Supplement 6a: Characteristics included studies

Study authors Publication year	Study design	Geographical location	Research period	Study population	Definition of inappropriate antibiotic prescription	Number of patients/practices/general practitioners
Akkerman 2005	Prospective cohort study	Netherlands	2003	RTI	Not according to the guidelines	146 GP's/1469 consultations
Akkerman 2005	Prospective cohort study	Netherlands	2003	Acute otitis media	Not according to the guidelines	146 GP's/458 consultations
Biezen 2019	Focus-groups	Australia	2018	GPs	Not according to the guidelines	26 GPs
Cadieux 2007	Retrospective cohort study	Canada	1990-1998	Viral RTI, bacterial RTI and UTI	Antibiotic prescription for a viral infection	104,230 episodes viral infection/ 852 physicians
Damoiseaux 1999	Observational study with semi-structured interviews	Netherlands	1994-1995	Acute otitis media	Not according to the guidelines	22 GP's/362 patients
Dekker 2015	Observational study	Netherlands	2008-2010	RTI	Antibiotic prescription not according to the guidelines	2739 consultations/48 practices
Eggermont 2018	Retrospective cross-sectional	Netherlands	2013	Sore throat symptoms (ICPC R21, R22, R72, R74, R76, R77)	Not indicated by the international guidelines	11,285 consultations/ 25 GP's
Fernandez-Alvarez 2019	Questionnaire	Spain	2010	GPS	Not according to indicators	2100 GPs
Fletcher-Lartey 2016	Cross-sectional survey and semi-structured survey	Australia	2014	GP's	Not indicated	584 GP's filled in survey (response rate 23.7%), 32 GP's interviewed
Malo 2016	Retrospective cross-sectional	Spain	2011	acute bronchitis (ICPC code R78)	Not according to the guidelines	36955 episodes of acute bronchitis
Nowakowska 2019	Observational study	United Kingdom	2010-2014	sinusitis otitis externa	Not according to the guidelines	1,151,105 antibiotic prescriptions

				otitis media		
				upper respiratory tract infection (URTI) (including unspecified URTI, tracheitis, laryngitis, sore throat and tonsillitis)		
				lower respiratory tract infection (LRTI) (including bronchitis, unspecified chest infection and unspecified LRTI)		
				urinary tract infection (UTI)		
O'Doherty 2019	Explorative qualitive design	Ireland		Acute RTI	Antibiotic prescription for acute RTI	13 GP's
Pouwels 2018	Retrospective cohort	United Kingdom	2013-2015	Acute cough	Not indicated by the guidelines and above the range of a quality indicator	3.7 mil patients, 2,046,095 consultations
				Acute bronchitis		
				Asthma exacerbations		
				COPD exacerbations		
				Acute sore throat		
				Acute rhinosinusitis		
				AOM		
				Upper RTI		
				Lower RTI		

				Influenza-like illness		
				UTI		
				Impetigo		
				Acne		
				Gastroenteritis.		
Silverman 2017	Retrospective database cohort	Canada	2012	Patients > 65 years with nonbacterial acute upper RTI.	Antibiotic prescription for a non-bacterial acute upper RTI	185,014 patients and visits/ 8990 primary care physicians
				Acute nasopharyngitis (common cold)		
				Acute bronchitis		
				Acute sinusitis		
				Acute laryngitis/tracheitis		
Singer 2018	Retrospective cohort	Canada		Acute mild-to-moderate sinusitis (ICD-9 461)	Antibiotic prescription for a viral infection as indicated in the disease group	16,742 patients (15,6%)/ 239 GP's
				Upper respiratory tract infection (ICD-9 465)		
				Bronchitis (ICD-9 466)		
				Acute rhinitis (ICD-9 460)		
				Acute laryngitis and tracheitis (ICD-9 464)		

				Nasopharyngitis (ICD-9 477)		
				Influenza (ICD-9 487/488)		
Singer 2018	Retrospective cohort	Canada	1999-2016	All antibiotic prescriptions	Not according to the guidelines	32 clinics/196,923 patients
van Esch 2018	Retrospective cohort	Netherlands	2016	Acute cough ICPC codes, 31% of the patients;	Antibiotic prescription not indicated by the guideline.	8192 adults (15 practices)
				Acute cough (R05)		
				Whooping cough (R71)		
				Laryngitis/tracheitis (R77)		
				Acute bronchitis/bronchiolitis (R78)		
				Acute rhinosinusitis ICPC codes, 34% of the patients		
				Sinus symptom/complaint (R09)		
				Upper respiratory infection acute (R74)		
				Acute/ chronic sinusitis (R75)		
				Urinary tract infection ICPC codes, 36% of the patients.		

