The high global prevalence of depression, together with the recent acceleration of remote care owing to the COVID-19 pandemic, has prompted increased interest in the efficacy of digital interventions for the treatment of depression. We provide a summary of the latest evidence base for digital interventions in the treatment of depression based on the largest study sample to date. A systematic literature search identified 83 studies ($N = 15,530$) that randomly allocated participants to a digital intervention for depression versus an active or inactive control condition. Overall heterogeneity was very high ($I^2 = 84\%$). Using a random-effects multilevel metaregression model, we found a significant medium overall effect size of digital interventions compared with all control conditions ($g = .52$). Subgroup analyses revealed significant differences between interventions and different control conditions (WLC: $g = .70$; attention: $g = .36$; TAU: $g = .31$), significantly higher effect sizes in interventions that involved human therapeutic guidance ($g = .63$) compared with self-help interventions ($g = .34$), and significantly lower effect sizes for effectiveness trials ($g = .30$) compared with efficacy trials ($g = .59$). We found no significant difference in outcomes between smartphone-based apps and computer- and Internet-based interventions and no significant difference between human-guided digital interventions and face-to-face psychotherapy for depression, although the number of studies in both comparisons was low. Findings from the current meta-analysis provide evidence for the efficacy and effectiveness of digital interventions for the treatment of depression for a variety of populations. However, reported effect sizes may be exaggerated because of publication bias, and compliance with digital interventions outside of highly controlled settings remains a significant challenge.