Public target interventions to reduce the inappropriate use of medicines or medical procedures: a systematic review

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Abstract

Background: An epidemic of health disorders can be triggered by a collective manifestation of inappropriate behaviors, usually systematically fueled by non-medical factors at the individual and/or societal levels. This study aimed to (1) landscape and assess the evidence on interventions that reduce inappropriate demand of medical resources (medicines or procedures) by triggering behavioral change among healthcare consumers, (2) map out intervention components that have been tried and tested, and (3) identify the “active ingredients” of behavior change interventions that were proven to be effective in containing epidemics of inappropriate use of medical resources.

Methods: For this systematic review, we searched MEDLINE, EMBASE, the Cochrane Library, and PsychINFO from the databases’ inceptions to May 2019, without language restrictions, for behavioral intervention studies. Interventions had to be empirically evaluated with a control group that demonstrated whether the effects of the campaign extended beyond trends occurring in the absence of the intervention. Outcomes of interest were reductions in inappropriate or non-essential use of medicines and/or medical procedures for clinical conditions that do not require them. Two reviewers independently screened titles, abstracts, and full text for inclusion and extracted data on study characteristics (e.g., study design), intervention development, implementation strategies, and effect size. Data extraction sheets were based on the checklist from the Cochrane Handbook for Systematic Reviews.

Results: Forty-three studies were included. The behavior change technique taxonomy v1 (BCTTv1), which contains 93 behavioral change techniques (BCTs), was used to characterize components of the interventions reported in the included studies. Of the 93 BCTs, 15 (16%) were identified within the descriptions of the selected studies targeting healthcare consumers. Interventions consisting of education messages, recommended behavior alternatives, and a supporting environment that incentivizes or encourages the adoption of a new behavior were more likely to be successful.

Conclusions: There is a continued tendency in research reporting that mainly stresses the effectiveness of interventions rather than the process of identifying and developing key components and the parameters within which they operate. Reporting “negative results” is likely as critical as reporting “active ingredients” and positive findings for implementation science. This review calls for a standardized approach to report intervention studies.

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Contributions to the literature

- This review identifies the types, components, and combinations of interventions more likely to successfully initiate and sustain public behavior change in the context of complexity.
- It can inform practitioners’ decisions about designing, implementing, and reporting interventions to reduce inappropriate use/demand of medical interventions while researchers and funders can use this review to determine where research is needed.
- No community-based interventions were found in LMICs; interventions were limited to primary care settings or policy restrictions on the supply side (e.g., ban on over-the-counter purchases).
- There is a need for standardized reporting of intervention development, adaptation, and implementation to maximize generalisability and replicability.

Background

Epidemics, which traditionally refer to a widespread occurrence of an infectious disease in a community at a particular time, have in recent years been used to describe large-scale public health issues caused by a shared pattern of human behaviors that impact public health and well-being. An epidemic of health disorders can not only be triggered by organisms that cause communicable diseases, such as bacteria, viruses, fungi, or parasites, but also by a collective manifestation of inappropriate behaviors, usually systematically fueled by non-clinical factors at the individual and/or societal levels. When medicines or medical procedures are used for conditions for which they should not be used, they are deemed as inappropriate use of medical interventions. For example, the World Health Organization and governments have warned about the recent spike in the use of prescription drugs [1] and cesarean sections [2] globally, which has formed an epidemic that has caused avoidable damage to individual health and introduced excessive burdens on health systems [3, 4].

There have been experiments with programs specifically designed to address factors driving the epidemics of inappropriate use of medical interventions. These countermeasures are often non-clinical behavioral change interventions targeting physicians and pharmacists as a point-of-entry for interventions and are designed to improve clinical practices and policies that restrict unnecessary dispensing [5, 6]. These programs usually employed educational materials (e.g., guidelines, lectures, workshops) [7, 8], auditing and feedback on prescribing practices [9–12], or computer-aided clinical decision support systems [13]. A 2005 Cochrane review concluded that, for interventions occurring on multiple levels to be effective, local barriers to change—including the role patients play in driving inappropriate demand—must be addressed [14]. Current interventions to address the pressure of inappropriate demands outside the clinical setting range from national mass media campaigns to local interventions targeted at smaller communities [15], aiming to influence the knowledge, attitudes, and practices towards medical use of the general public who have yet to become healthcare consumers: namely patients and caretakers of patients [15–17]. However, recent reviews highlighted that critical knowledge gaps exist in the evidence for engaging healthcare consumers as active decision-makers for appropriate medical use (as opposed to passive receivers of education materials) [18, 19]. Furthermore, the lack of evidence in the development of and evaluation of the impact of these interventions, especially in low- and middle-income countries (LMICs), complicates replication efforts [16, 17, 20].

The Behavioral Change Wheel (BCW) [21] and the behavior change techniques taxonomy volume 1 (BCTTv1) [22], developed by Michie and colleagues, facilitate researchers in organizing the content and components of behavioral interventions into nine intervention functions: education, persuasion, incentivization, coercion, training, enablement, modeling, environmental restructuring, and restrictions and assists them in translating specific techniques that were employed in a given intervention into change behaviors. Scientists have supported the use of BCW and BCTTv1 as a reliable and validated methodology that offers a common language for describing intervention components that can be used for the standardization of intervention content analysis and the development of interventions [23–25].

In this study, we aimed to (1) landscape and critically assess the evidence on non-clinical programs that reduce inappropriate or unnecessary use of medical interventions (i.e., medicines or medical procedures) by triggering behavioral change among healthcare consumers, (2) map out intervention components that have been tried and tested, and (3) identify the “active ingredients” of behavior change intervention programs that were proven to be effective in containing “epidemics of inappropriate use of medical interventions.”

Methods

Searches

For this systematic review, we searched MEDLINE, EMBASE, the Cochrane Library, and PsychINFO from the databases’ inceptions to May 2019, without language restrictions, for behavioral intervention studies. A search strategy was first developed for MEDLINE and adapted to other databases. The full-search strategy is detailed in
appropriate use was an outcome of a clinical condition, excluded interventions for substance abuse, where health conditions such as addiction or depression, we excluded interventions from therapies/treatments addressing mental health care consumers rather than providers, studies that aimed to modify clinical practices (e.g., prescribing) were excluded. Also, to differentiate behavior change interventions directed at healthcare staff, hospitals, inpatients, emergency care, or non-essential use of medicines and/or medical procedures for clinical conditions that do not require them. 

Four major types of behaviors were identified, namely inappropriate antibiotic consumption (e.g., for viral infections or self-limiting conditions), elective cesarean section, demand for brand-name drugs that are available as generics, and non-medical use of prescription drugs, defined as “use without a prescription or use for reasons other than what the medication is intended for” [16, 26, 27]. Studies that focused only on change of knowledge or attitudes and did not report actual behavioral data were excluded. Studies mainly targeting clinicians, other healthcare staff, hospitals, inpatients, emergency care, or patients with mental health conditions were excluded. To create a distinction between interventions directed at health care consumers rather than providers, studies that aimed to modify clinical practices (e.g., prescribing) were excluded. Also, to differentiate behavior change interventions from therapies/treatments addressing mental health conditions such as addiction or depression, we excluded interventions for substance abuse, where inappropriate use was an outcome of a clinical condition, not a cause.

Study inclusion and exclusion criteria
Inclusion and exclusion criteria used for all stages of the screening process are stated in Additional file 2. Studies had to be empirically tested by either randomized controlled trial (RCT), cluster-RCT (CRT), nonrandomized controlled trial (NCT), or interrupted times series (ITS) where the intervention time was clearly defined, and there were at least three data points both before and after the intervention, or quasi-experiments with a control group. To enable assessment of effectiveness in included interventions, this review excludes before/after evaluations of public campaigns or interventions that failed to employ a control group and therefore cannot show whether the effects of the campaign extended beyond trends occurring in the absence of the intervention. Outcomes of interest were reductions in inappropriate or non-essential use of medicines and/or medical procedures for clinical conditions that do not require them. We extracted the data on study characteristics: the country where the study was conducted, type of inappropriate use, target population, study design (e.g., RCT, controlled pre- and post-study [CPP]), data collection methods (e.g., survey, interview, medical records), and, when focused on a population study, sampling methodology (e.g., cluster, convenience), primary or main outcome measure, and conclusions reported. We further examined reporting on intervention development/adaptation, design, and implementation strategies. Additionally, we extracted underlying theoretical domains, effect size, and risk of bias by two independent review authors, who determined the domains within the Behavioral Change Wheel (BCW) and identified the “active ingredients” of the interventions according to BCTTv1. Data extraction sheets were based on the checklist from the Cochrane Handbook for Systematic Reviews [28]. The forms were modified after piloting on a sample of studies. When coding, we adopted the coding assumptions reported by Presseau et al. [25] that BCTs worked through targeting the behavior of health care consumers, or both the behavior of health care consumers and providers. We also assumed policy interventions and national campaigns were driven by governments and therefore coded governments as implementers for respective interventions. After the data extraction phase, we identified critical evidence gaps in evaluation data and processes of intervention development and implementation. We therefore conducted another round of targeted, investigative searches, involving citation and publication searches on first, last, and corresponding authors of selected interventions, seeking formative, process, and impact evaluation data.

Study quality assessment
We conducted and reported the review in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (PRISMA). Risk of bias was assessed by two reviewers using the Effective Public Health Practice Project’s (EPHPP) Quality Assessment Tool for Quantitative Studies [29], which includes eight components (21 items): selection bias, study design, confounders, blinding, data collection methods, withdrawals or dropouts, intervention, and integrity. A rating of
weak, moderate, or strong was given to each of the first six components, and these scores contributed to a global rating for the study. Qualitative data was assessed by the Critical Appraisal Skills Programme (CASP) checklist.

**Data synthesis on active ingredients**

Using BCW domains and BCT taxonomies, we analyzed descriptions of all interventions and identified the commonly targeted aspects by looking at the frequency with which BCW domain and BCT of the interventions were incorporated in the studies. We also explored the nature and pattern of the use of these active ingredients across the different studies, and the associated magnitude of effect size. We descriptively reported the active ingredients and primary outcomes’ effect sizes at the study level, counting the number of times a BCW domain and a BCT had been identified across studies and in different types of use behaviors and presented a description of features of included interventions.

**Results**

**Review statistics**

Our systematic search of the literature yielded 4045 results through database searching and an additional 238 were identified through bibliography searches. After de-duplication and title and abstract screening, 347 references were assessed in full text. A flow diagram of the study selection process is shown in Fig. 1. Forty-three studies (representing 43 interventions, see Additional file 3)—conducted between 1994 and May 2019 and meeting inclusion criteria—were included in the systematic review. Twenty-five studied interventions focused on the reduction of antibiotic...
use—eight on elective cesarean section, four on the conversion from brand name drugs to generic equivalents, and six on nonmedication use of prescription drugs. Table 1 provides an overview of the included intervention studies for full-text extraction including intervention aims and components.

**Study characteristics**
All included studies were published in English. Twenty-four in North America (excluding Mexico; USA: n = 21, Canada: n = 3), four in Latin America (Chile, Colombia, Venezuela, Brazil, and Mexico), four in the Middle East (Iran), eight in Europe (France, UK, Italy, Spain, and Moldova), three in East Asia and Pacific (Australia and Singapore), and none from sub-Saharan Africa, South Asia, or the Caribbean. The imbalance between high-income countries (HICs) and low- and middle-income countries (LMICs) is apparent when characterizing types of inappropriate use. Multifaceted interventions are scarce and limited to HICs while interventions in LMICs were limited to primary care settings or policy restrictions (on over-the-counter purchases) with zero community-based programs identified. No studies from LMICs focused on demands for brand-name drugs or non-medical use of prescription drugs.

