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Publication of comparative effectiveness research has not increased in high-impact medical journals, 2004-2013

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INTRODUCTION

Patient-centered research informs patients, physicians and other stakeholders about the benefits and risks of different healthcare options using findings from comparative effectiveness research (CER) and patient-reported outcomes.[1-4] Interest in patient-centered research has risen over the past decade to fill evidence gaps unanswered by placebo-controlled trials. Consequently, US governmental investment in this research has also increased, including $1.1 billion allocated for CER by the 2009 American Recovery and Reinvestment Act (ARRA)[5] and establishment of the Patient Centered Outcomes Research Institute by the 2010 Affordable Care Act (ACA).[6] We conducted a systematic review to explore whether rising interest and investment in patient-centered research has increased use of CER and PROs among pharmacologic intervention studies published in widely-read medical journals from 2004-2013.

MATERIALS/METHODS

We randomly selected 468 studies (20% sample) from 2335 original research articles with ≥1 pharmacologic interventions published from 2004-2013 in five widely-read medical journals (*Annals of Internal Medicine (Annals), British Medical Journal (BMJ), Journal of the American Medical Association (JAMA), Lancet, New England Journal of Medicine (NEJM)*). Reviews/meta-analyses, modeling studies, cost-effectiveness studies, cross-sectional studies, and case studies were excluded. Six reviewers abstracted study attributes using standardized guidance.

Comparisons between pharmacologic interventions and other interventions were classified as non-treatment, placebo, head-to-head (comparator=≥1 other active intervention), additive (comparator=main intervention plus other active interventions), treatment-varying (comparator=different dose/duration/order), and external (comparator=other time/population). CER was considered studies using head-to-head comparisons. PROs were defined as a patient's health status directly reported by the patient without outside interpretation.[7] Studies using CER or PROs were summarized by characteristics and trends were graphed with locally weighted smoothing curves using SAS 9.4 (SAS Institute, Cary, NC).

RESULTS

Of 468 sampled pharmacologic intervention studies, 30.3% used CER and 32.9% collected PROs. The *Lancet* (35.6%) and *JAMA* (32.5%) had the greatest percentage of published CER studies. PROs were most common in the *Annals* (41.9%) and *NEJM* (40.1%).

Among CER studies, 86% were randomized and 14% were non-randomized (Table 1). CER studies were generally larger than other studies and commonly assessed pharmacologic interventions for cardiovascular/renal, endocrine, and rheumatologic/orthopedic indications. Approximately 29% of CER studies used PROs.

The percentage of pharmacologic intervention studies using CER changed minimally among high-impact journals from 2004-2013, while the percentage with ≥1 PRO(s) noticeably

increased (Figure 1). Neither the ARRA nor ACA visibly impacted trends, even after considering a 2-year lag between policy approval and publication.

DISCUSSION

Despite growing interest and investment in patient-centered research, CER did not increase among pharmacologic intervention studies published in high-impact medical journals from 2004-2013. Placebo-controlled trials continue to dominate this literature. Concerns about lower power in head-to-head comparisons and bias in real-world studies may underlie a reluctance to publish CER.[8] Our analysis may be premature if governmental investments had not yet influenced publication trends by December 2013. We did observe increased use of PROs, especially among randomized trials, potentially reflecting recent FDA guidance supporting PROs as evidence of clinical benefit. Additional research should explore why CER has not increased in widely-read medical journals despite demand for such evidence.

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Highlights

- Despite increasing governmental interest and investment in comparative research, the proportion of studies published in high-impact medical journals using comparative effectiveness research (CER) did not change from 2004-2013.
- The proportion of studies published in high-impact medical journals using patient-reported outcomes has increased from 2004-2013, suggesting that more evidence is available to help clinicians make treatment decisions incorporating the patient viewpoint.

