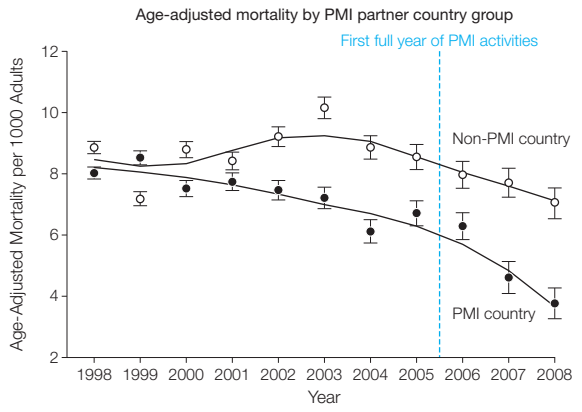
Figure. Age-Adjusted Mortality by the President's Malaria Initiative (PMI) Partner Country Group



Differential mortality trends are not obvious between PMI partner and non–PMI partner countries while PMI was implemented. A narrow-bandwidth (0.6) lowess curve was used to fit the trend. Lowess (locally weighted scatterplot smoothing) is a nonparametric method of fitting a curve using local regressions for each point. Error bars indicate 95% confidence intervals.

all mortality risk reduction. Shelton's point about the expectation of smaller effect on all-cause adult mortality from expansion of antiretroviral therapy in places where HIV prevalence is low is well taken. However, our country-specific estimates were based on the difference in the predicted mortality rates with and without PEPFAR for each country. As a result, the estimates of number of deaths averted in each of the 9 focus countries ranged from 2.4% to 17.4%. Our estimates involved substantial uncertainty (95% CI, 443 300-1 808 500 deaths averted), and our point estimate (740 800) should be viewed in that context.

Shelton's other concern is the possibility that the mortality effect may be related to PMI, which partially overlapped with PEPFAR geographically and temporally. The argument that malaria control efforts can reduce adult mortality, while feasible, is unproven. Although the recent analysis by Murray et al[1] suggests malaria mortality among adults is substantial, this notion challenges World Health Organization estimates[2] and requires further confirmation. Shelton also mentions that Rwanda and Tanzania (the countries we used in the subnational analysis) had particularly intensive PMI interventions. However, to make a causal argument, one would have to align the districts with PMI activity intensity, as we did for PEPFAR.

This issue can also be addressed empirically. Figure 2 from our article was altered to illustrate trends in adult mortality by PMI partner country group (FIGURE). The data in the Figure fail to suggest an obvious overlap between declines in adult mortality and PMI's coverage and timing. A statistical analysis exploring the independent and joint effects of the programs could provide additional insights.

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RESEARCH LETTER

Changes in Direct-to-Consumer Pharmaceutical Advertising Following Shifts From Prescription-Only to Over-the-Counter Status

To the Editor: Direct-to-consumer advertising (DTCA) can influence the use of prescription drugs.[1,2] The US Food and Drug Administration (FDA) regulates prescription drug advertising, including requirements to provide consumers with a "fair balance" of risks and benefits. When prescription drugs switch to over-the-counter (OTC) status, regulatory oversight of their advertising shifts to the Federal Trade Commission (FTC). Unlike the FDA, the FTC holds drug advertisements to the same standards as any consumer product: it applies a "reasonable consumer" standard of truthfulness and nondeception that does not require any balancing of potential benefits and harms. Such a shift may be associated with changes in content.

Methods. We analyzed all print and broadcast advertisements from 4 commonly used prescription drugs that were the subject of extensive DTCA promotion before and after OTC shift: loratidine (OTC in 2002), omeprazole (in 2004), orlistat (in 2007), and cetirizine (in 2008). Television and print materials spanning 24 months before and 6 months following OTC shift for each drug were obtained from an advertising database compiled by VMS Adsight, an archiver of print and broadcast advertising media.[3] The longer preshift period was required to obtain comparable numbers of prescription and OTC advertisements. Reproductions of 133 discrete advertisements were obtained, stratified by whether they appeared in print or television, and coded for descriptive characteristics, presentation of health benefits (specific indications and claims of general health improvement), and potential health harms (adverse effects, contraindications, warnings, and precautions) by 2 independent researchers. A third coder settled disagreements in 52 (13%) of 399 coding judgments. Prevalence ratios (PRs) of characteristics before and after the OTC switch were compared using the Fisher exact test and Stata statistical software version 7.2 (StataCorp). All tests were 2-tailed and the level of significance was $P < .05$; multiple comparisons used a Bonferonni-corrected α level of .002.

