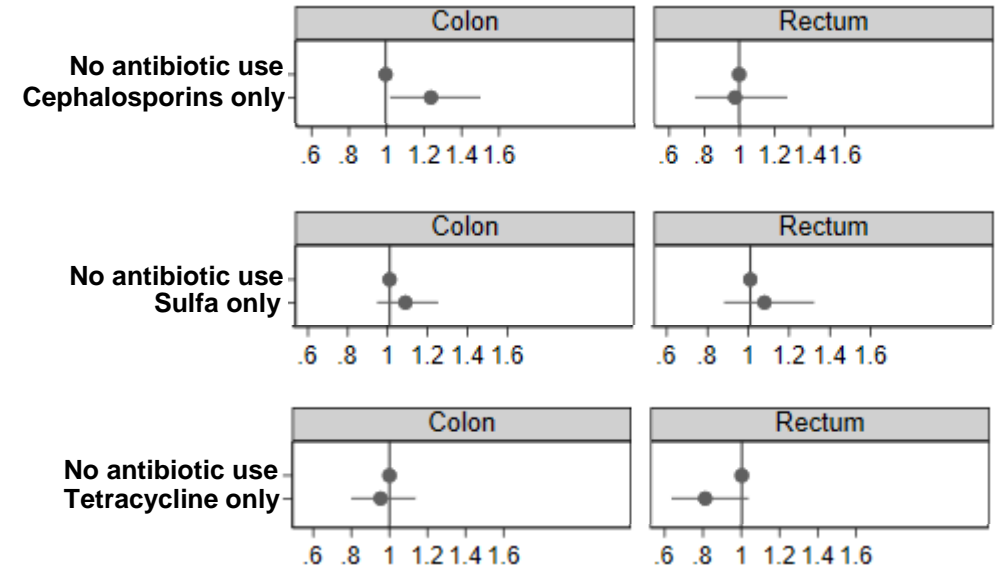
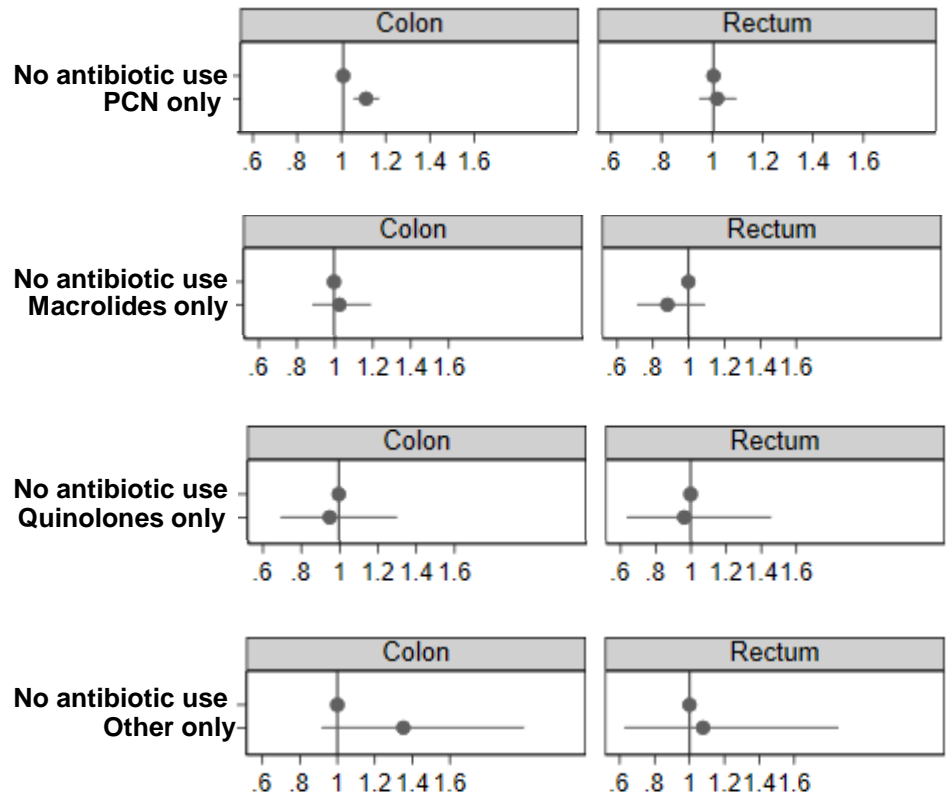
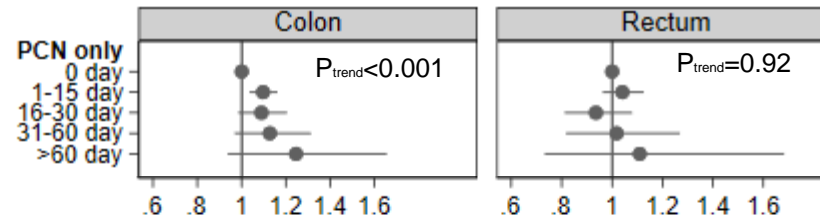


