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Abstract (or Book Review):	**Objective.** We conducted a systematic literature review of clinical trials to assess the comparative effectiveness of treatments for fibromyalgia in subgroups of highly affected or clinically complex adults. We focused on patient subgroups rather than overall treatment effects to complement a large systematic review being conducted on fibromyalgia treatments at McMaster University. **Methods.** Two investigators screened abstracts of identified references for eligibility (enrolled adults with fibromyalgia, examined treatment effects, had a control group, and assessed outcomes at least 3 months after treatment initiation). Full-text articles were reviewed to identify outcomes reporting for at least one adult subgroup: women, older or obese adults, individuals with coexisting mental health conditions, high severity or longer fibromyalgia duration, multiple medical comorbidities, or other chronic pain conditions. Primary outcomes included pain, symptom improvement, function, fatigue, sleep quality, participation, and health-related quality of life. We extracted data, assessed risk of bias of individual studies, and evaluated strength of evidence for each comparison and outcome. **Results**. We identified 22 randomized controlled trials (RCTs), 8 pooled analyses of patientlevel RCT data, and 4 observational studies that met inclusion criteria; 59 percent were drug trials. Adults with fibromyalgia and major depressive disorder (MDD) were studied most often; drug studies also reported outcomes by age, sex, race, and anxiety. Most drug trials examined duloxetine effects on pain and global improvement; trial duration was typically 3 months. Lowstrength evidence for duloxetine suggests that subgroups of adults with fibromyalgia and MDD do not experience differential short-term treatment effects. Other subgroup evidence is largely insufficient. For nearly all comparisons, treatment-by-subgroup interactions were not significant. Most interaction results were reported in text; only two RCTs and five pooled RCT analyses displayed data on subgroup outcomes. Losses to followup were considerable; dropout reporting was not subgroup specific. Adverse effects were reported for the MDD subgroup in one duloxetine pooled analysis; these were similar to overall adverse effects. Studies were not powered to detect subgroup effects. **Conclusion.** Despite the prevalent belief that fibromyalgia treatments may behave differently in subgroups, evidence to date is largely insufficient for fibromyalgia subgroup effects of interventions other than duloxetine in adults with concomitant MDD. Future studies should be designed to support subgroup analysis to improve clinical applicability.