



UNIVERSIDADE DA BEIRA INTERIOR
Ciências da Saúde

Intervenção educativa em farmacêuticos para melhorar o consumo de antibióticos: ensaio controlado aleatório por *clusters*

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Aos meus filhos Maria e João

Aos meus pais

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PREFÁCIO

O trabalho de doutoramento desenvolvido e apresentado nesta tese constitui uma parte do plano de trabalhos de um projeto financiado pela Fundação para a Ciência e Tecnologia (FCT) designado “Intervenção educativa para melhorar o uso de antibióticos em profissionais de saúde portugueses: ensaio aleatório por *clusters*” (PTDC/SAL-ESA/105530/2008) do Centro de Biologia Celular da Universidade de Aveiro.

O projeto de doutoramento foi submetido à FCT no âmbito do Programa de apoio à formação avançada de docentes do Ensino Superior Politécnico, 2009 (PROTEC) tendo sido atribuída a bolsa SFR/PROTEC/67544/2010, no ano letivo 2010/2011.

A tese aqui apresentada reflete o trabalho de doutoramento desenvolvido e consta de uma **introdução**, que permite contextualizar o problema de saúde pública que as resistências bacterianas e o consumo inadequado de antibióticos representam na atualidade e que justifica a necessidade de intervenção. Seguem-se os **objetivos** do estudo que serão desenvolvidos ao longo de **cinco capítulos**. Quatro dos quais são apresentados sob a forma de artigos publicados em revistas indexadas à *ISI Web of Knowledge (Thomson Reuters Journal Citation Report®)* com fator de impacto (FI). O sétimo capítulo é um artigo em fase de submissão e que compreende a intervenção educativa realizada. Segue-se uma **discussão** sobre o trabalho realizado, as **conclusões e implicações** do trabalho realizado para o conhecimento científico, profissional e para a sociedade em geral. Nas **perspetivas de investigação futura** apresentam-se novos estudos que estão a ser desenvolvidos, em estudantes dos cursos de ciências farmacêuticas, enfermagem, farmácia e medicina, para avaliar a influência dos planos curriculares nas atitudes e comportamentos relacionados com o uso de antibióticos dos futuros profissionais de saúde. De seguida apresenta-se a **lista de publicações e comunicações científicas** desenvolvidas. No final apresenta-se uma secção de **anexos**, onde se inclui, entre outros documentos, a autorização do estudo pela Comissão Nacional da Proteção de Dados, o registo do protocolo do estudo no ClinicalTrials.gov, o consentimento informado utilizado no estudo qualitativo, o questionário aplicado no estudo transversal, a apresentação em *Powerpoint* realizada aos farmacêuticos e os *poster* e *flyers* distribuídos aos doentes e à população em geral.

RESUMO

O desenvolvimento de resistências bacterianas tornou-se um importante problema de saúde pública, contribuindo para uma maior morbidade e mortalidade dos doentes e, também, com forte impacto nos custos associados aos cuidados de saúde. O consumo excessivo e inadequado de antibióticos é uma das principais causas responsáveis pela propagação de bactérias resistentes como evidenciado por vários estudos ecológicos em que a prevalência de resistências é maior em regiões com grande consumo de antibióticos. O surgimento de infeções graves, por bactérias multirresistentes para as quais os antibióticos disponíveis deixaram de ser eficazes, representa uma importante ameaça a nível mundial, a qual é agravada pela falta de investimento em novos fármacos antibacterianos, demonstrando a necessidade de promover o uso racional de antibióticos. Os farmacêuticos comunitários são importantes intervenientes na decisão do consumo de medicamentos pelos doentes, pelo que intervenções para promover o uso adequado de antibióticos na comunidade devem incluir estes profissionais de saúde. Tendo em conta estes factos, com este trabalho pretendeu-se realizar uma intervenção educativa em farmacêuticos comunitários com o objetivo de diminuir o consumo de antibióticos na população.

Inicialmente realizou-se uma revisão sistemática da literatura sobre intervenções educativas dirigidas a médicos e/ou farmacêuticos para melhorar a prescrição e dispensa de antibióticos. Verificou-se que as intervenções educativas multifacetadas, desenhadas tendo em conta as atitudes e conhecimentos dos profissionais de saúde e focando as habilidades de comunicação com os doentes, são muito eficazes.

Para explorar as atitudes e conhecimentos dos farmacêuticos em relação às resistências bacterianas e ao consumo de antibióticos realizou-se um estudo qualitativo na forma de grupos focais.

Com base nos dados obtidos no estudo qualitativo foi construído um questionário para determinar as atitudes e conhecimentos dos farmacêuticos em relação às resistências bacterianas e ao consumo de antibióticos e avaliar a sua influência na propensão para dispensar antibióticos sem receita médica. Através de um estudo piloto, provou-se a fiabilidade e reprodutibilidade do questionário.

Realizou-se um estudo transversal, que consistiu na aplicação do questionário aos farmacêuticos comunitários da região centro de Portugal. Os resultados mostraram que a complacência com o doente, a atribuição da responsabilidade a causas externas e a precaução/medo são atitudes que influenciam a propensão para dispensar antibióticos sem receita médica.

Com base nas atitudes identificadas, desenhou-se uma intervenção educativa ativa dirigida aos farmacêuticos comunitários, que inicialmente incidiu na gravidade do problema das resistências bacterianas e do consumo inadequado de antibióticos, na análise das atitudes identificadas e por último na definição de estratégias de comunicação com o doente.

De seguida, realizou-se um ensaio controlado aleatório por *clusters* em que 4 clusters pertenciam ao grupo controlo e outros 4 ao grupo intervenção. Cerca de 55% (n=173) dos farmacêuticos pertencentes ao grupo intervenção assistiram à intervenção educativa. A intervenção teve um impacto positivo na redução do consumo total de antibióticos nos 12 meses após a intervenção.

Palavras-chave: antibióticos; intervenções educativas, farmacêuticos comunitários; resistências bacterianas.

ABSTRACT

The emergence of bacterial resistance has become a significant public health problem, contributing to patients' morbidity and mortality, with a major impact on the costs of health care. Excessive or inappropriate use of antibiotics is one of the main causes for the spread of bacterial resistance, as evidenced by various ecological studies in which the prevalence of resistance is greater in regions where antibiotic use is more widespread. The rise of severe infections by multidrug-resistant bacteria for which the available antibiotics are no longer effective is a major threat worldwide, aggravated by the lack of investment in new antibacterial drugs, demonstrating the need to promote the rational use of antibiotics. Community pharmacists are key decision makers regarding which drugs patients will use and how they will use them, such that, any interventions to promote the appropriate use of antibiotics in the community should include pharmacists. Accordingly, a study was carried out based on an educational intervention with community pharmacists to reduce antibiotic use in the population.

Initially it was carried out a systematic review of the literature on educational interventions directed at physicians and/or pharmacists to improve, respectively, the prescribing and dispensing of antibiotics was carried out. These interventions were found to be multifaceted and very effective, designed taking into account the attitudes and knowledge of health professionals and focusing on communication skills with patients.

To explore the attitudes and knowledge of pharmacists regarding bacterial resistance and antibiotic use, a qualitative study was carried out in the form of focus groups.

Based on the data obtained from the qualitative study, a questionnaire was prepared to determine the attitudes and knowledge of pharmacists regarding not only bacterial resistance and antibiotic use but also to evaluate their propensity to dispense antibiotics without a prescription. The reliability and reproducibility of the questionnaire was proved through a pilot study.

A cross-sectional study was conducted by applying the questionnaire to community pharmacists in the central region of Portugal. The results showed that complacency with patients, the attribution of responsibilities to external causes and precaution/fear are attitudes that influence their propensity to dispense antibiotics without a prescription.

Based on the identification of these attitudes, an active educational intervention aiming community pharmacists was designed to focus on the seriousness of bacterial resistance, the

attitudes that had been discovered and, additionally, on communication strategies with the patient.

A random controlled trial was finally carried out by clusters, of which four belonged to the control group and the other four to the intervention group. About 55% (n=173) of pharmacists in the intervention group attended the educational intervention, which had a positive impact on reducing the overall use of antibiotics in the 12 months after the intervention.

Key-words: antibiotics; bacterial resistance; community pharmacists; educational intervention.

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LISTA DE ABREVIATURAS E ACRÓNIMOS

ARS Centro	Administração Regional de Saúde do Centro, IP
ARS Norte	Administração Regional de Saúde do Norte, IP
ATC	<i>Anatomical Therapeutic Chemical</i> (Classificação Anatómica Terapêutica e Química)
DDD	<i>Defined Daily Dose</i> (Dose Diária Definida)
DID	<i>Defined Daily Dose per 1000 inhabitants and per day</i> (Doses Diárias Definidas por 1000 habitantes por dia)
EARS	<i>European Antimicrobial Resistance Surveillance</i> (Vigilância Europeia de Resistências aos Antimicrobianos)
EARS-Net	<i>European Antimicrobial Resistance Surveillance Network</i> (Rede de Vigilância Europeia de Resistências aos Antimicrobianos)
ECDC	<i>European Centre for Disease Prevention and Control</i> (Centro Europeu de Prevenção e Controlo de Doenças)
EMA	<i>European Medicines Agency</i> (Agência Europeia do Medicamento)
ESAC	<i>European Surveillance of Antimicrobial Consumption</i> (Vigilância Europeia do Consumo de Antimicrobianos)
ESAC-Net	<i>European Surveillance Antimicrobial Consumption Network</i> (Rede de Vigilância Europeia de Consumo de Antimicrobianos)
EU/EEA	<i>European Union/European Economic Area</i> (União Europeia/Área Económica Europeia)
OMS	Organização Mundial de Saúde
PID	<i>Package per 1000 inhabitants and per day</i> (Embalagens por 1000 habitantes por dia)

CAPÍTULO 1

INTRODUÇÃO

1 INTRODUÇÃO

A resistência aos antimicrobianos é um importante problema de saúde pública a nível mundial. A Organização Mundial de Saúde (OMS) alerta-nos para o risco de regressarmos à era pré-antibiótica se nada for feito para combater esta grave ameaça para a saúde pública, uma vez que, estamos a ser conduzidos para uma época pós-antibiótica [1]. A emergência de resistências aos antimicrobianos tem sido associada ao uso inadequado de medicamentos antimicrobianos, a programas de prevenção e combate às infeções deficitários ou inexistentes, à falta de medicamentos adequados, à incapacidade de diagnóstico, à vigilância inadequada e à falta de regulamentação ou de medidas de implementação e controlo da regulamentação existente para assegurar o uso adequado de medicamentos antimicrobianos [2].

Já em 1945 Alexander Flemming, no seu discurso quando recebeu o Premio Nobel alertou que não é difícil criar micróbios resistentes à penicilina ao expô-los a doses de penicilinas incapazes de os matar e que, o mesmo poderia ocorrer no corpo humano [3]. Em entrevista ao *Financial Times* reforçou a ideia de que o uso inadequado da penicilina poderia conduzir à seleção de bactérias resistentes [4].

A resistência das bactérias é um fenómeno biológico natural, no entanto é exacerbada pela pressão seletiva que o uso inadequado de antibióticos exerce, tal como previsto por Flemming, desde o início da introdução dos primeiros antibióticos no mercado. Cada vez é mais frequente o surgimento de situações provocadas por bactérias que são resistentes à maior parte ou mesmo a todos os antibacterianos disponíveis, causando infeções graves que já foram outrora facilmente tratáveis [5].

Em 2011, a OMS dedicou o Dia Mundial de Saúde, 7 de abril, ao problema das resistências bacterianas com o lançamento da campanha “*Antimicrobial resistance: no action today, no cure tomorrow*” com o alerta “*urgent and consolidated efforts needed to avoid regressing to the pre-antibiotic era*”. Esta campanha incluía a introdução de um pacote de políticas com as ações críticas a desenvolver pelos governantes para estimular a mudança em todos os intervenientes de forma a promover o combate a este flagelo público. Foi então proposto aos diferentes países que desenvolvessem estratégias de forma a implementar as seguintes atividades [6]:

- Adesão a um plano nacional global, financiado, e com o envolvimento e responsabilização de toda a sociedade civil;
- Fortalecer a vigilância e capacidade laboratorial;
- Assegurar o acesso contínuo a medicamentos essenciais e de qualidade garantida;

-
- Regular e promover o uso racional de medicamentos (incluindo na produção animal) e assegurar os cuidados adequados a prestar aos doentes;
 - Reforçar a prevenção e controle de infeções;
 - Estimular a inovação, investigação e desenvolvimento de novas ferramentas.

As infeções por bactérias resistentes aos antibióticos são uma importante causa de morbidade e mortalidade, havendo diferenças significativas nos resultados em saúde entre indivíduos infetados com bactérias sensíveis e indivíduos infetados pelas mesmas espécies mas que desenvolveram resistências. O relatório da OMS “*Antimicrobial Resistance - Global Report on Surveillance*” [1] identificou que existe um aumento significativo, aproximadamente o dobro, para todas as causas de mortalidade, em indivíduos infetados com *Escherichia coli* ou *Klebsiella pneumoniae* resistentes a cefalosporinas de 3ª geração assim como por *Escherichia coli* resistente às fluorquinolonas ou por *Klebsiella pneumoniae* resistente aos carbapenemes ou *Staphylococcus aureus* resistente à meticilina.

A resistência aos antibióticos é muito elevada quer para bactérias Gram-positivas quer para bactérias Gram-negativas, verificando-se uma crescente resistência para as bactérias Gram-negativas, como é o caso da *Escherichia coli*. Segundo dados do Centro Europeu para a Prevenção e Controlo das Doenças (ECDC - *European Centre for Disease Prevention and Control*) [7], o surgimento de infeções graves provocadas por bactérias resistentes representa mais de 25% das infeções que surgem anualmente na Europa. Em 2007, cerca de 25 mil doentes morreram na Europa (dados da União Europeia, Islândia e Noruega) em consequência de infeções por bactérias resistentes, sendo dois terços atribuídas a infeções por bactérias gram-negativas. Além disso, as infeções por bactérias resistentes levaram a um aumento de cerca de 2,5 milhões de dias de internamento extra, em hospitais na Europa. Estas infeções são responsáveis por aumento dos custos em saúde, associados à necessidade de mais cuidados em saúde e perda de produtividade prevendo-se que anualmente os custos sociais das infeções por bactérias resistentes possam atingir um custo extra de cerca de 1,5 biliões de euros, atribuindo-se mais de 900 milhões de euros a custos hospitalares [7].

Para além dos dados do ECDC, muitos estudos têm demonstrado que as resistências contribuem para um aumento da morbidade, mortalidade e internamentos hospitalares com grande impacto no aumento de custos em saúde [8-12]

A dificuldade de tratamento de infeções provocadas por bactérias resistentes aos antibióticos disponíveis no mercado parece ser um problema sem resolução nos próximos tempos, uma vez que não se tem verificado grande investimento por parte da indústria farmacêutica para desenvolver novos antibióticos capazes de combater as infeções provocadas pelos microrganismos multirresistentes. Um grupo de trabalho constituído por membros da Agência Europeia do Medicamento (EMA - *European Medicines Agency*) e do ECDC realizaram um estudo de revisão que consistiu na análise, em março de 2008, de 3 bases de dados comerciais (Pharmprojects, T& I Informa UK Limited London, UK; Biopharm Insight, Infinata Norwood MA-

USA; Adis Insign R&D, Wolters Kluwer Health Amsterdam, NL) para obter informação sobre o desenvolvimento de novos agentes antibacterianos que se encontrassem em fase de ensaio clínico (Fase I, Fase II ou Fase III de ensaios clínicos) [7]. Desta análise verificou-se que dos 167 agentes antibacterianos identificados em fase de desenvolvimento clínico, 66 eram novas substâncias que apresentavam atividade *in vitro*. Dos 15 agentes que podiam ser administrados por via sistêmica, apenas quatro apresentavam atividade contra bactérias Gram-negativas, com base em dados reais, e, destes, apenas dois atuavam em novos ou possíveis novos locais alvo, sendo que nenhum atuava através de novos mecanismos de ação. Como tal, é de prever que nos próximos anos as resistências bacterianas continuem a ser um dos principais problemas de saúde pública, uma vez que existem poucos agentes antibacterianos em fase de desenvolvimento clínico que apresentem novos mecanismos de ação com o objetivo de combater as bactérias multirresistentes e de tratar as infeções provocadas por bactérias Gram-negativas multirresistentes.

A importância da necessidade de novos tratamentos para o tratamento de infeções por microrganismos resistentes assumiu tal dimensão que no Relatório de 2013 da OMS “*Priority Medicines for Europe and the World 2013 Update*” e à semelhança do Relatório de 2004, é considerada uma área terapêutica prioritária dado o potencial impacto para a saúde pública [13]. No entanto, alguns estudos têm demonstrado que existe pouco investimento por parte da indústria no desenvolvimento de novos fármacos antibacterianos [14-16].

Tendo em conta a emergência das resistências bacterianas e o declínio na taxa de desenvolvimento de novos fármacos, deverão ser estudadas e implementadas estratégias envolvendo os profissionais de saúde e a população em geral que promovam o uso adequado de antibióticos de forma a preservar atividade antibacteriana dos fármacos que atualmente existem no mercado.

1.1 Mecanismos de ação dos antibióticos e principais mecanismos de resistência bacteriana

Em termos gerais, os principais mecanismos de ação dos antibióticos disponíveis no mercado são inibição da síntese da parede celular, inibição da síntese de proteínas, inibição da síntese do DNA, inibição da síntese do RNA, inibição da síntese do ácido fólico e modificação da membrana bacteriana (Tabela 1) [4, 17].

Tabela 1 - Principais mecanismos de ação dos antibióticos [4, 17].

Mecanismo de ação antibacteriana	Antibióticos
Inibição da síntese da parede celular	Beta-lactâmicos (penicilinas, cefalosporinas, carbapenemes e monobactams) Glicopeptidos (Vancomicina) Lipopeptidos cíclicos (daptomicina)
Inibição da síntese proteica	Tetraciclinas Aminoglicosídeos Oxazolidononas (linezolid) Estreptograminas (quinupristina/dalfopristina) Cetolidos Macrólidos Lincosamidas Cloranfenicol
Inibição da síntese do DNA	Fluorquinolonas
Inibição da síntese do RNA	Rifampicina
Inibição da síntese do ácido fólico	Sulfonamidas, trimetoprim
Modificação da membrana bacteriana	Polimixinas (polimixina B e colistina)
Outros mecanismos	Metronidazol

Ao longo dos anos as bactérias foram desenvolvendo mecanismos de resistência para cada uma destas classes de antibióticos, sendo que algumas são capazes de desenvolver simultaneamente resistências a diferentes classes de antibióticos tornando-se multirresistentes, dificultando o tratamento com as opções de antibióticos disponíveis no mercado sendo por isso responsáveis por uma elevada taxa de mortalidade e morbidade [7].

Os primeiros casos de resistências bacterianas surgiram no final de 1930 e na década de 1940, logo após a introdução no mercado das penicilinas e das sulfonamidas [17]. O desenvolvimento de resistências bacterianas é um fenômeno natural e os polimorfismos genéticos que determinam as resistências já existiam mesmo antes da aplicação terapêutica dos antibióticos. A seleção positiva das modificações genéticas nas bactérias conduz à seleção do material genético mutado que se propaga a outras bactérias, por diferentes mecanismos de transferência genética (conjugação, transformação e transdução). A resistência aos antibióticos pode ser natural (intrínseca), resultando de mutação genética espontânea, ou adquirida [17, 18]. A resistência adquirida é a forma mais comum de resistências e resulta da pressão seletiva devida à presença de antibióticos promovendo respostas de adaptação por parte das bactérias.

Associados a estas mutações genéticas existem mecanismos biológicos nas bactérias afetadas que determinam o tipo de resistência desenvolvido (Tabela 2) [4, 17].

Tabela 2 - Mecanismos biológicos de resistências bacterianas [4, 17].

Mecanismo biológico de resistência		Principais grupos de antibióticos identificados
Destruição ou transformação do antibiótico	As bactérias produzem enzimas que quimicamente destroem ou modificam o antibiótico tornando-o inativo contra as bactérias	Antibióticos beta-lactâmicos
Efluxo ativo do antibiótico	As bactérias expulsam o antibiótico para o meio extracelular não deixando atingir concentrações eficazes	Antibióticos que atuam no interior da célula, como as tetraciclina, macrólidos e fluorquinolonas.
Modificação do recetor	<p>As bactérias alteram o recetor ou o alvo intracelular do antibiótico</p> <ul style="list-style-type: none"> · modificação na conformação das proteínas penicilina-ligantes · alterações ribossomais · modificações da DNA-girase 	<p>Penicilinas</p> <p>Aminoglicosídeos, macrólidos e tetraciclina</p> <p>Fluorquinolonas</p>

Inicialmente o problema das resistências bacterianas era considerado um problema apenas para os doentes hospitalizados, pois percebeu-se que as bactérias não só eram capazes de desenvolver resistências aos agentes antibacterianos, mas que permaneciam vivas e viáveis em ambiente hospitalar, causando graves infeções nosocomiais. Mais tarde percebeu-se que as resistências também são um grave problema de saúde pública nos cuidados de saúde primários, sendo responsáveis por muitas infeções adquiridas na comunidade [19].

Como referido anteriormente, a investigação de novos agentes antibacterianos é bastante deficitária para as necessidades que existem. No entanto, é importante refletir que mesmo que a investigação nesta área fosse promissora, se não houver mudança de comportamentos identificados como responsáveis pelo desenvolvimento de resistências bacterianas, muito rapidamente as bactérias desenvolverão mecanismos de adaptação aos novos agentes antibacterianos através do desenvolvimento de mecanismos de resistências.

Deste modo, se por um lado é importante o desenvolvimento de novos agentes antibacterianos com espectro de atividade contra as bactérias resistentes é também muito importante identificar os fatores responsáveis e criar medidas que diminuam o desenvolvimento de resistências aos antibacterianos.

1.2 Fatores de risco para o desenvolvimento de resistência aos antibióticos

Têm sido identificados vários fatores e comportamentos que contribuem para a emergência de resistência aos antibióticos, destacando-se [5, 17]:

- Uso excessivo e irracional de antibióticos quer em meio hospitalar, quer em cuidados primários, seja com fins curativos, seja com fins profiláticos;
- Uso de antibióticos na indústria agrícola principalmente para a produção de alimentos;
- Pouca adesão às medidas efetivamente comprovadas de prevenção e controle tais como lavagem das mãos, restrições de utilização de antibióticos e isolamento adequado de doentes com infecções por bactérias resistentes.

Para além destes fatores associados a comportamentos inadequados, também o próprio desenvolvimento da medicina associado à maior esperança de vida contribuem para uma maior sobrevivência de doentes com alto risco de infecções (por ex. idosos, doentes imunodeprimidos, doentes em estado crítico) que necessitam de tomar antibióticos frequentemente. Também o uso de procedimentos invasivos assim como o uso de dispositivos de prótese são intervenções médicas passíveis de infecção por microrganismos resistentes [17].

O uso inadequado de antibióticos e a inexistência de programas adequados de prevenção e controle da infecção são fatores modificáveis sobre os quais nos parece ser fundamental atuar.

O uso excessivo e irracional de antibióticos tem sido atribuído essencialmente a [6]:

- Prescrição inapropriada, incluindo a sua prescrição quando não é necessário, escolha incorreta do medicamento, ou em uma dosagem incorreta;
- Automedicação em países nos quais se consegue adquirir antibióticos sem receita médica;
- Interrupção de um ciclo de tratamento ou toma de antibióticos por muito tempo;
- Falta de regulamentos ou normas para os profissionais de saúde;
- Uso indevido e excessivo de antibióticos na pecuária e agricultura.

Estudos ecológicos baseados nos dados recolhidos pela rede Europeia de Vigilância do Consumo de Antimicrobianos (*European Surveillance of Antimicrobial Consumption* - ESAC) e pela rede Europeia de Vigilância da Resistência aos Antimicrobianos (*European Antimicrobial Resistance Surveillance* - EARS), indicam haver uma relação entre o consumo de antibióticos e as resistências desenvolvidas em cada um dos países [20-22], mostrando que a variação geográfica nas resistências pode ser explicada pela variação da pressão seletiva exercida pelas diferenças de consumo de antibióticos entre os diferentes países. Duas recentes meta-análises [23, 24], também evidenciaram a relação entre o consumo de antibióticos em cuidados de saúde

primários e as resistências bacterianas quer a nível individual [23, 24] quer a nível da comunidade [24], demonstrando também haver uma correlação mais forte nas regiões do sul da Europa, relativamente a outras regiões [24]. Esta forte relação é um fator muito importante pois estas regiões, a par das regiões de leste, são as que apresentam maiores taxas de consumo de antibióticos na Europa.

Para além dos sistemas de vigilância quer das resistências aos antimicrobianos quer da utilização destes na Europa, têm sido desenvolvidas pela Comissão Europeia estudos de monitorização dos níveis de utilização de antibióticos assim como do nível de conhecimento da população sobre os antibióticos, através de sondagens do Eurobarómetro com questionários aplicados diretamente à população em geral. O questionário aplicado em 2013, à semelhança do aplicado em 2009 tinha como principais objetivos [25]: (i) identificar o uso de antibióticos pela população em geral na União Europeia (frequência de utilização, como são obtidos, e porque razão eram utilizados); (ii) medir os níveis de conhecimento sobre a natureza e efetividade dos antibióticos e dos riscos associados ao seu uso desnecessário; (iii) determinar o impacto das campanhas de sensibilização sobre o conhecimento e comportamento dos Europeus.

Alguns dos resultados do último estudo realizado, em 2013, e publicados no relatório “*Special Eurobarometer 407 - Antimicrobial Resistance*” [25], relativos a Portugal, permitem-nos perceber qual a perceção, conhecimento e hábitos dos Portugueses em relação aos antibióticos. Os resultados mostram que a informação recebida através dos profissionais parece ser mais efetiva que a informação recebida através dos *media*, já que 80% dos europeus que receberam informação sobre antibióticos através dos profissionais de saúde referiram que no futuro iriam consultar o médico, e apenas 69% dos que receberam informação pelos *media* referiram essa situação. No entanto, os médicos e os farmacêuticos, são referidos como apresentando um papel fundamental na mudança dos pontos de vista e dos comportamentos na população. De 2009 para 2013, verificou-se uma diminuição de 5% de respondentes que afirmaram tomar pelo menos um antibiótico nos últimos 12 meses, no entanto em Portugal aumentou 5%. Outro dado importante relativamente aos respondentes de Portugal, é que 5% parece terem tomado antibióticos no ano anterior por automedicação, sendo que 2% afirmaram ter tomado antibióticos que sobram de tratamentos anteriores e 2% afirmaram ter tomado antibióticos adquiridos diretamente na farmácia sem prescrição médica e 1% obtiveram antibióticos sem prescrição em qualquer outra fonte. Comparando com os dados de 2009, houve menos 4% de respondentes que afirmaram ter obtido os seus antibióticos com receita médica. Os portugueses que participaram no estudo também demonstraram um nível de conhecimento sobre os antibióticos muito baixo, sendo dos países com mais baixo conhecimento. Também apenas 12% disse ter recebido alguma informação sobre o uso incorreto de antibióticos (menos 1% que em 2009), sendo que apenas 5% disseram ter recebido informação através dos *media* (mais 1% que em 2009), e 6% através dos profissionais de saúde (menos 2% que em 2009). Provavelmente devido a esta perceção de baixa informação que os respondentes portugueses referem, também

foram os que demonstraram estar menos recetivos a mudar os seus comportamentos, pois apenas 10% (mais 2% que em 2009) responderam que não tomariam mais antibióticos sem terem uma prescrição médica, sendo que apenas 4% (menos 18% que em 2009) referiram não voltar a automedicar-se e 8% dizem não voltar a guardar antibióticos que sobrem de um tratamento para voltar a tomar quando estiverem doentes (mais 2% que em 2009). Quando questionados sobre quais as fontes de informação que consideram credíveis, 90% dos portugueses inquiridos indicaram os médicos e 38 % as farmácias, sendo que neste caso aumentou 9% de 2009 para 2013.

As conclusões que evidenciamos deste estudo são o alerta de que as campanhas para melhorar o uso e o conhecimento sobre os antibióticos serão mais eficazes se forem direcionadas para os grupos que têm um conhecimento mais baixo. No entanto, as estratégias para melhorar o conhecimento e o uso de antibióticos por estes grupos, devem envolver os profissionais de saúde, nomeadamente os médicos e os farmacêuticos. Se por um lado os *media* são mais eficazes na disseminação do conhecimento, os médicos e os farmacêuticos têm maior capacidade de influenciarem as pessoas menos informadas a usar os antibióticos de forma adequada.

Entre setembro de 2011 e março de 2012 decorreu em Portugal uma campanha de sensibilização do cidadão para a correta utilização de antibióticos, designada “Preserve os antibióticos”, promovida pela Direcção Geral da Saúde e o Grupo de Infecção e Sepsis [26]. Esta campanha incluiu divulgação de flyers e de informação através dos *media* (radio e televisão) enfatizando a necessidade de restringir o uso de antibióticos através de duas estratégias fundamentais, a prevenção da infeção e o fim da automedicação, com o objetivo principal de alterar atitudes e comportamentos dos portugueses relativamente ao consumo de antibióticos. Tendo esta campanha terminado no ano anterior à aplicação do questionário do Eurobarómetro 407 , seria de prever melhores resultados neste questionário. Provavelmente o conhecimento, as atitudes e os comportamentos dos portugueses, não foram alterados como desejado, devido ao não envolvimento ativo dos profissionais de saúde nesta campanha, nomeadamente médicos de cuidados de saúde primários e farmacêuticos comunitários.