Results. After the OTC switch, 62 of 64 (97%) advertisements described benefits of medications compared with 57

of 69 (83%) during the prescription only period (PR, 1.17 [95% CI, 1.04-1.32]; $P=.01$; TABLE). The difference was not statistically significant for individual drugs. Differences existed in the presentation of potential harms during the prescription-only period in 48 of 69 advertisements (70%) vs 7 of 64 (11%) after OTC shift (PR, 0.17 [95% CI, 0.09-0.35]; $P<.001$). With the exception of print advertisements for orlistat, no postswitch advertisements mentioned contraindications or adverse effects. Print and broadcast advertisements after OTC switch were less likely to mention drugs' generic names (33 of 64 [52%] vs 65 of 69 [94%]; PR, 0.55 [95% CI, 0.43-0.70]; $P<.001$).

Comment. Our results support and extend initial reports on the practical outcomes of the shift in regulatory oversight in drug promotion from the FDA to the FTC that accompany OTC shift.[4] In addition to less presentation of potential harms, DTCA for OTC medications frequently omitted identification of drugs by their generic names, both of which are key tools for consumers seeking independent information on risks, benefits, and costs.[5]

These 4 products may not be representative of all prescription drugs, OTC drugs, or drugs undergoing OTC shift. Our study omitted online and radio advertisements, and advertisements may have been missed by the VMS algorithms. This analysis cannot distinguish between overrepresentation of insignificant harms in DTCA for prescription drugs vs the underrepresentation of significant harms in DTCA for OTC drugs.

The FDA's "fair balance" requirements covering prescription DTCA do not necessarily result in balanced presentations of risks and benefits, and these guidelines are known to be inconsistently enforced. However, our analysis suggests that DTCA after OTC switch presents even less information for making an informed decision, at a time when consumers must have more knowledge of whether medications' potential benefits are worth their

Table. Characteristics of Direct-to-Consumer Advertising for 4 Pharmaceutical Products Both Before Prescription and After Over-the-Counter Shift[a]