**Study design**
The included studies consisted of 18 RCTs and five NCTs, eight ITS, and 12 quasi-experimental studies. These studies varied in their quality, methodological design, and implementation. Twenty-four studies reported longitudinal data; the rest employed cross-sectional study designs. All were outcome evaluation studies. In terms of data collection methods for evaluation, 23 studies employed surveys and 30 utilized medical record data—these were not mutually exclusive. Four studies reported cost data. One study employed interviews as part of the intervention procedure, but not for evaluation purposes [51]. No qualitative data were reported in the initial included studies; we therefore conducted a targeted, investigative search on the selected interventions, but only located minimal formative data on some of the studies [30, 45–47, 50]. One UK-based project that aimed to improve the decision-making around mode of delivery among pregnant women published comprehensive implementation research data from pilot results [48] and study protocol [47] to outcome and economic evaluation [45, 46, 49, 52, 53]. Table 2 presents a summary of the key characteristics of each study measuring behavioral outcomes and reported formative and relevant evaluation data of the included interventions.

**Study quality assessment**
Study quality varied by domain assessed based on the primary behavioral outcomes (Additional file 4). There were 11 studies of overall strong quality, 12 of overall moderate quality, and 20 of overall low quality. In order to provide an overview of the entire literature, no studies were excluded based on their methodological quality. The majority of behavior outcomes were derived from medical records, leaving minimal room for reporting errors with the exception that some only relied on self-reported data for evaluation.

**Active ingredients of the behavior change interventions**
All of the interventions utilized multiple behavior change techniques (BCTs) with a primary aim to improve health care consumers’ behavior. Table 3 presents the features of all the included interventions; the frequency distributions of BCTs employed are presented in Fig. 2. Of all 93 BCTs in the taxonomy, 19 (19/93, 22.9%) were used as active ingredients in the included interventions: four BCTs were used exclusively for interventions targeting health care consumers (BCTs 3.3, 6.1, 9.2, 12.2); another four were used exclusively for multifaceted interventions that also targeted providers (BCTs 1.3, 2.2, 3.2, 14.2), with 11 BCTs used for both (BCTs 3.1, 4.1, 4.2, 5.1, 5.2, 8.2, 9.1, 10.1, 10.2, 12.1, 12.5; see Tables 4 and 5 for details). When compared with the principles in the Behavioral Change Wheel, 39 interventions employed education as an active ingredient followed by enablement (n = 12), environmental restructuring (n = 8), and restriction (n = 4). Of the 43 included studies, 22 were interventions delivered only at the community level, 12 in primary care settings, six in both community and primary care settings, and three in schools. Nineteen interventions were delivered on an individual basis, which tended to be shorter in duration, ranging from one to multiple short sessions. The majority of studies focused on evaluation design and outcomes and only provided high-level descriptions of the intervention, with or without details on the development or implementation processes. Twenty studies provided clear descriptions on the intervention adaption/development process, all on implementation strategies (e.g., channels and timing of dissemination), and, to a certain level, 15 on intervention dose (intensity) [54–56] and nine on designs (e.g., color and format) [55–58]. Some studies provided links to intervention designs, but most of these links had expired. Only eight interventions explicitly reported having adopted a theory or model of behavioral change, which included social marketing [56, 59, 60], social cognitive theory [55], precede/precede model [61], social development model [39, 40], and the health belief model [62]. However, little was reported on
| First author, year | Context | Target illness/condition | Country | Last month of data collected | Setting | Intervention elements | Name | Slogan | Target audience | Healthcare providers | Healthcare consumers | BCT-provider | BCT-consumer | Behavioural Change Theory-based |
|--------------------|---------|--------------------------|---------|----------------------------|---------|-----------------------|------|--------|-----------------|-------------------|--------------------|--------------|--------------|--------------------------------|
| Belongia, 2001     | RTIs    | USA                      | June 1998 | Community and primary care setting | Knowledge (including awareness), cultural, and doctor-patient relationship | – | None | Community and healthcare providers | Physician education (parent education pamphlets, parent information sheets, a sample letter, "prescription pad," CDC fact sheets) | Public education materials: programs, pamphlets and posters, presentations and "Cold kits" | 4.1 | 4.1 | 4.2 | 4.2 | Education | – |
| Belongia, 2005     | Not specified | USA                      | December 2003 | Community | Knowledge (including awareness) | Wisconsin antibiotic resistance network | – | “There’s no excuse for overuse” and “Get smart about antibiotics.” | Community and healthcare providers | Physician education (mailings, susceptibility reports, practice guidelines, satellite conferences, and presentations) | Mass media campaign (television, radio, newspapers, press conference; paid ad); Patient education materials | 4.1 | 4.1 | 4.2 | 4.2 | Education | – |
| Berrier, 2014      | Not specified | France                    | December 2010 | Community | Knowledge (including awareness) | – | “Antibiotics are not automatic!” and “antibiotics, used unnecessarily, lose their potency!” | Community | Guidelines, seminars, academic detailing, letters | Pamphlets and posters, print media, radio, television, website | 4.1 | 4.1 | 4.2 | 4.2 | Education | – |
| Cebotarenco, 2008  | RTIs    | Moldova                  | March 2004 | School setting | Knowledge (including awareness) peer | – | None | Community-students and guardians | – | Peer education, parents’ meetings, booklet, vignette video, newsletter, poster, and poster contest | – | 4.1 | 4.1 | 4.2 | Education | Social cognitive theory |
| Finkelstein, 2001  | RTIs    | USA                      | December 1998 | Community and primary care setting | Knowledge (including awareness), doctor-patient relationship, peer leader | – | – | Community and healthcare providers | Guideline dissemination, small-group education, educational materials, and | Educational materials for parents by mail and in primary care practices, | 2.2 | 2.2 | 3.2 | 3.2 | Education | – |
| First author, year | Context | Target illness/ condition | Country | Last month of data collected | Setting | Intervention elements | Name | Slogan | Target audience | Healthcare providers | Healthcare consumers | BCT-provider | BCT-consumer | Behavioral Change Wheel | Theory-based |
|-------------------|---------|---------------------------|---------|----------------------------|---------|-----------------------|------|--------|-----------------|----------------------|---------------------|-------------|-------------|----------------------|--------------|
| Finkelstein, 2008 | RTIs   | USA                       | August 2003 | Community Knowledge (including awareness), doctor-patient relationship | Reducing antibiotics for children in Massachusetts (REACH Mass) | None | Community and healthcare providers | Guideline dissemination, small-group education, educational materials, “prescription pad”, and prescribing feedback | pharmacies, and childcare settings | 9.1 | 2.2 | 3.2 | 4.1 | 4.2 | 5.1 | 8.2 | Education Social marketing |
| Formoso, 2013 | RTIs | Italy                       | March 2012 | Community Knowledge (including awareness), cultural, and doctor-patient relationship | Antibiotics, solution or problem | “Antibiotics, solution or problem?” | Community and healthcare providers | a newsletter on local AMR campaign materials (highlighting how to deal with patients’ expectations, occurrence of AMR and of side effects.) | mass media spaces (television, radio, newspapers) written materials (brochures, posters, newsletters) | 4.1 | 4.1 | 4.2 | 5.1 | 5.1 | 5.2 | 8.2 | 12.5 | Education Social marketing |
| Fuertes, 2010 | Not specified | Canada                       | December 2008 | Community Knowledge (including awareness) | Do bugs need drugs? | None | Community and healthcare providers | Television campaign | Television campaign | 4.1 | 4.2 | 5.1 | 5.1 | 5.2 | 5.2 | 8.2 | 8.2 | Education – |
| Gonzales, 2004 | RTIs | USA                       | February 2002 | Community & primary care setting Knowledge (including awareness) and doctor-patient relationship | Minimizing antibiotic resistance in Colorado | Be SMART about antibiotics | Community and healthcare providers | Antibiotic prescribing profiles and practices guidelines | Waiting room materials, examination room posters; mailing campaign packets household- and office-based patient education materials | 1.3 | 12.5 | 4.1 | 4.2 | 5.1 | 9.1 | 12.5 | Education – |
| Gonzales, 2005 | RTIs | USA                       | February 2002 | Community & primary care setting Knowledge (including awareness) and doctor-patient relationship | Minimizing antibiotic resistance in Colorado | Be SMART about antibiotics | Community and healthcare providers | antibiotic prescribing profiles and practices guidelines | Waiting room materials, examination room posters; mailing campaign | 1.3 | 12.5 | 4.1 | 4.2 | 5.1 | 9.1 | 12.5 | Education – |
| First author, year | Target illness/condition | Country | Last month of data collected | Setting | Intervention elements | Context | Target drivers/factors | Name | Slogan | Target audience | Healthcare providers | Healthcare consumers | BCT-pro | BCT-con | Behavioral Change Wheel | Theory-based |
|-------------------|--------------------------|---------|-------------------------------|---------|-----------------------|---------|------------------------|------|--------|-----------------|----------------------|---------------------|---------|---------|--------------------------|-------------|
| Henrysson, 2002   | RTIs                     | USA     | December 2000                 | Community | Knowledge (including awareness) | Knowledge (including awareness) | Workshops and follow-up visits | Printed information and newsletters | 4.1 4.2 | Community and healthcare providers | Restriction on sale of antibiotics without prescription | 12.1 12.1 | Education | – | Restriction, environmental restructuring |
| Lambert, 2007     | RTIs                     | UK      | February 2005                 | Community | Knowledge (including awareness) | Antibiotics – tracking down the trust | Professional education and prescribing support | Mass media with printed materials | 4.1 8.2 | Community and healthcare providers | – | 12.5 12.5 | Education | – |
| Lee, 2017         | RTIs                     | Singapore | Not specified              | Primary care setting | Knowledge (correcting misconceptions) | – | Community - patients | Educational pamphlets and verbal counseling | – | 4.1 4.2 | Education | – |
| Mainous, 2009     | RTIs                     | USA     | June 2008                     | Community | Knowledge (including misconceptions), cultural | “Solo Con Receta” (only with a prescription) | Community | Cultiy sensitive community intervention with multiple media sources | – | 4.1 5.1 | Education | – |
| McNulty, 2010     | RTIs                     | UK      | January 2009                  | Community & primary care setting | Knowledge (correcting misconceptions) | – | Community - patients | Three posters displayed in magazines and newspapers | 4.1 4.2 | 8.2 8.2 | Education | – |
| First author, year | Context | Target illness/condition | Setting | Last month of data collected | Intervention elements | Name | Slogan | Target audience | Healthcare providers | Healthcare consumers | BCT-provider | BCT-consumer | Behavioral Change Wheel | Theory-based |
|-------------------|---------|--------------------------|---------|-----------------------------|----------------------|------|--------|---------------|---------------------|---------------------|--------------|--------------|------------------------|--------------|
| Perz, 2002        | RTIs    | USA                      | Community | April 1999                  | Knowledge (including awareness), peer | Antibiotics and your child | Community and healthcare providers | Educating peer leader presentations | Public education via printed material | 4.1 4.2 4.2 | 8.2          | Education             | –            |
| Sabuncu, 2009     | RTIs    | France                   | Community | December 2007                | Knowledge (including awareness) | Keep antibiotics working | Community | Guidelines, seminars, academic detailing, letters | Pamphlets and posters, print media, radio, television, website | 4.1 4.2 5.1 12.5 | 12.5 | Education | –            |
| Santa-Ana-Tellez, 2013 | Not specified | Brazil and Mexico | June 2012 | Community | Access to non-prescription antibiotics | – | Community and healthcare providers | Restriction on sale of antibiotics without prescription in pharmacies, and introduction of fine on owners of pharmacies for non-compliance. | 12.1 14.2 (only Mexico) | 12.1 | Restriction, coercion, environmental restructuring | – |
| Santa-Ana-Tellez, 2015 | Not specified | Brazil and Mexico | March 2012 | Community | Access to non-prescription antibiotics | – | Community and healthcare providers | Restriction on sale of antibiotics without prescription in pharmacies, and introduction of fine on owners of pharmacies for non-compliance. | 12.1 14.2 (only Mexico) | 12.1 | Restriction, coercion, environmental restructuring | – |
| Taylor, 2005      | RTIs    | USA                      | Primary care setting | April 2002                  | Knowledge, doctor-patient relationship | Puget Sound Pediatric Research Network | Community - parents and children | Educational pamphlets and a video | – | 4.1 9.1 | Education | –            |
| Trepka, 2001      | RTIs    | USA                      | Community & primary care setting | August 1998                  | Knowledge (including awareness), cultural, and doctor-patient relationship | “Grand rounds” presentations, small-group academic detailing, and distribution of written materials (clinical practice) | Community and healthcare providers | Public education materials: programs, pamphlets, and posters, presentations and newspapers | 4.1 4.2 5.1 8.2 12.5 | 12.5 | Education | – |