Resultados semelhantes, demonstrando a falta de conhecimento dos Portugueses em relação aos antibióticos foram obtidos através de um estudo em estudantes do secundário realizado no distrito de Braga entre fevereiro e abril de 2007 [27]. Também em relação a estes resultados é importante refletirmos, pois este estudo surge nos finais de uma campanha que decorreu em Portugal em três períodos sazonais, entre 2004 e 2007, promovida pela Indústria Farmacêutica, Direcção Geral de Saúde e Organizações Profissionais, com o tema “Antibióticos, utilize-os de forma adequada”, através da disseminação de informação em panfletos e *posters*, em websites e na radio [28].

Parece-nos pois fundamental que qualquer intervenção educativa para melhorar o uso de antibióticos na população deverá, ter como principais alvos os médicos e farmacêuticos, para além da própria população.

1.3 Resistência aos antibióticos na Europa e em Portugal

A resistência aos antimicrobianos, na União Europeia é monitorizada através da base de dados interativa de resistência aos antimicrobianos (EARS-Net - *European Antimicrobial Resistance Surveillance Network*), uma rede de sítios de vigilância nos países da União Europeia coordenada pelo ECDC.

Para melhor entendermos a situação de Portugal em relação à prevalência de resistências bacterianas, de seguida apresenta-se uma análise dos últimos dados publicados no relatório anual de 2014 “*Antimicrobial resistance surveillance in Europe*”, com dados de 2013 sobre resistências aos antibióticos na Europa pelo EARS-Net [29]. As figuras que se apresentam (Fig. 1 à Fig. 4), foram retiradas deste relatório e de um documento sumário do mesmo [30], em que as cores dos mapas representam intervalos de percentagem de isolados bacterianos resistentes em relação aos isolados bacterianos analisados: verde escuro (<1%); verde claro ($\geq 1\%$ e <5%); amarelo ($\geq 5\%$ e <10%); amarelo torrado alaranjado ($\geq 10\%$ e <25%); vermelho ($\geq 25\%$ e <50%) e vermelho escuro ($\geq 50\%$).

Entre 2010 e 2013, a percentagem de *Klebsiella pneumoniae* resistente às fluorquinolonas, cefalosporinas de terceira geração e aminoglicosídeos assim como a resistência combinada a estes três grupos aumentou significativamente a nível dos países da União Europeia e da Área Económica Europeia (EU/EEA - *European Union/European Economic Area*). No entanto Portugal manteve-se no mesmo intervalo de percentagem de isolados invasivos com resistência combinada às fluorquinolonas, cefalosporinas de terceira geração e aminoglicosídeos ($\geq 10\%$ e <25%) (Figura 1). Em 2013, mais de um terço dos isolados de *Klebsiella pneumoniae* notificados na europa eram resistentes a pelo menos um dos grupos de antimicrobianos em estudo. Em Portugal as resistências são superiores à média ponderada da EU/EEA, sendo respetivamente 35,7% e 29,2% para as fluorquinolonas, 37% e 30% para as cefalosporinas de 3º geração e 30,3% e 24,5% para os aminoglicosídeos.

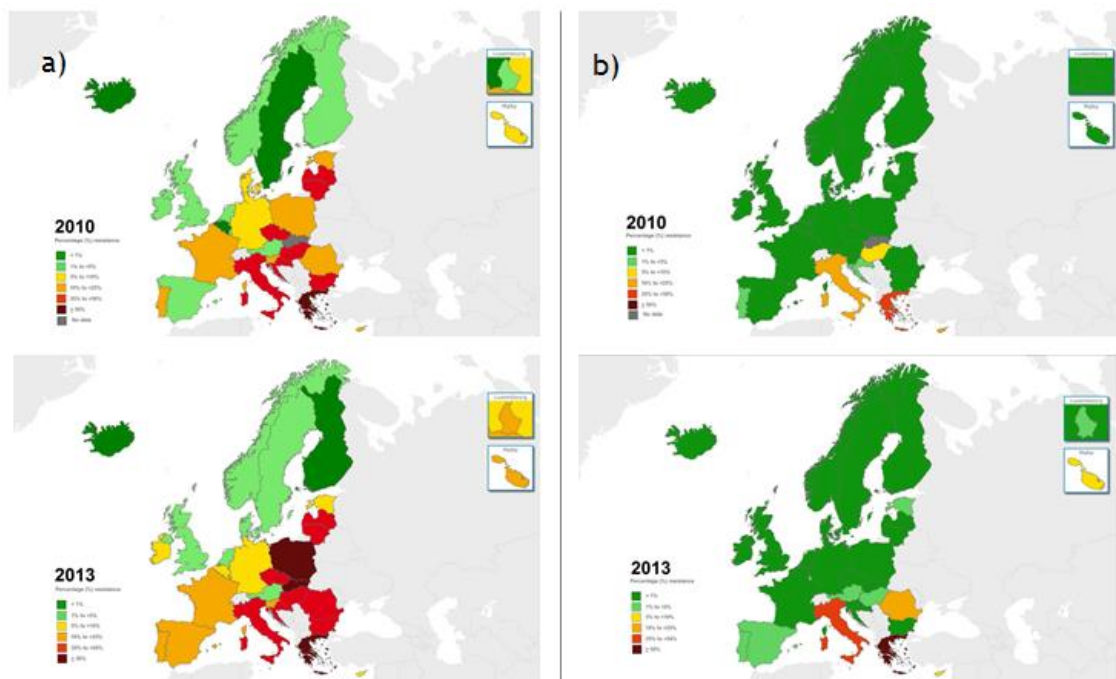


Figura 1 - *Klebsiella pneumoniae*: a) percentagem de isolados invasivos com resistência combinada às cefalosporinas de 3ª geração, fluorquinolonas e aminoglicosídeos. b) percentagem de isolados invasivos com resistência aos carbapenemes. EU/EEA, 2010 e 2013 [30].

Para além disso, também foi reportada a presença isolados de *Klebsiella pneumoniae* resistente à polimixina com resistência adicional às fluorquinolonas, cefalosporinas de 3ª geração, aminoglicosídeos e carbapenemes, em alguns países do sul da Europa.

Este relatório do ECDC alerta-nos para o facto de que o aparecimento de resistência às polimixinas é um importante aviso de que as opções terapêuticas estão a ficar cada vez mais limitadas, principalmente nos países onde já existe uma elevada taxa de resistências aos carbapenemes.

Também para a *Escherichia coli* houve um aumento de resistência às cefalosporinas de 3ª geração, sendo que para Portugal os valores para 2013 mantiveram-se no mesmo intervalo (10-25%) que em 2010 (Figura 2). As percentagem de isolados de *Escherichia coli* resistentes aos antibióticos normalmente utilizados, continua a aumentar na Europa e mais de metade dos isolados de *Escherichia coli* reportados em 2013 eram resistentes a pelo menos um dos antibióticos em estudo. A maior notificação de resistências verificou-se para as aminopenicilinas e para as cefalosporinas. Em Portugal a percentagem de resistências da *Escherichia coli* às aminopenicilinas é de 59,4% e às fluorquinolonas é de 31,6%, valores superiores à média ponderada da EU/EEA (57,8% às aminopenicilinas e 22,5% às fluorquinolonas).

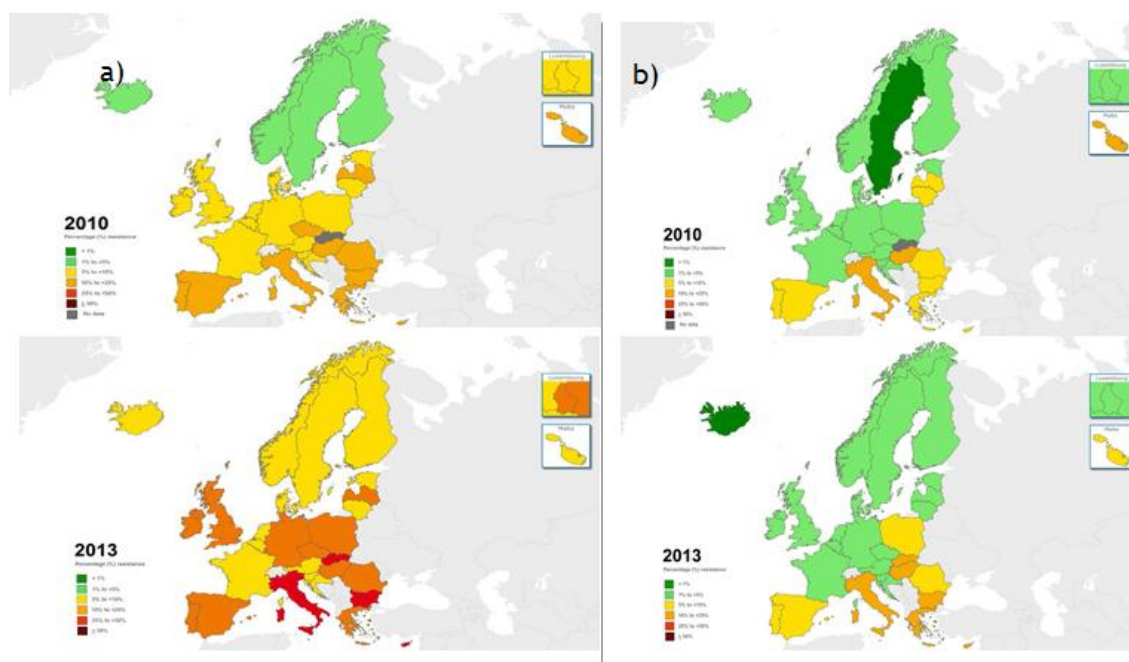


Figura 2 - *Escherichia coli*: a) percentagem de isolados invasivos com resistência às cefalosporinas de 3ª geração. b) percentagem de isolados invasivos com resistência combinada às cefalosporinas de 3ª geração, fluorquinolonas e aminoglicosídeos, EU/EEA, 2010 e 2013 [30].

Relativamente ao *Staphylococcus aureus* resistente à meticilina, no período 2005 a 2010, houve uma diminuição da sua percentagem na Europa, resultante dos esforços desenvolvidos para diminuir a sua prevalência [13]. No entanto, Portugal não seguiu esta tendência, tendo em 2010 aumentado para mais de 50% [13, 30]. Nos quatro anos seguintes a percentagem de *Staphylococcus aureus* resistente à meticilina continuou a diminuir na Europa, mas em menor intensidade que no período anterior. Em Portugal também houve uma diminuição neste período (figura 3), continuando no entanto com uma percentagem bastante superior à média ponderada da EU/EEA (46,8% vs 18 %).



Figura 3 - *Staphylococcus aureus*: percentagem de isolados invasivos com resistência à Meticilina (MRSA), EU/EEA, 2010 e 2013 [30].

Os dados de 2013 sobre as resistências às espécies de *Acinetobacter*, mostram uma grande variabilidade entre países, existindo uma elevada percentagem (>25%) de isolados com resistências combinadas às fluorquinolonas, aminoglicosídeos e carbapenemes nos países do sul da Europa, sendo que Portugal é dos países que apresenta valores mais elevado (>50%), quer

para resistência combinada quer para resistência a cada um dos grupos de antibacterianos em estudo (Figura 4).

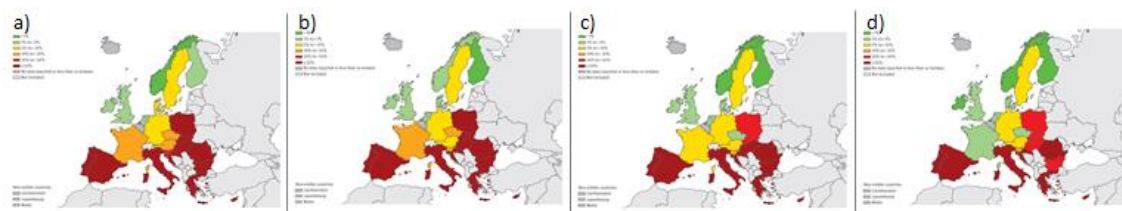


Figura 4 - Espécies de *Acinetobacter*: percentagem de isolados invasivos com resistência a) fluorquinolonas, b) aminoglicosídeos; c) carbapenemes e d) combinada às fluorquinolonas, aminoglicosídeos e carbapenemes EU/EEA, 2013. [29]

As resistências da *Pseudomonas aeruginosa* aos antimicrobianos é também bastante comum na Europa, apresentando uma elevada resistência combinada, com 14,3% dos isolados resistentes a pelo menos três grupos de antibióticos em estudo e 4,6% são resistentes aos 5 grupos. Em Portugal a percentagem de isolados resistentes encontra-se no intervalo ($\geq 10\%$ e $<25\%$), para todos os grupos, mas com valor superior à média ponderada da EU/EEA para as fluorquinolonas, carbapenemes e para os fármacos ceftazidima e piperacilina+tazobactam.

A sensibilidade *Streptococcus pneumoniae* apresenta também grandes diferenças entre os diferentes países europeus, a não sensibilidade aos macrólidos é superior à não sensibilidade às penicilinas. Em Portugal a não-sensibilidade aos macrólidos diminuiu de 2010 (21,8%) para 2011 (14,9%), no entanto, a partir daí tem vindo sempre a aumentar, aproximando-se em 2013 (20,6%) ao valor de 2010.

As resistências dos enterococos também têm estado a aumentar significativamente na Europa. Em 2013, em Portugal a percentagem de isolados de *Enterococcus faecalis* resistentes aos aminoglicosídeos foi de 37,2% e de *Enterococcus faecium* foi de 22%, sendo para ambas as bactérias superior à média ponderada da EU/EEA (30,9% e 8,9%, respetivamente).

Nos mapas apresentados, é notório que a resistência aos antibacterianos na Europa varia em termos de microrganismos, de agente antibacteriano e da região geográfica. Para muitos agentes antibacterianos e combinações é evidente um gradiente geográfico, geralmente com percentagem de resistências mais baixas nos países do norte da Europa, em relação aos países de leste e sul da Europa [5, 29, 31].

1.4 Consumo de antibióticos em cuidados de saúde primários na Europa e em Portugal

Os dados sobre o consumo de antimicrobianos são recolhidos através da Rede Europeia de Vigilância do Consumo de Antimicrobianos (ESAC-Net - *European Surveillance Antimicrobial Consumption Network*) a partir dos países da EU/EEA, pelo ECDC. Os dados de consumo são

apresentados por Doses Diárias Definidas (DDD) por 1000 habitantes por dia (DID), e os antibióticos são classificados de acordo com o sistema de classificação *Anatomical Therapeutic Chemical* (ATC). Também são incluídos alguns dados de consumo, expressos em número de embalagens por 1000 habitantes por dia (PID), que são dados que poderão ser uma previsão do número de prescrições e de tratamentos, principalmente em países onde os antibióticos são dispensados em embalagens completas, como é o caso de Portugal, e não de forma unitária [32-34].

No último relatório publicado pelo ESAC-Net, o relatório “*Surveillance of antimicrobial consumption in Europe 2012*” [35], podemos verificar que o consumo de antibióticos em cuidados de saúde primários mostra grande variabilidade de consumo entre os diferentes países da EU/EEA (Figura 5).

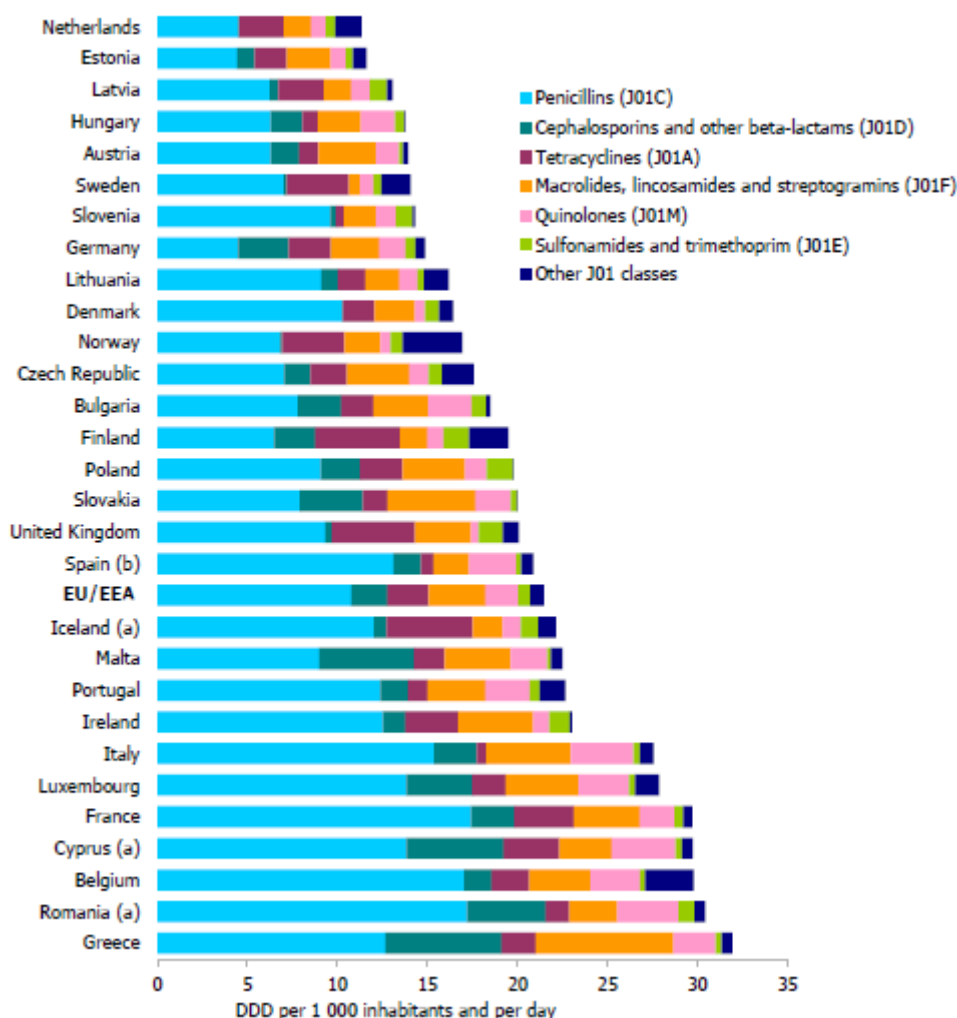


Figura 5 - Distribuição do consumo de antibacterianos de uso sistémico (Grupo ATC J01) em ambulatório para o nível 3 do Grupo ATC, expresso em DDD por 100 habitantes por dia, EU/EEA, 2012.

a) Os dados do Chipre, Islândia e Roménia são dados de consumo em cuidados primários e em hospitais.
b) Em Espanha os dados são dados de reembolso, e não de vendas [35].

De seguida fazemos uma análise do relatório com interpretação dos dados de consumo para os diferentes grupos ATC de antibióticos em Portugal relativamente ao resto da Europa.

A média ponderada do consumo da população EU/EEA, para o total de antibióticos sistémicos (J01) foi de 21,5 DID, correspondendo a 3,1 PID. Os subgrupos de antibióticos mais utilizados foram as penicilinas (J01C) incluindo a combinação de penicilinas com inibidores das beta-lactamases (J01CR) e penicilinas de largo espectro (J01CA), seguido dos macrólidos (J01FA) e das tetraciclina (J01A).

Portugal apresenta valores de consumo de antibióticos superiores à média ponderada do consumo a nível europeu, quando o indicador de consumo é expresso em DID (22,7 DID e 21,5 DID, respetivamente) mas inferior quando o indicador de consumo é expresso em PID (2,3 PID e 3,1 PID respetivamente). As penicilinas são o grupo de antibióticos mais consumido em toda a Europa, assim como em Portugal.

Entre 2011 e 2012 o consumo de antibióticos diminuiu (mais de 1%) em 15 (56%) dos 27 países em análise, sendo este o caso de Portugal.

No período de 2008-2012 o consumo de penicilinas aumentou em seis países, sendo Portugal um desses países. A média anual de aumento do consumo de penicilinas em Portugal foi de 0,18 DID, com significância estatística. A associação de penicilinas com inibidores das beta-lactamases também aumentou significativamente em Portugal, assim como em mais 9 países.

Relativamente às cefalosporinas, a média de variação anual no período 2008-2012 em Portugal foi estatisticamente significativa e correspondeu a uma diminuição de 0,12 DID. As cefalosporinas mais consumidas em Portugal em 2012 foram as cefalosporinas de 2ª geração, tendo no entanto havido uma diminuição muito significativa do seu consumo, desde 2008.

O consumo de sulfonamidas e trimetoprim também parece ter aumentado em Portugal numa média anual de 0,04 DID no período em estudo, no entanto sem significância estatística.

Em 2012 o consumo de macrólidos em Portugal (3,17 DID) foi superior ao consumo médio ponderado da população na zona EU/EEA (2,8 DID). No entanto, verificou-se uma diminuição significativa de 2008 a 2012, correspondendo a uma diminuição anual média de 0,18 DID. A maioria dos macrólidos consumidos em Portugal são de espectro de ação intermédia e de largo espectro de ação.

O padrão de consumo de quinolonas mostra haver um gradiente de consumo do norte para o sul da Europa. Em 2012 o consumo de quinolonas em Portugal (2,47 DID) foi bastante superior à média ponderada de consumo na EU/EEA (1,81 DID). O consumo de quinolonas de segunda geração foi três vezes superior ao consumo de quinolonas de primeira e terceira geração. Apesar do consumo de quinolonas em Portugal ser superior à média ponderada na EU/EEA, verificou-se, entre 2008 e 2012, uma diminuição do consumo médio anual em Portugal de 0,015 DID, com significado estatístico.

Relativamente às tendências de consumo de outros antibacterianos (J01X), verificou-se um aumento significativo do consumo em 12 países, incluindo Portugal com um aumento médio anual de 0,16 DID. No entanto, houve uma diminuição significativa do consumo de

antibacterianos esteroides (J01XC). Em Portugal, o consumo total de antimicrobianos do grupo J01X (1,44 DID), deve-se essencialmente ao consumo de derivados do nitrofurano (J01XD) como a nitrofurantoína (1,21 DID) e do grupo J01XX (outros antibacterianos), como a fosfomicina (0,18 DID). O consumo destes subgrupos de antibióticos, no período 2008 a 2012, aumentou significativamente em 12 países, incluindo Portugal.

Apesar da tendência de diminuição do consumo de antibióticos em Portugal, a verdade é que o consumo ainda é muito elevado. No mesmo relatório são também apresentados valores para os indicadores de consumo de antibióticos validados por *Coenan et al.* [36]. Se compararmos o valor de cada um destes indicadores em Portugal com os valores mínimo (p0), percentil 25 (p25), mediana (p50), percentil 75 (p75) e valor máximo (p100) para cada indicador na Europa, verificamos que para os indicadores de consumo Portugal está sempre acima do p50, exceto para as cefalosporinas (Tabela 3).

Para todos os indicadores, exceto o indicador J01CE_% (Consumo de penicilinas sensíveis às beta-lactamases expresso em percentagem em relação ao consumo total de antibacterianos do grupo J01), baixos valores indicam melhor qualidade do consumo, sendo considerado que o indicador apresenta melhor qualidade quando se encontra no primeiro quartil ($p0 \leq \text{valores} \leq p25$). Para o indicador J01CE_% considera-se que indica melhor qualidade de consumo, quando o valor se encontra no quarto quartil ($p75 < \text{valores} \leq p100$).

Tabela 3 - Indicadores de Qualidade, em 2012 em Portugal e respetivos percentis [35, 36].

Indicador	Descrição do indicador	Valor do indicador em Portugal em 2012 e intervalo de percentil em que se encontra.
J01_DID	Consumo de antibacterianos para uso sistémico expresso em DID	p50 < 22,66 <p75
J01C_DID	Consumo de penicilinas expresso em DID	p50 < 12,38 <p75
J01D_DID	Consumo de cefalosporinas expresso em DID	P25 < 1,55 <p50
J01F_DID	Consumo de macrólidos, lincosamidas e estreptograminas expresso em DID	p50 < 3,21 <p75
J01M_DID	Consumo de quinolonas expresso em DID	P75 < 2,47 <p100
J01CE_%	Consumo de penicilinas sensíveis às beta-lactamases expresso em percentagem em relação ao consumo total de antibacterianos do grupo J01	p0 < 0,1 <p25
J01CR%	Consumo de combinações de penicilinas incluindo inibidores das beta-lactamases,	p75<41,1~p100
J01DD+DE_%	Consumo de cefalosporinas de 3ª e 4ª geração expresso em percentagem em relação ao consumo total de antibacterianos do grupo J01	p50 < 1 <p75
J01 MA%	Consumo de fluorquinolonas expresso em percentagem em relação ao consumo total de antibacterianos do grupo J01	p75 < 10,9 <p100
J01_B/N	Razão entre o consumo de penicilinas, cefalosporinas e macrólidos de largo espectro em relação ao consumo de penicilinas, cefalosporinas e macrólidos de espectro estreito.	P50 < 34,85 <p75
J01_SV	Varição sazonal do consumo total de antibióticos.*	p25< 23,1 <p50
J01M_SV	Varição sazonal do consumo de quinolonas*	p0 < 6,4 <p25

* Variação Sazonal: comparação dos trimestres de inverno (outubro a dezembro e janeiro a março) com os trimestres de verão (julho a setembro e abril a junho) durante um ano a começar em julho, expresso em percentagem: $[\text{DDD}(\text{trimestres de inverno})/\text{DDD}(\text{trimestres de verão}) - 1] \times 100$

O indicador de consumo J01M_DID apresenta-se no quarto quartil, indicando que Portugal apresenta uma taxa muito elevada de consumo de quinolonas, comparando com os outros países da zona EU/EEA.

Da análise dos quartis em que se encontravam os valores dos indicadores de qualidade de consumo de antibióticos em cuidados de saúde primários em Portugal em 2012, parece haver uma baixa qualidade de consumo de antibióticos, indiciando a necessidade intervenções que melhorem o seu uso no país.

Da análise dos dados de consumo na Europa são visíveis as grandes diferenças de consumo que existem entre os diferentes países, diferenças de tal ordem que não parecem ser justificadas

apenas por possíveis diferenças de situações clínicas entre os países. Estas diferenças de consumo estarão provavelmente mais relacionadas com questões culturais, políticas nacionais de utilização de antibióticos, regulamentação (ou falta de políticas de controlo de execução das medidas regulamentares) e ainda na estrutura do mercado farmacêutico de cada país [37, 38], podendo mesmo influenciar os hábitos de consumo dos indivíduos que migram para países de maior consumo [39].

No estudo realizado pela OMS em 2013 [2], para avaliação da situação de cada país em relação às medidas propostas em 2011 no dia Mundial de Saúde, verificou-se que dos 53 países que constituem a Região Europeia da OMS, 43% referem que os medicamentos antimicrobianos estão disponíveis sem receita médica e que poderiam ser criadas *guidelines* de tratamento, 55% considera poder aplicar restrições ou reforço das restrições de acesso a medicamentos sujeitos a receita médica e, apenas 66% dos países refere que houve monitorização de antimicrobianos nos 5 anos anteriores. Relativamente à implementação de campanhas de informação pública, 79% dos países informaram ter organizado pelo menos uma campanha nos últimos dois anos. Apesar da implementação de campanhas de informação na maioria dos países, as conclusões desta análise indicam que o uso excessivo de antibióticos quer pela população em geral quer pelos profissionais de saúde continua a ser um potencial problema em todas as regiões. É também referido a falta de conhecimento que existe sobre as resistências bacterianas a nível da população, e a nível de alguns setores como nos cuidados de saúde, a nível político e académico e dos próprios *media*, revelando a necessidade de campanhas educativas em todos estes setores.

A atual falta de novos antibióticos para substituir os que se tornaram ineficazes, sem resolução previsível nos próximos anos alerta-nos para a urgente necessidade de proteger a eficácia dos fármacos que existem atualmente.

Sendo a resistência aos antibióticos um problema que afeta toda a comunidade parece importante, tal como alguns investigadores têm sugerido, que todos tentem descobrir a sua "pegada de resistência" para ajudar a identificar e medir os riscos associados aos antibióticos [4]. Isto é, todos os intervenientes no circuito dos antibióticos, desde a produção, prescrição, dispensa e consumo devem avaliar qual o seu potencial contributo no agravamento deste flagelo, assim como qual o seu papel na prevenção da disseminação de resistências aos antibióticos.

1.5 Fatores associados ao consumo inadequado de antibióticos e intervenções para melhorar o seu uso

Como referido anteriormente o uso excessivo e inadequado de antibióticos está relacionado com uma prescrição excessiva e inadequada, assim como com a automedicação, resultante da toma de medicamentos que sobraram de tratamentos anteriores ou da aquisição direta nas

farmácias sem uma receita. Apesar de os antibióticos serem de prescrição obrigatória na Europa, a verdade é que vários estudos têm revelado que existe dispensa de antibióticos nas farmácias sem receita médica [39-46]. Para além destes e outros estudos também os últimos dados publicados em 2013 pelo *Special Eurobarometer 407* [25] e à semelhança dos publicados em anos anteriores demonstram que a automedicação e a compra de antibióticos sem receita médica é uma realidade na Europa. Não existem estudos específicos na população portuguesa, que quantifiquem a quantidade de antibióticos que são dispensados sem receita médica, no entanto alguns estudos [46-49], assim como os dados do *Special Eurobarometer 407* [25], revelam que os portugueses também adquirem antibióticos sem receita médica nas farmácias e num estudo realizado na região sul de Portugal, cerca de 23 % da população estudada reconheceu ser fácil obter antibióticos sem receita médica nas farmácias [49].