	Benefits Presented					Harms Presented					Generic Name Mentioned				
	No. (%)		Prevalence (95% CI)			No. (%)		Prevalence (95% CI)			No. (%)		Prevalence (95% CI)		
Drug	Rx	OTC	Difference	Ratio	*P* Value[b]	Rx	OTC	Difference	Ratio	*P* Value[b]	Rx	OTC	Difference	Ratio	*P* Value[b]
Loratidine	21 (72)	8 (100)	0.28[c]	1.38	.16	15 (52)	0	–0.52[c]	NA	.01	26 (90)	7 (88)	–0.02 (–0.28 to 0.23)	0.97 (0.73 to 1.30)	>.99
TV	10 (71)	5 (100)	0.29[c]	1.40[c]	.53	8 (57)	0	–0.57[c]	NA	.04	11 (79)	4 (80)	0.01[c]	1.02[c]	>.99
Print	11 (73)	21 (91)	0.27[c]	1.36[c]	>.99	7 (47)	0	–0.47[c]	NA	.25	15 (100)	3 (100)	NA	NA	NA
Omeprazole	8 (80)	17 (74)	0.11 (–0.16 to 0.39)	1.14 (0.82 to 1.59)	.57	8 (80)	0	–0.26[c]	NA	>.99	10 (100)	2 (9)	–0.91[c]	0.09[c]	<.001
TV	3 (75)	6 (86)	0.11 (–0.39 to 0.60)	1.14 (0.60 to 2.17)	>.99	3 (75)	0	–0.75[c]	NA	.02	4 (100)	0	NA	NA	.003
Print	5 (83)	15 (94)	0.10 (–0.22 to 0.43)	1.13 (0.77 to 1.64)	.48	5 (83)	0	–0.83[c]	NA	<.001	6 (100)	2 (13)	–0.88[c]	0.13[c]	<.001
Orlistat	9 (82)	17 (100)	0.18[c]	1.22[c]	.15	7 (64)	7 (41)	–0.22 (–0.59 to 0.14)	0.65 (0.31 to 1.33)	.44	10 (91)	14 (82)	–0.09 (–0.33 to 0.16)	0.91 (0.69 to 1.21)	>.99
TV	3 (75)	4 (100)	0.25[c]	1.33[c]	>.99	2 (50)	0	–0.50[c]	NA	.43	4 (100)	3 (75)	–0.25[c]	0.75[c]	>.99
Print	6 (86)	13 (100)	0.14[c]	1.17[c]	.35	5 (71)	7 (54)	–0.18 (–0.61 to 0.25)	0.75 (0.38 to 1.50)	.64	6 (86)	11 (85)	–0.01 (–0.34 to 0.31)	0.99 (0.67 to 1.45)	>.99
Cetirizine	19 (100)	16 (100)	NA	NA	NA	18 (95)	0	–0.95[c]	NA	<.001	19 (100)	10 (63)	–0.38[c]	0.63[c]	.005
TV	7 (100)	2 (100)	NA	NA	NA	6 (86)	0	–0.86[c]	NA	.08	7 (100)	0	NA	NA	.03
Print	12 (100)	14 (100)	NA	NA	NA	12 (100)	0	NA	NA	<.001	12 (100)	10 (71)	–0.29[c]	0.71[c]	.10
Total	57 (83)	62 (97)	0.14 (0.04 to 0.24)	1.17 (1.04 to 1.32)	.01	48 (70)	7 (11)	–0.57 (–0.71 to –0.44)	0.17 (0.09 to 0.35)	<.001	65 (94)	33 (52)	–0.43 (–0.56 to –0.29)	0.55 (0.43 to 0.70)	<.001
TV	23 (79)	17 (94)	0.15 (–0.03 to 0.33)	1.19 (0.96 to 1.48)	.23	19 (66)	0	–0.66[c]	NA	<.001	26 (90)	7 (39)	–0.51 (–0.76 to –0.26)	0.43 (0.24 to 0.78)	<.001
Print	34 (85)	45 (98)	0.13 (0.01 to 0.25)	1.15 (1.00 to 1.32)	.05	29 (73)	7 (15)	–0.57 (–0.75 to –0.40)	0.21 (0.10 to 0.43)	<.001	39 (98)	26 (57)	–0.41 (–0.56 to –0.26)	0.58 (0.45 to 0.75)	<.001

Abbreviations: DTCA, direct-to-consumer advertising; NA, not able to calculate; OTC, over-the-counter; Rx, prescription.

[a] The Rx and OTC totals are: for loratidine: 29 and 8, respectively, for overall, 14 and 5 for TV, and 15 and 3 for print; for omeprazole: 10 and 23 for overall, 4 and 7 for TV, and 6 and 16 for print; for orlistat: 11 and 17 for overall, 4 and 4 for TV, and 7 and 13 for print; for cetirizine: 19 and 16 for overall, 7 and 2 for TV, and 12 and 14 for print; and for total: 69 and 64 for overall, 29 and 18 for TV, and 40 and 46 for print.

[b] Calculated using a 2-sided Fisher exact test.

[c] Confidence intervals could not be calculated in cases where a cell had a zero value.

risks and costs. Pharmaceuticals do not lose their capacity for harm after moving from behind the pharmacist's counter to in front of it; misuse of OTC drugs remains a major cause of emergency department visits, hospitalization, and death.[6] Closer attention should be paid to how such drugs are promoted to consumers.

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Study concept and design: Greene, Choudhry, Kesselheim, Shrank.
Acquisition of data: Greene, Brennan, Shrank.
Analysis and interpretation of data: Greene, Shrank.
Drafting of the manuscript: Greene.
Critical revision of the manuscript for important intellectual content: Greene, Choudhry, Kesselheim, Brennan, Shrank.
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CORRECTION

Incorrect Date: In the Viewpoint entitled "HIV/AIDS in 1990 and 2012: From San Francisco to Washington, DC," published in the July 25, 2012, issue of *JAMA* (2012;308[4]:345-346), a date was incorrectly reported. In the paragraph beginning "In contrast, a great success story is the advent of highly active antiretroviral therapy . . . ", the date at the end of that sentence should have been reported as 2003, rather than 1993. This article has been corrected online.