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discrepancies between physician and patient perceptions and emphasizes significant concerns among physicians regarding the quality of virtual care provision. They also suggest that patients, compared to physicians, value convenience when thinking about quality. These insights represent opportunities for technologic innovation but also indicate a need for caution as we integrate this care modality. Our study is limited by our sample size of 572 and the fact that patients who did not schedule video visits could not be included. Larger, multi-institutional studies are needed to better understand the limitations of, and opportunities afforded by, teledermatology during the public health crisis and beyond.

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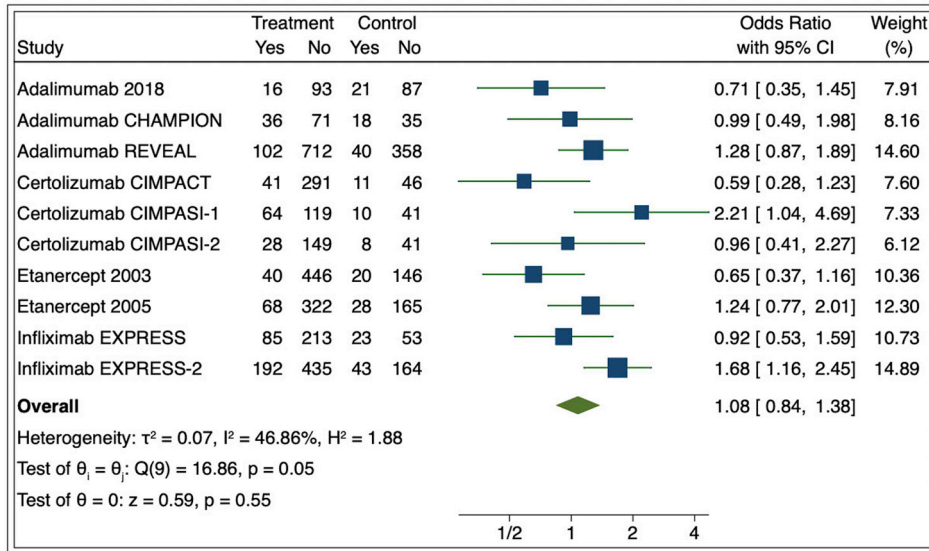
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Effect of anti-tumor necrosis factor therapy on the risk of respiratory tract infections and related symptoms in patients with psoriasis—A meta-estimate of pivotal phase 3 trials relevant to decision making during the COVID-19 pandemic



To the Editor: The COVID-19 pandemic turned attention to how immune-targeted therapies affect respiratory tract infections (RTIs). We reported meta-estimates of the risk of RTI associated with biologics that target interleukin (IL) 17 (odds ratio [OR], 1.56; 95% confidence interval [CI], 1.04-2.33)¹ and IL-23 (OR, 1.24; 95% CI, 0.98-1.56)² based on publicly available pivotal trial data. We now evaluate tumor necrosis factor inhibitors (TNFi) using a similar approach. TNF- α plays an important role in defense against viral infection, possibly through lysis of virus-infected cells and/or induction of an antiviral state in normal cells. In contrast, some models suggest that TNF may mediate significant tissue damage in RTIs.³ Despite extensive studies of TNF inhibitors over the past 2 decades, there are limited data on the effect of these biologics on the risk of RTIs.

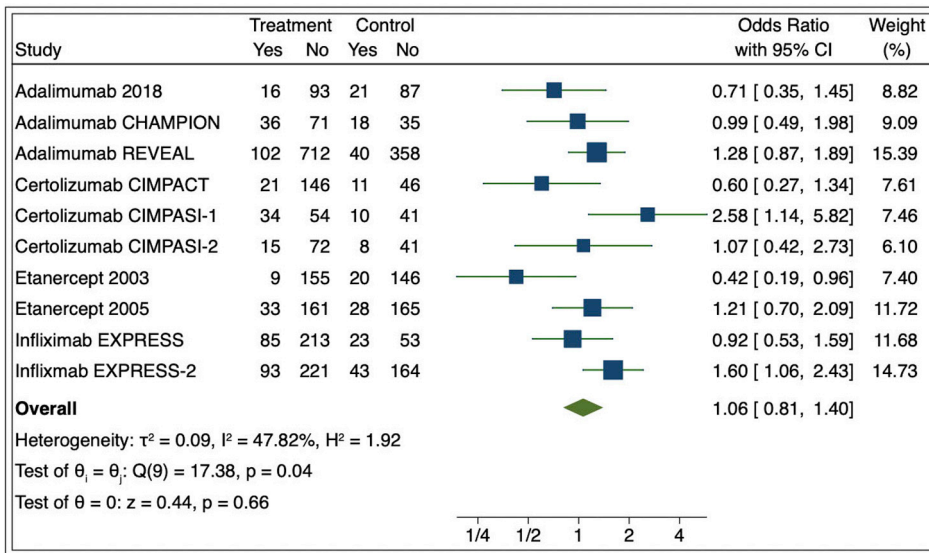
To rapidly assess the risk of RTI associated with TNFi, terms consistent with RTI were evaluated from data reported in publications of US Food and Drug Administration—approved, phase 3, placebo-controlled clinical trials listed in the prescribing information for adalimumab, infliximab, etanercept, and certolizumab. This data source was used because most trials were conducted before the initiation of clinicaltrials.gov. RTI events were summed and divided by the total number of individuals at risk in each study and compared to the placebo group by a meta-estimate. A significant increased risk of RTI was not observed in TNFi compared to placebo (OR, 1.08; 95% CI, 0.84-1.38; $P = .55$) (Fig 1). The events reported in our primary analysis used varying drug dosages. In our secondary analysis, we limited the exposure to only US Food and Drug Administration—approved dosing