As intervenções para melhorar o uso de antibióticos têm sido essencialmente dirigidas aos médicos e por vezes têm decorrido algumas campanhas gerais dirigidas à população em geral, esquecendo-se o problema da automedicação e não envolvendo os farmacêuticos comunitários que na nossa opinião são um importante foco de intervenção para combater a automedicação com antibióticos e para promover o uso racional de antibióticos. As intervenções para melhorar o uso através do combate à automedicação deverão apresentar soluções específicas para cada cultura, região e país [43].

Não se sabe qual a contribuição da utilização de antibióticos sem prescrição médica para o desenvolvimento e disseminação de bactérias resistentes [43]. Contudo os países com elevados níveis de resistências bacterianas na comunidade, são também países com elevados índices de automedicação com antibióticos, pelo que tem sido especulado que a automedicação desempenha um papel importante na seleção e manutenção de níveis elevados de resistências microbianas na comunidade [43]. Na Europa, os países onde se verificou maior consumo de antibióticos foi nos países de leste seguidos dos países do sul [44], que como vimos anteriormente são os países que na Europa apresentaram em 2012 maiores taxas de consumo [35] de antibióticos e em 2013 maiores percentagens de resistências [29].

Os potenciais fatores modificáveis associados à automedicação são a disponibilidade de antibióticos sem receita médica, não adesão ao tratamento (não completar um ciclo de tratamento), dimensionamento das embalagens não adequado aos tratamentos, e a prescrição pelos médicos de antibióticos para situações menores [45]. Para que qualquer medida de intervenção seja eficaz na modificação de comportamentos e da própria cultura de utilização de antibióticos é importante melhorar o conhecimento quer da população em geral quer dos profissionais de saúde sobre os antibióticos e os riscos associados ao seu uso, assim como desmistificar a crença de que os antibióticos são úteis para tratar males menores.

As expectativas dos doentes em relação à necessidade de antibióticos para situações menores são criadas por prescrições anteriores de forma inadequada também para situações menores, tendo sido demonstrada uma forte relação entre a automedicação principalmente por

antibióticos que sobraram de tratamentos anteriores e a prescrição médica para situações semelhantes [50].

Foram identificados fatores favoráveis e fatores predisponentes para a automedicação [38]. A percepção de que os antibióticos são adequados para situações menores, assim como as atitudes favorecedoras para o uso de antibióticos são fatores predisponentes para a automedicação. Por outro lado, a percepção de que os antibióticos podem ser adquiridos nas farmácias sem receita médica é o principal fator favorecedor para automedicação nível individual. Outros fatores favorecedores incluem as características dos países como a sua riqueza (número de médicos per capita), aplicação da regulamentação relacionada com a dispensa nas farmácias, dispensa de antibióticos por embalagem em vez de quantidade exata, o preço das consultas médicas, a satisfação com os cuidados médicos e a acessibilidade aos cuidados de saúde. Intervenções para diminuir a automedicação com antibióticos devem atuar quer nos fatores predisponentes quer nos fatores favorecedores de automedicação [38], diminuindo a disponibilidade de antibiótico sem aconselhamento de profissionais, facilitando a dispensa do número exato de comprimidos e através da educação do público em geral intervindo nas crenças sobre o uso de antibióticos em situações menores. Por outro lado, as expectativas dos doentes em relação aos antibióticos têm também sido identificadas como um fator importante que influencia as atitudes dos médicos durante a prescrição, devido à complacência com o doente [51, 52].

Em Portugal, apesar da dispensa de antibióticos ser por embalagens e não por unidades, em termos gerais, o dimensionamento está calculado tendo em conta os ciclos de tratamento para cada antibiótico e indicação clínica. Em relação a políticas de prescrição, e na sequência do Programa de Prevenção e Controlo de Infeções e de Resistência aos Antimicrobianos criado em fevereiro de 2013, foi publicado no mesmo ano o Despacho nº 15423/2013 no Diário da República, 2.ª série, n.º 229 de 16 de novembro de 2013, que tem como objetivo promover e corrigir as práticas de uso de antibióticos, nomeadamente através da implementação de programa de assistência à prescrição antibiótica, tanto em profilaxia como em terapêutica [53]. Como referido anteriormente também decorreram pelo menos duas campanhas nacionais com o objetivo de melhorar o conhecimento e o uso de antibióticos, uma em 2011 e a outra durante o período de 2004 e 2007 [28].

Os últimos dados do *Special Eurobarometer 407* assim como os dados de consumo de antibióticos em cuidados de saúde primários do ECDC e os dados de resistências bacterianas do ESAC já aqui analisados, sugerem-nos a necessidade de realizar intervenções, diferentes das campanhas já realizadas, de forma a melhorar o uso de antibióticos na comunidade em Portugal. Para além das medidas políticas que já estão a decorrer e outras que possam vir a ser implementadas, parece ser importante realizar intervenções educativas dirigidas quer à população em geral, quer aos profissionais de saúde essencialmente médicos e farmacêuticos comunitários, uma vez que estes têm um papel importante nas próprias atitudes, comportamentos e hábitos de utilização de medicamentos pelos doentes.

É pois necessário desenvolver estudos de investigação com intervenções dirigidas à modificação de hábitos de utilização de antibióticos pelos diferentes intervenientes desde a prescrição à dispensa. Segundo uma revisão da Cochrane [54] sobre a efetividade de intervenções para melhorar a prescrição de antibióticos em cuidados de saúde primários, para garantir a efetividade das intervenções, é importante ter em conta as características e barreiras no meio onde vai ser realizada a intervenção. É também importante realçar que as intervenções educativas multifacetadas envolvendo os médicos e outros profissionais de saúde, assim como, os doentes e a população em geral criam um ambiente altamente motivador com forte impacto na alteração de hábitos de prescrição.

Assim, as intervenções dirigidas aos profissionais de saúde devem ter em conta as barreiras, como as lacunas de conhecimento e as atitudes, que influenciam o seu desempenho quer na prescrição de antibióticos no caso dos médicos, quer na dispensa no caso dos farmacêuticos.

Vários estudos têm identificado que existem fatores intrínsecos e fatores extrínsecos ao médico que interferem com a prescrição de antibióticos [51, 52]. Também em relação à dispensa de antibióticos pelos farmacêuticos comunitários pensamos haver fatores extrínsecos e intrínsecos que podem interferir com o aconselhamento durante a dispensa de antibióticos através de uma receita médica assim como a possível propensão para dispensar antibióticos sem receita médica (Figura 6).

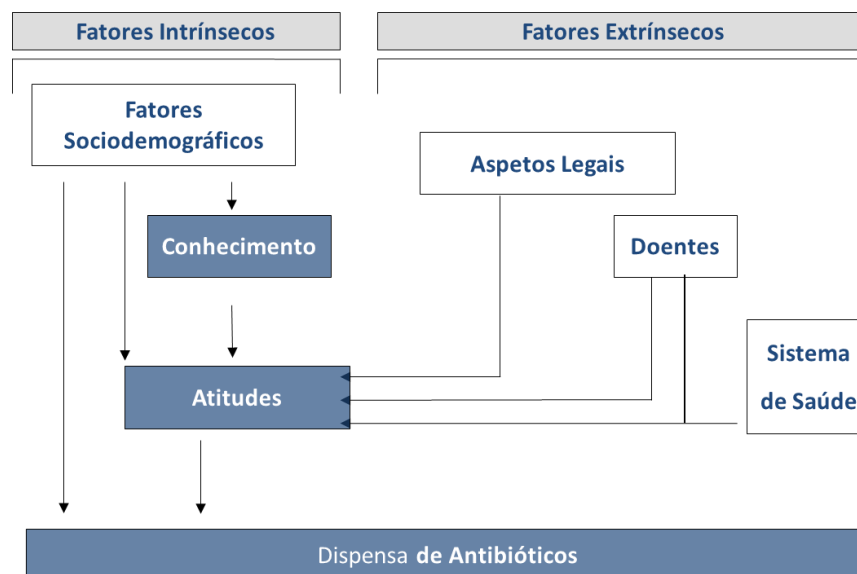


Figura 6 - Fatores intrínsecos e extrínsecos que poderão interferir com a dispensa de antibióticos pelos farmacêuticos comunitários (adaptado de [52]).

Face ao exposto, desenvolveu-se uma intervenção educativa dirigida a farmacêuticos comunitários, com o objetivo de promover o uso racional de antibióticos na comunidade. No estudo aqui apresentado neste documento, pretendeu-se explorar as atitudes e perceções dos farmacêuticos em relação aos antibióticos e às resistências bacterianas, de forma a desenhar uma intervenção educativa em farmacêuticos comunitários cuja implementação se fez através de um ensaio controlado aleatório na região abrangida pela Administração Regional de Saúde

do Centro (ARS Centro), de forma a avaliar o impacto no consumo de antibióticos. Para a implementação desta intervenção educativa seguiu-se o modelo de intervenções educativas desenvolvidas anteriormente, e que consiste num estudo sistemático a desenvolver em 5 fases [55]: (i) revisão bibliográfica, (ii) estudo qualitativo, (iii) desenho e validação de um questionário para avaliar atitudes e conhecimento dos farmacêuticos em relação aos antibióticos e às resistências bacterianas, (iv) estudo transversal para identificar que atitudes estão relacionadas com a propensão dos farmacêuticos para dispensar antibióticos sem receita médica (v) estudo experimental que consistiu na realização de um ensaio controlado aleatório por *clusters*.

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CAPÍTULO 2

OBJETIVOS

2 OBJETIVOS

Tendo em conta o elevado consumo de antibióticos em cuidados primários em Portugal, o principal objetivo deste estudo é diminuir o consumo de antibióticos na população, através de uma intervenção educativa dirigida a farmacêuticos comunitários na região definida pela ARS Centro. Para atingir este objetivo geral foram propostos os seguintes objetivos específicos a atingir durante o desenvolvimento do projeto:

- Realizar uma revisão bibliográfica dos estudos publicados para identificar que tipo de intervenções educativas, dirigidas a médicos e/ou farmacêuticos, têm sido desenhadas com o objetivo de melhorar a prescrição de antibióticos pelos médicos, em cuidados primários e/ou os hábitos de dispensa de antibióticos pelos farmacêuticos em farmácias comunitários.
- Explorar a perceção, atitudes e conhecimentos dos farmacêuticos, em relação à dispensa e ao consumo de antibióticos pela população e em relação às resistências bacterianas.
- Desenhar e validar um questionário que identifique as atitudes e conhecimentos dos farmacêuticos em relação às resistências bacterianas e ao consumo de antibióticos.
- Identificar as atitudes e conhecimentos dos farmacêuticos em relação aos antibióticos e às resistências microbianas e avaliar que influência têm na propensão para dispensar antibióticos sem receita médica.
- Desenhar uma intervenção educativa dirigida aos farmacêuticos comunitários, aos doentes e à população em geral, sobre as resistências bacterianas e o consumo inadequado de antibióticos.
- Realizar uma intervenção educativa a farmacêuticos comunitários, a doentes e à população em geral, através de um ensaio controlado aleatório na região abrangida pela ARS Centro.
- Avaliar o impacto da intervenção educativa realizada aos farmacêuticos em conjunto com uma intervenção educativa dirigida a médicos de clínica geral e familiar, sobre o consumo de antibióticos na população.

CAPÍTULO 3

**EDUCATIONAL INTERVENTIONS TO IMPROVE PRESCRIPTION AND
DISPENSING OF ANTIBIOTICS: A SYSTEMATIC REVIEW**

3 EDUCATIONAL INTERVENTIONS TO IMPROVE PRESCRIPTION AND DISPENSING OF ANTIBIOTICS: A SYSTEMATIC REVIEW

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Resumo

Realizou-se uma revisão sistemática dos estudos publicados na *MEDLINE - PubMed* sobre intervenções educativas desenhadas com o objetivo de melhorar a prescrição e/ou a dispensa de antibióticos em cuidados de saúde primários e em ambiente hospitalar, publicados entre janeiro 2001 e dezembro de 2011. Os dados relativos aos resultados extraídos de cada estudo incluiu as alterações resultantes da intervenção relativamente a: total de antibióticos prescritos/dispensados, prescrição do antibiótico adequado/adeseção às *guidelines* de tratamento incluindo dosagem e via de administração, atitudes e comportamentos, qualidade da prática de dispensa em farmácia. Foram incluídos 78 estudos para análise, 47 em cuidados primários e 31 em ambiente hospitalar, os quais diferiam bastante no desenho, definição da amostra, período de avaliação e resultados avaliados, mas a maioria reportou resultados positivos. Vinte e nove estudos (62%) em cuidados de saúde primários e vinte e quatro (78%) em ambiente hospital reportaram resultados positivos para todos os parâmetros avaliados; catorze estudos (30%) em cuidados de saúde primários e seis (20%) em ambiente hospitalar não reportaram resultados significativos de melhoria para todos os parâmetros medidos. A melhoria na adeseção às *guidelines* de prescrição e a diminuição no total de prescrição, foi observado, respetivamente, em 46% e 41% dos estudos analisados. A alteração do comportamento de prescrição de antibióticos foi observado em quatro estudos e a melhoria na qualidade da prática de dispensa de antibióticos na farmácia, foi observado em um estudo. Existem muitos mais estudos sobre intervenções educativas dirigidas a médicos que a farmacêuticos e as doenças respiratórias são o principal alvo das intervenções, principalmente em cuidados primários. Na maioria dos estudos os investigadores utilizam intervenções ativas ou multifacetadas, e em alguns estudos estas intervenções são desenhadas tendo em conta os conhecimentos e atitudes dos profissionais de saúde, focando-se nas barreiras identificadas. Os resultados mostraram que o uso de antibióticos pode ser melhorado através de intervenções educativas, sendo as mais usadas as intervenções multifacetadas.

RESEARCH ARTICLE

Open Access

Educational interventions to improve prescription and dispensing of antibiotics: a systematic review

Fátima Roque^{1,2,3}, Maria Teresa Herdeiro^{2,4*}, Sara Soares², António Teixeira Rodrigues², Luiza Breitenfeld¹ and Adolfo Figueiras⁵

Abstract

Background: Excessive and inappropriate antibiotic use contributes to growing antibiotic resistance, an important public-health problem. Strategies must be developed to improve antibiotic-prescribing. Our purpose is to review of educational programs aimed at improving antibiotic-prescribing by physicians and/or antibiotic-dispensing by pharmacists, in both primary-care and hospital settings.

Methods: We conducted a critical systematic search and review of the relevant literature on educational programs aimed at improving antibiotic prescribing and dispensing practice in primary-care and hospital settings, published in January 2001 through December 2011.

Results: We identified 78 studies for analysis, 47 in primary-care and 31 in hospital settings. The studies differed widely in design but mostly reported positive results. Outcomes measured in the reviewed studies were adherence to guidelines, total of antibiotics prescribed, or both, attitudes and behavior related to antibiotic prescribing and quality of pharmacy practice related to antibiotics. Twenty-nine studies (62%) in primary care and twenty-four (78%) in hospital setting reported positive results for all measured outcomes; fourteen studies (30%) in primary care and six (20%) in hospital setting reported positive results for some outcomes and results that were not statistically influenced by the intervention for others; only four studies in primary care and one study in hospital setting failed to report significant post-intervention improvements for all outcomes. Improvement in adherence to guidelines and decrease of total of antibiotics prescribed, after educational interventions, were observed, respectively, in 46% and 41% of all the reviewed studies. Changes in behaviour related to antibiotic-prescribing and improvement in quality of pharmacy practice was observed, respectively, in four studies and one study respectively.

Conclusion: The results show that antibiotic use could be improved by educational interventions, being mostly used multifaceted interventions.

Keywords: Drug resistance microbial, Review, Behavior change, Education medical continuing, Education pharmacy continuing

Background

Antibiotic resistance is an important public-health issue, which is aggravated by the lack of new antimicrobial agents [1,2]. Inappropriate use of antibiotics is the main factor underlying microbial resistance [3,4]. Ecological studies in Europe suggest that there is a clear association

between extent of antibiotic use and rate of resistance [5]. Excessive and inappropriate use of antibiotics is attributed to misprescription and to self-medication with “leftovers” from previous courses or with antibiotics dispensed in pharmacies without prescription [6,7]. In countries with a high incidence of self-medication with antibiotics, prescription of antibiotics is also high [7], suggesting that both practices are subject to the same cultural factors [8]. Physicians and pharmacists are the health professionals who exert most influence on patients’ medication-related behavior. Many educational interventions to improve antibiotic-prescribing and/or

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dispensing have targeted those health professionals. Previous systematic reviews of the topic include Steinman's [9], which covered reports published prior to 2004 and on interventions directed at physicians. Other more recent reviews [10-13] have targeted specific areas, namely, respiratory tract infections [10,13], critical care [11], and acute care [12]. Therefore, there has been no general reviews, of the topic, including interventions on physicians a pharmacists to improve antibiotic prescription and dispensing. To close this gap, we carried out a critical review of educational programs aimed at improving antibiotic-prescribing by physicians and/or antibiotic-dispensing by pharmacists, in both primary-care and hospital settings.

Methods

Literature search methodology

For review purposes, we conducted a search of the MEDLINE-PubMED scientific database from January 2001 through December 2011. In addition, other papers were located by manual searches targeting journals, particularly those less likely to be indexed, and references cited by papers retrieved.

The search strategy was designed to identify relevant studies addressing antibiotic resistance and the prescribing/dispensing habits of health care providers (physicians and pharmacists) pre- and post-educational interventions. The following search terms and their equivalents were used in PubMed: ("intervention" OR "program" OR "health promotion" OR "education") AND ("pharmacists" OR "pharmacy" OR "physician" OR "health professionals" OR "clinician" OR "clinic" OR "practitioner" OR "general practitioner" OR "doctor") AND ("antibiotics" OR "antimicrobial").

Based on previous reviews [14-17], we apply this selection criteria: (i) language: papers had to be published in English, French, Spanish or Portuguese; (ii) type of intervention: studies had to describe educational interventions; (iii) target population: educational interventions had to target physicians (general practitioners and all specialties) and/or pharmacists (population studies were included only if they also included interventions on pharmacists and/or physicians); and (iv) outcome measures: studies had to measure the effect of educational interventions on the prescribing behavior of physicians and/or dispensing behavior of pharmacists. Insofar as study design was concerned, no inclusion or exclusion criteria were stipulated because our aim was to use quality methodology to conduct a critical review of all published studies.

Data-extraction

Study design

Adapted from Figueiras [18], study designs were classified as follows: (1) before/after study; (2) non-randomized

controlled study without cross-contamination control; (3) non-randomized controlled study with cross-contamination control; (4) randomized controlled study without cross-contamination control; and (5) randomized controlled study without cross-contamination control. Where authors reported the different groups as being in workplaces that were geographically far apart, the study was deemed to have cross-contamination control; and where no mention was made of distance between groups or specific implementation of cross-contamination control, the study was deemed to be without such control.

Target disease

In cases where studies identified specific diseases in which interventions were made to improve antibiotic use, this was recorded.

Type of intervention

Educational interventions include any attempt to persuade physicians to modify their practice performance by communicating clinical information strategies [19] and by communication skills training [13]. Strategies that were purely administrative or applied incentives or coercion were excluded from this definition of educational interventions. In our review, we only included studies that assessed educational interventions. However, in studies in which these types of interventions were associated with others, we extracted data on all strategies. Consequently, interventions were classified into the following categories, adapted from Davis [19] and Figueiras [18]: (1) dissemination of printed/audiovisual educational materials (mailed printed matter; protocols and guidelines; self-instruction materials; drug bulletins); (2) group education, including group-session rounds, conferences, lectures, seminars, and tutorials; (3) feedback of physician prescribing patterns (individually, or including a comparison between these patterns and peer behavior and/or accepted standards), or feedback of patient-specific lists of prescribed medication; (4) individual outreach visits; (5) reminders at the time of prescribing; (6) computer-assisted decision-making systems; (7) formulary control/restrictive formulary process; (8) patient education (pamphlets); (9) patient education (videotapes); (10) workshops on rapid tests/introduction of Rapid Antigen Detection Testing (RADT) in consulting offices; (11) enforcement of regulations; (12) prescription feedback, with recommendations to modify it made by pharmacists and/or infectious-disease physicians; (13) financial incentives.

Baseline and follow-up

Under this head, we included the period during which outcomes were measured (baseline, intervention period and follow-up).

Analysis

Studies were classified into different categories, namely: (1) comparison of post-intervention values between groups; (2) comparison of pre- and post-intervention values within each group; (3) comparison of pre- and post-intervention values between groups; (4) comparison of follow-up values between groups; (5) comparison of pre-, post, and follow-up values within each group; and, (6) comparison of pre-, post- and follow-up values between groups.

Statistical tests

We collected data yielded by statistical tests used to assess the effectiveness of interventions.

Results

The results extracted from studies consisted of changes in: total antibiotics prescribed/dispensed (T); choice of appropriate antibiotics/adherence to antibiotic guidance according to guideline algorithms, including dosages and administration routes (Ga); attitudes and behavior (At/Bh); quality of pharmacy practice (Qph).

Study results were classified as: positive (+), if reported as positive or if changes in outcomes measured were statistically significant; partially positive (\pm), if reported as positive for some variables and negative for others; and negative (-), if reported as negative.

Results and discussion

Selection of papers

The search yielded a total of 90,350 Abstracts, 47,535 of which were potentially eligible for inclusion. A reading of the titles and abstracts led to an initial selection of 571

papers for full-text analysis; of these, 65 were then selected, made up of 40 primary- and 25 hospital-care studies. After a search of the references cited, 7 papers were added to the primary-care and 6 to the hospital-care studies. A total of 78 papers were included, 47 primary- [20-66] and 31 hospital-care interventions [3,67-96] (Figure 1)

Interventions in primary care professionals

In the studies analyzed (Table 1), educational interventions in primary care mainly targeted physicians, and outcomes were assessed by reference to the total antibiotic prescription or appropriate antibiotic prescription rates. Educational interventions in pharmacists occurred in 8 studies [25,32,33,42,44,50,52,66], though in 6 cases the interventions covered both pharmacists and physicians. In 21 studies [20,22,23,25,31-33,35-37,39,43,45,46,50-53,55,57,60], the interventions were extended to patients and their caregivers or general population.

In primary care (table 2), 33 studies (70%) [20-24, 26,27,29,30,32-39,41,44,45,47,48,50,51,53,54,56,58-61,63,65] focused on the use of antibiotics in respiratory infections, and one focused on the use of antibiotics in infectious diseases and other infections (urinary infections, skin and soft tissue infections and septicemia) [27]; the remaining 30% failed to identify any target disease [25,28,31,40,42,43,46,49,52,55,57,62,64,66]. Of the 47 papers, 27 (57%) studied the efficacy/effectiveness of one or more interventions versus non-intervention, using a control group that received the intervention in four studies, dissemination of guideline information in three [56,57,65] and educational sessions on diagnosis of *otitis media* in one [58]. In this last study, the educational

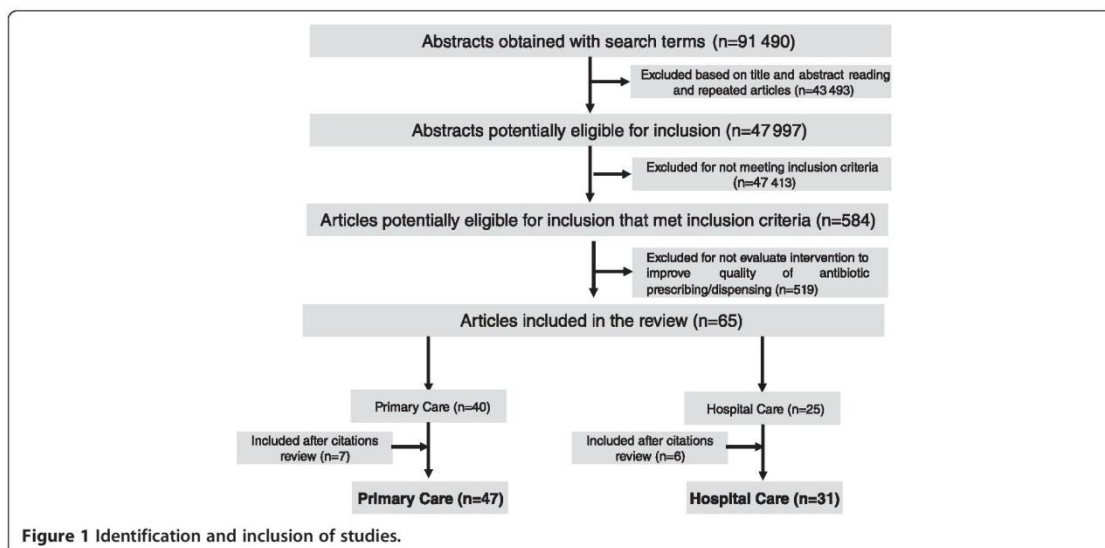


Figure 1 Identification and inclusion of studies.

Table 1 Studies analyzing educational interventions in health professionals to improve antibiotic use

<i>Author (year)</i>	<i>Country</i>	<i>Allocation unit (a)</i>	<i>Intervention population (b)</i>	<i>Type of patient</i>	<i>Sample size (%) (b), (c)</i>	<i>Statistical test</i>
Dollman, WB (2005) [20]	South Australia	PC	GPs, Pa	All	—	Bivariate
Hrisos, S (2007) [21]	UK	PC	GPs	—	340 GPs	Multivariate Bivariate
Hennessy, TW (2002) [22]	USA (Alaska)	PC	Py, Pa, O	All	3144 Pa	Multivariate Bivariate
Rubin, MA (2005) [23]	USA	PC	Py, Pa	All	—	Multivariate
Naughton, C (2009) [24]	Ireland	PC	GPs	All	110 GPs	Multivariate
Chazan, B (2007) [25]	Israel (Northern)	PC	Py, Nu, Ph, Pa	All	200 participants	Bivariate
Briel, M (2005) [26]	Switzerland	PC	Py	Adults	45 Py 624 Pa	Multivariate Bivariate
Monette, J (2007) [27]	Canada	PC	Py	Geriatric patients	36 Py	Multivariate
Enriquez-Puga, A (2009) [28]	England	PC	Py, GPs	All	28 practices	Multivariate Bivariate
Bjerrum, L (2006) [29]	Spain	PC	GPs	Adults	17 GPs in IG35 GPs in CG	—
Mcisaac, WJ (2002) [30]	Canada	PC	GPs	Children Adults	97 Py 621 patients	Multivariate Bivariate
Wheeler, JG (2001) [31]	USA	PC	Py, Pa	Pediatric patients	16 Py 771 parents	Bivariate
Juzych, NS (2005) [32]	USA	PC	Py, Ps, Nu, Ph, Pa	Adults Children	12 Py + 9 Ps in IG 6 Py + 9 Ps in CG	Univariate
Smeets, HM (2009) [33]	Netherlands	PC	GPs, Ph, Pa	—	131 practices in IG 127 practices in CG	Multivariate Bivariate
Mandryk, JA (2006) [34]	Australia	PC	GPs	—	—	Multivariate
Stille, CJ (2008) [35]	USA	PC	Py, Pa	Pediatric patients	168 Py	Multivariate Bivariate
Finkelstein, JA (2001) [36]	USA	PC	Py, Pa	<6 years	14468 Pa (pre-) 13461 Pa (post-)	Multivariate Bivariate
Altiner, A (2007) [37]	Germany	PC	GPs, Pa	≥16 years	104 GPs (pre-) 28 GPs + 787 Pa in CG 33 GPs + 920 Pa in IG	Multivariate
Légaré, F (2010) [38]	Canada	PC	Py	All	18 Py in IG + 15 Py in IG 245 Pa in IG + 214 Pa In CG	Multivariate
Kiang, KM (2005) [39]	USA	PC	Py, GPs, Ps, Nu, Pa, O	Adults and pediatric patients	1800 Py	Multivariate
Mohagheghi, MA (2005) [40]	Iran	PC	GP	Adults	40 GPs in CG 40 GPs in IG	—
Irurzun, C (2005) [41]	Argentina	PC	Py	≥15 years	19 Py	Bivariate
Chalker, J (2005)[42]	Vietnam and Thailand	Pharmacy	Ph	—	124 pharmacies	Multivariate

Table 1 Studies analyzing educational interventions in health professionals to improve antibiotic use (Continued)