**Table 1** An overview of the included studies: intervention aims, components, and reporting (Continued)
| First author, year | Target illness/condition | Country               | Last month of data collected | Setting                          | Context                  | Intervention elements                                                                 | Name                                                                 | Slogan                                                                 | Target audience                                                                 | Healthcare providers                                                                 | Healthcare consumers | BCT-provider | BCT-consumer | Behavioral Change Wheel | Theory-based       |
|-------------------|--------------------------|-----------------------|-------------------------------|---------------------------------|---------------------------|------------------------------------------------------------------------------|------------------------|---------------------------------|-----------------------------------------------|------------------------------------------------------------------|-------------------|--------------|-------------|--------------------------|------------------|
| Wirtz, 2013       | Not specified            | Chile, Colombia, Venezuela, Mexico | September 2009 | Community | Access to non-prescription antibiotics | –                       | Community and healthcare providers | –                       | Restriction on sale of antibiotics without prescription | Restriction on sale of antibiotics without prescription | 12.1              | 12.1         | –           | –                        | Restriction, coercion, environmental restructuring |
| Wutzke, 2007      | RTIs                     | Australia             | August 2004                 | Community & primary care setting | Knowledge, doctor-patient relationship, peer | The NPS common colds community campaign | Community and healthcare providers | “Common colds need common sense: they don’t need antibiotics.” | Prescription pads, patient information leaflets, prescribing software, newsletters, prescribing feedback, educational visiting, clinical audit with feedback and case studies (paper and peer group discussion). | Mass media activity using billboards, television, radio, and magazines and small grants to promote local community education | 2.2               | 4.1          | 8.2          | 12.5                      | –                |
| Beshears, 2013     | Not specified            | USA                   | October 2014                | Community | Knowledge (including awareness), peer influence | –                       | Community-union members | –                       | Informational letters with or without a testimonial from person with/without shared union affiliation | –                                                                  | 8.2               | 9.1          | 10.1         | 10.2                     | Education, incentivization |
| O’Malley, 2006     | Not specified            | USA                   | December 2003               | Community | Knowledge (including awareness), incentives | –                       | Community and healthcare providers | Free generic drug samples, physician financial incentives | Member mailings, advertising campaigns | –                                                                  | 3.2               | 4.1          | 8.2          | 10.1                     | Education, incentivization |
| Sedjo, 2009        | Not specified            | USA                   | December 2007               | Community | Knowledge (including awareness), incentives | –                       | Community-health plan enrollees | –                       | Targeted messaging to raise awareness | –                                                                  | 4.1               | 8.2          | 10.1         | 10.2                     | Education, incentivization |
| First author, year | Target illness/ condition | Country | Last month of data collected | Setting | Target drivers/factors | Name | Slogan | Target audience | Healthcare providers | Healthcare consumers | BCT-provider | BCT-consumer | Behavioral Change Wheel | Theory-based |
|-------------------|--------------------------|--------|-------------------------------|---------|-----------------------|------|--------|----------------|---------------------|---------------------|-------------|--------------|---------------------|-------------|
| Vallès, 2003      | Not specified            | Spain  | February 2000                 | Primary care setting | Knowledge (including awareness) | –    | –      | chronic disorders patients who attended general practices | –                   | –                   | –           | 4.1          | 8.2        | 9.2       | Education           | –           |
|                   | Non-medical use of prescription drugs |
| Hasak, 2018       | Pain management (short-term) | USA    | September, 2017               | Community | Knowledge (including awareness), enabling | –    | –      | –           | Information brochure, website | –                   | 4.1          | 4.2        | 5.1          | 5.2        | 12.1      | 12.5      | Education; enablement | –           |
| Lawrence, 2019    | Pain management (short-term) | USA    | January 2019                  | Community | Knowledge (including awareness), enabling | –    | –      | –           | Information brochure, video, Deterra bags | –                   | 4.1          | 4.2        | 5.1          | 5.2        | 12.1      | 12.5      | Education; enablement; environmental restructuring | –           |
| Maughan, 2016     | Pain management (short-term) | USA    | October 2015                  | Community | Knowledge (including awareness), enabling | –    | –      | –           | Information brochure, study hotline | –                   | 4.1          | 4.2        | 5.1          | 5.2        | 12.1      | 12.5      | Education; enablement; environmental restructuring | –           |
| Rose, 2016        | Pain management (short-term) | Canada | April 2015                    | Community | Knowledge (including awareness), enabling | –    | –      | –           | Information brochure | –                   | 4.1          | 4.2        | 5.1          | 5.2        | 12.1      | –         | Education; enablement | –           |
| Spoth, 2008       | Not specified            | USA    | December 2002                 | School setting | Enhance protective factors, Family dynamics | Strengthening Families Program (SFP) and Life Skills Training (LST) | –    | –      | Community students | Universal preventive interventions implemented during middle school (strengthening families program and | –                   | 3.1          | 12.2      | –         | –         | –          | –         | Social development model | –           |
| First author, year | Target illness/ condition | Country | Last month of data collected | Setting | Context | Intervention elements | Name | Slogan | Target audience | Healthcare providers | Healthcare consumers | BCT-provider | BCT-consumer | Behavioral Change Wheel | Theory-based |
|--------------------|---------------------------|---------|-----------------------------|---------|---------|----------------------|------|--------|-----------------|---------------------|---------------------|-------------|-------------|----------------------|-------------|
| Spoth, 2013        | Not specified             | USA     | December 2011               | School setting | Enhance protective factors, Family dynamics | Strengthening Families Program (ISFP) and Life Skills Training (LST) | –     | –     | Community - students | –               | Universal preventive interventions implemented during middle school (strengthening families program and life skills training) | –            | 3.1          | 12.2       | Education; enablement; environmental restructuring; Social development model |
| Eden, 2014         | Experienced previous cesarean birth | USA     | May 2007 | Community & primary care settings | Knowledge (including awareness), enabling | –     | –     | Community - pregnant women with one previous cesarean birth | –               | Evidence-base information brochure or facilitated decision analysis | –            | 4.1          | 5.1        | Education; enablement |
| Fraser, 1997       | Experienced previous cesarean birth | Canada  | November 1994               | Primary care setting | Knowledge (including awareness, predisposing, enabling, and reinforcing factors) | –     | –     | Community - pregnant women with one previous cesarean birth | –               | Educational pamphlet, prenatal education, and peer support program | –            | 3.3          | 4.1        | Education; enablement | The PRECEDE-PROCEED model |
| Hassani, 2016      | Not specified             | Iran    | NR                          | Primary care setting | Knowledge (including awareness) | –     | –     | Community - primiparous pregnant women | –               | Instructional sessions in the form of speech, group discussions, questions and answers, and presentations | 4.1          |             |             | Education; Health belief model |
| Montgomery, 2007   | Experienced previous cesarean birth | UK      | August 2006                 | Primary care setting | Knowledge (including awareness, enabling) | –     | –     | Community - pregnant women with one previous cesarean birth | –               | Information program and facilitated decision analysis | –            | 4.1          | 5.1        | Education; enablement |
| Navaee, 2015       | Fear of childbirth        | Iran    | NR                          | Primary care setting | Knowledge (including awareness, emotions) | –     | –     | Community - primiparous pregnant women | –               | Education through role play about advantages and disadvantages | –            | 4.1          | 4.2        | Education; modeling |

Elective cesarean section
| First author, year | Intervention adaption/development | Implementation strategy | Implementer(s) Unit of intervention | Dose/intensity |
|-------------------|----------------------------------|-------------------------|------------------------------------|----------------|
| Sharifirad, 2013  | Knowledge (including awareness), family dynamics | Community—spouses of primiparous pregnant women | Educational session about mechanism of normal vaginal and cesarean deliveries as well as their advantages and disadvantages. | 3.1 4.1 5.1 9.2 |
| Shorten, 2005     | Knowledge (including awareness), enabling | Community—pregnant women with one previous cesarean birth | Information materials and facilitated decision analysis | 4.1 5.1 9.2 |
| Valiani, 2014     | Knowledge (including awareness) | Community—primiparous pregnant women | Childbirth workshops | 4.1 4.2 5.1 6.1 9.2 |

Note: NR not reported, RTIs respiratory tract infections, GP general practitioner, CS elective cesarean section
| First author, year | Implementation/adaption/development | Implementation strategy | Implementer(s) | Unit of intervention | Dose/ intensity | Design | Costs | Duration | Data sources | Formative or process evaluation studies |
|-------------------|-----------------------------------|------------------------|----------------|---------------------|----------------|--------|-------|----------|-------------|--------------------------------------|
| Belongia, 2001    | Yes                               | Yes                    | Yes            | Community           | Partially reported | NR     | NR    | 4 months | Medical records + self-reports, lab testing |
| Belongia, 2005    | Yes                               | Yes                    | Yes            | Community           | Access expired    | NR     | NR    | 5 years  | Medical records                        |
| Bernier, 2014     | NR                                | NR                     | Yes            | Community           | NR               | NR     | NR    | 6 months (ongoing) | Medical records                        |
| Cebotarenco, 2008 | Yes                               | Yes                    | Yes            | Community           | Yes              | Yes    | NR    | 1 year   | Self-reports                          |
| Finkelstein, 2001 | Yes                               | Yes                    | Yes            | Community           | NR               | NR     | NR    | 1 year   | Medical records [30]                   |
| Finkelstein, 2008 | Yes                               | Yes                    | Yes            | Community           | Partially reported | NR     | NR    | 3 winters (Oct-March) | Medical records [30]                   |
| Formoso, 2013     | Yes                               | Yes                    | Yes            | Community           | Partially reported | Access expired   | $60,800 | 4 months | Medical records + self-reports         |
| Fuertes, 2010     | NR                                | Yes                    | Yes            | Community           | NR               | NR     | NR    | 5 months | Medical records                        |
| Gonzales, 2004    | Yes                               | Yes                    | Yes            | Community           | Access expired   | Access expired   | $196,745 | 1 year   | Medical records (see Gonzales, 2004)  |
| Gonzales, 2005    | Yes                               | Yes                    | Yes            | Community           | Access expired   | Access expired   | $63,745  | 1 year   | Medical records                        |
| Gonzales, 2008    | Yes                               | Yes                    | Yes            | Community           | Yes              | Yes    | $196,710 | 4 months | Medical records + self-reports         |
| Hennessy, 2002    | Yes                               | Yes                    | Yes            | Community           | Access expired   | Access expired   | $196,710 | 6 months | Medical records + lab testing + self-reports |
| Kliemann, 2016    | NA                                | Yes                    | Yes            | Community           | NA               | NA     | NA    | Ongoing  | Medical records                        |
| Lambert, 2007     | NR                                | Yes                    | Yes            | Community           | Partially reported | £25,000 |       | 2 winters | Medical records + self-reports         |
| Lee, 2017         | NR                                | NR                     | Yes            | Individual          | NR               | NR     | NR    | 2 weeks  | Medical records                        |
| Mainous, 2009     | NR                                | Yes                    | Yes            | Community           | Partially reported | NR     | NR    | 9 months | Medical records + self-reports         |
| McNulty, 2010     | NR                                | NR                     | Yes            | Individual          | NR               | Yes    | NR    | 2 months | Self-reports [32]                     |
| Perz, 2002        | Yes                               | Yes                    | Yes            | Community           | Partially reported | Partially reported | NR     | 1 year   | Medical records                        |
| Sabuncu, 2009     | NR                                | NR                     | Yes            | Community           | NR               | NR     | NR    | 5 years  | Medical records (see Bernier, 2014)   |
| First author, year | Intervention adaptation/development | Implementation strategy | Implementer(s) | Unit of intervention | Dose/ intensity | Design | Costs | Duration | Data sources | Formative or process evaluation studies |
|-------------------|-----------------------------------|-------------------------|----------------|---------------------|----------------|--------|-------|----------|-------------|-----------------------------------------|
| Santa-Ana-Tellez, 2013 | NA | Yes | Yes | Community | NA | NA | NA | Ongoing | Medical records | [33–36] |
| Santa-Ana-Tellez, 2015 | NA | Yes | Yes | Community | NA | NA | NA | Ongoing | Medical records | (see Santa-Ana-Tellez, 2013) |
| Taylor, 2005 | Yes | Yes | Yes | Community | NR | NR | NR | 1 year | Medical records | – |
| Trepka, 2001 | Yes | Yes | Yes | Community | Partially reported | NR | NR | 4 months | Self-reports | – |
| Wirtz, 2013 | NA | Yes | Yes | Community | NA | NA | NA | Ongoing | Medical records | [33–36] |
| Wutzke, 2007 | Yes | Yes | Yes | Community | Partially reported | Yes | NR | 6 years | Medical records + self-reports | – |

