Directed therapies exist. The aim of this systematic review is to summarize the existing therapies and determine how effective they are in reducing fatigue, and to conclude whether a superior effect of B cell directed therapies exist. The Medline and Embase databases were searched using the terms SS and fatigue between 1946 and 2013. The population included were adults over the age of 18, who met the American-European Consensus Criteria for pSS. The intervention was receiving biologic or pharmacological therapy. The outcome measured was an improvement in fatigue scores from baseline, using visual analogue scales, or the Multidimensional Fatigue Inventory. Randomized controlled trials [RCTs] and prospective studies that assessed improvement in fatigue as a primary or secondary outcome were included. Retrospective studies, case reports, and conference abstracts were excluded. The search yielded 8 suitable randomized controlled trials and 7 prospective studies. Two RCTs and three prospective studies involved rituximab, and all showed statistically significant improvements from baseline in fatigue scores. Small prospective studies of epratuzumab, LEF, infliximab and zidovudine also demonstrated statistically significant improvements in fatigue scores. RCTs using dehydroepiandrosterone showed significant improvements in fatigue scores, but also showed a placebo effect. Studies of HCQ, anakinra vs placebo, low dose doxycycline and a large RCT of infliximab did not produce significant results.

Conclusion: This is the first systematic review of treatments of fatigue in pSS. Overall there is a low level of evidence for treating fatigue in pSS, and studies are underpowered. There is no single effective treatment for fatigue in pSS, but the data suggest a promising role of B cell directed therapies. Fatigue is measured by a variety of scoring systems, which reflects multifactorial contributors, and the placebo effect found implicates a psychological component driving or maintaining fatigue. Future prospects include larger trials with more participants to study the role of B cells, some of which are underway. Studies should also be aimed at a multidimensional approach compared with single therapeutic agents, as the treatment of fatigue should include psychological input, and patients are likely to benefit from combined therapies.