Comparative efficacy of lamivudine with adefovir in patients with HBeAg-positive and negative CHB. Direct and indirect comparison methods to compare the relative efficacy of lamivudine with adefovir, or compared lamivudine (or adefovir) with placebo/non-treatment. Direct comparison was made by pooling the trials of lamivudine versus adefovir. An adjusted indirect comparison was performed by calculating the difference of pooled estimates of lamivudine and adefovir, which was obtained from trials of lamivudine (or adefovir) versus placebo/no treatment. RESULTS: Eight trials (n = 1324) were included. Of these, six were trials for HBeAg-positive CHB patients, and two for HBeAg-negative CHB patients. One trial compared lamivudine with adefovir in lamivudine-resistant patients with HBeAg-positive CHB, and seven trials compared lamivudine (or adefovir) with placebo/non-treatment in naive patients. Quality was medium-to-high in most trials. The direct comparison for lamivudine-resistant patients showed that lamivudine with adefovir were equivalent in clearing serological markers, lamivudine was less effective in normalizing ALT (OR = 0.11, 95% CI = 0.013–0.97) but superior in histological response (OR = 2.08, 95% CI = 1.08–4.04). Indirect comparison from four trials (n = 915) showed that lamivudine and adefovir were equally effective in serological and biomedical markers in naive patients with HBeAg-positive CHB. Indirect comparison from two trials (n = 282) showed that lamivudine was more effective in normalization of ALT than adefovir in HBeAg-negative CHB. But no data on serological and histological response were available. CONCLUSION: Lamivudine and adefovir was equally effective for naive patients with HBeAg-positive CHB. Larger direct comparison trials for lamivudine-resistant CHB and HBeAg-negative CHB should be further performed.