Demand of brand name drugs

| First author, year | Intervention adaptation/development | Implementation strategy | Implementer(s) | Unit of intervention | Dose/ intensity | Design | Costs | Duration | Data sources | Formative or process evaluation studies |
|-------------------|-----------------------------------|-------------------------|----------------|---------------------|----------------|--------|-------|----------|-------------|-----------------------------------------|
| Beshears, 2013 | NR | Yes | Yes | Individual | Partially reported | NR | NR | 1 letter | Medical records | – |
| O'Malley, 2006 | NR | Yes | Yes | Community | NR | NR | NR | 4 years | Medical records | – |
| Sedjo, 2009 | NR | Yes | Yes | Individual | NR | NR | NR | 1 call and quarterly mails | Medical records | – |
| Vallis, 2003 | NR | Yes | Yes | Individual | NR | NR | NR | 1 session | Medical records | – |

Non-medical use of prescription drugs

| First author, year | Intervention adaptation/development | Implementation strategy | Implementer(s) | Unit of intervention | Dose/ intensity | Design | Costs | Duration | Data sources | Formative or process evaluation studies |
|-------------------|-----------------------------------|-------------------------|----------------|---------------------|----------------|--------|-------|----------|-------------|-----------------------------------------|
| Haski, 2018 | Yes | Yes | Yes | Individual | Yes | Yes | NR | 2 times | Self-reports | [37] |
| Lawrence, 2019 | Yes | Yes | Yes | Individual | Yes | Yes | Partially reported (55–7 per bag) | 1 time | Medical records, self-reports | [38] |
| Maughan, 2016 | NR | Yes | Yes | Individual | Yes | NR | NR | 1 time | Self-reports | – |
| Rose, 2016 | Yes | Yes | Yes | Individual | Yes | Yes | NR | 1 time | Self-reports | – |
| Spoth, 2008 | NR | Yes | Yes | Individual | NR | NR | NR | 6.2 h sessions + 1 family follow-up + boosters (cohort) | Self-reports | [39–44] |
| Spoth, 2013 | NR | Yes | Yes | Individual | NR | NR | NR | 6.2 h sessions + 1 family follow-up + boosters (cohort study 1: 1993–2008; study 2: 1998–2011) | Self-reports | (see Spoth, 2008) |

Elective cesarean section

| First author, year | Intervention adaptation/development | Implementation strategy | Implementer(s) | Unit of intervention | Dose/ intensity | Design | Costs | Duration | Data sources | Formative or process evaluation studies |
|-------------------|-----------------------------------|-------------------------|----------------|---------------------|----------------|--------|-------|----------|-------------|-----------------------------------------|
| Eden, 2014 | Yes | Yes | Yes | Individual | NR | NR | NR | 1 session | Medical records + self-reports | – |
| Fraser, 1997 | NR | Yes | Yes | Individual | NR | NR | NR | 2 sessions | Medical records + self-reports | – |
| Hassani, 2016 | NR | Yes | Yes | Individual | NR | NR | NR | 6 sessions-50–60 min/session | Self-reports | – |
| Montgomery, 2007 | Yes | Yes | Yes | Individual | NR | NR | NR | 10 weeks | Medical records + self-reports | [45–49] |
| Nawaee, 2015 | NR | Yes | Yes | Individual | NR | NR | NR | 1 session-90 min | Self-reports | – |
| First author, year | Intervention adoption/development | Implementation strategy | Implementer(s) | Unit of intervention | Dose/ intensity | Design | Costs | Duration | Data sources | Formative or process evaluation studies |
|--------------------|-----------------------------------|-------------------------|----------------|---------------------|----------------|--------|-------|----------|-------------|--------------------------------------|
| Sharifrad, 2013    | NR                                | Yes                     | Yes            | Individual          | NR             | NR     | NR    | 1 session =90 min | Self-reports                         | –                                    |
| Shorten, 2005      | Yes                               | Yes                     | Yes            | Individual          | NR             | NR     | NR    | 1 session          | Medical records + self-reports        | [50]                                 |
| Valiani, 2014      | NR                                | Yes                     | Yes            | Individual          | NR             | NR     | NR    | 3-4 h/week         | Medical records                       | –                                    |
| First author, year | Study design | Study population | Study sample size | Primary outcome(s) |
|-------------------|--------------|------------------|------------------|-------------------|
| Belongia, 2001    | NCT          | Longitudinal     | Physicians and public | 111 facilities, 664 children | Pediatric antibiotic prescribing in child care facilities |
| Belongia, 2005    | CPP          | Longitudinal     | Parents and primary care clinicians | 4115 primary care physicians | Change in annual antimicrobial prescribing rate |
| Bernier, 2014     | ITS          | Longitudinal     | French citizens covered by NHI | Not reported | Change in antimicrobial prescribing rate |
| Cebotarenco, 2008 | CPP          | Cross-sectional  | Students and parents | ~6302 people | No antibiotic use for cold and flu |
| Finkelstein, 2001 | RCT          | Longitudinal     | Physicians and parents | 8815 children | Antibiotics dispensed per person-year of observation among children |
| Finkelstein, 2008 | RCT          | Longitudinal     | Physicians and parents | 223,135 person/years | Antibiotics dispensed per person-year of observation among children |
| Formoso, 2013     | NCT          | Longitudinal     | Modena and Parma, Emilia-Romagna region | 1,150,000 residents | Antibiotic prescription rate |
| Fuertes, 2010     | ITS          | Longitudinal     | Population in British Columbia, Canada | Not reported | Antibiotic utilization rate |
| Gonzales, 2004    | NCT          | Longitudinal     | Medicare enrollees with acute respiratory tract infections (ARIs) | 4270 patient visits | Decreased antibiotic prescription rates |
| Gonzales, 2005    | NCT          | Longitudinal     | Children with pharyngitis and adults with acute bronchitis | Baseline: 10128 patients; Study: 9586 patients | Decreased antibiotic prescription rates |
| Gonzales, 2008    | NCT          | Longitudinal     | Mothers of young children and primary care physicians | 922 households, 1.38+ million antibiotic prescriptions | Net change in antibiotic dispensed per 1000 persons |
| Hennessy, 2002    | NCT          | Longitudinal     | Medical providers and community | 10,809 | Antibiotic utilization |
| Kliemann, 2016    | ITS          | Longitudinal     | Residents of Sao Paulo | 41,262,199 | Antibiotic utilization |
| Lambert, 2007     | CPP          | Longitudinal     | Communities in North East of England | Not reported | Per person, per clinic visit |
| Lee, 2017         | RCT          | Cross-sectional  | Adult patients | 914 patients | Antibiotic prescriptions |
| Mainous, 2009     | QE (controlled post-test) | Cross-sectional | Latino adults | 500 adults | Use of non-prescription antibiotics |
| McNulty, 2010     | CPP          | Cross-sectional  | Adult ≥ 15 | Pre= (1999); post (1830) | Antibiotic use without professional advice |
| Perz, 2002        | CPP          | Longitudinal     | Children < 15 | 464200 person-years | Antibiotic prescription rates |
| Sabuncu, 2009     | ITS          | Longitudinal     | French citizens covered by NHI | Not reported | Change in winter antibiotic prescribing rate (Oct to Mar) |
| Santa-Ana-Tellez, 2013 | ITS  | Longitudinal     | Populations in Mexico and Brazil | Not reported | OTC antibiotics consumption |
| Santa-Ana-Tellez, 2015 | ITS  | Longitudinal     | Populations in Mexico and Brazil | Not reported | Seasonal variation in total Penicillin use |
| Taylor, 2005      | RCT          | Cross-sectional  | Parent/child dyads | 499 children | Total no. of prescriptions for antibiotics |
| Trepka, 2001      | CPP          | Cross-sectional  | Physicians and public | 365 children | Expected an antibiotic for their child and did not receive one and brought their child to another physician because they did not receive an antibiotic |
| First author, year | Study design | Study population | Study sample size | Primary outcome(s) |
|--------------------|--------------|------------------|-------------------|--------------------|
| Wirtz, 2013        | ITS          | Longitudinal     | Chile, Colombia, Venezuela, Brazil | Not reported | OTC antibiotics consumption |
| Wutzke, 2007       | ITS          | Longitudinal     | Australian community | Not reported | Change in use of antibiotics |
| Beshears, 2013     | RCT          | Cross-sectional  | Union members      | 5498 adults | Conversion rate to lower-cost alternatives |
| O'Malley, 2006     | QE (matched controlled) | Longitudinal | Adult patients | 9790064 claims | Generic dispensing rate |
| Sedjo, 2009        | QE           | Longitudinal     | Consumer-directed health care enrollees | 4026 people | Conversion rate to lower-cost alternatives |
| Vallès, 2003       | RCT          | Longitudinal     | Patients taking medications for chronic disorders | 4620 patients | Evolution of the percentage of generic prescribing |
| Hasak, 2018        | QE           | Cross-sectional  | Postoperative patients | 258 patients | Self-reported proper opioid disposal |
| Lawrence, 2019     | RCT          | Cross-sectional  | Parents of postoperative patients | 202 caregivers | Self-reported proper opioid disposal |
| Maughan, 2016      | RCT          | Cross-sectional  | Postoperative patients | 79 patients | Self-reported proper opioid disposal |
| Rose, 2016         | QE           | Cross-sectional  | Postoperative patients | 87 patients | Self-reported proper opioid disposal |
| Sprott, 2008       | RCT          | Longitudinal     | Late adolescents and young adults | 2651 (study 2 on prescription drugs) | Self-reported lifetime prescription drug misuse overall |
| Sprott, 2013       | RCT          | Longitudinal     | Late adolescents and young adults | Study 1: 667 students; Study 2: 2127 students | Self-reported lifetime prescription drug misuse overall |
| Eden, 2014         | RCT          | Cross-sectional  | Pregnant women with previous cesarean | 131 women | MoD (vaginal) |
| Fraser, 1997       | RCT          | Cross-sectional  | Pregnant women with previous cesarean section | 1275 women | MoD (vaginal) |
| Hassani, 2016      | QE           | Cross-sectional  | Primiparous women | 60 women | MoD (vaginal) |
| Montgomery, 2007   | RCT          | Cross-sectional  | Pregnant women with previous cesarean section | 742 women | MoD (vaginal) |
| Navaee, 2015       | RCT          | Cross-sectional  | Primiparous women | 67 women | MoD (vaginal) |
| Sharifiad, 2013    | RCT          | Cross-sectional  | Pregnant women and partners | 88 women and partners | MoD (vaginal) |
| Shorten, 2005      | RCT          | Cross-sectional  | Pregnant women with previous cesarean section | 227 women | MoD (vaginal) |
| Valiani, 2014      | RCT          | Cross-sectional  | Pregnant women and partners | 180 women and partners | MoD (vaginal) |

