day. Compared with placebo, the 60 mg QD dose was more consistently effective than the 20 mg BID dose. However, the incidence of certain treatment-emergent adverse events is likely to be lower at the 40 mg dose.' (p. 337)
Mallinckrodt et al. [68]	Comparison of MMRM vs. LOCF methods	Yes	[50, 51, 53, 54, 56, 57, 69, 70, 80, 81]	'Researchers may be able to take advantage of these easy-to-implement methods while we wait for further improvement in other areas.' (p. 101)
Nelson et al. [33]	Age ≥ 55	Yes	[51, 53]	'… duloxetine 60 mg/day was an efficacious treatment for MDD and also alleviated pain symptoms in depression patients age 55 and older.' (p. 227)
Nelson et al. [71]	Safety and tolerability compared with paroxetine and placebo	Yes	[50, 56, 57, 81]	'Duloxetine is safe and well tolerated in patients with MDD, with safety and tolerability comparable to that of paroxetine.' (p. 212)
Perahia et al. [28]	Discontinuation symptoms	Yes	[50, 51, 53, 54, 56, 57, 78, 80, 81]	'Abrupt discontinuation of duloxetine is associated with a [discontinuation-emergent adverse event] profile similar to that seen with other selective serotonin reuptake inhibitor (SSRI) and selective serotonin and norepinephrine reuptake inhibitor (SNRI) antidepressants.' (p. 207)

Table 1 (continued)

Study	Focus	Lilly authors?	Trials included	Conclusion
Perahia et al. [40]	Characteristics of depression	Yes	[50, 51, 53, 54, 56, 57, 78, 80, 81]	'Overall, changes on all outcome measures and response and remission rates were significantly greater in duloxetine-treated patients than in placebo-treated patients. Furthermore, the effect of duloxetine was similar across all episode characteristic groups (first/subsequent episode, short/medium/long episode duration).' (p. 285)
Perahia et al. [42]	Treatment of milder major depression	Yes	[51, 53]	'In conclusion, duloxetine 60 mg/day is effective and well-tolerated in milder MDD.' (p. 613)
Perahia et al. [72]	Depression: risk-benefit profile compared to venlafaxine	Yes	Two trials published after end of our search period	'Duloxetine 60 mg/day and venlafaxine XR 150 mg/day have similar benefit-risk profiles on the basis of a comparison utilizing [global benefit-risk assessment].' (p. 2)
Pritchett et al. [36]	Using effect size to determine optimal duloxetine dose	Yes	[50, 51, 53, 56, 57, 81]	'The effect size analyses demonstrate that duloxetine 40 mg has minimum efficacy, and that duloxetine 60–120 mg/day is effective in the treatment of patients with MDD. An initial dose less than 60 mg/day might provide better tolerability for some patients diagnosed with MDD.' (p. 42)
Raskin et al. [73]	Post-hoc analysis of single trial	Yes	[69]	'Duloxetine demonstrated a faster time to antidepressant response and improvement in self-reported pain as compared with placebo.' (p. 309)
Shelton et al. [39]	Level of depression severity as moderator of efficacy	Yes	[51, 53, 69, 74]	'Regardless of baseline MDD severity, duloxetine at one dose (60 mg/day) produced a significant improvement compared with placebo on the core emotional symptoms of MDD.' (p. 1345)
Shelton et al. [38]	Level of depression severity as moderator of efficacy	Yes	[50, 51, 53, 54, 56, 57, 69, 80, 81]	'Duloxetine demonstrated superior efficacy in the treatment of major depressive disorder, when compared with placebo, regardless of baseline severity of depressive symptoms, although effect sizes were largest in the most severely depressed patients.' (p. 348)
Stewart et al. [22]	Male vs. female: safety	Yes	[50–54, 80, 81]	'No evidence of clinically meaningful sex differences in the safety and tolerability of duloxetine were uncovered.' (p. 183)
Thase et al. [24]	Cardiovascular profile	Yes	[50, 51, 53, 54, 56, 57, 75, 80, 81]	'These data demonstrate that duloxetine has modest effects on heart rate and BP and no clinically meaningful effect on electrocardiogram profiles in a relatively healthy cohort of clinical trial patients.' (p. 132)
Van Baardewijk et al. [76]	Cost effectiveness of duloxetine versus venlafaxine	No	[50–54, 57]	'Differences in pharmacoeconomic outcomes found were modest, but in all cases, favoured venlafaxine-XR over duloxetine.' (p. 1271)
Viktrup et al. [31]	Urinary side effects	Yes	Eight depression trials; eight stress urinary incontinence trials; no individual studies cited	'Duloxetine treatment in women and men with depression and in women with SUI was rarely associated with obstructive voiding symptoms, and no subjects had objective acute retention requiring catheterization.' (p. 65)
Vis et al. [77]	Meta-analysis of indirect comparisons between duloxetine and venlafaxine	No	[50–54, 57]	'Venlafaxine-XR tends to have a favorable trend in remission and response rates compared with duloxetine. However, dropout rates and adverse events did not differ. A direct comparison is warranted to confirm this tendency.' (p. 1798)
Wernicke et al. [25]	Cardiovascular safety profile across several conditions	Yes	42 trials (including trials for other conditions) [50–54, 56, 57, 69, 74, 80, 81]	'Overall, the findings presented here support our conclusions that use of duloxetine does not appear to be associated with significant cardiovascular risks in patients with conditions for which the drug has been approved or studied.' (p. 438)
Wise et al. [26]	Effect on body weight	Yes	[50, 51, 53, 54, 56, 57, 78–81]	'Duloxetine-treated patients experienced weight loss after short-term treatment, followed by modest weight gain on longer-term treatment. The size of the weight changes observed suggests that the antidepressant duloxetine has minimal effects on weight for the majority of patients.' (p. 269)