				Dysuria/painful urination (U01)		
				Urinary frequency/urgency, (U02)		
				Cystitis/urinary tract infection (U71)		

GPs: General Practitioner
ICPC: International Classification Primary Care
ICPC R21: Throat symptoms
ICPC R22: Tonsils symptoms
ICPC R72: Strep throat
ICPC R74: Acute Upper Respiratory Infection
ICPC R76: Acute tonsillitis
ICPC R77: Laryngitis/tracheitis
RTI: Respiratory Tract Infection
UTI: Urinary Tract Infection

Supplement 6b: Determinants and their domains from included studies

Study authors Publication year	Determinants of inappropriate antibiotic prescription			Framework					
	Negative impact	**No impact**	**Positive impact**	**Culture of healthcare consumption**	**Patient factors and experiences**	**Culture of professional medicine**	**Clinician attitudes and beliefs**	**Practice environment**	**The patient-clinician interaction**
Akkerman 2005	More signs of inflammation (fever etc) GP's judgement of more severe illness GP's perception of high patient expectation for antibiotic	Patient age			More signs of inflammation (fever etc)		GP's judgement of more severe illness		GP's perception of high patient expectation for antibiotic
Akkerman 2005	Age of patient younger than 24 months GP's judgement of more severe illness GP's perception of high patient expectation for antibiotic				Age of patient younger than 24 months		GP's judgement of more severe illness		GP's perception of high patient expectation for antibiotic
Biezen 2019	Patients expect an antibiotic due to past experience and have high expectations of antibiotics		Imbedding guidelines in an EMR			No access to guidelines due to high cost			Patients expect an antibiotic due to past experience and have high expectations of antibiotics

	No access to guidelines due to high cost					Access to guidelines during consult is time-consuming			
	Access to guidelines during consult is time-consuming								
Cadieux 2007	Medical education outside Canada or United States					Medical education outside Canada or United States		More years in practice	
	More years in practice							Higher practice volume	
	Higher practice volume								
Damoiseaux 1999	Severity of illness at first contact				Severity of illness at first contact	Feeling how one should perform	Habit		Disease behaviour of the patient
	Co-morbidity						To ease the patient		Request by patient
	Young age (less than 2 years)				Co-morbidity		Negative events in the past		GP's perception of high patient expectation for antibiotic
	Belongs to risk group				Young age (less than 2 years)				
	Disease behaviour of the patient				Belongs to risk group				
	Request by patient				Many other non-medical problems presented				
	GP's perception of high patient expectation for				Impact of disease on patient				

	antibiotic								
	Many other non-medical problems presented								
	Impact of disease on patient								
	Habit								
	To ease the patient								
	Negative events in the past								
	Feeling how one should perform								
Dekker 2015	GP's perception of high patient expectation for antibiotic	Reduced general health			Presence of fever		GP's judgement of more severe illness		GP's perception of high patient expectation for antibiotic
	Presence of fever				Age >18 years				
	GP's judgement of more severe illness				Duration of symptoms ≥7 days				
	Age > 18 years				Presence of comorbidity				
	Duration of symptoms ≥ 7 days								
	Presence of comorbidity								
	Female gender								
Eggermont 2018	Comorbidity OR 1.21 (95% CI:1.01-1.32)	Concordance OR 0.92 (95% CI: 0.82-1.02)			Comorbidity				
		Gender GP OR 0.83 (95% CI:							

		0.58-1.08)							
		Gender patient OR 0.96 (95% CI: 0.85-1.06)							
		Age patient OR 1.00 (95% CI: 0.99-1.00)							
Fernandez-Alvarez 2019	Documentation of Pharmaceutical Industry OR 2.09 (95% CI: 1.70–2.87)	Pharmaceutical Industry Training 1.45 OR (95% CI: 0.93–1.15)	Clinical Practice Guidelines OR 1.25 (95% CI: 1.02–1.54)			Documentation of Pharmaceutical Industry			
	Medical Representatives OR 2.50 (95% CI: 1.63–3.66)	Previous clinical experience OR 1.27 (95% CI: 0.77–2.12)				Medical Representatives			
		Other specialists OR 1.03 (95% CI: 0.93–1.23)							
Fletcher-Lartey 2016	Patients expect an antibiotic prescription	Age of GP		Patients expect an antibiotic prescription		Medical liability	Diagnostic uncertainty	Time pressure	Preserving GP–patient relationships
	Time pressure	Years worked as a GP					Primary care considered not responsible for development of antibiotic resistance		Protecting business,