Notes: CS elective cesarean section, CPP controlled pre- and post-study, NA not applicable, NR not reported, PDMO prescription drug misuse overall, NCT nonrandomized controlled trial, OTC over-the-counter purchases, MoD mode of delivery, RCT randomized controlled trial, VD normal vaginal delivery.
| First author, year | Change in intervention group | Change in control group | Effect size (95% CI) | P value | Effective in changing public behaviors | Quality appraisal |
|--------------------|-----------------------------|------------------------|---------------------|---------|----------------------------------------|------------------|
| Belongia, 2001     | Baseline: 57.6%; post-intervention: 59.5% of initial visits | Baseline: 60.1%; post-intervention: 61.5% of initial visits | NR | Baseline: P = 0.56; post-intervention: P = 0.66 | No | Weak |
| Belongia, 2005     | − 20.4% | − 19.8% | − 0.6% | NR | No | Moderate |
| Bernier, 2014      | NA | NA | − 30% (− 36.3 to − 23.8%) | P < 0.001 | No | Mixed |
| Cebotareno, 2008   | Students: a 33.7% net increase in no antibiotic use; Adults: a 380% net increase in no use | Students − 0.4%; adults +0.1% | Students 3.694 (CI 2.516 to 5.423); adults 5.541 (CI 4.559 to 6.733) | P < 0.0001 | Yes | Weak |
| Finkelstein, 2001  | 3 to < 36 months (− 18.6%), 36 to < 72 (− 150%) | 3 to < 36 months (− 11.5%), 36 to < 72 (− 9.8%) | 3 to < 36 months (− 16%), 36 to < 72 (− 12%) | 3 to < 36 months (P < 0.001), 36 to < 72 (P < 0.001) | Yes | Strong |
| Finkelstein, 2008  | 3 to < 24 months (− 20.7%), 24 to < 48 (− 103), 48 to < 72 (− 2.5) | 3 to < 24 months (− 21.2), 24 to < 48 (− 145), 48 to < 72 (− 93) | 3 to < 24 months (− 0.5), 24 to < 48 (− 4.2), 48 to < 72 (− 6.7) | 3 to < 24 months (P = 0.69), 24 to < 48 (P < 0.01), 48 to < 72 (P < 0.0001) | Mixed | Strong |
| Formoso, 2013      | − 11.9 | − 7.4 | − 4.3% (− 7.1 to − 1.5%) | P = 0.008 | Yes | Strong |
| Fuertes, 2010      | − 5.8% | NA | NR | NR | No | Strong |
| Gonzales, 2004     | − 5% | − 2% | NR | P = 0.79 | No | Moderate |
| Gonzales, 2005     | Children: − 4%; Adults: − 24% | Children: − 2% at local control; 1% at distant control; Adults: − 10% at local control; − 6% at distant control | NR | Children: P = 0.18, P = 0.48 compared with distant and local control; Adults: P < 0.002 and P = 0.006, for distant and local control | Mixed | Moderate |
| Gonzales, 2008     | − | − | − 3.8% in retail pharmacy antibiotic dispenses and − 88% in managed care organization (MCO)-associated dispenses | P = 0.30 for public, P = 0.03 for MOC members | Mixed | Strong |
| Hennessy, 2002     | − 31% (P ≤ 0.01) | − 10% (P ≥ 0.05) | − 21% | NR | Mixed | Moderate |
| Kliemann, 2016     | − 1.616 DID | NA | NR | P = 0.002 | Yes | Moderate |
| Lambert, 2007      | Initial: − 31%; Expanded: − 35% | NA | NR | P < 0.01 | Mixed | Weak |
| First author, year | Change in intervention group | Change in control group | Effect size (95% CI) | P value | Effective in changing public behaviors | Quality appraisal |
|--------------------|-----------------------------|-------------------------|---------------------|---------|--------------------------------------|------------------|
| Lee, 2017          | 20.6%                       | 17.7%                   | 1.20 (0.83–1.73)    | 0.313   | No                                   | Weak             |
| Mainous, 2009      | 1.3%                        | 3.2%                    | NR                  | 0.90    | No                                   | Weak             |
| McNulty, 2010      | − 0.5%                      | 0%                      | NR                  | NA      | No                                   | Weak             |
| Perz, 2002         | Year 3:19%                  | Year 1: 8%              | 11% (8–14%)         | < 0.001 | Yes                                  | Moderate         |
| Sabuncu, 2009      | NA                          | NA                      | NR                  | NR      | NR                                   | Strong           |
| Santa-Ana-Tellez, 2013 | Brazil = −1.35; Mexico = −1.17 | NA                      | NR                  | Brazil P < 0.01; Mexico P < 0.01 | Mixed           | Strong           |
| Santa-Ana-Tellez, 2015 | Brazil = 0.077; Mexico = −0.359 | NA                      | Brazil = 0.077 (-1.142 to 1.297); Mexico = −0.359 (-0.613 to −0.015) | Brazil P > 0.05; Mexico P < 0.01 | Mixed           | Strong           |
| Taylor, 2005       | 2.2 ± 2.6                   | 2.5 ± 2.9               | NR                  | 0.23    | No                                   | Weak             |
| Trepka, 2001       | Expected an antibiotic for their child and did not receive one: − 5.1% brought their child to another physician because they did not receive an antibiotic: − 2.9% | Expected an antibiotic for their child and did not receive one: − 8.4% (− 13.9 to − 2.8); brought their child to another physician because they did not receive an antibiotic: − 4.5% (− 8.0 to − 0.9); they did not receive an antibiotic: 1.6% | Expected an antibiotic for their child and did not receive one: P = 0.003 brought their child to another physician because they did not receive an antibiotic: P = 0.02 | | |
| Wirtz, 2013        | Colombia: − 2.4 DID; Chile: − 3.8 DID; Venezuela: + 5.39 DID and Mexico: − 2.4 DID | NA                      | Colombia: − 1.00; Chile: − 5.56; Venezuela: opposite impact; Mexico: no difference | Colombia: P = 0.001; Chile: P < 0.05 | Mixed           | Moderate         |
| Wutzke, 2007       | − 3.40%                     | NA                      | 1.3–5.5             | < 0.05  | Yes                                  | Moderate         |
| Beshears, 2013     | Unaffiliated testimonial group 11.3%; Affiliated testimonial group 11.7% | 12.20%                   | NR                  | NR (insignificant)                   | No               | Moderate         |
| O'Malley, 2006     | Mailing: − 4.94; Advertising: − 0.13; Generic sampling: − 0.02; physician incentive: − 0.33 | Doubling co-payment for brand-name drugs: 8.60 | NR                  | P > 0.05 | No                                   | Moderate         |
| Sedjo, 2009        | 0.30%                       | 9.30%                   | 29.82 (4.41–201.93) | 0.05    | Yes                                  | Moderate         |
| Vallés, 2003       | 5.10% (1999–2000)           | 1.90% (1999–2000)       | NR                  | 0.01    | Yes                                  | Strong           |
| Hasak 2018         | 28 (22)                     | 14 (11)                 | NR                  | 0.02    | Yes                                  | Weak             |
| First author, year | Change in intervention group | Change in control group | Effect size (95% CI) | P value | Effective in changing public behaviors | Quality appraisal |
|-------------------|-----------------------------|-------------------------|---------------------|--------|----------------------------------------|------------------|
| Lawrence, 2019    | 66 (71.7)                   | 50 (56.2)               | 15.5 (1.7 to 29.3)  | P = 0.03. | Yes                                    | Moderate         |
| Maughan, 2016     | 52% (16/31)                 | 30% (8/27)              | NR                  | P = 0.11. | No                                     | Weak             |
| Rose, 2016        | 12 (27%)                    | 2 (5%)                  | 22% (5 to 38)       | P = 0.005 | Yes                                     | Weak             |
| Spath, 2008       | 11th graders: 3.9%; 12th graders: 7.7% | 11th graders: 7.7%; 12th graders: 10.5% | NR                  |          | Yes                                    | Weak             |
| Spath, 2013       | Study 1: 5.4; Study 2: 2.5 in age 21; 4.4 in age 22; 6.3 in age 25. | Study 1: 15.5; Study 2: 6.5 in age 21; 8.9 in age 22; 94 in age 25. | Study 1: 65%; Study 2: 62% in age 21; 51% in age 22; 33% in age 25. | Study 1: P < 0.01; Study 2: P = 0.015, age 21; P = 0.019, age 22; P = 0.064 | Yes                   | Weak             |
| Eden, 2014        | 41%                         | 37%                     | NR                  | P = 0.724 | No                                     | Weak             |
| Fraser, 1997      | 53%                         | 49%                     | 1.1 (1.0 to 1.2)    | P > 0.05 | No                                     | Weak             |
| Hassani, 2016     | 30%                         | 10%                     | NR                  | NR      | Yes                                    | Weak             |
| Montgomery, 2007  | Decision analysis group: 37% Info: 25% | Usual care: 30% | Info v. usual care: 0.93 (0.61,1.41) | Decision v. usual care: 1.42 (0.94,2.14) | P > 0.9          | Strong           |
| Havaee, 2015      | 62.9%                       | 43.8%                   | NR                  | P = 0.117 | No                                     | Weak             |
| Sharifrad, 2013   | 71.5%                       | 50.0%                   | NR                  | P < 0.05 | Yes                                    | Weak             |
| Shorten, 2005     | VD: 49.2%                   | CS: 50.8%               | NR                  | NR      | No                                     | Weak             |
| Vali, 2014        | Mothers alone intervention = 60%; Couples = 56.7% | 26.7% | NR | P = 0.017 | Yes                                    | Weak             |
Table 3 Features of included interventions

