Three−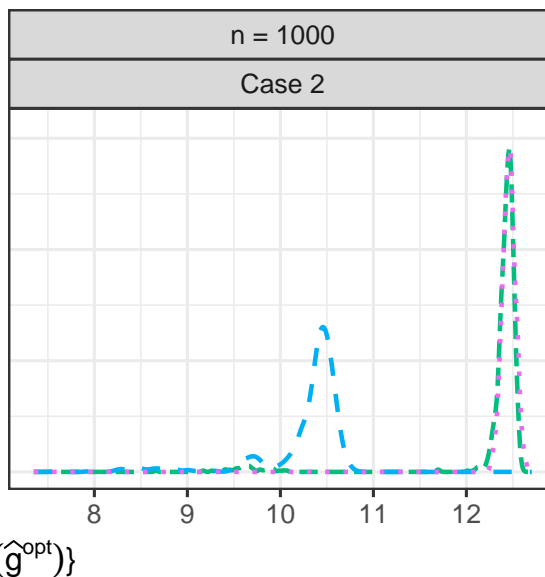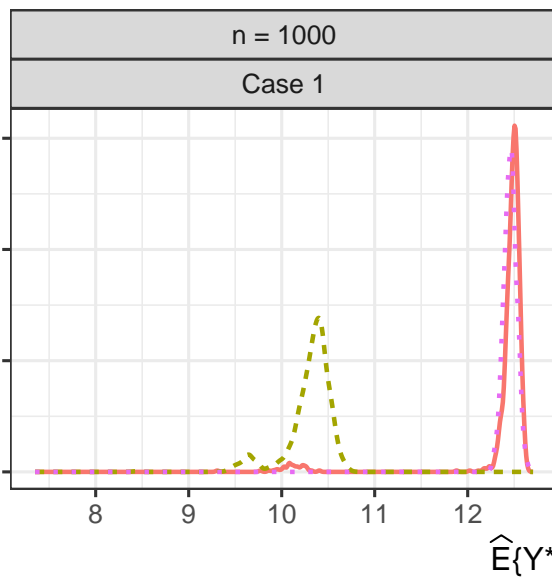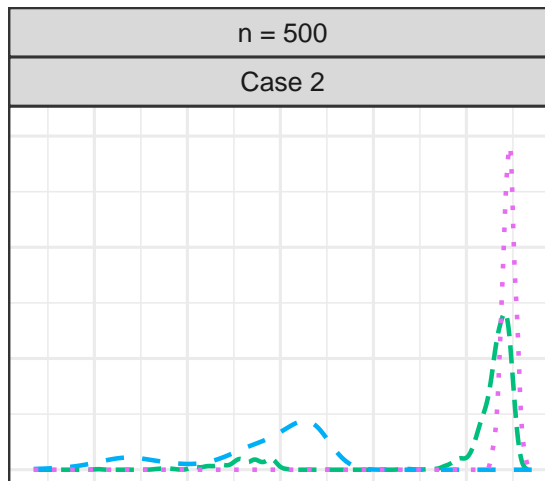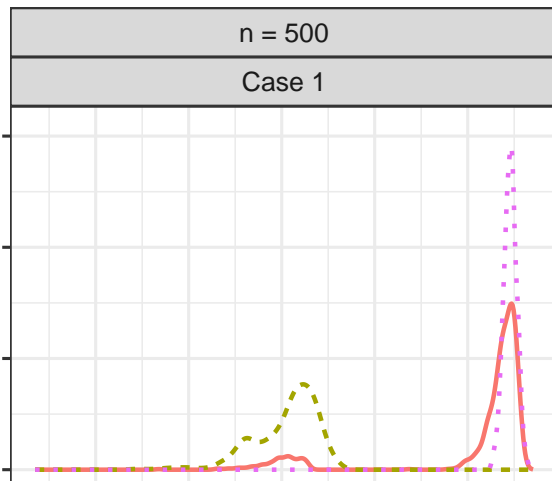stage Study