Finkelstein, JA (2008) [43]	USA	PC	Py, Pa	≤6 years	223 135 person/years	Multivariate
Chuc, NTK (2002) [44]	Vietnam	Pharmacy	Ph	—	58 pharmacies	Bivariate
Belongia, EA (2001) [45]	USA	PC	Ps, Pa	Children	109 Py in IG 52 in CG	Multivariate Univariate
Belongia, EA (2005) [46]	USA	PC	Py, Ps, Pa	—	12790 Py	Multivariate Univariate
Greene, RA (2004) [47]	USA	PC	Py, Ps	Adults Children	900 Py and Pa	Bivariate
Teng, CL (2007) [48]	Malaysia	PC	GPs	—	29 GPs	Bivariate
Awad, AI (2006) [49]	Sudan	PC	GPs	—	1800 Pa	Bivariate
Welschen, I (2004) [50]	Netherlands	PC	GPs, Ph, Pa, O	—	89 GPs	Bivariate
Gonzales, R (2004) [51]	USA	PC	Py, Pa,	Elderly	51 office practice in CG 4 office practices in IG	Multivariate
Colomina Rodríguez, J (2010) [52]	Spain	PC	Py, Ph, Pa, O	All	—	Bivariate
Hickman, DE (2003) [53]	USA	PC	Py, Nu, Pa	Adults Children	—	Bivariate
Coenen, S (2004) [54]	Belgium	PC	GPs	Adults	42 GPs in IG 43 GPs in CG	Multivariate Bivariate
Perz, JF (2002) [55]	USA	PC	Py, Ps, Pa	Pediatric patients	464200 person-years	Multivariate
Sondergaard, J (2003) [56]	Denmark	PC	Py	—	299 GPs	Bivariate
Doyne, EO (2004) [57]	USA	PC	Ps, Pa	Pediatric patients	6 practices - IG 6 practices - CG	Multivariate
Bauchner, H (2006) [58]	USA	PC	Ps	Children (3–36 months)	1368 Pa - IG 1138 Pa - CG	Multivariate Bivariate
Christakis, DA (2001) [59]	USA	PC	Ps, Nu, O	Children	16 providers - IG 12 providers - CG	Bivariate
Smabrekke, L (2002) [60]	Norway	PC	Ps, Nu, Pa	Children (1–5 years)	819 Pa	Bivariate
Bjerrum, L (2011) [61]	Several	PC	GP	Adults	47011	—
Regev-Yochay, G (2011) [62]	Israel	PC	GP	Children	3636	Multivariate
Llor, C (2011) [63]	Spain	PC	GP	—	235 (full) 97 (partial)	Univariate Multivariate
Weiss, K (2011) [64]	Canada	PC	GP	—	All GP	Multivariate
Llor, C (2011) [65]	Spain	PC	GP	Adults (14-60 years)	10 first patients	—
McKay, RM (2011) [66]	Canada	PC	Py, Ph, O	—	—	Bivariate
Deuster, S (2010) [3]	Switzerland	HC	Py	Adults	292 Pa	Bivariate

Table 1 Studies analyzing educational interventions in health professionals to improve antibiotic use (Continued)

Chang, MT (2006) [67]	Taiwan	HC	GPs	—	5046 Pa (pre-) 5054 Pa (post-)	Bivariate
Naughton, BJ (2001) [68]	USA	HC	Py, Nu	Geriatric patients	350 episodes	Bivariate
Lutters, M (2004) [69]	Switzerland	HC	Py	Geriatric patients	3383 Pa	Bivariate
Loeb, M (2005) [70]	Canada and USA	HC	Py, Nu	Geriatric patients	4217 residents	Bivariate
Lesprit, P (2009) [71]	France	HC	Py	—	786 Pa	Bivariate
Akter, SFU (2009) [72]	Bangladesh	HC	Py	Pediatric patients	2171 Pa (pre-) 1295 Pa (post-)	Bivariate
Paul, M (2006) [73]	Israel Germany Italy	HC	Py	Adults	1203 Pa (pre-) 2326 Pa (post-) (1245 IG and 1801 CG)	Bivariate
Camins, BC (2009) [74]	USA	HC	Py (internists)	—	784 new prescriptions	Multivariate Bivariate
Westphal, JF (2010) [75]	France	HC	Py	—	471 cases of pneumonia 104 (pre-); 367 (post-)	Bivariate
Mullet, CJ (2001) [76]	USA	HC	Ps, Nu	Pediatric > 6 months	809 Pa (pre-) 949 Pa (post-)	Bivariate
von Gunten, V (2005) [77]	Switzerland	HC	Py	—	1200 Pa	Multivariate Bivariate
Ansari, F (2003) [78]	UK	HC	Py	—	40 medical and surgical wards	Multivariate
Kisuule, F (2008) [79]	USA	HC	Py, Nu	—	17 hosp. practitioners	Bivariate
Halm, EA (2004) [80]	USA	HC	Py, Nu, Pa, O	Adults	2094 cases 1013 (pre-) 1081 (post-)	Bivariate
López-Medrano, F (2005) [81]	Spain	HC	Py	—	1280 treatments	Bivariate
Agwu, AL (2008) [82]	USA	HC	Py, Ps	Children	—	Bivariate
Barenfanger, J (2001) [83]	USA	HC Pharmacy	Ph	—	378 Pa (188 IG and 190 CG)	Bivariate
Rüttiman, S (2004) [84]	Switzerland	HC	Py	Adults	500 Pa	Bivariate
Martin, C (2005) [85]	USA	HC	Py	—	—	—
Solomon, DH (2001) [86]	USA	HC	Py	—	4500 Pa	Bivariate
Fowler, S (2007) [87]	UK	HC	Py	Elderly ≥ 80 years	6129 admissions	Multivariate
Sintchenko, V (2005) [88]	Australia	HC	Py	—	12 internists	Bivariate
Yong, MK (2010) [89]	Australia	HC	Py	—	—	Bivariate
Meyer, E (2010) [90]	Germany	HC	Py	Adults	4684 Pa (pre-) 7203 Pa (post-)	Multivariate

Table 1 Studies analyzing educational interventions in health professionals to improve antibiotic use (Continued)

Thursky, KA (2006) [91]	Australia	HC	Py	Adults	489 Pa (pre-) 497 Pa (post-)	Multivariate
Petterson, E (2011) [92]	Sweeden	HC	Nu, Py	Elderly	60 residents	—
Tangden, T (2011) [93]	Sweeden	HC	Py	elderly	—	Multivariate Bivariate
Talpaert, MJ (2011) [94]	UK	HC	Py	Adults	—	Multivariate
Bevilacqua, S (2011) [95]	France	HC	Py	Adults	—	Bivariate
Shen, J (2011) [96]	China	HC	Py	Adults	354 patients	Multivariate Bivariate

(a) PC – primary care; HC – hospital care.

(b) GPs – general practitioners; Ps – pediatrics; Py – physicians; Pa – patients or their caregivers; Ph – pharmacists; Nu – nurses; O – others.

(c) CG – control group; IG – intervention group.

Table 2 Interventions to improve antibiotic use in primary care

Author (year)	Study design (a)	Program description		Baseline and follow-up			Analysis (e)	Results (f)
		Disease (b)	Intervention type (c,d)	Baseline	Intervention period	Follow-up		
Dollman, WB (2005) [20]	1	URTI	IG: 1, 2, 8 CG: 0	5 months	5 months	—	2	T (+)
Hrisos, S (2008) [21]	4	URTI	IG1: 3 IG2: 3 IG1 + 2: 3 CG: 0	—	3 months	—	3	At/Bh (+)
Hennessy, TW (2002) [22]	3	RTI	IG: 8, 2 CG: 0	2 months	12 months (6 each year of intervention)	2 months	2, 3	T (+)
Rubin, MA (2005) [23]	2	URTI	IG: 1, 2, 8, 9 CG: 0	6 months	6 months	—	2, 3	T (+) Ga (+)
Naughton, C (2009) [24]	4	RTI	IG1: 3, 4 IG2: 3	12 months	—	12 months	2, 3	T (+) (-) ^a Ga (+) (-) ^a
Chazan, B (2007) [25]	1	Infectious disease	IG1: 1, 2 IG2: 1, 2, 8	4 months	4 months	—	2, 3	T (+)
Briel, M (2005) [26]	4	ARTI	IG1: 1,2 IG2: 1,2 CG: 0	—	5 months	—	1	T (+)
Monette, J (2007) [27]	4	Lower RTI UTI Skin and soft-tissue infections septicemia	IG: 1, 3 CG: 0	3 months	2 x 3 months	3 months	5, 6	Ga (+)
Enriquez-Puga, A (2009) [28]	4	—	IG: 1, 3, 4	2 periods of 6 months	6 months	24 months	5, 6	Ga (-)
Bjerrum, L (2006) [29]	2	RTI	IG: 2, 3, 10 CG: 0	3 weeks during 3 months	3 weeks during 3 months	—	1, 2	T (+) Ga (+)
Mcisaac, WJ (2002) [30]	4	Sore throat	IG: 1, 5 CG: 0	—	—	—	1	T (-) Ga (-)
Wheeler, JG (2001) [31]	1	Viral infections	IG: 2, 8, 9	1 week	3 weeks during 3 years	6 months (qualitative)	3	T (-) At/Bh (+)
Juzych, NS (2005) [32]	3	URTI	IG: 1, 2, 8 CG: 0	4.5 months	4.5 months	—	2, 3	Pa (+) (-) ^b T (+)
Smeets, HM (2009) [33]	2	RTI	IG: 2, 3, 8	6 months	6 months	—	5, 6	T (-)

Table 2 Interventions to improve antibiotic use in primary care (Continued)

			CG: 0			6 months (one year later)		Ga (-)
Mandryk, JA (2006) [34]	1	URTI	IG: 1, 2, 3, 4	33 months	51 months	—	2	Ga (+) T (+)
Stille, CJ (2008) [35]	4	RTI	IG: 1, 2, 8 CG: 0	—	—	6 months	1	At/Bh (+) (-) ^c
Finkelstein, JA (2001) [36]	4	<i>Otitis media</i> Pharyngitis Sinusitis Cold Bronchitis	IG: 1, 2, 3, 8 CG: 0	12 months	12 months	—	2, 3	T (+)
Altiner, A (2007) [37]	4	Acute cough	IG: 4, 8 CG: 0	3 months	—	3 months after 6 weeks 3 months after 1 year after	5, 6	T (+)
Légaré, F (2010) [38]	4	Acute RI	IG: 1, 2 CG: 0	—	—	—	2, 3	T (+)
Kiang, KM (2005) [39]	1	Respiratory illnesses	IG: 1, 2, 8	—	—	—	2, 3	Ga (+) At/Bh (+)
Mohagheghi, MA [40]	4	—	IG: 2 CG: 0	60 months	—	3 months afterwards 1 year afterwards	2, 3	T (+) (-) ^d
Irurzun, C (2005) [41]	1	Pharyngitis and tonsillitis	IG: 1, 2, 3, 4, 10	—	12 months	—	2	T (+) Ga (+)
Chalker, J (2005) [42]	5	—	IG: 2, 4, 11 CG: 0	—	—	3x3 months (one month after each intervention)	1	T (+) (-) ^e
Finkelstein, JA (2008) [43]	4	—	IG: 1, 2, 3, 8 CG: 0	24 months	6 months during 3 years	—	2, 3	T (+) (-) ^f Ga (+)
Chuc, NTK (2002) [44]	4	ARTI	IG: 2, 4, 11	—	—	—	2, 3	T (+) Qh (+)
Belongia, EA (2001) [45]	3	ARTI	IG: 1, 2, 8	6 months	—	6 months (every two years)	7, 8	T (+)
Belongia, EA (2005) [46]	2	—	IG: 1, 2, 8, 9	12 months	48 months	—	3, 4	T (+) (-) ^g
Greene, RA (2004) [47]	1	Acute sinusitis	IG: 1, 2, 3, 13	22 months	14 months	—	2	Ga (+) T (+)
Teng, CL (2007) [48]	2	URTI and others	IG: 1, 2, 4	3 months	—	3 months	2	T (+)

Table 2 Interventions to improve antibiotic use in primary care (Continued)

Awad, AI (2006) [49]	4	—	CG: 0 IG1: 1, 3 IG2: 2, 3 IG3: 3, 4	—	—	1 and 3 months afterwards	2, 3	T (+) ^h Ga (+)
Welschen, I (2004) [50]	4	ARTI	IG: 1, 2, 3, 8	3 months	—	3 months	2, 3	T (+)
Gonzales, R (2004) [51]	2	ARTI	IG: 1, 8	4 months	4 months (study period)	—	2, 3	T (+) (-) ⁱ
Colomina Rodríguez, J (2010) [52]	1	—	IG: 1, 2, 6, 8	48 months	36 months	24 months	5	T (+) Ga (+)
Hickman, DE (2003) [53]	4	Acute bronchitis	IG: 1, 2, 8 CG: 0	6 months	—	6 months	2, 3	T (+)
Coenen, S (2004) [54]	4	Acute cough	IG: 1, 4 IG: 0	3 months	1 month (without outcomes)	—	2,3	T (+) Ga (+) (-) ^j
Perz, JF (2002) [55]	1	—	IG: 1, 2, 8, 9 CG: 0	12 months	12 months	12 months	5,6	T (+)
Sondergaard, J (2003) [56]	4	RTI	IG: 1, 3 CG: 1	3 periods of 3 months	3 periods of 3 months	3 months (not shown)	2,3	T (-) Ga (-)
Doyne, EO (2004) [57]	4	—	IG: 1, 2, 3, 8 CG1: 1, 3 CG: 1	12 months	12 months	—	2,3	T (+) (-) ^k
Bauchner, H (2006) [58]	5	Acute otitis media	IG: 1, 2, 3 CG: 2	—	—	—	1	Ga (+) (-) ^l
Christakis, DA (2001) [59]	4	Acute otitis media	IG: 6 CG: 0	7 months	8 months	—	2,3	T (-) Ga (+)
Småbrekke, L (2002) [60]	2	Acute otitis media	IG: 1, 2, 8 CG: 0	4 months	4 months	—	2,3	T (+) Ga (+)
Bjerrum, L (2011) [61]	1	RTI	IG = 2, 3, 9, 10	3 weeks (x2years)	3 weeks (x1 year)	—	2, 3	T (+) Ga (+)
Regev-Yochay, G (2011) [62]	4	—	IG = 2 CG = 0	2 years	1 year	—	2, 3	T (+) Ga (+)
Llor, C (2011) [63]	4	Pharyngitis	IG1 = 2, 8, 10 IG2 = 2, 8, 10 (sem)	15 days	15 days	—	2, 3	T (+)
Weiss, K (2011) [64]	1	—	IG = 1 CG = 0	2 years	7 years	—	2, 3	T (+)

Table 2 Interventions to improve antibiotic use in primary care (Continued)

Llor, C (2011) [65]	4	Acute pharyngitis	IG = 1, 10 CG = 1	—	—	—	1	Ga (+)
McKay, RM (2011) [66]	1	—	IG = 1, 2, 8, 9	9 years	3 years	—	2	Pa (+) (-) ^m

^aIn [24], significantly positive in post-intervention period but no significant change post-follow-up.

^bIn [32], while prescriptions for pharyngitis, otitis media and URTI decreased significantly post-intervention, the decrease in the case of bronchitis was not as significant.

^cIn [35], comparison between attitudes, knowledge and behavior of physicians in the intervention versus the control group showed no significant differences. Physicians in the intervention group reported that they had changed their prescribing in the preceding 3 years.

^dIn [40], after one year, there was a reduction in the percentage of antibiotic prescribing in the intervention group but this was not statistically different from the control group.

^eIn [42], interventions resulted in improved antibiotic use, which was statistically significant in the Hanoi but not in the Bangkok study.

^fIn [43], there was no significant decrease in one age group (3–24 months).

^gIn [56], the reduction in antibiotic prescribing by pediatricians was greater in the control than in the intervention group.

^hIn [49], audit and feedback combined with academic detailing or seminars appeared to be more effective in changing antibiotic prescribing practices than audit and feedback alone.

ⁱIn [51], there was a moderate decrease in total antibiotics prescribed but this was not statistically significant.

^jIn [54], appropriate antibiotic prescribing improved post-intervention but did not prove statistically significant.

^kIn [57], the prescribing rate decreased in all groups but there were no statistically significant differences between groups.

^lIn [58], adherence was high though not statistically significant in the intervention group, but, in second episodes there were no differences in adherence, between groups.

^mIn [66], utilization rates for acute bronchitis are at the same level as when intervention began, but other acute respiratory tract infections declined.

(a) Disease: URTI – upper respiratory tract infections; RTI – respiratory tract infections; ARTI – acute respiratory tract infections; UTI – urinary tract infections.

(b) Study design (SD): (1) before/after studies; (2) – nonrandomized controlled trial without cross-contamination control; (3) – nonrandomized controlled trial with cross-contamination control; (4) - randomized controlled trial without cross-contamination control; (5) - randomized controlled trial with cross-contamination control.

(c) IG – intervention group; CG – control group.

(d) Type of intervention (TI): (0) no intervention; (1) dissemination of printed/audiovisual educational materials (mailed printed matter; protocols and guidelines; self-instruction materials; drug bulletins); (2) group education, including group-session rounds, conferences, lectures, seminars and tutorials; (3) feedback of physician prescribing patterns (individually or including a comparison of these patterns with peer behavior and/or accepted standards) or feedback of patient-specific lists of prescribed medication; (4) individual outreach visits; (5) reminders at the time of prescribing; (6) computer-assisted decision-making systems; (7) formulary-control/restrictive formulary process; (8) patient education (pamphlets); (9) patient education (videotapes); (10) workshops on rapid tests / introduction of Rapid Antigen Detection Tests (RADTs) in consulting offices; (11) enforcement of regulations; (12) prescription feedback with recommendations to modify it by pharmacists and/or infectious-disease physicians; (13) financial incentives.

(e) Type of data-analysis (T): (1) comparison of post-test values between groups; (2) comparison of pre- and post-values within each group; (3) comparison of pre- and post-values between groups; (4) comparison of follow-up values between groups; (5) comparison of pre-, post- and follow-up values within each group; (6) comparison of pre-, post- and follow-up values between groups.

(f) Results analyzed (R): (T) total antibiotics prescribed/dispensed; (Ga) choice of appropriate antibiotics/adherence to antibiotic guidance according to guideline algorithms, including dosages and routes of administration; (Pa) prescription rate per disease; (At/Bh) attitudes and behavior; (Qph) quality of pharmacy practice.

Table 3 Interventions to improve antibiotic use in hospital settings

Author (year)	Study design (a)	Program description		Baseline and follow-up			Analysis (d)	Results (e)
		Disease	Intervention type (b, c)	Baseline	Intervention period	Follow-up		
Deuster, S (2010) [3]	1	Most common hospital infections	IG: 1, 2	8 weeks	8 weeks	8 weeks (1 year after)	5	Ga (+) (-) ^a
Chang, MT (2006) [67]	1	—	IG: 1, 7	3 months	3 months	—	2	T (+) Ga (+)
Naughton, BJ (2001) [68]	4	Pneumonia	IG: 1, 2 CG: 1, 2	6 months	6 months	—	2, 3	T (-)
Lutters, M (2004) [69]	1	RTI and UTI	IG: 1, 2, 4	12 months	24 months	—	2	T (+) Ga (+)
Loeb, M (2005) [70]	4	UTI	IG: 1, 2, 4 CG: 0	—	—	—	1	T (+)
Lesprit, P (2009) [71]	2	Various	IG: 1, 2, 12 CG: 1, 2	—	8 weeks	—	1	Ga (+)
Akter, SFU (2009) [72]	2	Common pediatric infections	IG: 2	4 months	4 months	—	2, 3	T (+) Ga (+)
Paul, M (2006) [73]	5	—	IG: 6 CG: 0	7 months	7 months	—	1, 2	Ga (+)
Camins, BC (2009) [74]	4	—	IG: 1, 3, 4 CG: 1 (guidelines)	—	10 months	—	1	Ga (+)
Westphal, JF (2010) [75]	1	Pneumonia	IG: 2, 5, 6	18 months	54 months	—	2	Ga (+) (-) ^b
Mullet, CJ (2001) [76]	1	—	IG: 6	6 months	6 months	—	2	T (+) (-) ^c Ga (+)
von Gunten, V (2005) [77]	5	—	IG _B : 1 IG _C : 1, 2, 12 CG _A : 0	6 months	6 months	—	2, 3	T (+) Ga (+)
Ansari, F (2003) [78]	1	—	IG: 12	24 months	24 months	—	2	Ga (+) (-) ^d T (+)
Kisuule, F (2008) [79]	1	—	IG: 1, 3, 4	Period until 20 prescriptions	2 months	1 month	2	Ga (+)
Halm, EA (2004) [80]	1	Pneumonia	IG: 1, 2, 8, 9	5 months	—	5 months	2	Ga (+)
López-Medrano, F (2005) [81]	1	—	IG: 12	12 months	12 months	—	2	T (+) Ga (+)
Agwu, AL (2008) [82]	1	—	IG: 6, 12	12 months	12 months	—	2	Ga (+)
Barenfanger, J (2001) [83]	4	—	IG: 6 CG: 0	—	5 months	—	1	T (+)
Rüttiman, S (2004) [84]	1	—	IG: 1, 2, 3	—	—	—	2	T (+) Ga (+)

Table 3 Interventions to improve antibiotic use in hospital settings (Continued)

Martin, C (2005) [85]	1	Pneumonia Meningitis UTI	IG: 1, 2	—	60 months	—	2	Ga (+)
Solomon, DH (2001) [86]	4	—	IG: 1, 3, 4, 12 CG: 0	4 weeks	18 weeks	—	2, 3	Ga (+)
Fowler, S (2007) [87]	1	—	IG: 1, 3	21 months	21 months	—	2	Ga (+)
Sintchenko, V (2005) [88]	1	Intensive care	IG: 6	6 months	6 months	—	2	T (+) Ga (+)
Yong, MK (2010) [89]	1	Intensive care	IG: 6	30 months	54 months	—	2	Ga (+)
Meyer, E (2010) [90]	1	Intensive care	IG: 2	24 months	36 months	—	2	T (+)
Thursky, KA (2006) [91]	1	Intensive care	IG: 2, 6	6 months	6 months	—	2	T (+) Ga (+)
Petterson, E (2011) [92]	4	UTI	IG = 1, 2, 3 CG = 0	3 months	3 months	—	2, 3	T (+) Ga (+)
Tangden, T (2011) [93]	1	Pneumonia (Intravenous)	IG = 1, 2	7 years	—	2.5 years	3	T (+) Ga (+) (-) ^e
Talpaert, MJ (2011) [94]	1	—	IG = 2	12 months	12 months	—	3	T (+) (-) ^f
Bevilacqua, S (2011) [95]	2	—	IG = 3, 7, 12 CG = 0	12 months	12 months	—	2, 3	Ga (+)
Shen, J (2011) [96]	2	Bronchitis Community acquired pneumonia Acute exacerbation of COPD	IG = 12 CG = 0	—	10 months	—	1	Ga (+)

^aIn [3], the follow-up analysis showed sustained adherence to guidelines in hospital-acquired pneumonia but a decrease in guideline adherence in the case of UTI.

^bIn [75], there was a significant decrease in the proportion of antibiotic orders containing at least one criterion that was not in line with the guideline, but the choice of antibiotics according to the context of acquisition of pneumonia, improvement was not statistically significant.

^cIn [76], total of antibiotics used was similar but the number of orders placed per antibiotic course decreased post-intervention.

^dIn [78], there was a significant decrease in use of total and alert antibiotics, except in the case of ceftriaxone and meropenem.

^eIn [93], there was a reduction of cephalosporines consumption, but piperacillin/tazobactam and penicillin increased

^fIn [94], there was a reduction in fluoroquinolone and cephalosporine but no significant change total of antibiotics neither clindamicine, amoxiciline and co-amoxclav use.

(a) Disease: URTI – upper respiratory tract infections; RTI – respiratory tract infections; ARTI – acute respiratory tract infections; UTI – urinary tract infections; COPD-Chronic obstructive pulmonary disease.

(b) Study design (SD): (1) before/after studies; (2) – nonrandomized controlled trial without cross-contamination control; (3) – nonrandomized controlled trial with cross-contamination control; (4) – randomized controlled trial without cross-contamination control; (5) – randomized controlled trial with cross-contamination control.

(c) IG – intervention group; **CG** – control group.

(d) Type of intervention (TI): (0) no intervention; (1) dissemination of printed/audiovisual educational materials (mailed printed matter; protocols and guidelines; self-instruction materials; drug bulletins); (2) group education, including group-session rounds, conferences, lectures, seminars and tutorials; (3) feedback of physician prescribing patterns (individually or including a comparison of these patterns with peer behavior and/or accepted standards) or feedback of patient-specific lists of prescribed medication; (4) individual outreach visits; (5) reminders at the time of prescribing; (6) computer-assisted decision-making systems; (7) formulary-control/restrictive formulary process; (8) patient education (pamphlets); (9) patient education (videotapes); (10) workshops on rapid tests / introduction of Rapid Antigen Detection Tests (RADTs) in consulting offices; (11) enforcement of regulations; (12) prescription feedback with recommendations to modify it by pharmacists and/or infectious-disease physicians; (13) financial incentives.

(e) Type of data-analysis (T): (1) comparison of post-test values between groups; (2) comparison of pre- and post-values within each group; (3) comparison of pre- and post-values between groups; (4) comparison of follow-up values between groups; (5) comparison of pre-, post- and follow-up values within each group; (6) comparison of pre-, post- and follow-up values between groups.

(f) Results analyzed (R): (T) total antibiotics prescribed/dispensed; (Ga) choice of appropriate antibiotics/adherence to antibiotic guidance according to guideline algorithms, including dosages and routes of administration; (Pa) prescription rate per pathology; (At/Bh) attitudes and behavior; (Qph) quality of pharmacy practice.

session in the intervention group included diagnosis of *otitis media* and information on recommendations for antibiotic use.

Only two studies [51,64], evaluated the efficacy of passive interventions in physicians and in one of them interventions was in combination with educational campaigns directed at patients and their caregivers [51]. All the other studies included active interventions in health professionals (whether or not associated with passive interventions). Three studies [22,46,66], involved active interventions in patients and health professionals, and in four studies [26,33,50,62] the interventions included improvement of doctor-patient communication skills.

Twenty-nine studies (62%) [20-23,25-27,29,34,36-39,41,44,45,47-50,52,53,55,60-65] reported positive results for all outcomes measured; fourteen studies (30%) [24,31,32,35,40,42,43,46,51,54,57-59,66] reported positive results for some outcomes, and results that were not statistically influenced by the intervention for others; only four studies [28,30,33,56] failed to report significant post-intervention improvements for all outcomes.

While some studies conducted no post-intervention follow-up of participants [20,21,23,25,26,29,30,32,34,36,38,39,41,43,44,46,47,54,57-66], others followed up their participants for different periods, ranging from two months [22] to three [27,37,40,42,48-50,56], six [31,33,35,45,53], twelve [24,55] and twenty-four months [28,52].

Interventions that included improving diagnostic procedures to help physicians distinguish bacterial from viral infections led to very positive results [29,41,61,63,65].

Interventions in hospital care professionals

Whereas most interventions concentrated on physicians (Table 1), some included a multidisciplinary intervention targeting physicians and nurses [68,70,76,79,92], patients [80], and in one case, solely pharmacists [83]. Some studies identified the patients targeted, with these being elderly in five instances [68-70,87,92,93] children in three [72,76,82]. Table 3 summarizes the studies retrieved containing interventions for improving antibiotic use in hospital care. The diseases targeted were as follows: pneumonia in four cases [68,75,80,93]; urinary infections in two [70,72]; urinary and upper respiratory tract infections in one [69]; pneumonia, meningitis and urinary infection in one study [85], and bronchitis, community acquired pneumonia and chronic obstructive pulmonary disease in other [96]. Of the thirty-one papers, 6 (20%) studied the efficacy/effectiveness of one or more interventions versus no intervention, using a control group [70,71,73,77,83,86]. Naughton [68] compared two strategies, a multidisciplinary intervention in physicians and nurses, and a physician-only intervention in ten

skilled nursing facilities randomized into two groups, and reported no statistically significant differences between the two groups. Most of the reported hospital-based interventions coincided with the implementation of protocols or new computer systems, with the result that post-intervention were compared with pre-intervention outcomes without the use of control groups.

While some studies [67,73,76,83,87-89] used passive interventions, all the others used active interventions or passive and active simultaneously. Twenty-four papers (78%) [67,69-74,77,79-92,95,96] reported positive results for all outcome measures; 6 papers (20%) [3,75,76,78,93,94] reported some outcomes as positive and others as positive statistically non-significant; and Naughton reported negative results [68].

In contrast to primary care in which only three studies [24,26,32] analyzed clinical outcomes, in hospital care some studies [67,69,70,72,74,81,84,86,96] compared outcomes pre- and post-intervention to assess whether a reduction in antibiotic use might cause clinical alterations, and no influences were observed, namely, to length of hospital stay, and mortality, morbidity and/or readmission rates.

Many of the hospital-care studies highlighted the important role of clinical pharmacists in drawing up and implementing guidelines and policies for antibiotic use in hospital settings [3,67,69,74,75,77-80,82,85,86,91,96].

Studies design

While 25 papers (53%) [21,24,26-28,30,35-38,40,42-44,49,50,53,54,56-59,62,63,65] reported randomized controlled studies in the case of primary care, a far lower number, i.e., 8 (26%) [68,70,73,74,77,83,86,92], reported this type of study in the case of hospital care, and only one of these included cross-contamination control. Cross-contamination can occur when the participants of different intervention or control groups have close working relationships and might share information about the intervention, and this is important because differences in the results between the intervention and the control group may be influenced by this factor. In some studies physicians participated on a voluntary basis (they were invited to participate in the study), and their prescribing habits recorded during the intervention may not represent their real use of antibiotics [24,26-30,33,37,50,61-63,65,70].

