Dr. Pincus *et al*, reply

To the Editor:

We appreciate Dr. Anderson's interesting comments, and would offer the following:

1. The data presented did not involve a metaanalysis, but rather a compilation of reports that included data concerning mortality in patients with rheumatoid arthritis (RA) that included a baseline erythrocyte sedimentation rate (ESR). As noted in the report[1], a computer search for "erythrocyte sedimentation rate (ESR)" and "rheumatoid arthritis (RA)" yielded about 86,000 reports. Even if it were possible to examine all these reports (which would require years), the results would likely have been similar to the reported data, which are consistent with clinical findings[2,3].

2. ESR tests were performed according to the Westergren sedimentation rate, although in several reports the method was not mentioned. Nonetheless, the Wintrobe sedimentation rate, with a maximum of 100, yields lower values, and its use would have lowered the ESR in earlier studies, contrary to the findings.

3. Patients included in databases analyzed in this study were not participants in clinical trials, but rather in observational studies. This matter is relevant because inclusion criteria for clinical trials have remained relatively similar over the last 50 years, such as an ESR > 28 mm/h. Most patients with RA seen in our clinical settings did not meet inclusion criteria for current clinical trials[4,5], in part as ESR was not > 28. In our opinion, the ESR requirement in clinical trials is undesirable, particularly as patients with normal and elevated ESR at baseline had a similar likelihood of taking methotrexate or biological agents (manuscript in preparation).

4. We would agree that the observation of lower levels of ESR may reflect nonspecifically milder inflammatory disease at this time compared to earlier periods. This phenomenon may meet a definition of an epiphenomenon, i.e., "an occurrence that is accidental, accessory, or incidental to a cause-and-effect relationship." Nonetheless, there is no currently available measure of RA status, ranging from swollen joints to patient self-report scores for pain, that addresses a cause-and-effect relationship, and all clinical measures may be regarded as "epiphenomena." All 7 RA Core Data Set measures are better in RA patients seen in recent years compared to the 1980s, although ESR remains elevated in individuals of low socioeconomic status in advantaged countries[6], and in general in disadvantaged individuals[7].

The primary basis for any measure in clinical medicine is to provide guidance for clinical decisions. ESR is less likely to be abnormal than any of the other 6 Core Data Set measures for RA, including joint counts, questionnaire scores, and global measures, as noted in several recent poster presentations at the ACR and EULAR annual meetings. We recently recognized data from 4 additional sites from the early 1990s from the EURIDISS (European Research on Incapacitating Diseases and Social Support) study[8], in which the mean ESR was < 30 mm/h in RA patients from Oslo (Norway), Nancy (France), Groningen (The Netherlands), and Belfast (Northern Ireland), now bringing to 7 the total number of locales with similar findings (Table 1).

We thank Dr. Anderson for his comments, and hope this correspondence will further alert rheumatologists to the likelihood of a normal ESR in a large fraction of patients with RA.

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Table 1. Erythrocyte sedimentation rate in 7 locations, 1980–2005.

Location	n	Patients with ESR < 28 mm/h, %	ESR (mm/h)	
			Mean	Median
Wichita, KS, USA, 1994[2]	1556	37% F, 45% M	37 F, 34 M	38 F, 33 M
Oslo, Norway, 1996[8]	237	—	26	—
Nancy, France, 1996[8]	135	—	29	—
Groningen, The Netherlands, 1996[8]	283	—	28	—
Belfast, Northern Ireland, 1996[8]	51	—	28	—
Jyvaskyla, Finland, 2009[3]	1892	45%	—	30
Nashville, TN, USA, 2009[3]	738	47%	—	30