| First author, year | Gov't support | Policy | Professional target |
|--------------------|---------------|--------|---------------------|
|                    |               |        | Letters to doctors | Educational meetings | Written materials | Clinical practice guidelines | Prescribing feedback | Physician financial incentives |
| Belongia, 2001     | Yes           | x      | x                   | x                    | x                  | x                           | x                 | x                        |
| Belongia, 2005     | Yes           | x      | x                   | x                    | x                  | x                           | x                 | x                        |
| Bernier, 2014      | Yes           | x      | x                   | x                    | x                  | x                           | x                 | x                        |
| Cebotarenco, 2008  | No            |        |                      |                      |                    |                             |                   |                          |
| Finkelnstein, 2001 | Yes           | x      | x                   | x                    | x                  | x                           | x                 | x                        |
| Finkelnstein, 2008 | Yes           | x      | x                   | x                    | x                  | x                           | x                 | x                        |
| Formosa, 2013      | Yes           | x      |                      |                      |                    |                             |                   |                          |
| Fuentes, 2010      | Yes           | x      |                      |                      |                    |                             |                   |                          |
| Gonzales, 2004     | Yes           | x      | x                   | x                    | x                  |                             |                   |                          |
| Gonzales, 2005     | Yes           | x      | x                   | x                    | x                  |                             |                   |                          |
| Gonzales, 2008     | Yes           | x      |                      |                      |                    |                             |                   |                          |
| Hennessey, 2002    | Yes           | x      |                      |                      |                    |                             |                   |                          |
| Kliemann, 2016     | Yes           | x      |                      |                      |                    |                             |                   |                          |
| Lambert, 2007      | Yes           | x      |                      |                      |                    |                             |                   |                          |
| Lee, 2017          | No            |        |                      |                      |                    |                             |                   |                          |
| Mainous, 2009      | No            |        |                      |                      |                    |                             |                   |                          |
| McNulty, 2010      | Yes           | x      | x                   | x                    | x                  |                             |                   |                          |
| Perz, 2002         | Yes           | x      | x                   | x                    | x                  |                             |                   |                          |
| Sabuncu, 2009      | Yes           | x      | x                   | x                    | x                  |                             |                   |                          |
| Santa-Ana-Tellez, 2013 | Yes     | x      |                      |                      |                    |                             |                   |                          |
| Santa-Ana-Tellez, 2015 | Yes   | x      |                      |                      |                    |                             |                   |                          |
| Taylor, 2005       | Yes           | x      |                      |                      |                    |                             |                   |                          |
| Trepka, 2001       | Yes           | x      | x                   | x                    | x                  |                             |                   |                          |
| Wirtz, 2013        | Yes           | x      |                      |                      |                    |                             |                   |                          |
| Wutzke, 2007       | Yes           | x      | x                   | x                    | x                  |                             |                   |                          |
| Behears, 2013      | Yes           | x      |                      |                      |                    |                             |                   |                          |
| O'Malley, 2006     | No            |        |                      |                      |                    |                             |                   |                          |
| Sedjo, 2009        | No            |        |                      |                      |                    |                             |                   |                          |
| Valle, 2003        | No            |        |                      |                      |                    |                             |                   |                          |
| Hasok, 2018        | No            |        |                      |                      |                    |                             |                   |                          |
| Lawrence, 2019     | No            |        |                      |                      |                    |                             |                   |                          |
| Maughan, 2016      | No            |        |                      |                      |                    |                             |                   |                          |
| Rose, 2016         | No            |        |                      |                      |                    |                             |                   |                          |
| Spoth, 2008        | No            |        |                      |                      |                    |                             |                   |                          |
| First author, year | Grant support | Professional target | Public target | Policy | Written materials | Educational materials | Written feedback | Prescribing feedback | Clinical practice guidelines | Physiological incentive | Clinical decision support | Other mass media campaign activities | Decision aids/Enabling tools | NR
|-------------------|---------------|---------------------|--------------|--------|------------------|----------------------|------------------|----------------------|-------------------------|----------------------|-------------------------|----------------------------|-------------------------|-------|
| Spoth, 2013       | No            | No                  | NR           |        |                  |                      |                  |                      |                         |                      |                         |                            |                        |       |
| Eden, 2014        | No            | No                  | NR           |        |                  |                      |                  |                      |                         |                      |                         |                            |                        |       |
| Fraser, 1997      | Yes           | Yes                 | NR           |        |                  |                      |                  |                      |                         |                      |                         |                            |                        |       |
| Hassani, 2016     | No            | No                  | NR           |        |                  |                      |                  |                      |                         |                      |                         |                            |                        |       |
| Montgomery, 2007  | No            | No                  | NR           |        |                  |                      |                  |                      |                         |                      |                         |                            |                        |       |
| Navaee, 2015      | No            | No                  | NR           |        |                  |                      |                  |                      |                         |                      |                         |                            |                        |       |
| Sharifirad, 2013  | No            | No                  | NR           |        |                  |                      |                  |                      |                         |                      |                         |                            |                        |       |
| Shorten, 2005     | No            | No                  | NR           |        |                  |                      |                  |                      |                         |                      |                         |                            |                        |       |
| Valiani, 2014     | No            | No                  | NR           |        |                  |                      |                  |                      |                         |                      |                         |                            |                        |       |
| First author, year | Public target | TV | Video | Newsletters/mails | Poster | Radio | Press conferences | Newspapers or advertisements (including billboards, bus signs) | Websites | Informational written materials (including pamphlets/brochures) | Education meetings | Mascots | School program (including peer-education) | Family and friends | Decision-aid/enabling tools | Other mass media campaign activities | Multilingual |
|-------------------|---------------|----|-------|-------------------|--------|-------|------------------|------------------------------------------------|-----------|---------------------------------|-----------------|---------|------------------------------------------|---------------|-----------------|-------------------------------|-------------|
| Belongia, 2001    |               | X  | X     |                   |        |       |                   |                                               |           |                                 |                 |         |                                          |               |                 |                               | NR          |
| Belongia, 2005    |               | X  | X     | X                 | X      |       | X                | X                                             | X         |                                 |                 |         |                                          | X             |                 |                               | NR          |
| Bernier, 2014     |               | X  | X     | X                 | X      |       | X                | X                                             | X         |                                 |                 |         |                                          | X             |                 |                               | NR          |
| Cebotareno, 2008  |               | X  | X     |                   |        |       | X                | X                                             | X         |                                 |                 |         |                                          | X             |                 |                               | NR          |
| Finkelstein, 2001 |               | X  |       |                   |        |       | X                | X                                             |           |                                 |                 |         |                                          |               |                 |                               | NR          |
| Finkelstein, 2008 |               | X  |       |                   |        |       | X                | X                                             | X         |                                 |                 |         |                                          |               |                 |                               | NR          |
| Formosa, 2013     |               | X  | X     | X                 | X      |       | X                |                                               |           |                                 |                 |         |                                          |               |                 |                               | NR          |
| Fuertes, 2010     |               | X  |       |                   |        |       | X                |                                               |           |                                 |                 |         |                                          |               |                 |                               | NR          |
| Gonzales, 2004    |               | X  |       |                   |        |       | X                | X                                             |           |                                 |                 |         |                                          |               |                 |                               | Yes         |
| Gonzales, 2005    |               | X  |       |                   |        |       | X                | X                                             |           |                                 |                 |         |                                          |               |                 |                               | Yes         |
| Gonzales, 2008    |               | X  |       |                   |        |       | X                | X                                             |           |                                 |                 |         |                                          |               |                 |                               | Yes         |
| Hennessy, 2002    |               | X  |       |                   |        |       | X                |                                               |           |                                 |                 |         |                                          |               |                 |                               | NR          |
| Kliemann, 2016    |               |    |       |                   |        |       |                 |                                               |           |                                 |                 |         |                                          |               |                 |                               | NA          |
| Lambert, 2007     |               | X  |       |                   |        |       | X                | X                                             |           |                                 |                 |         |                                          |               |                 |                               | NR          |
| Lee, 2017         |               |    |       |                   |        |       |                 |                                               |           |                                 |                 |         |                                          |               |                 |                               | Yes         |
| Mainous, 2009     |               | X  |       |                   |        |       | X                |                                               |           |                                 |                 |         |                                          |               |                 |                               | Yes         |
| McNulty, 2010     |               | X  |       |                   |        |       | X                |                                               |           |                                 |                 |         |                                          |               |                 |                               | NR          |
| Perz, 2002        |               | X  | X     |                   |        |       | X                | X                                             |           |                                 |                 |         |                                          |               |                 |                               | NR          |
| Sabuncu, 2009     |               | X  | X     | X                 | X      |       | X                |                                               |           |                                 |                 |         |                                          |               |                 |                               | NR          |
| Santa-Ana-Tellez, 2013 |           | X  | X     | X                 | X      |       | X                |                                               |           |                                 |                 |         |                                          |               |                 |                               | NR          |
| Santa-Ana-Tellez, 2015 |           | X  | X     | X                 | X      |       | X                |                                               |           |                                 |                 |         |                                          |               |                 |                               | NA          |
| Taylor, 2005      |               |    |       |                   |        |       | X                |                                               |           |                                 |                 |         |                                          |               |                 |                               | NR          |
| Tieple, 2001      |               | X  |       |                   |        |       | X                | X                                             |           |                                 |                 |         |                                          |               |                 |                               | NR          |
| Wirtz, 2013       |               |    |       |                   |        |       | X                |                                               |           |                                 |                 |         |                                          |               |                 |                               | NA          |
| Wurtze, 2007      |               | X  |       |                   |        |       | X                | X                                             |           |                                 |                 |         |                                          |               |                 |                               | NR          |
| Besehers, 2013    |               | X  |       |                   |        |       | X                |                                               |           |                                 |                 |         |                                          |               |                 |                               | NR          |
| O’Malley, 2006    |               | X  |       |                   |        |       | X                |                                               |           |                                 |                 |         |                                          |               |                 |                               | NR          |
| Sedjo, 2009       |               | X  |       |                   |        |       | X                |                                               |           |                                 |                 |         |                                          |               |                 |                               | NR          |
| Vallée, 2003      |               | X  |       |                   |        |       | X                |                                               |           |                                 |                 |         |                                          |               |                 |                               | NR          |
| Hasak, 2018       |               |    |       |                   |        |       | X                |                                               |           |                                 |                 |         |                                          |               |                 |                               | NR          |
| Lawrence, 2019    |               | X  |       |                   |        |       | X                |                                               |           |                                 |                 |         |                                          |               |                 |                               | NR          |
| Maughan, 2016     |               |    |       |                   |        |       | X                |                                               |           |                                 |                 |         |                                          |               |                 |                               | NR          |
| First author, year | Public target | TV | Video | Newspapers/ | Poster | Radio | Press | conferences | Newspapers or advertisements (including bill boards, bus signs) | Websites | Informational written materials (including pamphlets/brochures) | Education meetings | Mascots | School program (including peer-education) | Family and friends | Decision-aid/enabling tools | Other mass media campaign activities | Multilingual |
|-------------------|--------------|----|-------|-------------|--------|-------|-------|-------------|-------------------------------------------------|-----------|--------------------------------------------------|-----------------|----------|-------------------------------|----------------|-----------------------|--------------------------|-------------|
| Rose, 2016        | X            | X   |       |             |        |       |       |            |                                                 |           |                                                  |                 |          |                               |               |                      |                           | NR          |
| Spoth, 2008       | X            | X   |       |             |        |       |       |            |                                                 |           |                                                  |                 |          |                               |               |                      |                           | NR          |
| Spoth, 2013       | X            |     |       |             |        |       |       |            |                                                 |           |                                                  |                 |          |                               |               |                      |                           | NR          |
| Eden, 2014        | X            |     |       |             |        |       |       |            |                                                 |           |                                                  |                 |          |                               |               |                      |                           | Yes         |
| Fraser, 1997      | X            | X   |       |             |        |       |       |            |                                                 |           |                                                  |                 |          |                               |               |                      |                           | Yes         |
| Hassani, 2016     | X            |     |       |             |        |       |       |            |                                                 |           |                                                  |                 |          |                               |               |                      |                           | NR          |
| Montgomery, 2007  | X            |     |       |             |        |       |       |            |                                                 |           |                                                  |                 |          |                               |               |                      |                           | NR          |
| Navare, 2015      | X            | X   |       |             |        |       |       |            |                                                 |           |                                                  |                 |          |                               |               |                      |                           | NR          |
| Sharifrad, 2013   | X            | X   |       |             |        |       |       |            |                                                 |           |                                                  |                 |          |                               |               |                      |                           | NR          |
| Shorten, 2005     | X            |     |       |             |        |       |       |            |                                                 |           |                                                  |                 |          |                               |               |                      |                           | NR          |
| Valiani, 2014     | X            |     |       |             |        |       |       |            |                                                 |           |                                                  |                 |          |                               |               |                      |                           | NR          |
how these underlying theories were used in the development and evaluation of the interventions.