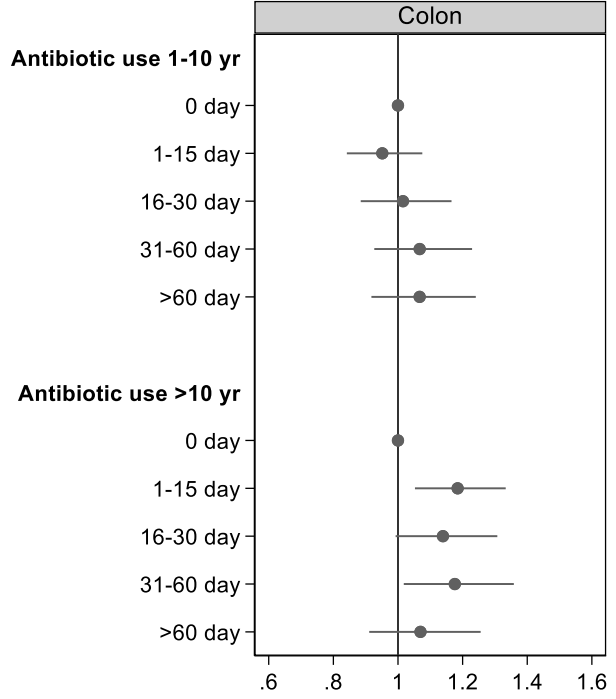
Appendix Figure 1. Forest plot of aORs for classes of antibiotics and cancer site. ORs estimated using a separate model for each site (colon, rectal, proximal colon, distal colon) with use of different classes of antibiotics as binary term, adjusted for BMI, smoking, alcohol use, diabetes status, chronic NSAIDs and aspirin use, and number of colonoscopies. PCN, Penicillins; Sulfa: Sulpha and trimethoprim



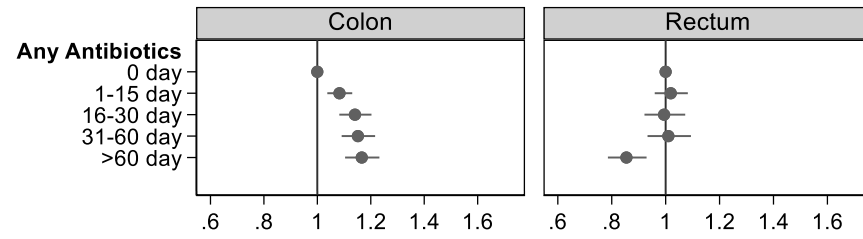
Appendix Figure 2: **Forest plot of aORs for single classes of antibiotics use and CRC risk.** ORs estimated using a separate model for each single class of antibiotics as binary term, adjusted for BMI, smoking, alcohol use, diabetes status, chronic NSAIDS and aspirin use, and number of colonoscopies. PCN, Penicillins; Sulfa: Sulpha and trimethoprim



