Supplementary materials

Description of candidate determinants

Patient-related determinants included age, gender, and whether the participant had a co-morbidity (at least one of the following: Chronic Obstructive Pulmonary Disease (COPD), asthma, other lung disease, heart failure, ischemic heart disease, other heart disease, or diabetes).

Illness-related determinants included presenting symptoms (cough, phlegm, shortness of breath, wheeze, coryza, fever, chest pain, muscle aching, headache, disturbed sleep, feeling generally unwell, interference with normal activities, confusion/disorientation, and diarrhoea), clinician-rated symptom severity score (a summation of the severity of the 14 symptoms previously described scaled to range from 0 to 100, where 100 represented the maximum severity on all 14 symptoms and 0 represented no problems on any of the 14 symptoms), phlegm colour (categorised as no phlegm, normal coloured phlegm (white or clear), and discoloured phlegm (yellow, green, or bloodstained)), whether an abnormality was found when performing an auscultation examination (at least one of the following: diminished vesicular breathing, wheeze, crackles, or rhonchi), and the number of days of symptoms prior to consulting (categorised as seven days or less, eight to 14 days, or 15 days or more).

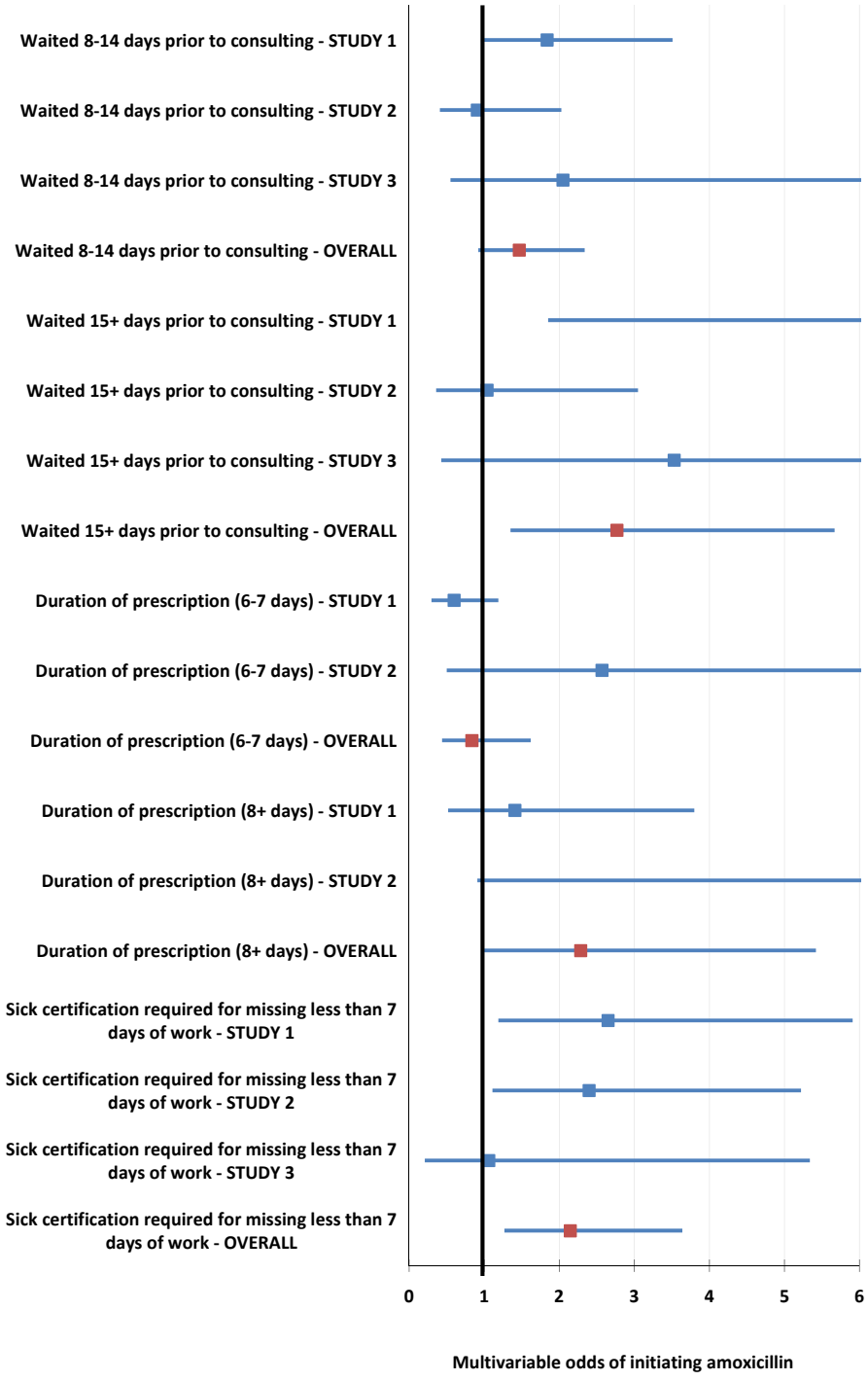
Prescription-related determinants included the dose (categorised as less than 500mg, 500mg, between 500 and 1000mg (not inclusive), and 1000mg or more), frequency (categorised as twice a day or more than twice a day), and duration (categorised as five days or less, six to seven days, or eight or more days) of the amoxicillin prescription. For the participants in study 3 (i.e. the placebo-controlled trial), this was fixed, as all participants were prescribed 1000mg of amoxicillin, three times a day for seven days.