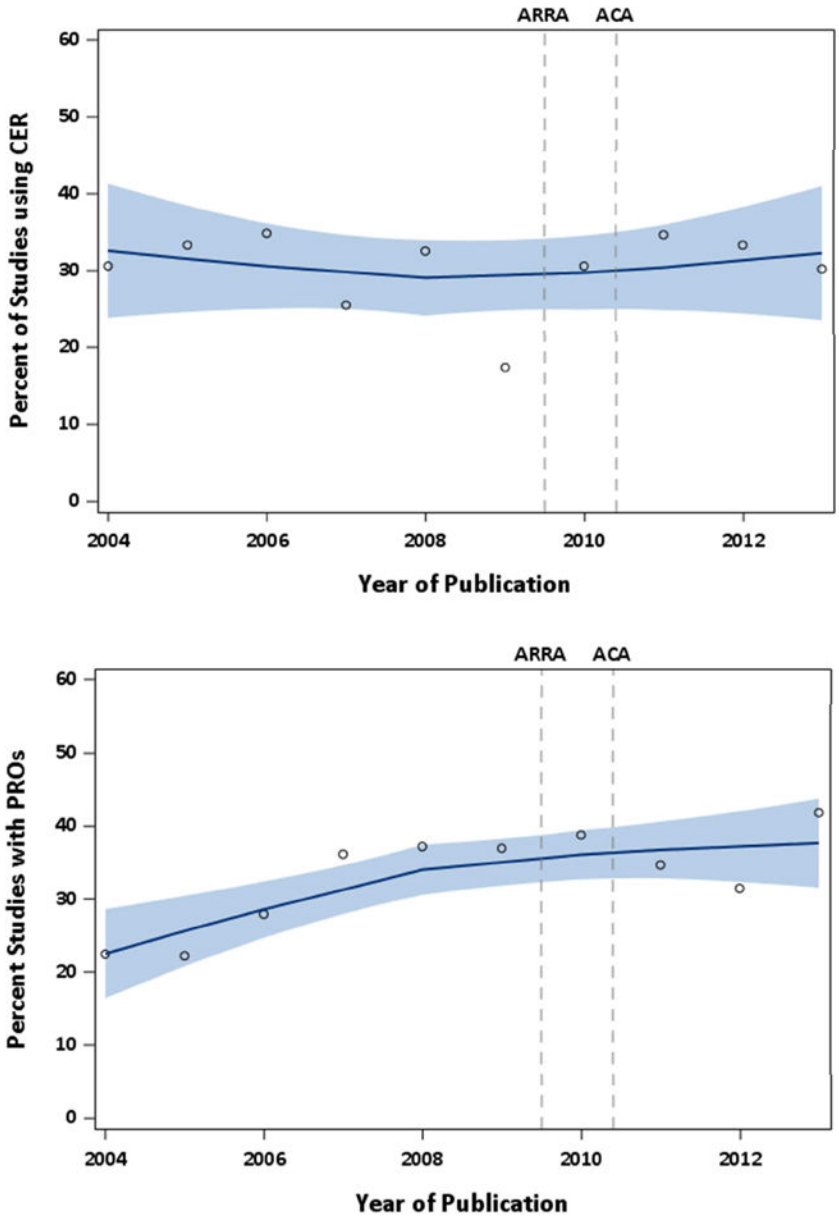

FIGURE 1.

Trends in the percentage of studies on pharmacologic interventions published in high-impact medical journals from 2004-2013 using comparative effectiveness research (top) and patient-reported outcomes (bottom). Blue shading represents 95% confidence bands.

TABLE 1

Journal and study attributes of a 20% random sample of studies on pharmacologic interventions (n=468) published in five high-impact medical journals from 2004-2013

Characteristic	CER, n(%)		PRO, n(%)	
	Yes (n=142)	No (n=326)	Yes (n=154)	No (n=314)
Journal				
NEJM	51 (35.9)	126 (38.7)	71 (46.1)	106 (33.8)
Lancet	47 (33.1)	86 (26.4)	33 (21.4)	100 (31.8)
JAMA	26 (18.3)	54 (16.6)	30 (19.5)	50 (15.9)
BMJ	11 (7.7)	36 (11.0)	7 (4.5)	40 (12.7)
Annals	7 (4.9)	24 (7.4)	13 (8.4)	18 (5.7)
Size				
<250	26 (18.3)	89 (27.3)	59 (38.3)	56 (17.8)
251-2500	74 (52.1)	140 (42.9)	76 (49.4)	138 (44.0)
>2500	42 (29.6)	97 (29.8)	19 (12.3)	120 (38.2)
Randomization				
Non-randomized	20 (14.1)	65 (19.9)	4 (2.6)	82 (26.1)
Randomized	122 (85.9)	261 (80.1)	150 (97.4)	232 (73.9)
Study Purpose				
Effectiveness	20 (14.1)	43 (13.2)	9 (5.8)	54 (17.2)
Efficacy	49 (34.5)	173 (53.1)	90 (58.4)	132 (42.0)
Efficacy/Safety	64 (45.1)	76 (23.3)	52 (33.8)	88 (28.0)
Safety	9 (6.3)	34 (10.4)	3 (2.0)	40 (12.7)
Comparison Type[a]				
Placebo	-	-	90 (58.4)	119 (37.9)
No treatment	-	-	10 (6.5)	50 (15.9)
Head-to-head[b]	-	-	39 (25.3)	101 (32.2)
Additive[c]	-	-	14 (9.1)	25 (8.0)
Treatment-varying	-	-	18 (11.7)	75 (23.9)
Other	-	-	2 (1.3)	20 (6.4)
Treatment indication[d]				
Cardiovascular/Renal	33 (23.2)	68 (20.9)	20 (13.0)	81 (25.8)
Endocrine	10 (7.0)	19 (5.8)	11 (7.1)	18 (5.7)
Gastrointestinal	5 (3.5)	8 (2.5)	1 (0.7)	12 (3.8)
Hematology/Oncology	21 (14.8)	50 (15.3)	25 (16.2)	46 (14.7)
Infectious disease	35 (24.7)	91 (27.9)	35 (22.7)	91 (29.0)
Neurologic	4 (2.8)	14 (4.3)	10 (6.5)	8 (2.6)
Psychiatric	6 (4.2)	10 (3.1)	11 (7.1)	5 (1.6)
Reproductive	5 (3.5)	6 (1.8)	6 (3.9)	5 (1.6)

Characteristic	CER, n(%)		PRO, n(%)	
	Yes (n=142)	No (n=326)	Yes (n=154)	No (n=314)
Respiratory	5 (3.5)	18 (5.5)	9 (5.8)	14 (4.5)
Rheumatologic/orthopedic	12 (8.5)	13 (4.0)	9 (5.8)	16 (5.1)
Other	6 (4.2)	29 (8.9)	17 (11.0)	18 (5.7)
Patient reported outcome (PRO)				
No PRO	101 (71.1)	213 (65.3)	-	-
≥1 PRO	41 (28.9)	113 (34.7)	-	-

Abbreviations: CER, comparative effectiveness research; PRO, patient-reported outcome.

[a] Each study could have more than one comparison type. Percentages may add to >100%.

[b] Comparison of a pharmacologic intervention with any other non-placebo intervention.

[c] Comparisons between a pharmacologic intervention alone and with the addition of ≥1 interventions.

[d] Disease that is being treated by the main pharmacological intervention.