**Interventions targeting health care consumers**

Table 4 reports the individual BCTs identified within the descriptions as active ingredients of the selected interventions targeting health care consumers. Of the 93 BCTs, the most frequently used active ingredients in the selected interventions targeting health care consumers were BCTs: 4.1-Instruction on how to perform the behavior (n = 34), 4.2 Information about antecedents (n = 22), 5.1 Information about health consequences (n = 22), followed by 12.5 Adding objects to the environment (n = 12), 8.2 Behavior substitution (n = 11), and 12.1 Restructuring the physical environment (n = 8). Most studies employed education interventions aiming to improve public knowledge (including awareness or correcting misconceptions). Mass media campaigns were widely used to reduce antibiotic misuse [54–56, 60, 63–68] and demand for brand-name drugs [69], all in HIC. The effectiveness of such behavioral change interventions was mixed. Decision aids to assist pregnant women making decisions about mode of delivery were tested in three different trials in Australia, UK, and USA; all reported to be ineffective [52, 70, 71]. Taylor et al. [72], Lee et al. [73], and Vallès et al. [51] trialed patient-based education interventions in primary care settings to reduce antibiotic use or to substitute generic for brand-name drugs; only Vallès et al.’s [51] intervention found a positive impact on behavior change. Mainous et al. and McNulty et al. assessed community-wide education interventions in the USA and UK on their effectiveness in improving public antibiotic use and found the provision of educational messages itself was insufficient to overcome the influence of past attitudes and behaviors [57, 66]. Formal and informal social support networks can be leveraged to influence individuals’ behaviors through improving doctor-patient communication [58–60, 64, 72, 74] or by actively engaging family members in the process [39, 40, 75]. Four interventions aimed to encourage disposal of leftover opioids among postoperative patients by employing a combination BCWs of education, enablement, and environment restructuring (BCTs: 4.1, 4.2, 5.1, 5.2, 8.2, 12.1, 12.5), which reported positive impact [76–79]. Two longitudinal RCTs on school-based universal preventive interventions in the USA that aimed to strengthen families and build life skills were introduced to middle schoolers [39, 40] and reported a lasting impact on preventing non-medical use of prescription drugs into adulthood. Structural environmental conditions regarding access to healthcare services and medicines, and promotive and restrictive policies—or the lack thereof—can be pathways to shaping individual behaviors. Two trend analyses assessing the effectiveness of French public education campaigns [63, 68] reported a significant reduction in antibiotic consumption rates; however, trials on community-wide public campaigns with academic detailing for practitioners did not demonstrate comparable levels of improvement in public antibiotic use. Belongia et al. and Fiskelstein et al. found little or no evidence—attributable to multi-year interventions in Wisconsin and Massachusetts—on reductions in antibiotic prescribing in the intervention areas, despite improved public knowledge [54, 59, 74]. Gonzales et al. found that the state-wide “Get Smart Colorado” campaign did not improve prescription rates, but might be associated with a reduction in antibiotic use in the community through decreases in office visit rates among children [56, 64]. Four studies evaluated the effectiveness of the restrictions on OCT purchases on antibiotic consumption in five Latin American countries with mixed results [33–35, 80].

**Interventions also targeting health care providers**

Table 5 reports the individual BCTs identified within the descriptions as active ingredients of the selected interventions targeting health care providers. The most frequently used BCTs targeting health care providers were similar with those targeting consumers, with small differences in the ranking: BCTs: 4.1 Instruction on how to perform the behavior (n = 15), 4.2 Information about antecedents (n = 13), 12.5 Adding objects to the environment (n = 10), followed by 5.1 Information about health consequences (n = 9), 8.2 Behavior substitution (n = 9), and 12.1 Restructuring the physical environment (n = 4). We noticed that, except for programs aiming to contain inappropriate use of antibiotics, other interventions had limited engagement between consumers and providers.

**Discussion**

**Summary of findings**

Using the Behavioral Change Wheel (BCW) domains to identify the theoretical concepts underlying interventions and the behavior change technique taxonomy v1 (BCTTv1) to identify the active ingredients of interventions, we found that the domain of education was the most commonly targeted by a majority of interventions with primary focus on the provision of information on BCTs 4.1 how to perform the behavior and 4.2 about antecedents and 5.1 the associated health consequences. A plethora of evidence supports the view that human behaviors should be understood in their social ecological context, as products of intertwined influences at the personal, communal, societal, and structural levels [81–83]. Studies show that improving knowledge and awareness does not equate with appropriate behavior change, as lack of information is often not the only barrier to changing behavior [64, 66, 84–86]. The effects of education
Interventions have been mixed—most likely due to heterogeneity in context, population served, and intervention design and measures. Cabral et al. examined how communication affects prescription decisions for acute illnesses and demonstrated a clear miscommunication with cross-purposes between health care consumers and providers, as patients and/or caregivers focused on their concerns and information needs, which clinicians interpreted as an expectation for antibiotics [87]. This review supports the use of multifaceted (complex) interventions that incorporate BCTs related to provision of information (BCTs 4.1, 4.2, or 5.1) and, as an alternative to antibiotics, prescription pads with clear explanations on symptoms, and appropriate treatment options (BCT 8.2).
as education alone is not sufficient to be effective. Interventions consisting of health education messages (e.g., BCTs 4.1, 4.2, 5.1), recommended behavior alternatives (BCT 8.2), and a supporting environment that incentivizes or encourages the adoption of a new behavior (e.g., BCTs 10.1, 10.2, 12.1, 12.5) are more likely to be successful. Other types of utilized behavior change techniques often aimed to encourage alternative behaviors and improve the physical environments via regulations or mass media.

The continuing tendency in research reporting has been to stress the effectiveness of interventions rather than the process of identifying and developing key components and the parameters within which they operate. There is a lack of detail on how the intervention components were selected, designed, and the process of implementing them, with limited descriptions provided on the “contexts” and “mechanisms” that determine the effectiveness of interventions. Few studies provided sufficient details on intervention development, dose/intensity, and design; some provided links to project materials that had expired [54–56, 60]. The majority of the selected interventions did not describe the pilot or process data for implementation, nor did they discuss the dissemination of findings and pathways to impact. Even after identifying active ingredients of interventions using BCTTv1, without a complete “recipe,” one cannot recreate successes in other contexts. Just like there are agreed-upon

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**Table 4** Behavior change techniques and number of interventions targeting health care consumers and included specific behavior change techniques, behavior change techniques taxonomy volume 1 (BCTTv1) hierarchical clusters, and intervention content examples

| BCT | BCTTv1 hierarchical clusters | Examples extracted from descriptions of the interventions | Frequency |
|-----|------------------------------|----------------------------------------------------------|-----------|
| 3.1 | Social support (unspecified) | Educational programs for husbands of pregnant women that aimed to provide social support of husbands, which consequently reduces the rate of elective cesarean section. | 3 |
| 3.3 | Social support (emotional)   | A resource person will provide peer influence during decision making process about mode of delivery | 1 |
| 4.1 | Instruction on how to perform the behavior | Information about when antibiotics are and are not needed (e.g., rarely for bronchitis, not for colds). | 34 |
| 4.2 | Information about Antecedents | Information about bacterial and viral infections | 22 |
| 5.1 | Information about health consequences | Information about bacterial resistance or side effects of antibiotic use | 22 |
| 5.2 | Salience of consequences     | Emphasis on the consequences inappropriate use of antibiotics (e.g., antimicrobial resistance or side effects of antibiotic use) | 6 |
| 6.1 | Demonstration of the behavior | Role play education to reduce the fear of childbirth | 3 |
| 8.2 | Behavior substitution        | Alternative remedies instead of antibiotics for colds | 11 |
| 9.1 | Credible source              | Endorsement by CDC was designed to increase the credibility of key messages | 4 |
| 9.2 | Pros and cons                | Information about the differences between generic and brand-name drugs in terms of advantages (high-quality bioequivalent formulations, health professionals’ preferences, avoidance of confusions) and disadvantages (popularity, fidelity to branded products) | 8 |
| 10.1 | Material incentive (behavior) | Switching to a lower-cost generic medication is cost-saving | 3 |
| 10.2 | Material reward (behavior)   | Associated cost savings to the recipient from switching to each of these alternatives | 3 |
| 12.1 | Restructuring the physical environment | Restriction on sale of antibiotics without prescription | 8 |
| 12.2 | Restructuring the social environment | Interventions focused on empirically supported family risk and protective factors, such as parental nurturing, child management skills, improved parent–adolescent communication skills and adolescent prosocial skill development (e.g., managing conflict and stress, handling peer pressure, developing positive friendships) | 3 |
| 12.5 | Adding objects to the environment | Mass media strategies were undertaken including advertising using billboards, television, radio, and magazines. | 12 |

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elements that constitute a rigorous and comprehensive reporting of evaluation studies, publications on behavioral change interventions should systematically cover a standardized list of intervention elements from the development, adaptation and refinement, feasibility and pilot-testing, implementation, evaluation, and reporting of BCTs. The CONSORT-SPI team [88] has developed guidance and checklists for the reporting of BCT trials; however, the required details on the reporting are still primarily focused on evaluation study designs (e.g., process of randomization) rather than BCT development and implementation. From implementation research perspective and following the Medical Research Council (MRC) guidance on developing and evaluating complex interventions, reporting of BCT development and implementation should include descriptions on the context, target behavior determinants, theories and rationale (theory of change), intervention design features, adaptation/development process, implementation strategy (e.g., implementor, dose/intensity), modifications made between the feasibility and effective assessment phases, and evaluation outcomes. The lack of detailed reporting

| BCT | BCTTv1 hierarchical clusters | Examples extracted from descriptions of the interventions | Frequency |
|-----|------------------------------|----------------------------------------------------------|-----------|
| 1.3 Goal setting (outcome) | 1. Goals and planning | Provision of individual prescribing profiles depicting: (1) the proportion of adult bronchitis patients receiving antibiotic treatment (target 10 percent or less); (2) the proportion of these antibiotics belonging to a first-line group (erythromycin, doxycycline, tetracycline) (target 70% or more); and (3) the proportion of these antibiotics that are ineffective against proven bacterial causes of uncomplicated acute bronchitis (target 0%). | 1 |
| 2.2 Feedback on behavior | 2. Feedback and monitoring | Prescribing feedback, clinical audit with feedback | 3 |
| 3.1 Social support (unspecified) | 3. Social support | Interventions that inform best practice prescribing and that support health professionals manage patient expectations | 1 |
| 3.2 Social support (practical) | 3. Social support | This intervention will (1) provide a range of patient education materials to physician offices without charge, (2) provide ongoing information about antibiotic-use rates and resistance in the community, (3) provide feedback about prescribing by practice, and (4) serve as a general resource on issues of antibiotic prescribing and resistance | 3 |
| 4.1 Instruction on how to perform the behavior | 4. Shaping knowledge | Academic detailing to promote appropriate antibiotic use; practice guidelines which included with the patient profiles for adults with bronchitis and children with pharyngitis were compatible with those produced by the Centers for Disease Control and Prevention (CDC) | 15 |
| 4.2 Information about Antecedents | 4. Shaping knowledge | Clinical practice guidelines for common respiratory illnesses | 13 |
| 5.1 Information about health consequences | 5. Natural consequences | A reference card providing easy-to-read facts about symptoms and treatments for ARIs | 9 |
| 5.2 Salience of consequences | 5. Natural consequences | Emphasis on AMR | 2 |
| 8.2 Behavior substitution | 8. Repetition and substitution | Prescription pads with explanations on symptoms and appropriate treatment options (to be given to patients instead of antibiotic prescriptions) | 9 |
| 9.1 Credible source | 9. Comparison of outcomes | Endorsement by CDC was designed to increase the credibility of key messages. | 1 |
| 10.1 Material incentive (behavior) | 10. Reward and threat | An intervention intends to reward physicians for reducing pharmacy costs for their patients, one component of which was to increase their prescribing of generic drugs | 1 |
| 10.2 Material reward (behavior) | 10. Reward and threat | Reward given to physicians for reducing pharmacy costs for their patients, one component of which was to increase their prescribing of generic drugs | 1 |
| 12.1 Restructuring the physical environment | 12. Antecedents | Waiting room materials (CDC posters and patient reference cards) | 4 |
| 12.5 Adding objects to the environment | 12. Antecedents | Mass media strategies were undertaken including advertising using billboards, television, radio and magazines. | 10 |
| 14.2 Punishment | 14. Scheduled consequences | Regulations that require prescriptions for antibiotics to be retained and registered in pharmacies and imposes fines to the owners of the pharmacies for non-compliance. | 2 |
| 15 | 10 | 75 |
among included intervention studies on evidence-based development and implementation processes undermines the generalizability of study findings, makes cross-intervention comparisons difficult, and complicates future adaption and replication efforts.