While there were no specific healthcare professional-related determinants available consistently across all three datasets, responsible clinician identifiers were available and could be used to determine whether variation in adherence could be attributed to the influence of individual clinicians.

Participants were recruited from several European countries (Belgium, England, Finland, France, Germany, Hungary, Italy, Norway, Poland, Slovakia, Slovenia, Spain, Sweden, The Netherlands, and Wales), and healthcare setting-related determinants were established from work carried out as part of the GRACE project (GRACE website. Available from: http://www.grace-lrti.org/portal/en-gb/), and subsequent surveys among clinicians from countries that were not represented in this work. These included whether single-handed practices were common (e.g. representing at least a quarter of all practices), whether there had been public campaigns related to antibiotic use, whether patients had to pay to see a general practitioner, whether clinicians were required to certify sickness for less than seven days of absence from work, whether amoxicillin was the first-line choice of antibiotic for a respiratory infection in primary care, and the country-level antibiotic prescribing rate. The prescribing rate was obtained from the European Surveillance of Antimicrobial Consumption Network (ESAC) antimicrobial consumption interactive database (ESAC-Net. Available from: http://ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/esac-net-database/Pages/overview-country-consumption.aspx.), defined as the Defined Daily Dose (DDD) per 1000 inhabitants per day, averaged across the years 2007 to 2010.

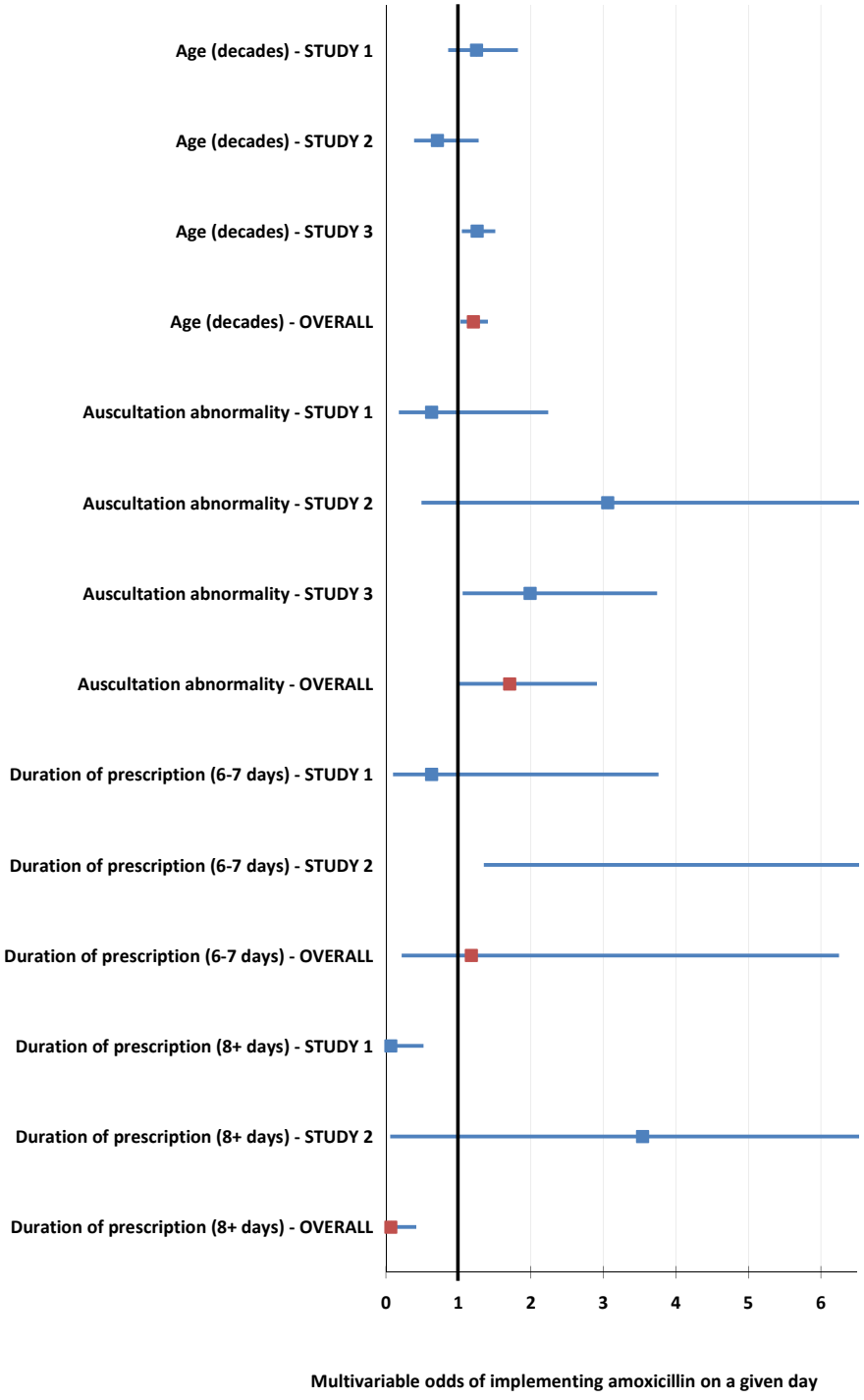
Finally, the study in which the patient participated was evaluated as a potential determinant in all analyses.