Table 2. Trials most frequently cited in pooled analyses

Study	Number of pooled analyses including data from trial
Detke et al. [53]	33
Detke et al. [51]	33
Goldstein et al. [50]	27
Eli Lilly Study 4091a [80][1]	23
Goldstein et al. [54]	22
Detke et al. [57]	20
Eli Lilly Study 3327b [81][1]	18
Perahia et al. [56]	17

[1] Indicates study that was not published as a standalone article. Data from these trials are available from the Eli Lilly online clinical trial registry.

Discussion

Our findings suggest that many pooled analyses regarding the efficacy and safety of duloxetine have substantial redundancy. In many instances, it was difficult to ascertain how such salami publications were making substantial contributions to the scientific literature. Several clinical trials were included in over 20 pooled analyses.

We do not claim that the scientific questions examined in the pooled analyses lacked legitimate scientific importance. For example, the potential interaction of gender and race with treatment response is certainly a topic of interest. However, given that Latinos, Blacks, and Whites all tended to respond similarly to duloxetine and that gender also did not moderate outcome, it seems that such data could easily have been presented in a single publication rather than in 3 published pooled analyses. Likewise, data on safety outcomes were sliced into several pieces. It is unclear how an individual publication is needed to report data separately for safety outcomes such as nausea, sexual side effects, urinary side effects, and several others. Multiple publications based on similar data which conclude that duloxetine is effective for mild depression, melancholic depression, and across differing lengths of depressive episodes likewise seem redundant. A much smaller number of publications could likely have communicated such data just as clearly. Further, the sample size of some pooled analyses was rather small; 6 pooled analyses included only data from 2 clinical trials. It is likely that exceedingly few meta-analyses have been published based on only 2 trials, raising the question of why pooled analyses based on only 2 trials warrant publication in the absence of novel scientific data.

A limitation of the current investigation is that the inappropriateness of 'salami slicing' is not universally agreed upon. What may be considered redundant information by some may be considered an important scientific contribution by others. Thus, we acknowledge that different evaluators may draw different conclusions regarding whether these publications were appropriate. However, we believe that publishing similar outcomes from the same dataset of publications on several occasions better serves the curricula vitae of researchers and, potentially, goals of drug marketers, than it does science and patient care.

Outside of Melander et al. [15], we are aware of no other investigation which has examined the prevalence of redundant pooled analyses. We only included publications on a single drug and focused on only the literature related to one of its multiple indications. It is certainly possible that pooled analyses regarding duloxetine are not representative of the broader scientific literature. Indeed, given our limited focus, it is likely inappropriate to generalize that pooled analyses containing redundant data are widely spread in the psychiatric or wider medical literature. We have simply demonstrated that in the instance of duloxetine in the treatment of depression, 'salami slicing' appears to have taken place with substantial frequency via pooled analyses.

Writings from the drug industry indicate that medical journal publications, rather than just communicating scientific findings, are an important part of the drug marketing process. As written in a medical marketing trade publication, 'the goal of strategic publication planning is to accelerate the adoption of a new chemical entity and, by doing so, accelerate uptake after it enters the market' [47, p. 41]. The same author noted that a good strategic publication plan supports a product's 'selling platform' [47, p. 41]. Documents from Pfizer and Eli Lilly indicate similar views, that journal publications are linked to product sales [7, 8].

Journal editors, peer reviewers, and researchers should be aware that salami publication wastes valuable resources of editors, reviewers, and journals [1–6]. Further, salami publications may be more representative of propaganda than of actual contributions to science [48]. The fact that such redundant publications have appeared in a wide variety of medical journals raises questions about the quality of peer review and what passes for 'original' science. A recent editorial raised concerns that the medi-

cal literature has a 'bias in favour of valuable commercial content as opposed to tough-minded critical analysis' [49, p. 199]; our findings lend credence to such views. Greater vigilance on the part of reviewers and editors may help to curb such publication practices, but the ultimate responsibility lies with authors, who should understand that 'salami science' does little to advance either science or patient care.

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