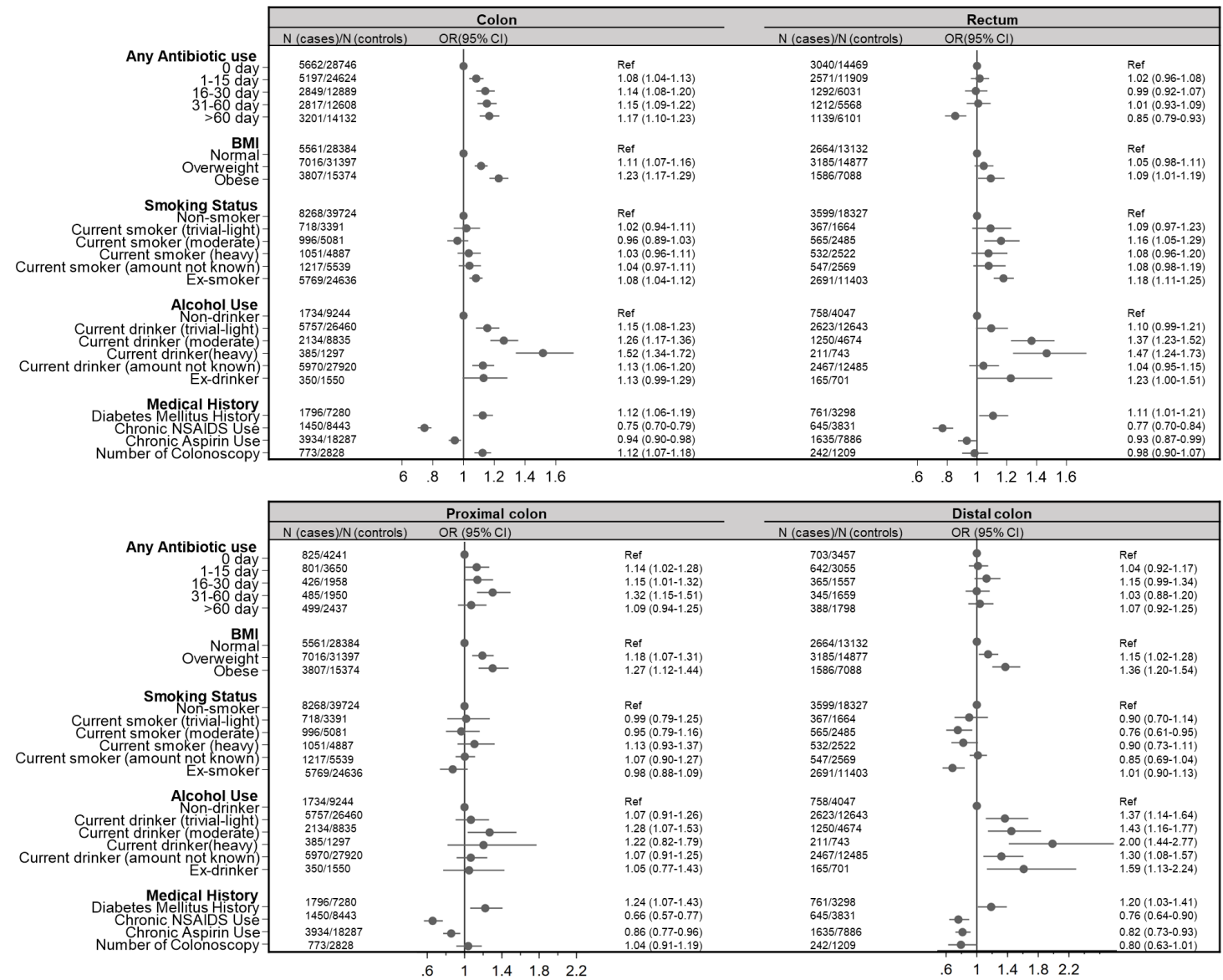
Appendix Figure 3. Subgroup analysis of PCN use only on CRC risk, stratified by anatomic location. ORs estimated using separate models for colon and rectum, with days of antibiotic use as categorical term, adjusted for BMI, smoking, alcohol use, diabetes status, chronic NSAIDs and aspirin use, and number of colonoscopies; Missing data were imputed for BMI, smoking and alcohol use in the above models.