*Forest plot illustrating the odds ratios and 95% confidence intervals for the initiation model for each individual study and overall**



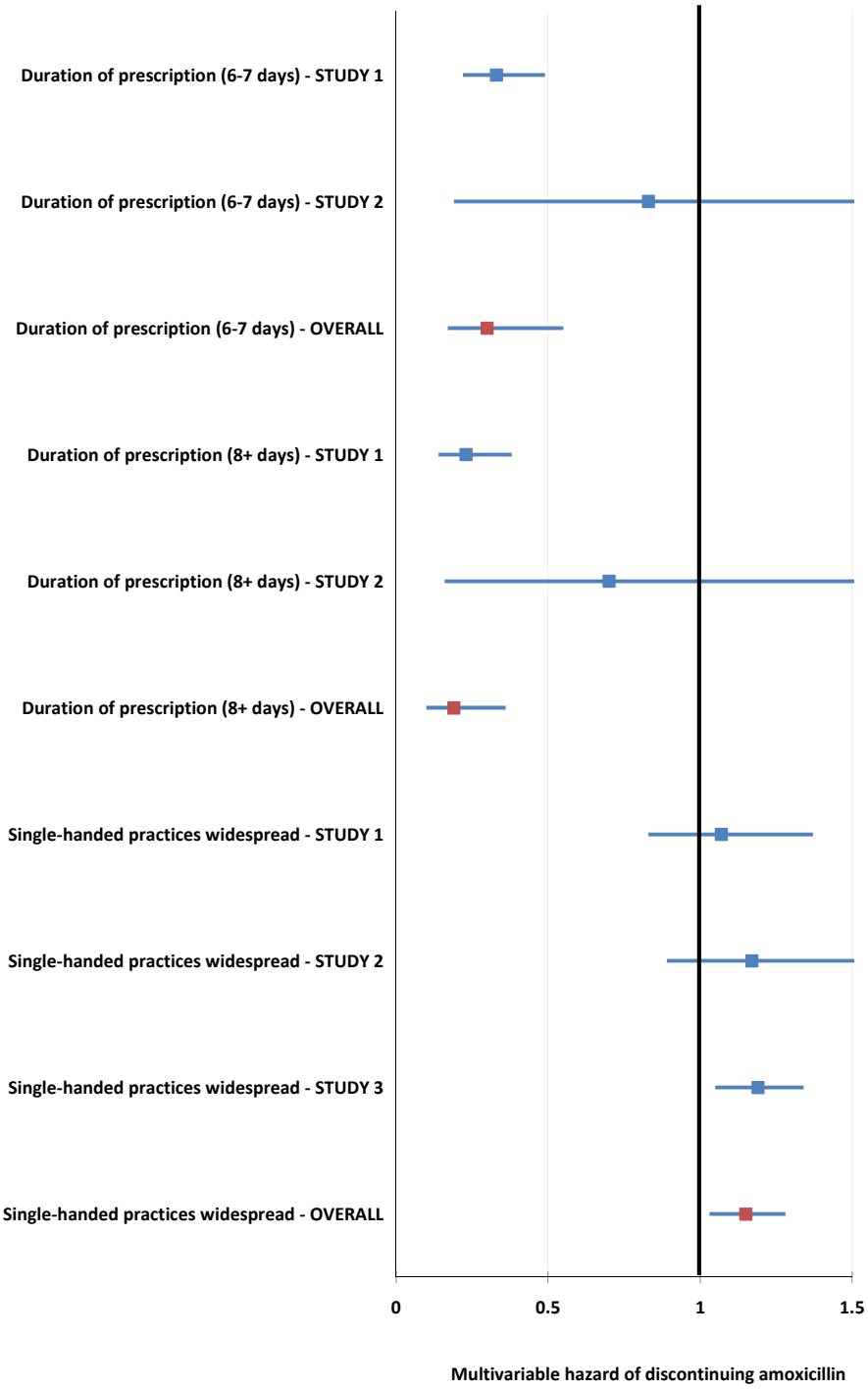
*Days waited prior to consulting compared to a reference category of 7 days or less. Duration of prescription variable compared to a reference category of 5 days or less.

*Forest plot illustrating the odds ratios and 95% confidence intervals for the implementation model for each individual study and overall**



*Duration of prescription variable compared to a reference category of 5 days or less

*Forest plot illustrating the hazard ratios and 95% confidence intervals for the discontinuation model for each individual study and overall**



*Duration of prescription variable compared to a reference category of 5 days or less