There were many differences in the analytical approaches adopted by the different studies: while some compared the results of the intervention with the situation at baseline, and some compared the results between groups pre- and post-intervention, others focused exclusively on the position post-intervention. There were few studies that conducted a follow-up after the intervention

Table 4 Review studies covering interventions to improve antibiotic use

Author (year)	Title of study	Study objectives	Inclusion criteria	Methods	Number of studies included	Review period
van der Velden (2012) [13]	Effectiveness of physician-targeted interventions to improve antibiotic use for respiratory tract infections	To assess the effectiveness of physician-targeted interventions aiming to improve antibiotic prescribing for respiratory tract infections in primary care, and to identify intervention features mostly contributing to intervention success.	Studies with an intervention primarily targeted at physicians in a primary care setting aiming to improve antibiotic prescribing for RTIs, conducted in a high-income country, presenting a standardized outcome of (first choice) prescription measured in defined daily dosage, prescription or rates.	Systematic review of studies published in MEDLINE, EMBASE, and the Cochrane Library. Quantitative analysis to assess the association between effectiveness rates and intervention features.	58	January 1990 through July 2009
Charani, E (2011) [12]	Behaviour Change Strategies to Influence Antimicrobial Prescribing in Acute Care: A Systematic Review	To assess the effectiveness of antimicrobial prescribing interventions that either alone or in combination, aim to influence behaviors in acute care.	Effective Practice and Organization of Care (EPOC) model was adapted to include additional criteria for review of uncontrolled studies. Studies were included only if they were conducted in countries defined as having a developed health care system.	Systematic review of studies published in MEDLINE, Applied Social Sciences Index and Abstracts (ASSIA), Business Source Complete, The Cochrane Library, PsycINFO, and the Database of Abstracts of Reviews of Effectiveness (DARE) and Health Management Information Consortium (HMIC)	10	January 1999 through April 2011
Tonkin-Crine, S (2011) [97]	Antibiotic prescribing for acute respiratory tract infections in primary care: a systematic review and meta-ethnography.	To evaluate general practitioners' perceptions about antibiotic prescribing, and interventions aimed at prudent prescribing.	Studies that used qualitative methods and analysis.	Meta-synthesis of qualitative research examining GP attitudes and experiences of antibiotic prescribing, and interventions aimed at more prudent prescribing for ARTI.	12	1950-May 2011
Kaki, R (2011) [11]	Impact of antimicrobial stewardship in critical care: a systematic review.	To evaluate the evidence for antimicrobial stewardship interventions in the critical care unit.	Studies that evaluate the effectiveness of application of any intervention to improve antimicrobial utilization and within an intensive care setting, using a modified Cochrane Registry EPOC Database inclusion criteria.	Systematic review of studies published in OVID MEDLINE, Embase and Cochrane databases	24	January 1996 through December 2010
Boonacker, CWB (2010) [10]	Interventions in health care professionals to improve treatment in children with upper respiratory tract infections.	To analyze which strategies are used to promote evidence-based interventions in the management of children with URTI and assess the related effectiveness and costs.	Randomized controlled trials, non-randomized controlled trials and controlled before/after studies using implementation methods to change health care professionals' attitudes to the treatment of children with URTI and investigate the effectiveness of implementation strategies.	Systematic review of studies published in Pubmed, Embase and Cochrane Central Register of Controlled Trials.	17	Last search, February 2009
Steinman, MA (2006) [9]	Improving antibiotic selection. A systematic review and quantitative analysis of quality improvement strategies.	To assess which interventions are most effective in improving the prescribing of recommended antibiotics for acute outpatient infections.	Clinical trials with contemporaneous or strict historical controls that reported data on antibiotic selection in acute outpatient infections	Systematic review with quantitative analysis of the EPOC Database, supplemented by MEDLINE and hand-searches	24	Last search, November 2004

had ended, and those which did reported that the majority of positive results observed in the post-intervention period were lost over time.

No studies were found in which the interventions had been designed on the basis of the attitudes and behavior responsible for antibiotic prescribing or dispensing habits, despite the fact that many authors contend that this knowledge contributes to the success of educational interventions in health professionals [69,79,80]. In some studies [28,33,49,79], however, interventions addressed barriers facing the individual prescriber, particularly when it came to dealing with diagnostic uncertainty, and were tailored to: overcoming any identified barriers and enable general practitioners (GPs) to reflect on their own prescribing; helping decrease uncertainty about appropriate disease management and appropriate prescribing; facilitating more patient-centered care; and being beneficial to implementation in practice. One study [39] assessed the impact of interventions on the knowledge, beliefs, and decision-making of primary care physicians, and two others, used workshops and focus-group discussions to determine the possible motivating factors underlying observed prescribing practices [49,62]. The importance of interventions being acceptable to physicians was highlighted by a recent systematic review [97].

All the studies underlined the importance of appropriate use of antibiotics to prevent the problem of microbial resistance, and stated that the most important aim of interventions to improve antibiotic use was to reduce this important public health problem. Even so, only one primary-care [46] and eight hospital-care studies [67,84,85,87,89-91,93] analyzed improvement in bacterial susceptibility during the intervention. While some studies reported the reduction in the cost of antibiotic use, only five studies analyzed the effectiveness of intervention in terms of the cost of the intervention versus the cost of reducing antibiotic use [73,78,81,84,86,96].

We found only two studies that addressed interventions (undertaken in Thailand and Vietnam, respectively) [42,44] specifically designed to improve pharmacists' to combat the dispensing of antibiotics without prescription, despite there were studies which established that the sale of antibiotics without a prescription are a reality in some European countries [98-102]. Although some of the studies reviewed -mainly those pertaining to hospital care- reported the important role played by pharmacists in developing interventions to be undertaken in physicians and implementing antibiotic treatment guidelines and protocols in hospital settings, there were few studies with interventions targeted at pharmacists. Some authors stressed the usefulness of including pharmacists in teams tasked with drawing up recommendations and making decisions about antibiotic use in certain countries [54,96,103,104].

Results obtained by our search showed that the majority of published studies about educational interventions describe active and multifaceted interventions. This finding is in accordance with a number of systematic meta-analyses of randomized controlled trials to improve health care practice, which conclude that highly interactive learning methods, such as educational outreach visits [105] workshops [106,107], small discussion groups [107,108], individualized training sessions [107,108], practice-based interventions [19] and case-based learning [109], are the most effective strategies.

Some recent review papers on interventions to improve antibiotic prescribing [9-11,97] (Table 4) focus on a limited set of intervention targets, such as acute outpatient infections, and more specifically on clinical knowledge and decision-making processes [9], specific populations (children), specific diseases (upper respiratory tract infections) [10] or purpose-designed noneducational (stewardship) interventions in specific hospital divisions, such as critical care [11] and acute care [12]. One paper [97] reviewed studies that evaluated GPs' perceptions about antibiotic prescribing and interventions aimed at prudent prescribing. Our study only analyzed educational interventions but was more extensive, in that it included interventions aimed at physicians and/or pharmacists in both primary-care and hospital settings, and focused on any disease with antibiotic prescribing for child, adult or geriatric patients. In contrast to Steinman [9], who made a quantitative analyses of quality-improvement strategies, our review, like those of Boonacker [10], Kaki [11] and Charani [12], was a qualitative analysis.

As in the case of any systematic review, ours suffers from the limitation of publication bias. The inclusion criteria allowed for the review to cover a wide range of studies with different designs, something hindered us in making comparisons and performing a meta-analysis. Identification of the design proved a complex task, and it is therefore possible that some study may have been misclassified as regards design, due to an incomplete description of the methodology used. In many cases, deficiencies in the design and description of the intervention and identification of the sample made tabulating the study characteristics difficult.

Conclusions

The results yielded by our search show that there are many more papers on educational interventions in physicians than pharmacists. Respiratory disorders were the disease targeted by most studies, mainly in primary care. Published studies varied widely in terms of study design, outcome measures, outcome period, and definition of sample. Most studies used active or a mix of active and passive interventions, and reported that active

interventions were more effective. Notwithstanding these heterogeneity, it can be concluded from the above: first, that educational interventions to improve antibiotic use are essential; and second, that in many studies such interventions are active and multifaceted, some of them include both physicians and pharmacists, and were designed taking these health professionals' attitudes and knowledge into account, in order to focus on the barriers so identified.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

FR, LB, MTH, AF – concept the study and participated actively in the design of the study. FR and SS – performed the bibliographic search. FR, ATR and SS – extract data from the studies. FR, LB, MTH, AF – interpreted and discuss the data. FR writes the manuscript. All authors read and approved the manuscript.

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CAPÍTULO 4

ATTITUDES OF COMMUNITY PHARMACISTS TO ANTIBIOTIC
DISPENSING AND MICROBIAL RESISTANCE: A QUALITATIVE STUDY IN
PORTUGAL

4 ATTITUDES OF COMMUNITY PHARMACISTS TO ANTIBIOTIC DISPENSING AND MICROBIAL RESISTANCE: A QUALITATIVE STUDY IN PORTUGAL

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Resumo

Com este estudo pretendemos explorar a percepção, conhecimentos e atitudes dos farmacêuticos em relação aos antibióticos e às resistências antibacterianas, assim como aos hábitos de dispensa, com o objetivo de recolher informação para desenhar um questionário para usar nos estudos seguintes. Realizou-se um estudo qualitativo na forma de Grupos Focais (FG), na região abrangida pela Administração Regional de Saúde do Norte (ARS Norte), que decorreu entre dezembro de 2010 e março de 2011. Foram convidados a participar no estudo farmacêuticos comunitários dos 5 distritos que pertencem a esta região, tendo-se realizado seis FG com 4 a 7 farmacêuticos cada, nos distritos onde trabalhavam os farmacêuticos que participaram. Após revisão bibliográfica, desenvolveu-se um guião que foi usado pelo moderador para guiar as discussões durante as sessões. No início de cada sessão os participantes assinaram um consentimento informado, após serem informados acerca do estudo, quais os objetivos e de que as sessões iriam ser gravadas. Para evitar enviesamentos de interpretação, as gravações foram transcritas por um investigador diferente do moderador, e foi atribuído um código a cada sessão para que a informação fosse tratada sem identificar os participantes. Os farmacêuticos conhecem o problema das resistências bacterianas quer em cuidados de saúde primários quer em ambiente hospitalar e têm a percepção que é um importante problema de saúde pública resultante e relacionado com o uso excessivo e inadequado de antibióticos devido à prescrição inadequada, à automedicação e também à não adesão ao tratamento por parte dos doentes. Todos os farmacêuticos atribuíram o problema das resistências a causas externas, incluindo doentes, médicos, outras farmácias e consumo em veterinária. Relativamente às atitudes relacionadas com os hábitos de dispensa de antibióticos, em particular com a prática de dispensa de antibióticos sem receita médica, foram identificadas a complacência com o doente, a responsabilidade externa, e precaução. Os farmacêuticos tinham a percepção de que têm um papel importante no combate às resistências bacterianas e a maioria defende uma

maior interação entre médicos e farmacêuticos nos cuidados primários e entre cuidados de saúde primários e cuidados hospitalares e são de opinião que deveriam existir intervenções educativas nos profissionais de saúde e na população em geral sobre o uso de antibióticos e as resistências bacterianas.

Attitudes of community pharmacists to antibiotic dispensing and microbial resistance: a qualitative study in Portugal

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Abstract *Background* The inappropriate use of antibiotics is considered a main cause of microbial resistance. This is an important public health problem. Community pharmacists have an important role in the management of drugs for outpatients. *Objective* Our study sought to explore pharmacists' knowledge, attitudes, perceptions and dispensing habits insofar as to antibiotics and microbial resistance. *Setting* The study was developed with community pharmacists in the North of Portugal. *Methods* Qualitative research in the form of focus groups (FG). Focus groups were conducted with 4–7 pharmacists, using a moderator. A topic guide was developed to lead the discussions, which were audio-recorded and transcribed. The study was carried out between December 2010 and March 2011 in the five districts of the Northern Health Region of Portugal (ARS-N). Pharmacists from different regions of each district were invited to participate in the study by an investigator responsible for the study. Participants were informed about the study and that sessions were

audio-recorded to facilitate data interpretation. They signed an informed consent form before taking part in the focus groups. The Ethical Committee of ARS-N was informed of this study. *Main outcome measure* Pharmacists' knowledge and perceptions on antibiotic use and microbial resistance, attitudes related to antibiotic dispensing habits, and pharmacists' suggestions to improve antibiotic use. *Results* A total of 6 focus groups were conducted with community pharmacists (n = 32). Attitudes related to the problem of resistance were attributed external responsibility, to patients, to physicians, to other pharmacies, and to veterinary consumption. Some attitudes were identified that could lead to antibiotic dispensing without a prescription. These attitudes are complacency, precaution and external complacency. *Conclusions* Portuguese pharmacists perceive that antibiotic use and bacterial resistance could be improved, showing a behavioural intention to improve antibiotic dispensing habits.

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Keywords Antibiotic dispensing · Antimicrobial drug resistance · Community pharmacists · Pharmacist attitudes · Portugal · Qualitative study

Impact of findings on practice

- A tailored interventions should be developed to improve the quality of pharmacists' practices related to antibiotic dispensing.
- Portuguese pharmacists are aware of the risks of resistance, when dispensing antibiotics.

Introduction

In recent decades, antibiotic resistance has become one of the main public health problems worldwide. Resistance is directly associated with increased use of antimicrobial drugs, thereby leading to a major clinical and public health problem [1–8]. As antibiotics become less effective due to the increased number of organisms that develop antibiotic resistance, the threat to disease management increases [2, 4]. The problem of antibiotic resistance leads to consequences such as increased health-treatment costs and a rise in new adverse reaction to antibiotics [9, 10].

Some factors have been indicated as the main causes of antibiotic resistance, and inappropriate use of antibiotics [2, 5, 11–14] is regarded as one of these. This incorrect use can be ascribed to both health professionals and consumers. Excessive use of antibiotics is attributed to inappropriate prescription by physicians and self-medication (particularly the use of leftover antibiotics from previous courses of treatment and acquisition from pharmacies without a prescription). These are three, potentially modifiable factors that would enable resistance to be reduced.

Given that self-medication is now a reality in Europe, especially in countries to the south and in the east [15, 16], possible forms of intervention should include pharmacists [17]. In Portugal, antibiotics may only be dispensed by community pharmacies under medical prescription, which means that actions to improve antibiotic use and combat self-medication must necessarily include community pharmacists.

Aim of the study

This study sought to explore pharmacists' knowledge, attitudes, perceptions and dispensing habits with respect to antibiotics and microbial resistance, with the aim of collecting information so as to design a questionnaire for use in further studies.

Methods

Study design

Qualitative research, in the form of focus groups (FGs), was designed to explore the knowledge and attitudes of pharmacists with regard to antibiotic resistance, dispensing and consumer demand. Focus groups are a type of group interview which enables researchers to collect qualitative data [18, 19]. This informal discussion about a particular topic, led by a moderator, with participants who share similar characteristics or common interests [18–20] and following a guide with a series of questions, helps to keep the discussion flowing and enables all the group members to participate, by not allowing one person to overshadow another [18–20]. This methodology is important as an exploratory research technique for obtaining data on a specific research subject [20]. We decided to use focus groups because they allow for interaction with all the group members and discussion based on personal experience and subjective points of view, so ensuring that all dimensions of the problem are debated [18, 21].

A topic guide was constructed, based on a review of the literature and a previous study with physicians [21], to facilitate identification of pharmacists' attitudes to antibiotics, bacterial resistance and dispensing habits (“Appendix”). Information in this guide was grouped into the following three categories: (1) knowledge and perception of antibiotic use and resistance; (2) antibiotic dispensing process; and (3) suggestions for improving antibiotic use.

Study population and sample selection

The study was conducted in a NUTS II (*Nomenclatura das Unidades Territoriais para Fins Estatísticos*/Nomenclature of Territorial Units for Statistics) area of Portugal defined by the Northern Regional Health Administration (*Administração Regional de Saúde do Norte/ARS-N*), which includes five geographical districts. To obtain information on all geographic areas, focus-group sessions were carried out in the five districts, from December 2010 to March 2011.

Pharmacists working in community pharmacies in the ARS-N defined area and drawn from different regions of each district were invited by the study's principal investigator (MTH) to participate in focus-group sessions. Participation of all pharmacists was on a volunteer basis, without any incentives.

Procedures

Focus groups were conducted with 4–7 pharmacists, using a pharmacist investigator (FR) as a moderator, who

followed the purpose-designed topic guide but allowed the discussion to flow for 60–90 min until there were no more new ideas. Participants were informed about the study and as to the fact that sessions were being sound-recorded to facilitate data interpretation. They were told that all content was confidential and that, in general, the data would be handled and processed without any of the participants being identified. Pharmacists signed an informed consent form before taking part in the focus groups, and the ARS-N was informed of the study. To avoid any possible interpretation biases, the audio-taped FGs were transcribed by a different investigator (SS), who was not a pharmacist and who coded the FG sessions with serial numbers (FG1, FG2, FG3, FG4, FG5 and FG6). The method used by the researcher for literal transcription was to listen to the tape and take notes. Four weeks after the last hearing of the tape, the same researcher played the tape once again, and the transcription was deemed to be concluded.

Analysis

Transcriptions were analysed by two researchers who identified and took note of the different ideas from each group. The information retained was discussed by the researchers and was classified into different pre-defined categories, in order to process the results. We chose not to use computerised analysing software because this is useful for analyses involving a larger number of interviews, which was not the case here.

Results

A total of six FGs were conducted with 32 pharmacists, 28 women and 4 men, in the five districts of Portugal's Northern Health Region. In one district (with biggest geographical dispersion), two FG sessions were held, with the aim of obtaining a total sample of over 30 pharmacists, in the line to literature [18, 22, 23], and other similar studies [21].

Knowledge and perception of antibiotic use and microbial resistance

All groups identified resistance to antibiotics as an important public health problem, even in primary care, but considered it to be a greater problem in hospital settings. Resistance to antibiotics in the case of urinary infections (all FGs), odontology (FG3) and otitis (FG3) was identified. All pharmacists mentioned that patients exerted great pressure on health professionals, such as physicians and pharmacists, to obtain antibiotics (FG1, FG4, FG5): "... patients think that antibiotics solve all their problems ..." and "... many people use

pharmacy as a first resort to solve their health problems, and when they think that an antibiotic is necessary, they often ask the pharmacy for it and insist that we supply it...". Some pharmacists (FG3; FG4; FG5) commented, "... they insist on obtaining an antibiotic... but when we explain the consequences of using an unnecessary antibiotic, some patients understand and don't insist anymore. But if we just said no, without providing an explanation relating to their health... they would insist and think that we didn't believe them". Another participant stated, "... I did not sell an antibiotic without a prescription and the patient then came back to show me the box he purchased at another pharmacy ...". In FG4, one pharmacist said, "... one mother told me, very angrily, that I made her spend the entire afternoon with her son in the hospital... and the physician prescribed the antibiotic she wanted ...". The most common situations giving rise to this demand for antibiotics are respiratory infections and more specific infections, such as tooth and urinary infections. Topical ophthalmic use was observed (FG4) to be an important problem that warranted discussion by professionals and the scientific community, "... patients with recurrent conjunctivitis insist on buying ointments containing antibiotics and they never go to the doctor ... this is an important problem, and nobody worries about this...consequences of this must be investigated ..."

Factors associated with development of resistance to antibiotics

Pharmacists identified the following four factors as being the main causes of resistance: (1) self-medication with leftovers from previous treatment, and/or acquisition of antibiotics at certain pharmacies without a prescription; (2) patients' non-compliance with the prescribed dosages; (3) excess/inadequate antibiotic prescription by physicians; and (4) excessive use of antibiotics in animals used for human consumption, without respecting withdrawal periods. An important cause was reported (FG5) to be the fact that physicians often prescribed inadequate dosages, while another group (FG3) mentioned the absence of the dosage in the prescription as a problem, "The prescription does not always include the dosage ... and we can only advise the patient on the standard dosage... we do not know the severity of the infection ... and the correct dosage depends on the severity ...".

One group (FG4) identified drug interactions with alcohol as an important cause and went to state that, when they informed patients that alcohol might interfere with the antibiotic activity, some chose to stop the treatment, "... alcohol consumption is also a problem... interactions between alcohol and antibiotics could increase resistances ... we advise patients for alcoholic risks, and many times they refuse stop drinking ...". Excessive prescription of the

newer generation of antibiotics was reported by another group (FG5) as being the main reason for the emergence of multiresistance.

One important factor mentioned by FG2 was the fact that the presence of antibiotics in domestic waste continues to occur because not all patients make a practice of returning surplus or expired medicines to the pharmacy. This situation contributes greatly towards resistance in the environment, which affects everyone.

All pharmacists attributed the problem of resistance to external causes, including patients, physicians, other pharmacies and veterinary consumption.

Antibiotic dispensing process

In all groups, pharmacists said that they were under pressure to dispense antibiotics without a prescription, and they all identified a number of factors which they perceived as contributing to this demand (Table 1). The main reasons identified by pharmacists for patients demanding antibiotics without a prescription and pressuring pharmacists into selling these could be broken down into two categories: one was linked to patients' lack of knowledge about antibiotics, inasmuch as they believed that antibiotics were the cure for everything and that previously taken antibiotics could be used for similar situations without the need for medical diagnosis; and the other was linked to patients' socio-economic situation, inasmuch as pharmacists in some FGs mentioned that patients demanded antibiotics without a prescription because they could not afford fees or private medical consultations, and could not miss work to see a doctor (Table 1).

When dispensing habits were discussed, pharmacists were under the impression that some pharmacies sold antibiotics without a prescription, yet they felt that this situation was becoming less widespread because the new generation of pharmacists was more sensitive to the issue and the population was generally more receptive to pharmacists' information. There were some specific situations, however, which pharmacists recognised as contributing towards antibiotics being dispensed without a prescription, both by others and themselves (Table 2). They identified some clinical situations in which they acknowledged having occasionally dispensed antibiotics without a prescription; this mainly occurred in cases where they knew the patient personally, and where the patient often brought the prescription to them at a later point in time.

Two focus groups (FG1, FG6) admitted that attitudes towards known patients tended to be different because pharmacists knew the individual patient's history and could expect the prescription to be handed in later. In FG3, this situation was recognised in the case of recurrent tonsillitis.

Table 1 Factors that lead to patient demand for antibiotics without a prescription

Factors	Reported by
Patients recognise and request specific antibiotics that were effective in a previous situation	FG1; FG2; FG3; FG6
Belief that an "antibiotic is the cure for everything"	FG1; FG4; FG5
Difficult access to health care	FG1; FG3; FG4
Patients cannot miss work (docked from salary)	FG1; FG3
Patients have no money to pay fees or private medical consultations	FG1; FG2; FG4
Antibiotics for travelling	FG4; FG5; FG6

FG focus group

Table 2 Factors that pharmacists recognised could lead them to dispense an antibiotic without a prescription

Factors	Reported by
Lack of packages for a complete treatment	All
Prescription over the telephone	All
Known patient/clinical history, such as recurrent tonsillitis (patients bring prescriptions later)	FG1; FG3; FG6
For specific infections, such as tooth and urinary infections (they know that doctors will prescribe)	FG3

FG focus group

Although one of the factors most cited as increasing resistance was patient non-compliance, all pharmacists claimed that, when dispensing antibiotics, they were in the habit of urging patients to comply with the treatment regimens. None however expressed any intention of monitoring patients. Pharmacists acquired their perception of non-compliance with antibiotic treatment in cases where patients came to the pharmacy requesting antibiotics to continue a course of treatment initiated with leftovers from a previous prescription, or patients returned packages of antibiotics to the pharmacy on the expiration date.

At some sessions (FG4; FG5) pharmacists relayed the importance of the practice of warning patients about the interactions between antibiotics and other drugs.

Insofar as generic drugs were concerned, pharmacists considered that neither these, nor the selection of active substance, nor dispensing habits had any influence on the increase in the consumption of antibiotics. Some pharmacists (FG3; FG4) noted, however, that the lower prices of generics could have the advantage of influencing treatment compliance.

Suggestions for improving antibiotic use

Lastly, we recorded suggestions for improving antibiotic use (Table 3). Pharmacists felt that community microbial-resistance studies were called for and that discussing these issues with all the stakeholders involved was vital for improving antibiotic use. Participants reported that there was little communication between physicians and pharmacists, and between primary care and hospital settings.

Discussion

This is the first qualitative study to be conducted in Portugal with the aim of exploring pharmacists' knowledge of and perceptions about antibiotic use and microbial resistance. The results obtained enable pharmacists' attitudes relating both to the perception and attribution of the problem and to dispensing habits, to be identified. The problem of resistance was ascribed to external causes, including patients, physicians, other pharmacies and veterinary consumption. Self-medication with leftovers and non-compliance with the recommended treatment were attributed to patients. These causes have been pinpointed by various authors [3]. A further factor mentioned by pharmacists was the fact that some patients dispose of antibiotics along with their domestic waste. Although no studies have been conducted to evaluate the impact of antibiotics contained in household waste, the presence of wastewaters with antibiotics was evaluated by a Portuguese study [24] in which the authors analysed the presence of tetracyclines in four samples of hospital wastewater effluent and their eventual status in municipal wastewater

treatment plants (WWTPs). Minoxiline and tetracycline were found in 41.7 % of the samples; epitetracycline and doxycycline were found in 25 and 8.3 % of the samples, respectively. Their WWTP removal rate ranged from 89.5 to 100 % [24].

Pharmacists are of the opinion that the main factor associated with resistance is the great number of prescriptions, along with the prescribing of new-generation drugs, an external factor attributed to physicians. It is interesting to compare these pharmacists' views to physicians' attitudes studied in Spain, where the latter attributed the problem of resistance to pharmacist sales without a prescription [21]. Comparison of our results to those obtained from the Spanish study would seem to show that an important attitude common to all health professionals is that of attributing responsibility for resistance-related problems to others. In a recent review [25] of attitudes to antibiotic misprescription, the authors identified the responsibilities of others as a factor underlying misprescription, and went on to say that this factor motivates the belief that other professionals are responsible for generating antibiotic resistance. This similarity between pharmacists and physicians could explain the findings obtained in previous studies, namely, that self-medication and prescription are practices affected by the same cultural dimensions [26], thereby suggesting that in countries with a higher incidence of self-medication with antibiotics, the prescription rate is also high [16]. Inappropriate use of antibiotics in a population can substantially increase with change of location [27], which shows that attitudes to and habits of prescribing and dispensing medicine have an important role in antibiotic use. A recent study [2] revealed discrepancies in physicians', pharmacists' and nurses' respective levels of awareness as to frequently encountered resistance and the strategies available for limiting this phenomenon. In another study [28], pharmacists were more concerned about antibiotic resistance than were physicians, but the physicians' and pharmacists' knowledge of and beliefs about the effects of antibiotics were nevertheless very similar.

Among the attitudes to dispensing habits encountered by this study, those specifically relating to the dispensing of antibiotics without a prescription were attributed to external responsibility, complacency and precaution. External responsibility was variously ascribed to the health system, to physicians and to patients. When attitudes specifically relating to dispensing quality and information given to patients were considered, a positive attitude was observed with regard to informing patients, while engaged in dispensing, about the need for therapeutic compliance. However, there was an attitude of indifference, both to achieving patient compliance once the customer had left the pharmacy and to identifying possible interactions

Table 3 Recommendations proposed by the different Focus Groups for improving antibiotic use

Factors	Reported by
Periodic determination of resistance in the community	FG1; FG3
Regulatory measures to avoid prescription of new molecules	FG5
Disclosure of new antibiotic resistance and hospital studies to primary health care professionals	FG1
More interaction between pharmacists and physicians in pharmacotherapy decisions, and between primary care and hospitals	FG1;FG3; FG5
More control of antibiotic dispensing without a prescription	FG3; FG2
More information and awareness about the impact of antibiotics for animals	FG1; FG5
Educational intervention for health professionals and for the population	All

FG focus group

between antibiotics and other drugs in the same patient. One Portuguese-based study [29] into university students' attitudes to antibiotic use showed that their perceptions about antibiotic compliance was incorrect, which in turn may mean that the information conveyed by pharmacists and physicians had not been properly understood by these patients. This could be attributed to the above-mentioned indifference of pharmacists who did not carry out any type of follow-up of patients during their antibiotic treatment.

As reported in earlier studies [30], pharmacists tend to differentiate between well-known and unknown customers, mainly in recurrent situations, such as tonsillitis, and in clinical situations (dental and urinary infections) where, pharmacists argue, physicians will definitely prescribe antibiotics. The prescribing of antibiotics in these clinical situations has been widely discussed in the literature [31–33], and has revealed the need for educational interventions for physicians and pharmacists aimed at improving antibiotic use.

In recent decades, the professional activity of the community pharmacist has changed dramatically, as has the role of the community pharmacy. A considerable number of patients see pharmacists as first-line health professionals for solving their problems, and they exert great pressure on such pharmacists to obtain antibiotics without a prescription. In line with other European studies [9, 34], all FGs mentioned that illegal antibiotic dispensing without a prescription is still a reality. In our study, however, pharmacists felt that this was not as commonplace as it had been 5 years previously. A factor which has contributed towards this improvement in the quality of pharmaceutical care is the increase in the number of licensed pharmacists and the improved training of pharmaceutical technicians.

Pharmacists acknowledged that the relationship with physicians is very complex and that cooperation between these professions, in primary care, is very low. This is an issue reported by some authors [35]. Some pharmacists feel that a better relationship between health professionals, with periodic discussions about patient-related problems, coupled with the intervention of pharmacists in pharmacotherapy decision-making, could improve antibiotic use. Cooperation in primary care between physicians and pharmacists has yielded successful outcomes in the management of some diseases [35–39]. The important role of the pharmacist is cited by Coenen [40] as being one of the factors responsible for better use of antibiotics in the Netherlands than in Belgium, since in Belgium pharmacotherapy is not discussed on a regular basis in local groups involving pharmacists as it is in the Netherlands. Additionally, consumption in Belgium is nearly three times that of the Netherlands [41].