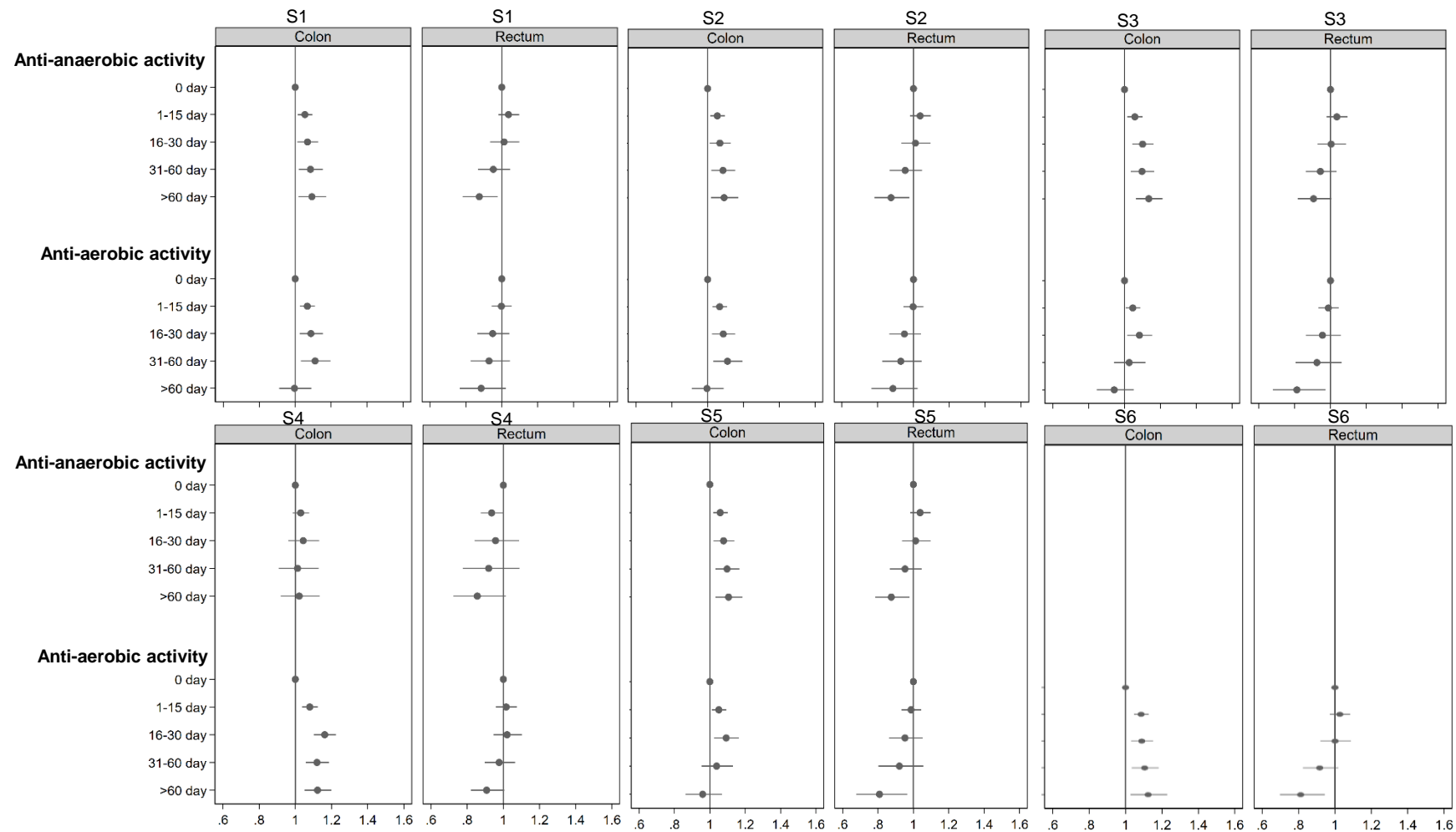
Appendix Figure 4: Antibiotic-cancer association by time window (1-10 years and >10 years) and total days of exposure in patients with at least 15 years of follow-up. ORs were obtained for use of antibiotics 1-10 years and >10 years preceding cancer diagnosis, adjusted for BMI, smoking, alcohol use, diabetes status, chronic NSAIDS and aspirin use, and number of colonoscopies; Missing data were imputed for BMI, smoking and alcohol use in the above models.