	Diagnostic uncertainty	Gender					Inability to effectively negotiate or explain antibiotic use		Empathy for patients and risk perception about the seriousness of the illness
	Medical liability	Location of practice and socioeconomic profile of practice population							
	Primary care considered not responsible for development of antibiotic resistance								
	Preserving GP–patient relationships								
	Protecting business								
	Inability to effectively negotiate or explain antibiotic use								
	Empathy for patients and risk perception about the seriousness of the illness								
Malo 2016	Increasing age		Female patient		Co-morbidity				
	Co-morbidity				increasing age				
	Ongoing use of corticosteroids				ongoing use of corticosteroids				

Nowakowska 2019	Comorbidity	Socioeconomic deprivation			Comorbidity				
	Received antibiotics in previous year				Received antibiotics in previous year				
O'Doherty 2019	Guideline is non-comprehensive and does not clearly outline for a multitude of factors and the best course of action for all conditions the GP's face during their consultations			A paying private patient versus patient with free access healthcare		Guideline is non-comprehensive and does not clearly outline for a multitude of factors such as cough, sinus pain and the best course of action for all conditions the GP's face during their consultations		Limited time for an consultation	Patients expect an antibiotic due to past experience and have high expectations of antibiotics
	Paying private patient versus patient with free access healthcare								
	Patients expect an antibiotic due to past experience and have high expectations of antibiotics								
	Limited time for an consultation								
Pouwels 2018	Comorbidity	Weekday of consultation			Comorbidity				
Silverman 2017	Received antibiotics in previous year	Payment model (fee for service, capitation)	Female physician		Received antibiotics in previous year		11-24 year career versus < 11 year career	Workload > 150 days/year	

	11-24 year career versus < 11 year career		Hospital affiliation (Canada)				>25 year career versus < 11 year career	25-44 patients/day versus < 25 patients/day	
	>25 year career versus < 11 year career						Medical education outside Canada or United States	> 45 patients/day versus < 25 patients/day	
	Medical education outside Canada or United States								
	Workload > 150 days/year								
	25-44 patients/day versus < 25 patients/day								
	> 45 patients/day versus < 25 patients/day								
Singer 2018	Female versus male patient OR 1.22 (95% CI: 1.15-1.30)	Practice location (urban versus Rural)		Fee for service provider versus salaried provider	Female				Frequency of office visits (per 2 visit increase to the same primary care provider)
	Age patient < 60 year versus > 60 year OR 1.19 (95% CI: 1.02–1.38)	Practice size (< 1055 patients versus > 1055 patients)			Age patient < 60				
	Comorbidity 3 or more versus 0 OR 2.02 (95% CI:1.90–2.14)	Provider age (= 43 year versus > 43 year)			Comorbidity 3 or more versus 0				

	Comorbidity 1 or 2 versus 0 OR 1.34 (95% CI: 1.28–1.39)	Provider sex (male versus Female)							
	Fee for service provider versus salaried provider OR 4.35 95% CI: (3.31–5.72)	No. Of encounters per week (< 53 versus ≥ 53)							
	Frequency of office visits (per 2 visit increase to the same primary care provider) OR 1.48 (95% CI: 1.30-1.69)								
Singer 2018	Patient age (per 10 year increase) OR 1.13 (95% CI: 1.03-1.24)	Female patients							
	Number of comorbid conditions OR 1.11 (95% CI: 1.07-1.17)	Country of graduation (other than Canada)							
	Office visit frequency 1.12 (95% CI: 1.08-1.22)	Higher prescriber age (per 10 years increase)			Female patients			Rural practice location	
	Rural practice location OR 1.47 (95% CI: 1.17-1.84)				Number of comorbid conditions			Larger practice size	
	Larger practice size OR 2.26 (95% CI: 1.76-3.16)				Office visit frequency				

Van Esch 2018		Shared decision making							

CI: Confidence interval
EMR: Electronic Medical Record
OR: Odds ratio