Our study has some limitations, which include specific limitations relating to the use of a qualitative study and the

fact that the pharmacists' discussion could be biased in view of their tendency to provide legally acceptable answers. Moreover, the low number of participants plus the fact that the focus group sessions were solely in the Northern Region of Portugal, mean that the study's conclusions cannot be freely generalised to other countries.

Conclusions

Some of the pharmacists interviewed were aware of their important role in fighting antibiotic resistance. This exploratory study enabled us to identify pharmacists' attitudes to the problem of antibiotic resistance and dispensing practices, and led pharmacists to reflect on their behaviour during the dispensing process. It was suggested that information on community-based resistance measures and enhanced interaction between physicians and pharmacists could improve antibiotic use.

The results obtained from this study are important for designing a questionnaire to assess pharmacists' attitudes and subsequently developing tailored interventions to improve the quality of pharmacists' antibiotic-dispensing practices.

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Conflicts of interest The authors declare that they have no conflicts of interest.

Appendix

Moderator's guide for focus groups

- “What are your opinions about the latest campaigns on the correct use of antibiotics? (latest years, type of campaign—pamphlets in pharmacies, television advertisements).”
- “Are there pharmacists that dispense antibiotics without a prescription? What about 5 years ago? Were there any?”
- “What are the causes of antibiotics being dispensed without a prescription? In case of no answer being forthcoming, specify:

- Difficult access to health care.
- Patient pressure. Aggressive attitudes, excuses such as they cannot miss work, travelling issues, patients known in the neighbourhood.
- Is pharmacists' behaviour towards a known patient different from that towards an unknown one? And towards a young patient versus an elderly patient?
- Are younger pharmacists more likely to ask for a prescription than older professionals?
- If the antibiotics are not sold at this pharmacy, can customers get them somewhere else?
- Will you dispense the antibiotic with the customer's commitment to bring you the prescription later?
- To maintain customers.
- In order to save time because you know that the doctor will prescribe it.
- Do you believe that there is some influence from the pharmaceutical industry?
- The antibiotic is dispensed because the prescription for the needed treatment was incomplete.
- Antibiotics were prescribed over the telephone.
- What can you say about antibiotic use on animals?"
- "Do you consider that the importance of antibiotic use is conveyed to patients? Do you think that recent graduate students are more or less aware of this transmission of information? What about pharmaceutical technicians?"
- "Do you believe that dispensing generics has any advantages?"
- "In your opinion, what is the percentage of pharmacies that sell antibiotics without a prescription?"
- "Out of every 10 boxes of antibiotics sold at your pharmacy, how many are sold without a prescription?"

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CAPÍTULO 5

**PORTUGUESE COMMUNITY PHARMACISTS, ATTITUDES TO AND
KNOWLEDGE OF ANTIBIOTIC MISUSE: QUESTIONNAIRE
DEVELOPMENT AND RELIABILITY**

5 PORTUGUESE COMMUNITY PHARMACISTS, ATTITUDES TO AND KNOWLEDGE OF ANTIBIOTIC MISUSE: QUESTIONNAIRE DEVELOPMENT AND RELIABILITY

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Resumo

Neste trabalho pretendeu-se, a partir dos dados obtidos no estudo qualitativo, construir um questionário que fosse válido para identificar as atitudes e conhecimentos dos farmacêuticos comunitários em relação às resistências microbianas e aos hábitos de dispensa de antibióticos. Após a construção do questionário, procedeu-se a dois estudos, com o objetivo de (i) avaliar a validade de face e conteúdo do questionário, utilizando um painel de peritos e realizando um pré-teste com 10 farmacêuticos comunitários e, (ii) avaliar a fiabilidade e reprodutibilidade, através de um estudo piloto que consistiu num teste reteste em 50 farmacêuticos pertencentes aos 5 distritos da região norte de Portugal. A reprodutibilidade foi quantificada através do Coeficiente de Correlação intraclasse (ICC; 95% intervalo de confiança). A consistência interna foi avaliada pelo alfa de Cronbach's. Os coeficientes de correlação variaram entre suficiente e bom para todas as frases (ICC>0,4) relativas ao conhecimento e atitudes em relação às resistências e uso de antibióticos, e, variou entre bom e excelente na secção com frases sobre situações com as quais os farmacêuticos concordavam que os antibióticos podiam, por vezes, ser dispensados sem receita médica (ICC>0,8). O alfa de cronbach's para esta secção é de 0,716. Obteve-se um questionário fiável, reprodutível e válido para determinar as atitudes e conhecimentos dos farmacêuticos relacionados com as resistências bacterianas, o uso de antibióticos e a propensão dos farmacêuticos para dispensa de antibióticos sem receita médica.

Portuguese Community Pharmacists' Attitudes to and Knowledge of Antibiotic Misuse: Questionnaire Development and Reliability

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Abstract

Objective: To develop and evaluate the reliability of a self-administered questionnaire designed to assess the attitudes and knowledge of community pharmacists in Portugal about microbial resistance and the antibiotic dispensing process.

Methods: This study was divided into the following three stages: (1) design of the questionnaire, which included a literature review and a qualitative study with focus-group sessions; (2) assessment of face and content validity, using a panel of experts and a pre-test of community pharmacists; and, (3) pilot study and reliability analysis, which included a test-retest study covering fifty practising pharmacists based at community pharmacies in five districts situated in Northern Portugal. Questionnaire reproducibility was quantified using the intraclass correlation coefficient (ICC; 95% confidence interval) computed by means of one-way analysis of variance (ANOVA). Internal consistency was evaluated using Cronbach's alpha.

Results: The correlation coefficients were fair to good ($ICC > 0.4$) for all statements (scale-items) regarding knowledge of and attitudes to antibiotic resistance, and ranged from fair to good to excellent for statements about situations in which pharmacists acknowledged that antibiotics were sometimes dispensed without a medical prescription ($ICC > 0.8$). Cronbach's alpha for this section was 0.716.

Conclusions: The questionnaire designed in this study is valid and reliable in terms of content validity, face validity and reproducibility.

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Introduction

The emergence and spread of microbial resistance to antibiotics is an important public health problem and has been linked to increased and inappropriate use of antibiotics worldwide [1,2]. This misuse of antibiotics, including self-medication, is known to contribute to infections with antibiotic-resistant micro-organisms, leading in turn to a rise in hospitalisations, length of hospital stays, mortality and health-care costs [3].

A review of antibiotic self-medication in Europe [4] repeatedly found high prevalences of self-medication in South and East European countries along with high levels of antibiotic resistance. Two major sources and practices involving self-medication were identified [4], namely: (1) over-the-counter dispensing of systemic antibiotics by community pharmacists; and, (2) the use of leftover antibiotics from previous treatments, resulting either from patients'

non-compliance or from a larger number of tablets than needed being dispensed.

In Portugal, antibiotics may only be legally dispensed by community pharmacies under medical prescription. Although no studies could be located which specifically addressed the prevalence of self-medication with antibiotics and their acquisition from pharmacies without a medical prescription, a number of population-based studies show that this does indeed exist [5,6].

It therefore follows that effective actions to improve antibiotic use and combat self-medication must necessarily include community pharmacists. This being so, it thus becomes essential to ascertain community pharmacists' knowledge of and attitudes to microbial resistances and antibiotic use, so that the pertinent educational interventions can be tailored to the task. No published, validated instrument designed for use on community pharmacists

was however found. Accordingly, the aim of this study was to develop and assess the reliability of a self-administered questionnaire, purpose-designed to elicit the knowledge and attitudes of community pharmacists in Portugal about microbial resistance and the antibiotic dispensing process.

Methods

Ethics statement

Authorisation for this study (Permit No. 2886/2013) was obtained from the Portuguese Data Protection Authorities (*Comissão Nacional de Proteção de Dados/CNPD*). Written informed consent was obtained from all pharmacists who participated in the focus group study. As Portuguese community pharmacies are private entities, agreement to participate in the pilot study was obtained from the individual pharmacists, by sending them a cover letter explaining the study and asking them to complete and sign the accompanying questionnaire.

Study population and sample selection

The study was conducted in a NUTS II (*Nomenclatura das Unidades Territoriais para Fins Estatísticos/Nomenclature of Territorial Units for Statistics*) area of Portugal defined by the Northern Regional Health Administration (*Administração Regional de Saúde do Norte, I.P./ARS-N*), and the target population included practising pharmacists based at community pharmacies in five Northern Portuguese districts (Braga, Bragança, Porto, Viana do Castelo and Vila Real).

Questionnaire design

To obtain attitude scale-items, a qualitative study was conducted: this took the form of focus-group sessions held with community pharmacists to explore their perceptions, attitudes and knowledge about microbial resistance and antibiotic use [7]. The topic guide for this qualitative study with pharmacists was based on a review of the literature [7].

Face and content validity

Two clinical psychology experts and one Portuguese language expert evaluated face-validity parameters, such as the grammar, syntax, organisation, appropriateness and logical sequence of the statements [8].

Content validity was assessed by an expert panel consisting of three pharmacologists and three specialist pharmacists (the latter being a grade awarded by the Portuguese Pharmaceutical College). This appraisal stage [9] is fundamental for assessing the accuracy, clinical terminology, completeness and meaning of items.

To clarify possible problems of comprehension with any questionnaire item, a pre-test was conducted on ten community pharmacists, who were invited to complete the questionnaire and comment on any difficulties experienced in interpreting the respective items.

Pilot study and reliability analysis

A test-retest study was conducted using a convenience sample of 50 community pharmacists drawn from all districts in Portugal's Northern Region. Questionnaires were delivered together with a cover letter, outlining the study objectives and highlighting the importance of each pharmacist's participation.

To assess reliability [10], questionnaires were delivered to each pharmacist twice, at an interval of two to four weeks, in line with the scientific literature [11] and previous studies [12].

Statistical analysis. Questionnaire reproducibility (degree of agreement among answers) was quantified using the intraclass correlation coefficient (ICC; 95% confidence interval) [13,14] computed by means of one-way analysis of variance (ANOVA) [10].

The internal consistency of the group of questions on the dispensing of unprescribed antibiotics by pharmacists, was evaluated using Cronbach's alpha [15,16].

Results

The different stages of the study and the outcomes obtained at each stage are shown in Figure 1.

Questionnaire design

The six focus-group sessions that were held during the qualitative study and involved a total of 32 pharmacists, enabled us to explore pharmacists' perceptions, knowledge and attitudes about microbial resistances and antibiotic use [7].

Data collected from this qualitative study were used to draw up a structured questionnaire containing scale-items that reflected pharmacists' attitudes to and knowledge of microbial resistance, antibiotic use and the antibiotic dispensing process.

The questionnaire obtained at this stage was one sheet long (two pages), divided into the following five sections: Section 1, containing a box with instructions on how to complete the form; Section 2, containing nineteen statements (scale-items) regarding pharmacists' attitudes to and knowledge of microbial resistance and antibiotic use, followed by a horizontal, continuous visual analogue scale (VAS) for respondents to mark with a cross; Section 3, containing four statements about the process of dispensing antibiotics without a medical prescription, followed by a VAS for respondents to mark with a cross; Section 4, containing personal and professional data, such as age, gender, workplace, job function and mean number of antibiotics dispensed; and, Section 5, containing a request to professionals to make suggestions about antibiotic use and microbial resistance.

Face and content validity

Clinical psychology and Portuguese language experts assessed the grammar, syntax, organisation, appropriateness and logical sequence of scale-items. Initially, Section 2 of the questionnaire contained 19 statements but after evaluation by the experts, 6 statements were redrafted and 2 statements were deleted. The statements deleted were, "Antibiotics are over prescribed" and "In situations where the patient is known, antibiotics may sometimes be sold without a medical prescription", because the experts felt that these two items were already included in other statements and in Section 3.

Expert pharmacologists and specialist pharmacists evaluated the accuracy, clinical terminology, completeness and meaning of all questions, and considered that the questionnaire was well constructed and included important issues, such as therapeutic compliance and drug-drug interactions that could influence the development of resistance.

The statement S11, "When antibiotics are returned to Valormed, patients should be alerted to the consequences of not complying with the treatment", gave rise to several problems: the clinical psychology expert did not understand the qualitative meaning of the statement, and of the ten pharmacists who completed the questionnaires designed to assess respondents' comprehension of each statement, two commented that the content of a Valormed bag cannot be evaluated (seen or commented upon) by pharmacists at the time it is delivered (Valormed is a Portuguese system which is available at Portuguese

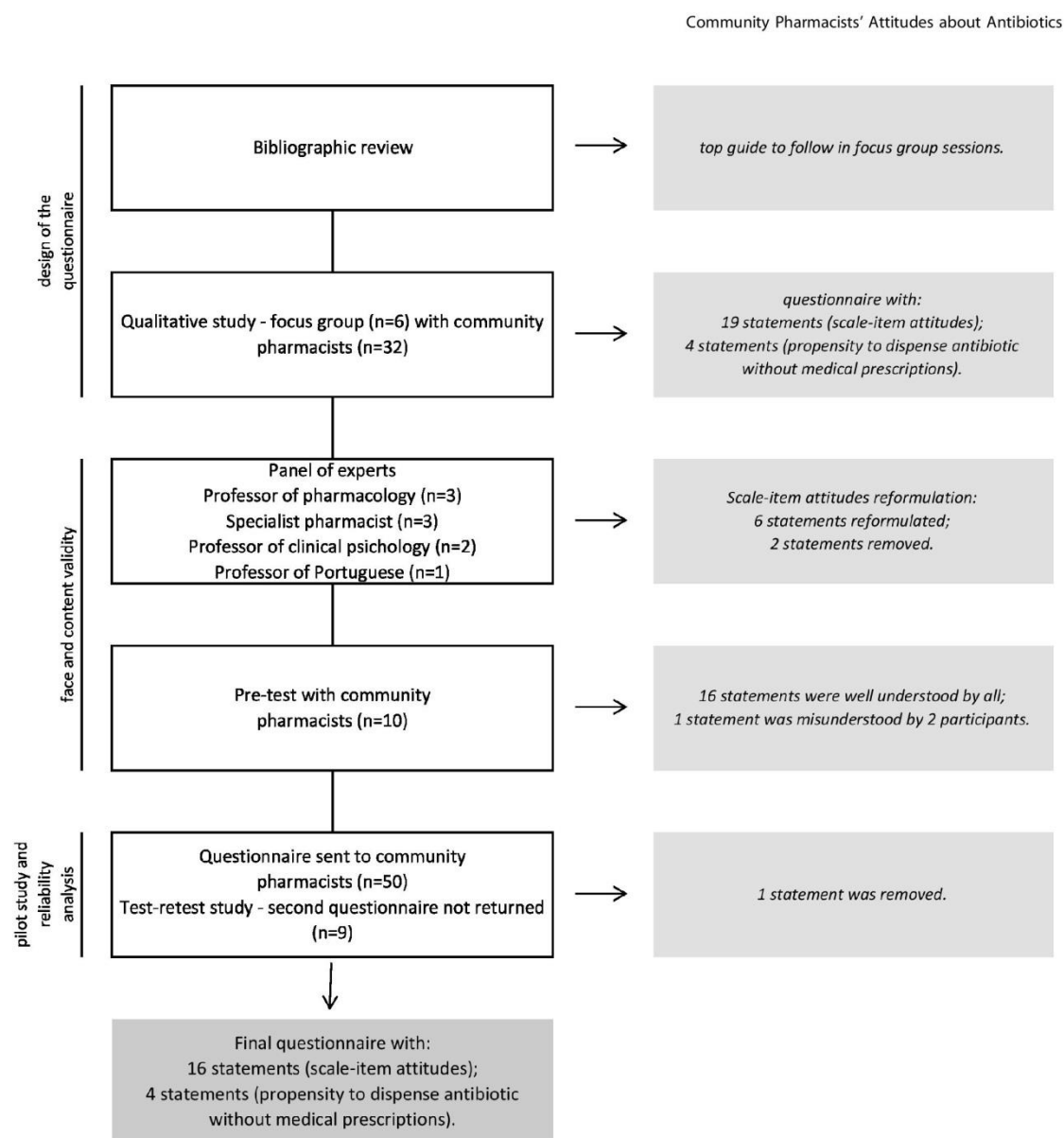


Figure 1. Flow Chart.

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pharmacies for collecting medicinal packaging and unused or expired medicines).

Even so, it was decided that, since the statement sought to respond to a major concern raised by those participating in the focus-group sessions, it would not be deleted but would instead be maintained during the pilot study.

Pilot study and reliability analysis

Of the 50 pharmacists initially invited, 41 completed the study (82%), and 9 (18%) did not complete the questionnaire used for retest purposes.

Reproducibility. ICCs were determined for all the statements contained in Sections 2 and 3 of the questionnaire (Tables 1 and 2).

The correlation coefficients for statements in Section 2 (Table 1) exceeded 0.4 ($p < 0.05$) for all attitudes, and ranged from 0.439 ($p < 0.01$) (statement S15: "Antibiotic prescribing should be more closely controlled") to 0.796 ($p < 0.001$) (statement S16: "Dispensing antibiotics without prescription should be more closely controlled").

The correlation coefficients for statements in Section 3 relating to antibiotic dispensing without a prescription (Table 2) exceeded 0.4 ($p < 0.05$), and ranged from 0.454 ($p < 0.05$) to 0.860 ($p < 0.001$).

Table 1. Intraclass correlation coefficients (ICCs) assessed for pharmacists' attitudes (Section 2 of the questionnaire).

Statements about knowledge of and attitudes to microbial resistance to antibiotics	ICC (95% CI)	p-value
S1: Antibiotic resistance is an important Public Health problem of ours.	0.778 (0.586–0.881)	<0.001
S2: The fact of a patient taking an antibiotic increases the risk of developing resistance.	0.777 (0.576–0.882)	<0.001
S3: In all cases where antibiotics are dispensed, it is essential that patients be advised about complying with the treatment.	0.678 (0.389–0.830)	<0.001
S4: An important cause of appearance of antibiotic resistance is long-term prescription of new molecular entities.	0.789 (0.606–0.887)	<0.001
S5: When dispensing, possible interactions between the antibiotic and other drugs that the patient is taking should be assessed.	0.463 (–0.002–0.713)	0.025
S6: Antibiotics are sometimes dispensed without medical prescription because the patient is known to have difficulty in obtaining a medical consultation.	0.760 (0.552–0.872)	<0.001
S7: Two of the main causes of the appearance of antibiotic resistance are patient self-medication and antibiotic misuse.	0.586 (0.228–0.779)	0.003
S8: Antibiotics are sometimes dispensed, even when it is known that they are not indicated, because there is no time to explain the reason why they are not called for.	0.469 (0.009–0.716)	0.023
S9: If a patient feels that he/she needs antibiotics and these are not dispensed, he/she will easily obtain the prescription and could accuse us of having delayed the treatment.	0.635 (0.319–0.805)	0.001
S10: I am convinced that new antibiotics will be developed to solve the problem of resistance.	0.608 (0.269–0.791)	0.002
*S11: When antibiotics are returned to Valormed [®] , patients should be alerted to the consequences of not complying with the treatment.	0.677 (0.392–0.829)	<0.001
S12: The use of antibiotics in animals for human consumption is an important cause of appearance of new resistance to pathogenic agents in humans.	0.610 (0.272–0.791)	0.002
S13: Antibiotics are sometimes prescribed without medical prescription because the patient is known to have neither the time nor the money to see a physician.	0.794 (0.615–0.810)	<0.001
S14: If a patient feels that he/she needs antibiotics and these are not dispensed, he/she will easily manage to obtain them at another pharmacy.	0.732 (0.501–0.857)	<0.001
S15: Antibiotic prescribing should be more closely controlled.	0.439 (–0.056–0.702)	0.0036
S16: Dispensing antibiotics without prescription should be more closely controlled.	0.796 (0.614–0.893)	<0.001
S17: The phenomenon of resistance to antibiotics is mainly a problem in hospital settings.	0.541 (0.143–0.754)	0.007

[®]VALORMED is a system for collecting medicinal packaging and unused or expired medicines.

*This item was removed from the final questionnaire.

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Internal consistency. Cronbach's alpha for Section 3 of the questionnaire was 0.716. To obtain one scale with higher internal reliability, statements were deleted one at a time until a group of items with the highest Cronbach's alpha values was obtained (Table 2).

Suggestions in Section 5 of the questionnaire. Six of the pharmacists included in this study added comments under the "suggestions" item, as requested by the questionnaire: in three cases these involved suggestions for new topics, such as diagnostic tests on susceptibility to antibiotics and the availability of

information on the interaction between antibiotics and other drugs; the remainder related to the wording of statement S11.

Discussion

This is the first study to design and validate an instrument for measuring pharmacists' attitudes to antibiotic misuse. Our questionnaire showed itself to be a valid, reliable and reproducible instrument for measuring pharmacists' attitudes to and knowledge of microbial resistance and antibiotic dispensing behaviour.

Table 2. Intraclass correlation coefficients (ICCs) assessed for situations in which pharmacists acknowledge that antibiotics are sometimes dispensed without a medical prescription (Section 3 of the questionnaire).

IN CASES WHERE THE PATIENT IS KNOWN, ANTIBIOTICS ARE SOMETIMES DISPENSED WITHOUT A MEDICAL PRESCRIPTION IN THE FOLLOWING SITUATIONS:	ICC	p-value	Cronbach's alpha, if item deleted
1. Dental diseases and ailments (e.g., dental abscesses).	0.823 (0.663–0.907)	<0.001	0.682
2. Upper respiratory infections (e.g., otitis media, pharyngitis, etc.).	0.454 (–0.035–0.713)	0.032	0.597
3. Urinary infections (cystitis).	0.860 (0.732–0.927)	<0.001	0.507
4. Any infection in which the patient undertakes to bring the prescription.	0.733 (0.488–0.861)	<0.001	0.773

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Attitude and knowledge scale-items were measured using an 8-centimetre long, unnumbered VAS, with answers scored from total disagreement to total agreement. Visual analogue scales are derived from the Likert scale, have shown themselves to be more sensitive for detecting small differences, and might possibly be more reliable and valid [17,18]. VAS-based questionnaires have been used in other studies to assess pharmacists' attitudes to adverse drug reaction (ADR) reporting [19], with the attitudes identified then being used to develop highly successful interventions to improve ADR reporting [20].

The results show that our questionnaire was well accepted and understood by pharmacists and that it enabled reliable results to be obtained. Furthermore, the test-retest study indicates that the responses to both Section two and Section three of the questionnaire displayed an acceptable degree of reproducibility. According to the values cited by Rosner [14], the ICCs obtained in our study show fair to good ($ICC > 0.4$) or excellent ($ICC > 0.7$) reproducibility for all scale-items. Despite the fact that Statement 11 displayed fair to good reproducibility ($ICC 0.677$; $p < 0.001$), it was nevertheless removed for further analysis because comments made during the test-retest study reinforced the opinion voiced by the clinical psychologist and pharmacists during the face- and content-validity stage. Statement 11 was intended to evaluate pharmacists' concern about prescription compliance but we concluded that this item was liable to misinterpretation. We therefore decided to eliminate it and propose a final questionnaire, containing 16 attitude and knowledge scale-items.

The statements in Section 3 (situations in which pharmacists acknowledged that antibiotics were sometimes dispensed without a medical prescription) showed a satisfactory level of internal consistency [15], thereby indicating that all items ($n = 4$) measured the same concept [16], i.e., the propensity to dispense antibiotics without a medical prescription. Cronbach's alpha was not calculated for attitude and knowledge scale-items in Section 2 of the questionnaire because this scale was designed to assess different attributes and to apply a measure of internal consistency would thus not make sense [16].

Our study's high degree of reliability may be due to data obtained from a previous qualitative study in the form of focus-group sessions with community pharmacists, and/or to one or more of the following: (1) the objectivity of the questions being first assessed by experts in linguistics and psychology; (2) the interest shared by the pharmacists in antibiotic resistance issues; (3) the fact that the questionnaire was also assessed by an expert panel of pharmacologists and specialist pharmacists; (4) the use of a continuous VAS; and, (5) the 2- to 4-week interval between two responses on the same subject [12].

The major limitations of this study lie in the fact that the pilot-study sample was not only very small but was a convenience sample, meaning in turn that the attitudes identified could not be extrapolated to a larger population. However, the main goal of the pilot study was to assess the reliability of the questionnaire developed during stages 1 and 2 of the study, and for this purpose, the most widely used approach relies on sample sizes of $n \geq 30$ and sample selection by a convenience method [21,22].

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Some studies focus on self-medication as a factor involved in the development of antibiotic resistance [4], while other authors point to the sale of antibiotics without a prescription as a reality in Europe [3,23] and pharmacies therefore being another link in the chain of antibiotic resistance [24]. Yet, we located only one study, conducted on community pharmacists in Southern Thailand [25], which reported that attitudes to microbial resistance could influence the dispensing of antibiotics for upper respiratory infections. There are no other studies in the literature addressing the validation of scales designed to assess pharmacists' attitudes vis-à-vis this important issue, thus ruling out comparisons between our study and others.

In a review [8] of the nature, validity, and reliability of measurement scales designed to assess factors linked to antibiotic misuse/overuse, the authors included 27 studies with scales aimed at patients/parents, 13 studies with scales aimed at physicians, and 15 studies with scales aimed at physicians and patients/parents: scales aimed at pharmacists were not included, revealing the lack of studies targeted at identifying community pharmacists' attitudes to and knowledge of antimicrobial resistance and the antibiotic dispensing process.

Despite the lack of studies into community pharmacists' attitudes to microbial resistance and antibiotic use, some studies, undertaken in hospital settings to compare the attitudes of pharmacists and physicians to hospital antibiotic policies [26], stress the important role played by pharmacists in hospital-guideline implementation [27,28] and the therapeutic decision-making process, even in primary care [29].

As mentioned above, pharmacists have an important role to play in policy and guideline implementation and patient management of medication, i.e., antibiotic use, but there are no validated tools for measuring their attitudes to these issues.

Accordingly, we feel that the instrument developed and validated in this study, in the form of a self-administered questionnaire, could prove very useful in future studies undertaken for the purpose of ascertaining community pharmacists' attitudes to and knowledge of microbial resistance and antibiotic use. Educational interventions addressing these attitudes could be designed to improve antibiotic dispensing practices, with the aim of combating microbial resistance and promoting public health.

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Author Contributions

Conceived and designed the experiments: FR LB AF MTH. Performed the experiments: FR SS. Analyzed the data: FR SS LB CG AF MTH. Contributed reagents/materials/analysis tools: FR CG AF MTH. Wrote the paper: FR LB AF MTH.

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CAPÍTULO 6

INFLUENCE OF COMMUNITY PHARMACISTS' ATTITUDES ON
ANTIBIOTIC DISPENSING BEHAVIOR: A CROSS-SECTIONAL STUDY IN
PORTUGAL

6 INFLUENCE OF COMMUNITY PHARMACISTS' ATTITUDES ON ANTIBIOTIC DISPENSING BEHAVIOR: A CROSS-SECTIONAL STUDY IN PORTUGAL

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Resumo

Realizou-se um estudo transversal que incluiu todos os farmacêuticos comunitários inscritos na Secção Regional do Centro da Ordem dos Farmacêuticos, com morada na região abrangida pela Administração Regional de Saúde do Centro. O questionário, desenvolvido no capítulo anterior foi enviado por correio, a 1197 farmacêuticos e obteve-se uma taxa de resposta de 64,8%. A associação entre possíveis fatores sociodemográficos e/ou as atitudes com a propensão para a dispensa de antibióticos sem receita médica foi avaliada por regressão logística. Todos os farmacêuticos reconheceram as resistências bacterianas como um importante problema de saúde pública revelando uma atitude positiva do ponto de vista coletivo, assim como em relação à informação prestada aos doentes na promoção da adesão ao tratamento. A concordância com a possibilidade dispensar antibióticos, por vezes, sem receita médica a doentes conhecidos foi superior para infeções dentárias, seguido das infeções urinárias e só depois doenças respiratórias. Os resultados obtidos demonstram que as atitudes e conhecimentos dos farmacêuticos podem influenciar a sua propensão para a dispensa de antibióticos sem receita médica, no entanto, o mesmo não foi demonstrado para os dados sociodemográficos. As atitudes que demonstraram estar significativamente associadas à propensão para dispensar antibióticos sem receita médica foram a complacência com o doente, a atribuição de responsabilidades a outros e o medo ou precaução.

Influence of Community Pharmacists' Attitudes on Antibiotic Dispensing Behavior: A Cross-sectional Study in Portugal

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ABSTRACT

Purpose: The emergence of microbial resistance is widely associated with inappropriate antibiotic use. Self-medication with antibiotics acquired directly from pharmacies without a medical prescription has been reported by several European countries as being an important cause of such inappropriate use. The goal of this study was to identify and evaluate community pharmacists' attitudes toward and knowledge of antibiotics and microbial resistance and to assess what influence, if any, these attitudes might have on their propensity to dispense unprescribed antibiotics.

Methods: We conducted a cross-sectional study covering all community pharmacists registered with the Official College of Pharmacists in Portugal's Central Region. A self-administered questionnaire on attitudes toward microbial resistance and antibiotic use was mailed to 1197 pharmacists. Responses ranged from 0 (total disagreement) to 10 (total agreement). Logistic regression was used to model the association between respondents' attitudes and their propensity to dispense antibiotics without an earlier medical prescription.

Findings: The overall response rate was 64.8%. Agreement with the dispensing of unprescribed antibiotics was highest in the case of dental diseases and ailments, followed by urinary tract infections. Although none of the sociodemographic data were associated with a propensity to dispense antibiotics without a medical prescription, the attitudes shown to be significantly associated with this propensity were complacency about patients, responsibility of others, and precaution or fear.