Appendix Figure 5: Forest plot of aORs for the effects of any antibiotic use on CRC risk, stratified by anatomic location, adjusting for BMI (continuous term), smoking, alcohol use, diabetes status, chronic NSAIDS and aspirin use, and number of colonoscopies in the final model.

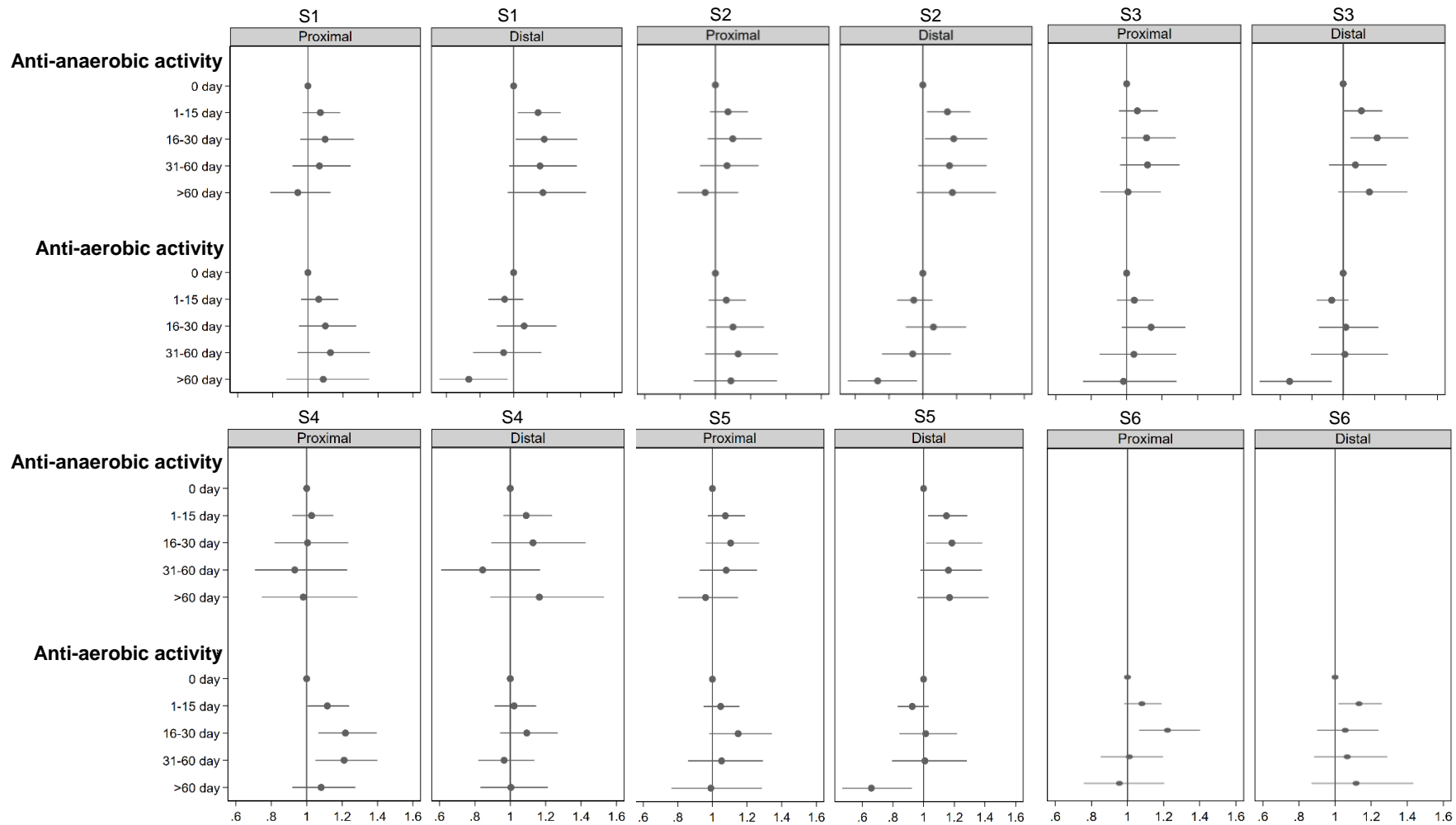


Appendix Figure 6. Forest plot of aORs for both antibiotic exposure and all co-variates included in the final model
 ORs estimated using separate models for each site, with days of antibiotic use as categorical term, adjusted for BMI, smoking, alcohol use, diabetes status, chronic NSAIDS and aspirin use, and number of colonoscopies; N, number. Missing data were imputed for BMI, smoking and alcohol use in the above models.