Random-effects REML model

Doses used in this meta-estimate: Adalimumab 40 mg; Infliximab 3&5 mg/kg; Etanercept 25 & 50 mg; Certolizumab 200 & 400mg for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy. The size of the square corresponds to the relative weight assigned in the pooled analysis, and the horizontal lines indicate the confidence interval (CI). The diamond denotes the overall effect size, and the lateral tips of the diamond indicate the associated CI.

Fig 1. Meta-estimate of respiratory tract infections from publications of US Food and Drug Administration–approved dosages of phase 3 pivotal trials adverse events tables (includes “upper respiratory tract infections,” “nasopharyngitis,” “rhinitis,” “rhinorrhea,” “pneumonia,” bronchitis,” “sinusitis,” “pharyngitis,” “flu syndrome,” and “cough”). *CI*, Confidence interval; *REML*, restricted maximum likelihood.



Random-effects REML model

Doses used in this meta-estimate: Adalimumab 40 mg; Infliximab 5 mg/kg; Etanercept 50 mg; Certolizumab 400mg for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy. The size of the square corresponds to the relative weight assigned in the pooled analysis, and the horizontal lines indicate the confidence interval (CI). The diamond denotes the overall effect size, and the lateral tips of the diamond indicate the associated CI.

Fig 2. Meta-estimate of respiratory tract infections from publications of US Food and Drug Administration–approved dosages of phase 3 pivotal trials adverse events tables (includes “upper respiratory tract infections,” “nasopharyngitis,” “rhinitis,” “rhinorrhea,” “pneumonia,” “bronchitis,” “sinusitis,” “pharyngitis,” “flu syndrome,” and “cough”). *CI*, Confidence interval; *REML*, restricted maximum likelihood.

regimens and found similar results (OR, 1.06; 95% CI, 0.81-1.40; $P = .66$) (Fig 2). Sensitivity analyses were conducted, combining drugs with similar mechanisms of action and structure (ie, adalimumab and infliximab), which yielded similar results (OR, 1.14; 95% CI, 0.86-1.51; $P = .36$). We also evaluated certolizumab individually because its clinical trials occurred more recently, but the results were similar (OR, 1.18; 95% CI, 0.50-2.79; $P = .70$).

In conclusion, we found no evidence of an increased risk of RTI in pivotal trials of TNFi in psoriasis. Caution is advised in comparing these results to our prior analyses of biologics targeting IL-17 and IL-23 because of statistical imprecision, different populations, and time periods studied; therefore, one should not necessarily conclude that TNFi are more or less safe than biologics targeting IL-17 and IL-23 with respect to risk of RTI and COVID-19. Furthermore, we could not estimate viral RTI specifically because objective confirmatory testing was not reported. Nevertheless, the findings are reassuring, and recent data suggest that TNFi are associated with a 60% reduction in the risk of hospitalization for patients with rheumatism infected with severe acute respiratory syndrome coronavirus 2, possibly related to a TNFi-suppressing cytokine storm.⁴ However, these data are derived from spontaneous case reports and should be interpreted with caution. TNFi are currently being tested in clinical trials of patients with COVID-19.⁵ Trial data and large-scale, prospective cohort studies are urgently needed to better define the impact of TNFi on infections with severe acute respiratory syndrome coronavirus 2 and outcomes from COVID-19 illness.

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