Implications: Because the attitudes of community pharmacists can influence their readiness to dispense

unprescribed antibiotics, educational interventions addressing such attitudes should be implemented to improve antibiotic use. (*Clin Ther.* 2015;37:168–177) © 2015 Elsevier HS Journals, Inc. All rights reserved.

Key words: antibiotics, attitudes, community pharmacists, microbial resistance, Portugal.

INTRODUCTION

Microbial resistance to antibiotics is an emerging public health issue worldwide and has been pinpointed as a major consequence of the inappropriate use of antibiotics.^{1–3} The emergence of microbial resistance has had a significant impact on patient morbidity and mortality, as well as on the increase in health care costs.^{4–6} Most antibiotics are consumed by outpatients,⁷ and nonprescription antibiotic consumption, obtained directly from pharmacies (even in countries where it is illegal) or with leftovers from previous courses of treatment, has been identified in several European countries.^{8–17} The use of unprescribed antibiotics could increase the risk of microbial resistance^{18,19} because it is associated with incorrect self-diagnosis,⁸ inappropriate selection of antibiotics and doses, and shorter courses of treatment.^{19–21}

Similar to other countries, Portugal has a high rate of outpatient antibiotic use,^{2,22} and some studies have identified instances of nonprescription antibiotic

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consumption.^{23–26} Despite the fact that the sale of antibiotics without a prescription is illegal in Portugal, a recent study reported that ~23% of respondents found it fairly easy to acquire antibiotics without a prescription from a community pharmacy.²⁶ Although pharmacists play a key role in preventing access to unprescribed antibiotics, there is a lack of research into their reasons for dispensing these drugs without a medical prescription. Accordingly, the aim of the present study was: (1) to estimate the percentage of pharmacists who have a propensity to dispense antibiotics without a medical prescription; and (2) to assess what attitudes and knowledge affect such behavior. Identification of factors that influence the propensity to dispense unprescribed antibiotics would enable specific purpose-designed intervention strategies to address this problem.

SUBJECTS AND METHODS

Study Setting and Population

The study was conducted in the area covered by Portugal's Central Regional Health Administration (Administração Regional de Saúde do Centro IP). To practice their profession, all community pharmacists in Portugal are required to be registered members of the Official College of Pharmacists. The study population thus comprised all community pharmacists (N = 1197) who were formally registered with the Official College of Pharmacists of the Central Region in September 2011 and had their address situated within the regional health administration's designated catchment area.

Community pharmacists in Portugal are divided into 3 categories: technical director, assistant pharmacist, and pharmacist. The technical director is the person in charge of the pharmacy and is replaced by the assistant pharmacist in his or her absence. Until August 2007, the owner of a pharmacy had to be both a pharmacist and the technical director. Hence, in most pharmacies, the technical director is also the owner.

Participants gave their consent to participate in the study after reading a cover letter with a detailed explanation of the study in which they were informed that all data are confidential. The completing and mailing of the questionnaire were completely voluntary, with no counterparties. Authorization for this study (permit no. 2886/2013) was obtained from the

Portuguese Data Protection Authorities (Comissão Nacional de Proteção de Dados).

Data Collection

A self-administered questionnaire, complete with a prepaid, self-addressed return envelope and pencil, was mailed to the 1197 registered community pharmacists. Also included were 2 cover letters: 1 from our research group outlining the study objectives and stressing the importance of participating, and another from the chairman of the Central Region's Official College of Pharmacists endorsing the study and encouraging participation. To boost the response rate, questionnaires were re-sent to nonrespondents up to a maximum of 4 times (at 4- to 8-week intervals).²⁷

The questionnaire was designed on the basis of results from a previous qualitative study, which consisted of 6 focus group sessions with a total of 32 pharmacists.²⁸ The final questionnaire was printed on a single sheet (2 pages), divided into the following 5 sections: section 1 contained a box with instructions on how to complete the form; section 2 contained 17 statements (scale items) regarding knowledge of and attitudes regarding antibiotic resistance and the antibiotic dispensing process, followed in each case by a continuous visual analog scale (VAS) for respondents to mark with a cross; section 3 contained an assessment of situations in which antibiotics would sometimes be dispensed without the necessary medical prescription provided that the patients were known, followed in each case by a continuous VAS for respondents to mark with a cross; section 4 contained sociodemographic data, such as age, sex, workplace, job function, and mean number of antibiotics dispensed; and section 5 contained a request to professionals to make suggestions about antibiotic use and microbial resistance.

The attitude and statement scale items in sections 2 and 3 of the questionnaire were measured by using a horizontal, continuous, unnumbered, 8-cm long VAS. Visual analogue scales (VAS) are derived from the Likert scale, are reputed to be highly sensitive for detecting small differences, and are also believed to be possibly more reliable and valid than Likert scales.²⁹ The position of the cross placed against each question by the respective participants was scored in a range from 0 (total disagreement) to 10 (total agreement), with a precision of 0.5. Face and content validity (ie, language, organization, appropriateness and logical sequence of statements, accuracy, clinical terminology, completeness

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and meaning of items, comprehension of the questionnaire) were assessed by experts in the respective fields, resulting in small amendments to the text.³⁰

To evaluate reliability and reproducibility, a pilot (test–retest) study was conducted on a sample of 41 community pharmacists, with questionnaires being delivered to each pharmacist twice, at intervals of 2 to 4 weeks.³⁰ Cronbach's α (internal consistency) for section 3 of the questionnaires was 0.716. Reproducibility (degree of agreement among answers), as shown by the intraclass correlation coefficient (95% CI), ranged from fair to good to excellent for sections 2 and 3 of the questionnaire.

Statistical Analyses

Logistic regression was used to model the association between independent variables and pharmacists' propensity to dispense antibiotics without a prescription (dependent variable). The dependent variable was determined by using section 3 of the questionnaire (situations in which pharmacists acknowledged that, in cases in which patients were known, antibiotics would sometimes be dispensed without a medical prescription). A propensity to dispense antibiotics without a medical prescription was presumed to exist in any case in which a pharmacist awarded a VAS score of ≥ 5 to at least 1 of the 4 situations identified in section 3 of the questionnaire (S1, dental diseases and ailments; S2, upper respiratory tract infections; S3, urinary tract infections; or S4, any infection in which the patients undertakes to bring in a prescription).

Statistical Models

A multivariate model was constructed, using variables of exposure (sociodemographic and professional [eg, age, sex, job function, years of experience in community pharmacies, hospitals and other areas]) and potential confounding. This model was adjusted for the effects of any potential confounder having a statistical significance < 0.2 in the bivariate model. Results were expressed as odds ratios (ORs) with their 95% CIs, which indicate the increase/decrease in the probability of dispensing antibiotics without a prescription for every increase of 1 unit on the continuous VAS (score range, 0–10). To consider the incremental exposure corresponding to the interquartile range of any given attitude, the interquartile OR (IqOR) was calculated taking into account the distribution of

independent variables among all participants. Because some of the ORs register values lower than unity, we calculated the inverse of the IqOR ($1/\text{IqOR}$), which can be interpreted as the increase in the probability of a propensity to dispense antibiotics without a medical prescription when the $1/\text{IqOR}$ decreases from the 75th to the 25th percentile of the sample.

RESULTS

There was an overall response rate of 64.8% ($n = 770$); of the 1197 questionnaires sent, 8 were returned due to change of address and 7 were excluded for lack of evidence to show that the respondents were community pharmacists (Figure). The sociodemographic data of the final study sample ($n = 763$) are shown in Table I. No multivariate analysis was performed because no potential confounders were found.

Propensity to Dispense Antibiotics Without a Medical Prescription

Table II shows the degree of agreement expressed by the study population with situations in which antibiotics would sometimes be dispensed without a medical prescription if the patient was known to the pharmacist. Agreement with the dispensing of unprescribed antibiotics was highest in the case of dental diseases and ailments, followed by urinary tract infections.

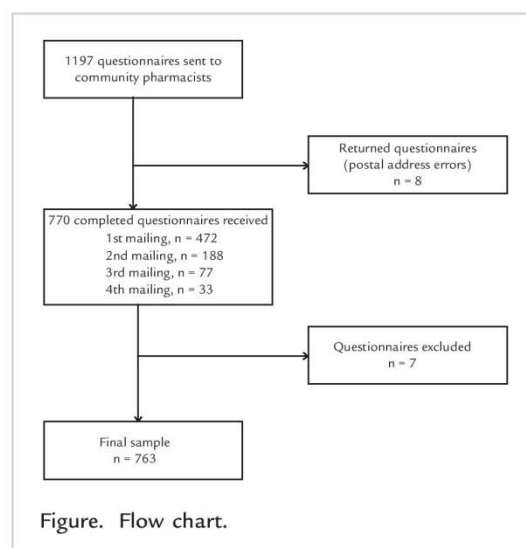


Table I. Influence of sociodemographic characteristics on pharmacists' propensity to dispense antibiotics without an earlier medical prescription.

Characteristic	% (n)	Propensity to Dispense Antibiotics Without Medical Prescription		OR (95% CI)	P
		Yes (n)	No (n)		
Age, y					
< 30	29.2 (225)	112	113	1	
30–40	35.8 (276)	131	144	1.038 (0.726–1.485)	0.837
≥ 41	33.5 (258)	126	132	0.953 (0.678–1.339)	0.782
Sex					
Male	19.0 (145)	75	70	1	0.396
Female	80.6 (615)	294	321	1.170 (0.814–1.680)	
Job function					
Technical director*	36.2 (272)	135	145	1.033 (0.747–1.428)	0.844
Assistant pharmacist†	40.4 (308)	151	157	0.987 (0.671–1.450)	0.945
Pharmacist	21.6 (165)	79	86	1	
Years of experience in community pharmacy					
< 5	33.4 (255)	123	132	1	
≥ 5	65.0 (496)	241	255	0.986 (0.729–1.334)	0.927
Experience in other areas					
Hospital pharmacist	5.4 (41)	16	25	1.511 (0.794–2.879)	0.209
Other	8.5 (65)	33	32	0.974 (0.586–1.619)	0.918

OR = odds ratio.

*Person in charge of the pharmacy.

†Replaces the technical director in the latter's absence.

Table II. Propensity of pharmacists to dispense antibiotics without an earlier medical prescription: calculation of dependent variable.

In cases in which the patient is known to the pharmacist, antibiotics are sometimes dispensed without a medical prescription in the following situations:	Percentile			
	25th	50th	75th	Scores ≥ 5*
1. Dental diseases and ailments (eg, dental abscesses)	0.5	2.0	6.5	293 (38.4%)
2. Upper respiratory tract infections (eg, otitis media, pharyngitis)	0.5	0.5	2.5	112 (14.7%)
3. Urinary tract infections (cystitis)	0.5	2.5	5.5	276 (36.2%)
4. Any infection in which the patient undertakes to bring the prescription	0.5	0.5	1.0	65 (8.5%)
At least 1 of the preceding statements (dependent variable)				371 (48.6%)

*Where the cross was placed at or above the 5-point mark on the continuous visual analog scale.

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Pharmacists' Attitudes to and Knowledge of Antibiotic Use

Pharmacists' degree of agreement with the respective attitude scale items is shown in percentile terms in [Table III](#). In general, pharmacists were in agreement (median, 10) with the statements S1, S3, S5, S7, S14, and S15. In contrast, pharmacists disagreed with the assertions of statements S8 and S12 (median, 0.5) and S6 (median, 1).

Factors Associated With a Propensity to Dispense Antibiotics Without a Medical Prescription

As can be seen in [Table I](#), none of the socio-demographic data were associated with a propensity to dispense antibiotics without a medical prescription. The relationship between knowledge/attitudes and a propensity to dispense unprescribed antibiotics is expressed statistically in [Table III](#). For every 1-unit increase in the VAS score (range of 0 [total disagreement] to 10 [total agreement]), this propensity was increased in several instances. First, in the case of complacency about patients, the propensity to dispense unprescribed antibiotics increased by 43% in response to "antibiotics are sometimes dispensed without medical prescription because the patient is known to have difficulty in obtaining a medical consultation," by 53% in response to "antibiotics are sometimes dispensed without medical prescription because the patient is known to have neither the time nor the money to see a physician," and by 18% in response to "if a patient feels that he or she needs antibiotics and these are not dispensed, he or she will easily manage to obtain them at another pharmacy." Second, propensity was increased in the case of the responsibility of others (patients), by 10% in response to "two of the main causes of the appearance of antibiotic resistance are patient self-medication and antibiotic misuse" and in the case of the responsibility of others (health care systems) by 9% in response to "dispensing antibiotics without prescription should be more closely controlled." Lastly, propensity to dispense unprescribed antibiotics increased in the case of fear/precaution by 8% in response to "if a patient feels that he or she needs antibiotics and these are not dispensed, he or she will easily obtain the prescription and could accuse us of having delayed treatment."

DISCUSSION

There have been few studies which identify knowledge and attitudes that might influence community pharmacists' propensity to dispense antibiotics without a medical prescription. However, many European studies¹¹⁻¹⁵ have found that it is possible to buy antibiotics directly from pharmacies without a prescription, even where this is a mandatory statutory requirement. Moreover, the opportunity to acquire unprescribed antibiotics from pharmacies has been identified as an important factor contributing to self-medication with these drugs,⁸ revealing the need to evaluate factors that could influence pharmacists' propensity to dispense antibiotics without a medical prescription.

Our results indicate that pharmacists' knowledge and attitudes could influence their propensity to dispense antibiotics without an earlier medical prescription. The attitudes that proved most significant in influencing this propensity were: complacency about patients, responsibilities of others (patients and the health care system), and fear or precaution. Socio-demographic characteristics, such as sex, age, job function, and years of experience, appeared to have no influence on the propensity to dispense unprescribed antibiotics. During the previous qualitative study,²⁸ the new generation of pharmacists was reported to be less closely associated with antibiotic dispensing without a medical prescription, but the present study detected no statistically significant difference between pharmacists with ≥ 5 years' and those with < 5 years' experience.

The clinical situations in which pharmacists registered the highest degree of agreement with dispensing without a medical prescription were dental diseases and ailments (38.4%), followed by urinary tract infections (36.2%), and, to a far lesser extent, upper respiratory tract infections (14.7%). In an European study involving 19 countries,⁸ the population was surveyed on their use of antibiotics without medical indication. The most commonly cited reasons for self-medication were throat symptoms, bronchitis, and tooth or gum complaints, followed by urinary tract infections. Because the Portuguese population was not included in this European study, it might be interesting to conduct a local survey in Portugal and compare the populations' stated intentions regarding self-medication with our results on pharmacists' propensity to dispense antibiotics without a medical prescription.

Table III. Influence of surveyed attitudes and knowledge on pharmacists' propensity to dispense antibiotics without an earlier medical prescription.

Attitude or Knowledge	Percentile			Units		Interquartile	
	25	50	75	OR (95% CI)	<i>P</i>	Interquartile OR (95% CI)	1/Interquartile OR (95% CI)
S1: Antibiotic resistance is an important public health problem of ours.	10	10	10	0.952 (0.845–1.071)	0.412	—	1
S2: The fact that a patient taking an antibiotic increases the risk of developing resistance.	5	7	10	0.974 (0.929–1.022)	0.286	—	1.14 (0.90–1.45)
S3: In all cases in which antibiotics are dispensed, it is essential that patients be advised about complying with the treatment.	10	10	10	1.003 (0.636–1.538)	0.989	1	—
S4: An important cause of the appearance of antibiotic resistance is long-term prescription of new molecular entities.	7	9	10	0.967 (0.985–1.022)	0.234	—	1.11 (0.94–1.05)
S5: When dispensing, possible interactions between the antibiotic and other drugs that the patient is taking should be assessed.	9	10	10	0.984 (0.891–1.087)	0.755	—	1.02 (0.92–1.12)
S6: Antibiotics are sometimes dispensed without a medical prescription because the patient is known to have difficulty in obtaining a medical consultation.	0.5	1	4.5	1.434 (1.338–1.537)	<0.0001	4.23 (3.2–5.58)	—
S7: Two of the main causes of the appearance of antibiotic resistance are patient self-medication and antibiotic misuse.	8.5	10	10	1.097 (1.024–1.175)	0.008	1.15 (1.04–1.27)	—
S8: Antibiotics are sometimes dispensed, even when it is known that they are not indicated, because there is no time to explain the reason why they are not called for.	0.5	0.5	1.5	1.03 (0.972–1.092)	1.319	1.03 (0.97–1.09)	—
S9: If a patient feels that he or she needs antibiotics and these are not dispensed, the patient will easily obtain the prescription and could accuse us of having delayed treatment.	0.5	4	7.5	1.078 (1.033–1.126)	0.001	1.69 (1.26–2.29)	—
S10: I am convinced that new antibiotics will be developed to solve the problem of resistance.	3.5	5.5	7.5	1.036 (0.982–1.093)	0.2	1.15 (0.93–1.43)	—

(continued)

Table III. (continued).

	Percentile			Units OR (95% CI)	<i>P</i>	Interquartile	
	25	50	75			Interquartile OR (95% CI)	1/Interquartile OR (95% CI)
Attitude or Knowledge							
S11: The use of antibiotics in animals for human consumption is an important cause of the appearance of new resistance to pathogenic agents in humans.	7	9	10	0.982 (0.920–1.049)	0.596	—	1.06 (0.87–1.28)
S12: Antibiotics are sometimes dispensed without a medical prescription because the patient is known to have neither the time nor the money to see a physician.	0.5	0.5	3	1.527 (1.403–1.661)	0.0001	2.88 (2.33–3.56)	—
S13: If a patient feels that he or she needs antibiotics and these are not dispensed, the patient will easily obtain them at another pharmacy.	3.5	5.5	8.5	1.180 (1.122–1.241)	<0.0001	2.29 (1.78–2.94)	—
S14: Antibiotic prescribing should be more closely controlled.	9.5	10	10	0.904 (0.837–0.982)	0.017	—	1.05 (0.9–0.94)
S15: Dispensing antibiotics without a prescription should be more closely controlled.	9.5	10	10	0.879 (0.806–0.959)	0.004	—	1.07 (1.02–1.11)
S16: The phenomenon of resistance to antibiotics is mainly a problem in hospital settings.	1	3	6	1.045 (0.996–1.097)	0.075	1.25 (0.98–1.59)	—

OR = odds ratio.

Few pharmacists (8.5%) showed a propensity to dispense antibiotics without a medical prescription for any infection in which the patient undertook to bring the prescription, revealing more concern about legal consequences than public health issues. Acquiring antibiotics from pharmacies without a prescription, whether by direct purchase or by providing a prescription retrospectively, has been reported in several studies.^{11–15} Enforcement of the laws regulating the sale of antibiotics was identified as a potentially modifiable factor facilitating self-medication.³¹ In Portugal, there is no official control by the authorities of the number of antibiotics that are sold with and without a prescription. Pharmacists were largely in agreement with enforcing control of both the dispensing and the prescribing of antibiotics (statements S14 and S15), disclaiming their own responsibility and instead placing it on others.

Difficulties in accessing health care, whether because of a lack of physicians or because patients have no money to pay fees, were identified as relevant determinants of self-medication.³¹ In some regions of Portugal, there are not enough general practitioners to manage the population, and access to the country's National Health System is not free of charge; therefore, patients view pharmacists as first-line health professionals for solving their problems, and they exert great pressure on these pharmacists to obtain what they think they need. In our study, pharmacists showed themselves to be complacent about patients precisely because they felt that patients had neither the time nor the money to see a medical physician. Complacency with patients strongly influences the propensity to dispense antibiotics, probably because patients exert great pressure to obtain these drugs. This is particularly true in the case of regular patients, when pharmacists know their clinical history and feel that they are competent to dispense antibiotics without a prescription for certain minor complaints.²⁸

Total agreement with statement S3 (“Antibiotic resistance is an important public health problem of ours”) revealed that pharmacists have a positive attitude from a collective point of view but, when faced by individual patients and customers, their behavior changes. However, when it came to information given to the patient, pharmacists not only had a positive attitude but were also unanimous regarding the need to advise patients about complying with treatment and to assess possible interactions between

the antibiotics prescribed and any other chronic medication being taken by patients. Indeed, therapeutic noncompliance has been described as having some impact on antibiotic resistance in the community.³² The paucity of studies evaluating the influence of pharmacists' attitudes and knowledge on antibiotic dispensing renders any possible comparison of results difficult. Nevertheless, some studies highlight the role of pharmacists in managing patients' medication in primary care.^{33,34}

One important limitation of our study is that the data were self-reported. The dependent variable (propensity to dispense antibiotics without a previous medical prescription) was calculated from self-reported, VAS-rated agreement with situations in which pharmacists considered that antibiotics were sometimes dispensed without a medical prescription. Responses were limited to 4 dispensing situations and did not explore all the possible situations that might lead a pharmacist to dispense antibiotics without a medical prescription. It must be noted, however, that the situations described were drawn from a previous qualitative study,²⁸ in which pharmacists recognized some upper respiratory tract infections, urinary tract infections, and dental diseases as constituting clinical scenarios in which antibiotics were sometimes dispensed without an earlier medical prescription. Other limitations of these types of studies include nonresponse bias and the fact that professionals may admit to less dispensing than they really engage in. Nevertheless, one of the strengths of this study was its high response rate, with no monetary inducements.

Our study found that both the dispensing of antibiotics without a previous medical prescription and the quality of the information given during the dispensing process may be related to pharmacists' attitudes. We feel that these attitudes should be discussed in all countries to clarify the role of pharmacists in managing patients' medicines and in promoting the appropriate use of such medicines and the health of their communities, both individual and public. The Portuguese authorities are currently discussing what should be included as pharmaceutical care in community pharmacies. The role of clinical pharmacists when it comes to interacting with physicians to solve urgent yet uncomplicated situations linked to infectious symptoms could serve to enhance antibiotic use, by reducing both the prescribing and the dispensing of these agents. Regular pharmacotherapy discussions

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between pharmacists and physicians are reported to be one of the possible factors responsible for the comparative improvement in antibiotic use in the Netherlands compared with Belgium.³³

CONCLUSIONS

Antibiotic dispensing at community pharmacies may be influenced by pharmacists' attitudes in general, and by complacency about patients, the alleged responsibility of others, and precaution or fear in particular. It is therefore essential that educational interventions addressing such attitudes be designed and implemented to prevent the use of antibiotics without a medical prescription.

Such interventions will reinforce the importance of the correct use of antibiotics, the consequences of dispensing antibiotics without an earlier medical diagnosis, and ways of improving pharmacist–patient communication. The general population will be exposed to the interventions through flyers and posters about the correct use of antibiotics and the need to have a medical diagnosis before taking these drugs.

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CONFLICTS OF INTEREST

The funders had no role in study design, data collection and analysis, or in the writing of the article.

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CAPÍTULO 7

IMPROVING ANTIBIOTIC USE THROUGH A JOINT INTERVENTION
TARGETING PHYSICIANS AND PHARMACISTS: A CLUSTER
RANDOMISED CONTROL STUDY IN PORTUGAL

7 IMPROVING ANTIBIOTIC USE THROUGH A JOINT INTERVENTION TARGETING PHYSICIANS AND PHARMACISTS: A CLUSTER RANDOMISED CONTROL STUDY IN PORTUGAL

Artigo em fase de submissão.

Resumo

Tendo em conta os dados obtidos nos trabalhos descritos nos capítulos anteriores e uma vez identificadas as atitudes e conhecimentos que influenciam o comportamento dos farmacêuticos durante a dispensa de antibióticos e que estão associadas à propensão de dispensa de antibióticos sem receita médica, desenhou-se uma intervenção educativa dirigida aos farmacêuticos que trabalham em farmácias comunitárias na região abrangida pela ARS Centro, aos doentes e à população em geral, através da divulgação de material educacional, flyers e posters, nas farmácias e centros de saúde. A intervenção educativa foi creditada pela Ordem dos Farmacêuticos, como formação contínua aos farmacêuticos participantes. A intervenção educativa decorreu em sessões com grupos de farmacêuticos ou em visitas individuais às farmácias e consistiu numa apresentação que inicialmente incidiu sobre o problema das resistências bacterianas a nível da Europa e em Portugal, quais os fatores desencadeantes e sobre o papel do farmacêutico no uso racional de medicamentos antibióticos. De seguida analisaram-se as atitudes dos farmacêuticos identificadas nos estudos anteriores e posteriormente foram apresentados diálogos entre farmacêuticos e doentes com soluções para modificar as atitudes incidindo na melhoria da capacidade de comunicação entre o farmacêutico e o doente. Neste capítulo pretende-se avaliar o impacto da intervenção nos farmacêuticos em conjunto com uma intervenção semelhante em médicos de clínica geral e familiar que decorreu no mesmo período. Com este objetivo foi realizado um ensaio controlado aleatório por *clusters*, entre 31 de maio e 3 de outubro de 2013, que incluiu todos os médicos e farmacêuticos a trabalharem, respetivamente, em centros de saúde e em farmácias comunitárias na zona abrangida pela ARS Centro. Foram definidos oito *clusters*, tendo como referência os hospitais centrais da região e, aleatoriamente, quatro *clusters* foram atribuídos ao grupo intervenção e outros 4 ao grupo controlo. Comparando a mudança nos dados de consumo entre o grupo controlo e o grupo intervenção, no período pré-intervenção e pós-intervenção verifica-se que há uma forte associação entre a intervenção e a diminuição

significativa do consumo de antibióticos nos 12 meses após a intervenção, revelando um impacto muito positivo desta intervenção educativa conjunta.

Improving antibiotic use through a joint intervention targeting physicians and pharmacists: a cluster randomised control study in Portugal

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Abstract

Objectives: To improve population antibiotic use through an educational intervention targeting primary-care physicians' and community pharmacists' attitudes and knowledge.

Methods: We conducted a cluster randomised trial. A combination of active (small group-session presentations and outreach visits) and passive interventions (distribution of posters, flyers and scientific papers) were conducted on physicians and pharmacists. In the intervention group, patients and the general public were exposed to the intervention through the dissemination of information materials. Antibiotic-consumption data were evaluated pre- and post-intervention for both the intervention and control groups, with a 12-month post-intervention follow-up. Data were expressed as the number of packages per 1000 inhabitants per day (PID). The study protocol was registered on ClinicalTrials.gov (NCT02173509).

Results: The intervention was associated with a significant decrease in overall antibiotic use (3.71% reduction, 95% CI: 0.00 to 8.30) at 12 months of the intervention. The effect was most marked for tetracyclines (15.63% decrease, 95% CI: 2.94 to 27.59), macrolides (9.37% decrease, 95% CI: 2.21 to 17.43) and cephalosporins (7.24% decrease, 95% CI: 0.00 to 15.80). No statistically significant differences were observed for fluorquinolone consumption.

Conclusions: Multifaceted interventions involving physicians, pharmacists and the general public proved effective in reducing antibiotic consumption.

Running title: Improving antibiotic use

Key words: educational interventions; antibiotic consumption; microbial resistance; primary-care physicians; community pharmacists.

INTRODUCTION

Antimicrobial resistance currently is a growing threat to public health world-wide, and indeed the World Health Organisation (WHO) has issued an alert warning of the possibility of a return to the pre-antibiotic era, during which even common infections could kill [1]. It is well known that the overuse and misuse of antibiotics are responsible for the emergence of microorganisms resistant to antibiotics [2-6]. The development of such resistance is responsible for treatment failure and deaths [7-9] (approximately 25,000 in Europe alone)[10], prolonged hospital stays, and increased costs (around 1.5 billion euros per year in Europe)[10].

In contrast to northern Europe and North America, where outpatient antimicrobials are largely restricted to prescription-only use, non-prescription access to antimicrobials is common in the rest of the world [11], including Portugal [12]. Nevertheless, studies on interventions to improve antibiotic use focus mainly on physicians[13-15], even though pharmacists play a key role in the use of antibiotics without prescription and in the changing views and behaviours of patients [12].

This trial sought: firstly, to evaluate the effectiveness of a joint educational intervention on overall antibiotic use, targeted at primary-care physicians and community pharmacists; and secondly, to evaluate the impact of the intervention on six main subclasses of antibiotics.

METHODS

Study population and setting

The study was conducted in the catchment area covered by Portugal's Central Regional Health Administration (*Administração Regional de Saúde do Centro IP/ARS-C*), with approximately 1,744 million inhabitants, 87 outpatient centres and 549 community pharmacies. The study population comprised all physicians working at Public National Health System outpatient centres (~1100 physicians) and all pharmacists working at community pharmacies (~1200 pharmacists) in the study area. Two communities belonging to different clusters were excluded from the study because data on antibiotic consumption were solely available in aggregated form.

Study design

We conducted a cluster randomised control trial, with small-area-wide evaluation (municipalities). To prevent cross-contamination between the intervention and control groups,

we formed 8 spatial clusters. Each cluster consisted of all of the municipal areas covered by 1 referral hospital, and included primary-care centres, community pharmacies and hospitals. The impact of the intervention on antibiotic use was evaluated at a municipal level, since it could not be measured at an inhabitant level (no data available) and it made no sense to do this at a pharmacist or physician level.

The clusters were distributed by equal randomisation, using a computer-generated procedure, with 4 clusters being assigned to the intervention group and 4 to the control group.

Ethical aspects and registration

The study protocol was registered on ClinicalTrials.gov (NCT02173509), was approved (Permit No. 015650) by Portugal's Central Regional Health Administration, and obtained official authorisation (Permit No. 2886/2013) from the Portuguese Data Protection Authorities (*Comissão Nacional de Proteção de Dados/CNPD*).