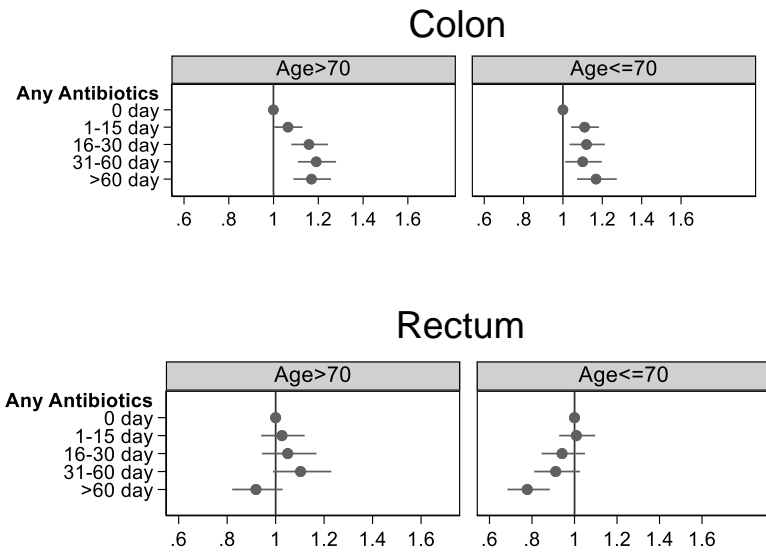
Appendix Figure 7. Forest plot of aORs for antibiotic use for colon and rectal cancer, from models classifying antibiotics based on anti-anaerobic/aerobic activity.

ORs estimated using a separate model for each site (colon, rectal) with days of antibiotic use as categorical term, adjusted for BMI, smoking, alcohol use, diabetes status, chronic NSAIDs and aspirin use, and number of colonoscopies. S1: restrict on antibiotics with significant/known anti-anaerobic (all ampicillin/penicillin, tetracycline, metronidazole/tinidazole, chloramphenicol, moxifloxacin and vancomycin) and anti-aerobic activity (all cephalosporins, all sulpha and trimethoprim, quinolones, flucloxacillin, nitrofurantoin, and nalidixic acid); S2: delete vancomycin from anaerobic list; S3: add cephalosporins to anaerobic list; S4: add ampicillin/amoxicillin to aerobic list; S5: Delete cephalosporins from aerobic list; S6: amoxicillin only in aerobic list.



Appendix Figure 8. Forest plot of aORs for proximal and distal colon cancer, from models classifying antibiotics based on anti-anaerobic/aerobic activity

ORs estimated using a separate model for each site (proximal colon, distal colon) with days of antibiotic use as categorical term, adjusted for BMI, smoking, alcohol use, diabetes status, chronic NSAIDs and aspirin use, and number of colonoscopies. S1: restrict on antibiotics with significant/known anti-anaerobic (all ampicillin/penicillin, tetracycline, metronidazole/tinidazole, chloramphenicol, moxifloxacin and vancomycin) and anti-aerobic activity (all cephalosporins, all sulpha and trimethoprim, quinolones, flucloxacillin, nitrofurantoin, and nalidixic acid); S2: delete vancomycin from anaerobic list; S3: add cephalosporins to anaerobic list; S4: add ampicillin/amoxicillin to aerobic list; S5: Delete cephalosporins from aerobic list; S6: amoxicillin only in aerobic list.



Appendix Figure 9: Stratified analysis by age subgroups (age>70 vs age <=70) for colon and rectum in the fully adjusted model. Forest plots show aORs and 95% confidence intervals.