This systematic literature review is the first on the effectiveness of public-targeted behavioral change interventions to reduce inappropriate use of medical interventions. It identified a serious lack of formative data, which means that interventions to change public use of medical interventions are often designed on the basis of “best guesses” of what needs to change, without an evidence base or explicit rationale for the selection of a specific intervention strategy. There is an urgent need to adopt a multidisciplinary, systematic approach to developing evidence-based behavioral change interventions to reduce inappropriate medical use and to develop an operational mechanism for knowledge translation and scale-up within and across different countries. We found limited evidence [39, 63] on evaluating the impact of previous or ongoing education interventions on inappropriate use in terms of long-term impact, scalability, and replicability. The root causes of why certain interventions were unsuccessful are not systematically explored or reported, yet reporting “negative results” is likely as critical as reporting “active ingredients” and positive findings for the development and sustainability of implementation science.

Relation to other studies
Like most stewardship programs, quaternary prevention—a relatively new category of medical prevention first raised in 1986 by Dr. Marc Jamoulle, a family physician, to addressing concerns around the protection of people and patients from being harmed by over-diagnosis or overtreatment—tends to focus mostly on health care providers while placing less attention on consumers [5, 89–91]. The definition of quaternary prevention was later expanded by Brodersen et al. in 2014 to include patients and medical interventions as an action taken to protect individuals (persons/patients) from medical interventions that are likely to cause more harm than good [92, 93]. The expanded definition recognizes the contemporary reality in medicine in which people may suffer harm from medical interventions throughout their entire lifetime—from conception to adulthood, in times of good health, as well as when experiencing self-limited disease, chronic conditions, or terminal disease. Therefore, quaternary prevention should include preventing all types of harm associated with medical interventions [92, 93]. From this perspective, quaternary prevention is aligned with the aims of the behavioral change interventions and techniques identified in our review and should be considered alongside the other four classical levels of preventive activities, i.e., primordial (e.g., laws that restrict over-the-counter purchases of antibiotics), primary (e.g., prescription drugs disposal programs), and secondary and tertiary preventions (e.g., interventions that reduce fear of childbirth or convert demand of brand-name drugs to generic drugs).

The use of medicine or medical procedures is a highly complex set of behaviors involving multiple actions, including the self-diagnostic process, assessing benefit/risk, decision-making around healthcare seeking and treatment choice, and review of treatment—each performed at different time points across the care continuum [94, 95]. It involves interactions with various stakeholders (i.e., family members and providers) and is often shaped more by individual and contextual factors than by a clinical diagnosis [94, 95]. Therefore, developers and implementers of behavioral change interventions should be clear as to whose and which behaviors are being targeted for change and how—namely, who needs to do what differently, how, to whom, where, when, and for how long. A set of precisely specified behaviors would allow for easier measurement and therefore would offer a baseline and metric for evaluating the success of an intervention.

In order to develop effective behavioral change interventions, we first need to explain why people behave in certain ways, yet a more in-depth look at people’s life-world is lacking from every reviewed article. As the dual processing theory (DPT) posits, human behavior is guided by two types of processing mechanisms: the implicit, intuitive system 1 and the explicit, rational system 2 [96]. Behavioral economists elaborate that, due to limited self-control, rationality and social preferences, actual decisions are less rational and stable than traditional normative theory suggests [96]. They are usually made with a range of biases resulting from the way people think and feel, rather than with rationality or full information. However, most of the included interventions—appealing to system 2 processing—attempted to influence behaviors via improved knowledge and attitudes; disappointingly, many trials indicated that this did not automatically lead to preferred behaviors [54, 59, 72, 74]. To complicate things further, Zinn argues that between rationality and irrationality, there is a third, “in-between” dimension that includes trust, intuition, and emotion, which is an important aspect of decision-making when people deal with risk and uncertainty, especially in anticipation of the possible undesired outcomes of decisions [97]. This may explain why three RCTs on decision aids (system 1) to address individual emotions (system 2) had no real impact on choice of vaginal birth [52, 70]. On the other hand, in addition to education programs, financial incentives (changes in copayment), free medicine, advertisements (print media), and health policies have been experimented with as
behavioral change interventions to influence healthcare consumers’ choice of medicine—in particular, to promote uptake of generic medicines—though they have demonstrated inconsistent results [98, 99].

The most promising measure was an intervention delivered face-to-face, where consumers were told that they had the option of switching back to brand-name drugs anytime [51, 100, 101]; hence, an intervention that leverages human behavioral mechanisms may be more effective and cost-effective in optimizing decision making than repeated, expensive education campaigns.

In response to the recent opioid epidemic across the globe, promising prevention programs aimed not only to improve the knowledge and awareness of the risk of nonmedical use of prescription drugs among at-risk individuals, but also to empower healthcare consumers by providing skills or tools that enable them to take action prior to the occurrence of misuse and/or before the development of poor habits [39, 40, 76–79]. These interventions further improved the socio-ecological surroundings of the target audience by involving family members and restructuring their social or physical environments [39, 40, 76–79].

Our review showed only 19% of BCTs have been utilized by included interventions (i.e., 81% of BCTs unexplored), with great variation between different types of misuse—most were limited to education. Future studies should explore other BCTs. A wide range of disciplines engaging in social and behavioral sciences, such as psychology, sociology, anthropology, communication, and marketing, can provide theories, models, and methods for a more comprehensive and coherent approach to understanding or even modifying contextual, organizational, and interpersonal determinants of behavior. In terms of sustainability of the interventions themselves, other than a few longitudinal studies [39, 40], we do not know how long the reported effect of behavioral change will sustain. Few studies incorporated economic evaluations, and therefore, it was not possible to determine the returns on investment (ROI) for these included interventions. Future intervention studies should consider the aspects of RE-AIM (Reach Effectiveness Adoption Implementation Maintenance) framework or follow the MRC Guidelines on Developing and Evaluating Complex Interventions during the planning stage to enhance the impact of interventions and the reporting of them.

Development of a behavioral change intervention has to start with a realist, comprehensive understanding of the complex environment that shapes individual and collective behaviors. The etiology of inappropriate use of medical interventions should be studied and addressed within the context of its biological, psychosocial, behavioral, and environmental factors and the interactions between them. In early 2000, Sallies et al. developed a behavioral epidemiology framework, which specified a systematic sequence of studies on health-related behaviors leading to evidence-based interventions directed at populations in the following five phases: (1) establish links between behaviors and health, (2) develop measures of the behavior, (3) identify influences on the behavior, (4) evaluate interventions to change the behavior, and (5) translate research into practice [21, 83, 102]. In 2011, Michie and colleagues mapped out various pathways to influencing behavioral change and recommended that interventions seeking to change behavior should be designed on the basis of a thorough “behavioral diagnosis” of why behaviors are the way they are and what needs to change in order to bring about the desired behavior [21]. Conducting such diagnosis should be facilitated by the use of behavioral theory. Not until recent years did researchers systematically report efforts in the identification of the root causes of operational barriers and facilitators in designing, implementing, and evaluating interventions. For instance, in 2018 and 2019, Langridge et al. have attempted to decipher the intervention elements and visual imagery used in public antimicrobial stewardship [23, 103].

Consistent with the findings from recent reviews by Cochrane and the Department of Health and Social Care and Public Health in England [5, 104, 105], our review found that few interventions employed behavior change theories or techniques. Behavioral determinants and social influences are often not given sufficient consideration in the design and evaluations of interventions. To inform the design of effective, context-specific behavior change interventions, one must first define the problem in both behavioral terms and in its current context and adopt a theory-driven, systematic approach to intervention design. This points to another critical knowledge gap identified by this review in implementation science, namely early studies that take place prior to the implementation of behavioral change interventions. Following the Medical Research Council (MRC) guidelines on developing and evaluating complex interventions [106], as presented in Table 1, we find there is little reporting on the feasibility, pilot, or process data that generates the needed contextual information and evidence base for acceptance, adaption, and uptake. Limited detail has been made available on the development of the included interventions regarding how key decisions were made, including feasibility and compliance. Future research on pilot and/or feasibility studies that aim to strengthen large-scale behavioral change intervention design can span the continuum of implementation science research from idea generation to intervention development, implementation, evaluation, and scale-up.
Limitations
This systematic review is subject to important limitations as we worked with interventions that are complex, heterogeneous, non-standardised, and targeted different types of inappropriate use of medical interventions and users. The diversity in the design and outcome measures of the included interventions prevents us from performing a meta-analysis. We demonstrated great variability in the effect size observed within each behavioral change intervention considered. We cannot make a conclusion that certain types of behavioral change intervention might be more effective than any other type of design due to the limitations of the literature relating to the lack of evidence-based development process and evaluation design. Behavioral data that were gathered via survey instruments were by nature self-reported from health care consumers who may have been reluctant to report practices that could be considered inappropriate or may have been subject to recall bias. Often there were more than one “active ingredient” identified for each included intervention, yet retrospective coding and the study design did not allow us to pinpoint which component was more effective. Further, some studies contained bundles of interventions while others contained similar, yet different interventions implemented in multiple countries; therefore, the results of this review may have been clouded by unconsidered/unreported intervention components in the studies included. The studies in this review were spread across a wide range of settings and populations, so general conclusions should be drawn with caution. Publication bias may be a critical problem since it implies that most interventions have a positive effect. We expect most interventions aimed at individuals to be much more complex in reality; however, this review was not able to capture how and why “active ingredients” were selected, implemented, or functioned in the respective socioeconomic, cultural, and healthcare settings. Future work should focus on addressing the limitations and uncertainties surrounding existing behavioral change interventions.

Conclusion
Systematically assessing the evidence across behavioral change interventions allows for the identification of the “active ingredients” of effective interventions that improve healthcare consumers’ use of medical interventions, as well as the identification of those with ineffective or uncertain outcomes. Although opportunities for behavioral change interventions are becoming more commonly recognized, multifaceted (complex) interventions are still new, scarce, limited to high-income countries, and, as is evident from our findings, highly heterogeneous. Public-targeted behavioral change interventions in low- and middle-income countries (LMICs) were exclusively limited to primary care settings. Interventions that consist of health education messages, recommended behavior alternatives, and a supporting environment that incentivizes or encourages the adoption of a new behavior are more likely to be successful. Future research should also seek to unpack the distinctions between various audience segments, the influence of the social ecological context, and the utility of the unexplored 81% of behavioral change techniques (BCTs). It is critical to adhere to a rigorous framework that guides the development, implementation, evaluation, and reporting of evidence-based interventions, so that generated evidence can be documented, disseminated, compared, and utilized for further research. The lack of reporting on evidence-based development and implementation processes makes cross-intervention comparisons and replication difficult. Our review further identified a need for standardized reporting of intervention development, adaptation, and implementation to maximize generalisability and replicability.

Supplementary information
Supplementary information accompanies this paper at https://doi.org/10.1186/s13012-020-01018-7.

Additional file 1: Search Strategy
Additional file 2: Inclusion and Exclusion Criteria
Additional file 3: List of included studies
Additional file 4: Summary of quality assessment of included studies

Abbreviations
ABR: Antibiotic resistance; AMR: Antimicrobial resistance; BCT: Behavior change technique; BCTT: Behavior change technique taxonomy; BCW: Behavioral Change Wheel; CPP: Controlled pre- and post-study; CRT: Cluster randomized control trial; CS: Elective cesarean section; DPT: Dual processing theory; EPHPP: Effective Public Health Practice Project's Quality Assessment Tool for Quantitative Studies; HIC: High-income country; ITS: Interrupted time series; LMIC: Low- and middle-income country; MoD: Mode of delivery; MRC: Medical research council; NA: Not applicable; NR: Not reported; NCT: Nonrandomized controlled trial; OTC: Over-the-counter purchases; PDM: Prescription drug misuse; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RCT: Randomized control trial; RO: Returns on investment; VD: Normal vaginal delivery; WHO: World Health Organization

Authors’ contributions
LL conceived of the study. LL developed the search string for analysis and contributed to piloting abstraction tools. LL and PA selected, reviewed, and coded the studies. EF or JH served as the third reviewer. LL wrote the first draft and revisions of the manuscript, and all authors commented on it and the subsequent drafts. The authors read and approved the final manuscript.

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