Intervention

We designed the educational intervention, taking into account data yielded by previous focus-group and cross-sectional studies on physicians' and pharmacists' attitudes and knowledge that influence antibiotic prescribing and dispensing respectively [16-18]. A combination of active (small group-session presentations and outreach visits) and passive interventions (distribution of posters, flyers and scientific papers) were conducted on physicians and pharmacists. The passive intervention, with information on resistance and the consequences of inappropriate antibiotic use (posters and flyers), was directed at patients and the general public. The educational intervention had the scientific support of Portugal's Central Regional Health Administration, the Official College of Physicians, the Official College of Pharmacists and the Portuguese Association of Family Medicine.

The trial lasted for four months (31 May 2013 to 3 October 2013), with the two interventions being respectively presented by two pharmacist researchers, one responsible for the physician intervention (ATR) and the other for the pharmacist intervention (FR).

Physician intervention

A letter was sent to the clinical director of each outpatient centre, inviting all physicians to participate in the intervention. The outreach visits were scheduled with the clinical director, were included in each facility's continuing medical education programme, and took place during weekly staff meetings to ensure that the greatest number of physicians were present. The presentation consisted of two parts: initially, data were presented, showing antibiotic resistance

in Europe and the relationship between this and antibiotic consumption, and highlighting the causes and consequences of inappropriate antibiotic use; at this juncture, pictures were shown which simulated dialogues between physicians and patients, pinpointing the attitudes previously identified as having the greatest influence on antibiotic prescribing quality (complacency with patients, ignorance and responsibility of others), explaining how to prevent such influence, and indicating the strategies to be used for improving communication skills.

Pharmacist intervention

By way of introduction, the Official College of Pharmacists sent an e-mail to all pharmacies falling within the intervention area, inviting all the pharmacists employed by these to participate in the educational intervention groups. After this first contact, the researcher would telephone the pharmacies to remind them of the intervention dates, and at those pharmacies where no-one was available to attend the intervention on the appointed date, the researcher would try to arrange for an outreach visit to the pharmacy.

The interventions lasted for about 2 hours, and consisted of a presentation followed by an explanation of the flyers and posters, with pharmacists being encouraged to place a poster in visible place in the pharmacy and distribute the flyers to the patients. The sessions ended with a discussion/debate about the topic and the presentation, stressing the crucial, uncompromising role played by pharmacists in promoting the rational use of medicines, and antibiotics in particular. While the initial presentation contained the same information as that included in the presentation to physicians, this was then followed by a list of the factors which could, according to previous studies, potentially influence the behaviour of pharmacists during the dispensing of antibiotics [16, 17]. During the presentation, pictures were shown, simulating dialogues between pharmacists and patients, representing the attitudes previously identified as having the greatest influence on the propensity to dispense antibiotics without a medical prescription (complacency about patients, responsibility of others, and fear/precaution), explaining how to prevent such influence, and indicating the strategies to be used for improving communication skills.

The educational intervention was included in the continuous education programmes for pharmacist and accredited by the Official College of Pharmacists, so that all pharmacists who participated in the intervention received an accreditation on their professional membership cards.

Patient intervention

The passive intervention directed at patients was implemented by means of posters displayed at pharmacies and outpatient centres, and flyers directly distributed to them by their physicians

and pharmacists. The information on the flyers intended for the general public was clear and simple: it included key messages about the global problem of microbial resistance, highlighting the importance of seeking a medical diagnosis before taking any antibiotic and focusing on situations, such as colds, in which antibiotics are not effective, with -as suggested for public health campaigns [19]- a mix of positive and negative values evoking the consequences if nothing is done.

Control group

The control group, which did not receive the intervention, comprised 4 clusters with 60 outpatient centres and 401 community pharmacies.

Follow-up and outcome measures

In each community, the follow-up period started after the last intervention had finished, and ended in September 2014.

Evaluation of the impact of the intervention was made at a municipal level rather than at a health-professional or patient level.

To quantify antibiotic drug consumption, we used monthly sales data for each community sourced from IMS Health® (for the period May 2012 to September 2014) and aggregated by active substance in accordance with the Anatomical Therapeutic Chemical (ATC) classification and DDD measurement unit (WHO version 2011) [20]. The IMS Health® Portugal database estimates consumption from the volume of antibiotics sold at community pharmacies, using information acquired from pharmaceutical sales distribution channels. In view of the fact that outpatient antibiotic use was assessed over time and that community pharmacies in Portugal dispense complete packages of antibiotics, in order to evaluate the impact of our intervention the data were expressed as number of packages per 1000 inhabitants per day (PID), as suggested in recent studies [21-23].

The consumption of antibiotics expressed in PID was measured for the following main antibacterial groups: antibacterials for systemic use (J01_PID); tetracyclines (J01A_PID); penicillins (J01C_PID); cephalosporins [(J01DB+J01DC+J01DD+J01DA)_PID]; sulphonamides and trimethoprim (J01E_PID); macrolides (J01 FA_PID) and quinolones (J01M_PID).

Statistical analysis

Linear mixed models (LMMs), fitted using restricted maximum likelihood (REML), were applied to the statistical analysis [24]. To construct the models, we used antibiotic consumption data as dependent variables, with individual observations (per month and municipality) as level 1, municipalities as level 2, and spatial clusters (as indicator variable) as level 3; random effects were considered, both among municipalities and among spatial clusters.

A dichotomous indicator variable was created for measurement of the intervention effect. This variable (denoted period) takes a value of 0 for the baseline period and 1 for months between the start of the intervention and the end of follow-up. The intervention effect was assessed by the interaction between the group (1 for intervention group, 0 for control group) and period variables.

Moreover, the individual observations (per month and municipality) for the respective warm (April-September) and cold periods (October-March) of the different years were assumed to be independent, whereas the individual observations within the respective warm and cold periods were deemed to be correlated.

All analyses were performed using the free R statistical software environment [25] (version 3.1.2) with the lme4 package [26]. The 95% confidence intervals (CIs) were computed using the profile likelihood method, and the *p*-values were calculated using Satterthwaite approximation of the degrees of freedom (lmerTest package) [27].

RESULTS

The intervention group comprised 4 clusters with 25 outpatient centres (~309 physicians) and 144 community pharmacies (~312 pharmacists).

All Public National Health System outpatient centres were visited and about 64 % of physicians attended the intervention. A total of 173 pharmacists (about 55% of all the pharmacists working at all pharmacies allocated to the intervention group) from 106 pharmacies (about 74% of all pharmacies allocated to the intervention group) attended the educational intervention (Figure 1).

Comparing the post-intervention to the baseline period (Table I), a decrease in total consumption of antibiotics was observed in both groups, with a reduction of 0.18 PID in the intervention group and 0.09 PID in the control group. Whereas consumption of penicillin decreased in the intervention group (0.04 PID), no changes were observed in the control group.

In the case of tetracycline, consumption decreased in the intervention group but increased in the control group. Cephalosporin, macrolide and quinolone consumption decreased in both the intervention and control groups, with consumption of macrolides registering a major sharp decline in the intervention group (0.06 PID).

Table 2 shows the effects of the intervention on post-intervention antibiotic use adjusting for baseline values, with a statistically significant reduction being observed in the intervention group for overall consumption of antibiotics (3.71% decrease, 95% CI: 0.00 to 8.30), tetracyclines (15.63% decrease, 95% CI: 2.94 to 27.59), macrolides (9.37% decrease, 95%CI: 2.21 to 17.43) and cephalosporins (7.24% decrease, 95% CI: 0.00 to 15.80). For the other antibiotic groups no statistically significant changes were in evidence.

DISCUSSION

This is the first large, cluster randomised controlled trial to evaluate the impact of a joint educational intervention on population antibiotic use in all clinical situations, targeted at community pharmacists and physicians. Overall consumption of antibiotics decreased by 3.71% at one year of the intervention, with impact being greatest in the case of tetracyclines, macrolides and cephalosporins.

The main *novelty of our study* lies in the fact that it is the first to evaluate simultaneous interventions among physicians and pharmacists, not at a prescribing or dispensing level but rather at a consumption level. Measuring the joint effect is particularly important, since it avoids the transfer of the demand for antibiotics between physicians and pharmacists. It is possible that, if an intervention targets physicians and these then restrict their prescription of antibiotics, some patients will demand them at pharmacies without a medical prescription (a phenomenon which may be more frequent in the south of Europe); and vice-versa, i.e., interventions among pharmacists which restrict dispensing may increase the demand for physicians' prescriptions. Our design makes it possible to avoid such transfers.

The *magnitude of the effect* was not high but might nonetheless be relevant for public health purposes. Our effect was less marked than that reported by nationwide campaigns in France [28] and Belgium [29]. However, these studies did not include a control group: the impact was calculated by comparing pre- to post-intervention data, and so it cannot be said with any certainty whether the use of antibiotics would have fallen or risen without the campaigns [19]. Indeed, if we had not adjusted for the changes in the control group, we would have observed a decrease of 9.5% (1.89 vs. 1.71) from pre- to post-intervention. Furthermore, it should be borne

in mind that the effect found by us may have been diluted by a number of factors, including: (1) the length of the post-intervention period, which was not just one quarter [30] but rather a full year; (2) to calculate drug consumption, our data source, IMS Health®, takes into account sales by and returns to pharmacies but not variations in pharmacy stocks, which, though inevitably present in the intervention and control groups, may nevertheless dilute the effect of the intervention; (3) the analysis was performed by reference to the effect of consumption on the population, so that it amounts to a way of measuring the effect by intention-to-treat, which also dilutes the effect because not all the physicians or pharmacists took part in the study; (4) although our intervention focused on public primary-care physicians and not those working in hospitals or private outpatient centres, the sales data used included prescription from all of these settings (including hospital prescriptions in cases where patients were discharged); and lastly, (5) conducting the study by geographical area of consumption renders it highly likely that a percentage of the dispensing (consumption) took place in areas other than those of prescription or residence, so that the effect would be shifted to other municipalities, some of which would correspond to the control group. This would likewise serve to dilute the effect.

Accordingly, we regard our results as *successful* and believe this to be due to the fact that we conducted an active educational intervention targeting primary-care physicians' and community pharmacists' attitudes and knowledge, which previous studies had identified as being associated with antibiotics [16]. In the literature, interventions are very frequent in the case of physicians [13] but much less so in that of pharmacists [31-33]. We feel that, outside the confines of northern Europe and north America, the role of the pharmacist is fundamental for the rational use of antibiotics, and should be borne in mind in all intervention studies. Our educational intervention included extensive training in communication skills, to equip participants to deal with patient pressure to obtain antibiotic prescriptions from physicians or antibiotics without prescription from pharmacies. In addition, we disseminated information to the patients themselves. In brief, we designed a multifaceted intervention, with training in the types of communication skills shown to be most effective [14].

Analysis of the effect *by therapeutic subgroup* shows that the impact of our intervention was highest for the consumption of antibiotics in the tetracycline group (decrease of 15.63%), followed by macrolides (decrease of 9.37%) and cephalosporins (decrease of 7.24%). The greater impact on these subgroups may possibly be due to the fact that the intervention was geared to restricting the prescribing/dispensing of antibiotics which were not first-line in the target population. A reduction in the use of penicillin, sulphonamides and trimethoprim was observed between the intervention and control groups, though without statistical significance, and no impact on quinolones was in evidence. These findings are similar to those reported by

other studies designed to improve antibiotic prescribing, in which quinolone prescriptions also failed to decrease [28, 32].

An improvement between the pre- and post-intervention periods (2.10 vs. 2.01) was likewise observed for the *control group*. This might be attributable to two factors: (1) a possible contamination of the clusters in the control group, whether due to a transfer of the educational intervention from some clusters in the intervention to the control group, or because the prescribing (physicians) and dispensing occurred in different clusters, one from the intervention and the other from the control group, which would dilute the effect of our intervention; and additionally, (2) our intervention may have coincided with governmental measures in 2013 [34], or this finding may even be due to the effect of the economic crisis.

Strengths and limitations of the study

Our study design has a number of strengths. The use of a control group served both to eliminate potential sources of bias, such as seasonal variation in antibiotic consumption due to external factors, and minimise the effects of changes in behaviour over time. These potential biases have limited the interpretation of other before-and-after studies that have sought to address this issue. Randomisation minimises the potential for selection bias, and a cluster-based distribution reduces the risk of cross-contamination between groups. Imbalances in baseline group composition were addressed, by adjusting for baseline differences in the dependent variables and comparing the changes in the intervention group against those in the control group. Another important strength resided in the fact that we designed the educational interventions taking into account physicians' and pharmacists' attitudes and knowledge identified in earlier studies.

Various limitations must also be considered when it comes to interpreting the results of our study. *Firstly*, there is the impossibility of measuring secondary outcomes, such as incidence of resistance or infection due to antibiotic-resistant organisms and the possible incidence of adverse events associated with reduced use of antibiotics. *Secondly*, IMS Health® data represent sales and not the real consumption because patients might buy a medication but then decide not to take it [35]. Even so, sales or reimbursement data have been rated as the best nationally available source of information closest to consumption data [23], and are considered to be similar to the number of treatments revealing patient exposure to antibiotics. Indeed, sales data are those used by the European Centre for Disease Prevention and Control to evaluate antimicrobial consumption trends in Portugal [36]. *Thirdly*, sales data do not enable us to

evaluate whether our intervention had an effect on the quality of antibiotic prescribing as judged by reference to patients' clinical status and/or on the frequency of self-medication. *Fourthly*, we know how many physicians and pharmacists attended the educational intervention but cannot measure the extent to which the message was successfully spread among the general public, and it would be of interest to design future interventions to measure this.

CONCLUSIONS

Like other countries in southern Europe, Portugal continues to have high levels of antibiotic use [37] as well as a pattern of considerable bacterial resistance [38]. In view of our results, we feel that if governmental measures were associated with active educational interventions directed at physicians, pharmacists and patients, the impact on antibiotic consumption would be much greater. It would be interesting to replicate this educational intervention in other regions and add it to any other ongoing campaigns, since in order to be most effective a combination of various interventions should be supported by government and regulatory institutions [39].

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Transparency declarations

The authors declare that they have no competing interests.

Author contributions

F. Roque, A Teixeira-Rodrigues, L Breitenfeld, A Figueiras, MT Herdeiro were responsible for designing the study. MT Herdeiro was the researcher responsible for the project grant. F Roque and A Teixeira-Rodrigues prepared the educational materials (power-point, flyers and posters) for the intervention, which were revised by all the authors. F Roque conducted the pharmacist interventions and A Teixeira-Rodrigues conducted the physician interventions. F Roque, A Teixeira-Rodrigues, M Piñero-Lamas and A Figueiras analysed the data, F Roque wrote the manuscript, and all authors were responsible for reviewing and revising the paper.

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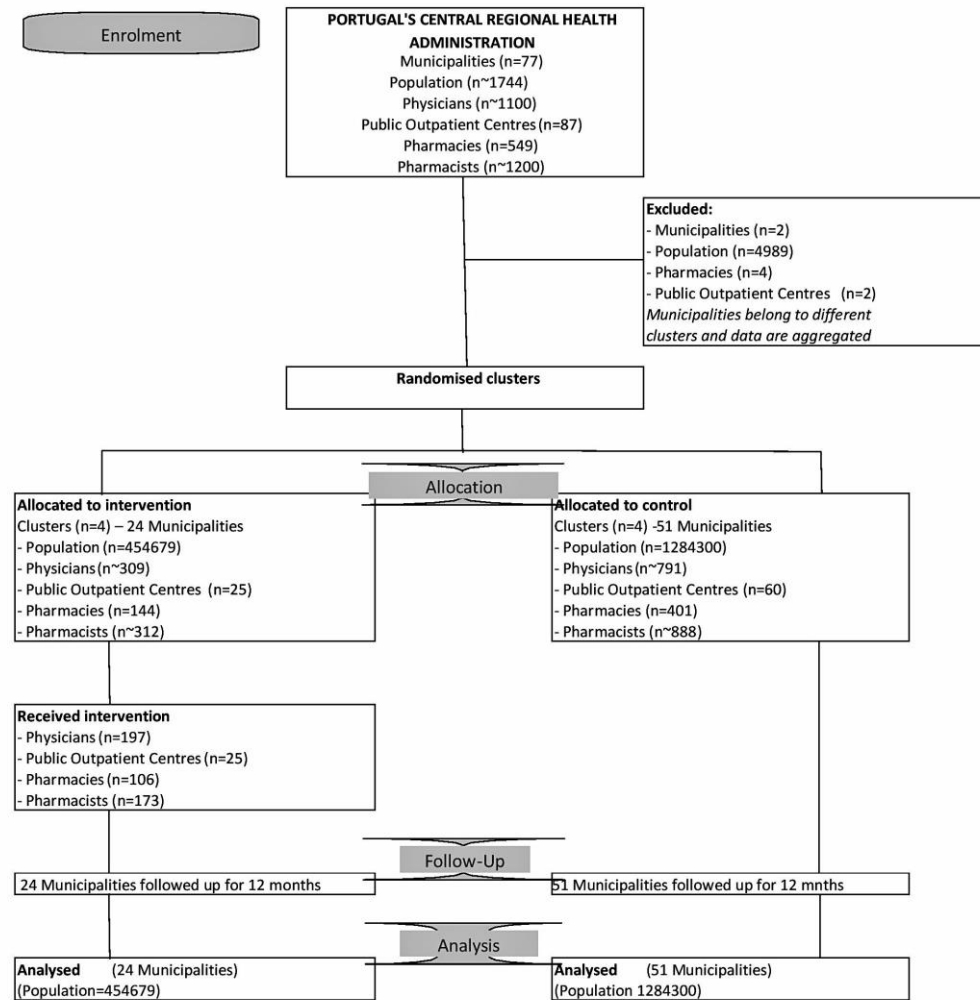


Figure 1 – Flow chart of the study, showing randomisation and intervention attendance.

Table 1. Antibiotic consumption at baseline and post-intervention in the intervention and control groups.

Antibiotic consumption (expressed in PID)	Group	Period	
		Baseline	Post-intervention Overall period
Antibacterial for systemic use	Intervention	1.89 (1.81 - 1.97)	1.71 (1.65 - 1.77)
	Control	2.10 (2.05 - 2.14)	2.01 (1.97 - 2.05)
Tetracycline	Intervention	0.032 (0.029 - 0.034)	0.030 (0.028 - 0.033)
	Control	0.037 (0.036 - 0.039)	0.041 (0.039 - 0.043)
Penicillins	Intervention	0.79 (0.75 - 0.82)	0.75 (0.72 - 0.77)
	Control	0.94 (0.92 - 0.96)	0.94 (0.92 - 0.95)
Cephalosporins	Intervention	0.28 (0.25 - 0.30)	0.24 (0.22 - 0.26)
	Control	0.27 (0.26 - 0.28)	0.25 (0.24 - 0.26)
Sulphonamides and trimethoprim	Intervention	0.069 (0.065 - 0.072)	0.063 (0.059 - 0.066)
	Control	0.080 (0.077 - 0.082)	0.078 (0.075 - 0.080)
Macrolides	Intervention	0.43 (0.40 - 0.45)	0.37 (0.35 - 0.39)
	Control	0.48 (0.46 - 0.50)	0.46 (0.45 - 0.48)
Quinolones	Intervention	0.28 (0.27 - 0.29)	0.25 (0.24 - 0.26)
	Control	0.27 (0.26 - 0.28)	0.23 (0.23 - 0.24)

Table II – Post-intervention changes in antibiotic consumption in the intervention versus the control group, adjusted for baseline values

Antibiotic consumption (expressed in PID)	Percentage change (95% CI)*	P-value
Antibacterials for systemic use	-3.71 (-8.30 , 0.00)	0.0459
<i>Tetracyclines</i>	-15,63 (-27.59 , -2.94)	0.0111
<i>Penicillins</i>	-2.55 (-7.98 , 1.22)	0.1907
<i>Cephalosporins</i>	-7.24 (-15.80 , 0.00)	0.0206
<i>Sulphonamides and trimethoprim</i>	-2.90 (-10.77 , 2.78)	0.2645
<i>Macrolides</i>	-9.37 (-17.43 , -2.21)	0.0214
<i>Quinolones</i>	3.59 (0.00 , 6.85)	0.1160

Abbreviations:

PID, number of packages per 1000 inhabitants per day

CI, confidence interval

* Post-intervention with respect to baseline

CAPÍTULO 8

DISCUSSÃO

8 DISCUSSÃO

Este é o primeiro estudo realizado em Portugal que avalia o impacto de uma intervenção educativa para diminuir o consumo de antibióticos na comunidade, através de um ensaio controlado aleatório. Do que nos foi possível avaliar na revisão sistemática realizada e em pesquisas mais recentes, existem poucos estudos publicados sobre intervenções educativas para melhorar o uso de antibióticos que incluam intervenções ativas dirigidas a farmacêuticos comunitários conjuntamente com intervenções ativas dirigidas a médicos, lacuna esta que quisemos preencher com o desenho do estudo que desenvolvemos.

A primeira fase do trabalho desenvolvido consistiu num estudo de revisão sistemática de estudos publicados sobre intervenções educativas para melhorar o uso de antibióticos quer em cuidados primários quer em ambiente hospitalar. A maioria dos estudos incluídos na análise, descrevem intervenções dirigidas a médicos e os dados analisados são dados sobre o total de antibióticos prescritos ou sobre taxas de prescrição adequada, focando algumas situações clínicas e não o consumo em geral, para além disso não consideram na análise um período de *follow-up*, e os que consideram fazem-no em períodos muito curtos, apenas quatro estudos fazem um *follow-up* igual ou superior a 12 meses. Verificou-se uma grande heterogeneidade entre os desenhos dos diferentes estudos publicados, havendo uma grande percentagem de estudos não controlados e/ou sem análise pré- e pós-intervenção. Estes são aspetos muito importantes a considerar no desenho de estudos que têm como objetivo avaliar o impacto de uma intervenção, pois sabe-se que o efeito de uma intervenção tem tendência a perder-se com o tempo e que, o grau de evidência é maior com um desenho controlado aleatório que inclua medidas de pré- e pós-intervenção. O grupo controlo permite eliminar ou minimizar a influência de fatores externos e as medidas pré- e pós- intervenção permitem ajustar as características basais de ambos os grupos quando estes não são equivalentes, proporcionando um maior poder estatístico aos resultados. Também foram poucos os estudos que desenharam as intervenções educativas tendo por base atitudes e conhecimentos previamente identificados, no entanto, alguns focavam a sua discussão na necessidade de desenhar intervenções com base nas barreiras associadas aos comportamentos dos profissionais. Apesar da heterogeneidade observada entre os estudos, demonstrou-se que as intervenções educativas para melhorar o uso de antibióticos são necessárias e têm geralmente resultados positivos, sendo na maioria intervenções ativas e multifacetadas e que, em cuidados de saúde primários, é importante dirigi-las a médicos e farmacêuticos, tendo em conta as atitudes e conhecimentos destes.

Existe uma grande lacuna de estudos publicados sobre atitudes e conhecimentos dos farmacêuticos comunitários em relação ao consumo e à dispensa de antibióticos, como demonstrado pela informação sistematizada nesta revisão sistemática e na pesquisa de informação sobre o tema.

Com o estudo qualitativo desenhado na forma de grupos focais pretendeu-se explorar a percepção, as atitudes e os conhecimentos dos farmacêuticos comunitários em relação às resistências bacterianas e ao consumo de antibióticos na população assim como em relação à dispensa de antibióticos nas farmácias. Esta metodologia qualitativa na forma de grupos focais revelou-se de grande importância pois é muito adequada para explorar o conhecimento, atitudes e experiências, permitindo identificar o que as pessoas pensam, como pensam e porque pensam dessa forma. Existe uma grande interação entre os participantes que permite evidenciar as prioridades dos participantes, encorajando-os a analisar as suas próprias experiências e a conversar sobre temas difíceis facilitando o aparecimento de ideias e experiências que dificilmente surgiriam por outras metodologias. Durante as sessões dos grupos focais, os farmacêuticos mostraram preocupação com o problema das resistências bacterianas, no entanto desresponsabilizam-se do problema, atribuindo a causa a causas externas como os doentes, os médicos, outras farmácias e consumo em veterinária. Também a responsabilidade pelo facto da possível dispensa de antibióticos sem receita médica é atribuída a responsabilidade externa como aos médicos, às políticas de saúde e aos próprios doentes, ocorrendo por complacência com os doentes ou por precaução.

A informação obtida durante o estudo qualitativo foi importante para o desenho de um questionário que permitisse identificar e quantificar a influência que as atitudes e o conhecimento dos farmacêuticos em relação às resistências bacterianas e ao consumo de antibióticos poderá ter sobre a propensão dos farmacêuticos comunitários para dispensar, nalgumas situações, antibióticos sem receita médica. O questionário foi validado quanto à validade de face e conteúdo e quanto à fiabilidade através de um ensaio piloto na região abrangida pela ARS Norte em que se analisou a reprodutibilidade e a consistência interna dos parâmetros a considerar como variável dependente, correspondendo à propensão dos farmacêuticos para dispensar antibióticos sem receita médica. Com esta fase do estudo foi possível obter um instrumento válido para utilizar no estudo transversal que se realizou na fase seguinte na região abrangida pela ARS Centro. O questionário foi validado numa região diferente da do estudo transversal para que não houvesse contaminação do estudo.

Na fase seguinte do projeto, utilizando o questionário obtido foi possível identificar quais os fatores que influenciam a propensão dos farmacêuticos para dispensar, nalgumas situações, antibióticos sem receita médica. As características sociodemográficas não mostraram influenciar os farmacêuticos, contrariamente a algumas atitudes. As atitudes que mostraram poder influenciar mais a propensão para a dispensa de antibióticos sem receita médica são a

complacência com o doente, a atribuição da responsabilidade a outros e ainda, o medo ou precaução. Este estudo não avaliou a taxa de dispensa de antibióticos dispensados sem receita médica, mas sim a concordância dos farmacêuticos com a dispensa de antibióticos em algumas situações clínicas quando o doente é conhecido. Muitos dos estudos europeus que avaliam a taxa de dispensa de antibióticos sem receita médica, fazem-no através de clientes simulados em que é avaliada a facilidade de aquisição por doentes que não são conhecidos. Apesar de em Portugal não haver estudos publicados, vários estudos têm indicado que a dispensa de antibióticos sem receita médica é maior para com os doentes conhecidos que para com os doentes desconhecidos.

A última etapa deste projeto consistiu no desenho de uma intervenção educativa focada nas atitudes e conhecimentos dos farmacêuticos, identificados nos estudos anteriores, com o objetivo de melhorar a prática farmacêutica quer na informação prestada quando dispensam antibióticos prescritos numa receita médica, quer através da não dispensa de antibióticos quando os doentes os solicitam sem receita médica. Realizou-se um ensaio controlado aleatório por *cluster*, e a intervenção consistiu numa intervenção ativa, através de sessões com pequenos grupos de farmacêuticos e de visitas às farmácias em que se trabalhou as barreiras identificadas e as habilidades de comunicação entre o farmacêutico e o doente. Também foi desenvolvido material educacional na forma de *posters* e *flyers* dirigidos aos doentes que foram distribuídos nas farmácias e centros de saúde.

A principal limitação do nosso estudo foi a impossibilidade de avaliar o impacto da intervenção sobre a dispensa de antibióticos sem receita médica, pois estes dados não estão disponíveis e não foi possível obtê-los. Como referido inicialmente este projeto é parte integrante de um projeto mais alargado que também inclui um estudo semelhante realizado com médicos no mesmo período. Desta forma avaliou-se o impacto que a intervenção conjunta em farmacêuticos comunitários (realizada no âmbito desta tese) e em médicos que trabalham em centros de saúde do Sistema Nacional de Saúde (realizada no âmbito do trabalho de doutoramento de outro investigador), teve no consumo de antibióticos na comunidade, utilizando os dados de consumo gentilmente cedidos pelo IMS® Portugal.

O impacto das intervenções foi bastante positivo, pois verificou-se uma diminuição significativa de 3,71% no consumo geral de antibióticos entre o período pré-intervenção e pós-intervenção após 12 meses de *follow-up*, no grupo intervenção comparando com o grupo controlo. Este efeito foi mais acentuado para as tetraciclina, seguido dos macrólidos e das cefalosporinas.

O sucesso desta intervenção deve-se ao facto da intervenção educativa ser uma intervenção ativa dirigida aos profissionais de saúde envolvidos, os médicos que prescrevem e os farmacêuticos que dispensam e ao facto de terem sido desenhadas tendo em conta os conhecimentos e atitudes que pode influenciar a sua prática profissional. Além disso os doentes

também foram envolvidos na intervenção educativa através da distribuição de material educativo.

Apesar das limitações associadas à impossibilidade de avaliar o impacto da intervenção educativa nos farmacêuticos sobre a dispensa sem receita médica, e de quantificar o seu contributo no impacto que a intervenção conjunta teve no consumo de antibióticos, a intervenção nos farmacêuticos foi um sucesso, dada a sua recetividade e o impacto com significância estatística que a intervenção conjunta teve no consumo de antibióticos. O efeito da intervenção em farmacêuticos poderá ter contribuído para o sucesso da intervenção conjunta, a vários níveis, quer pelo papel educativo que o farmacêutico passou a ter sobre o doente modificando as suas expectativas em relação aos antibióticos e a sua pressão sobre o próprio médico, quer pela diminuição de dispensa de antibióticos sem receita médica, quer ainda pelo efeito motivador que as intervenções educativas envolvendo médicos e outros profissionais de saúde têm sobre prescrição, como defendido numa revisão sistemática da *Cochrane*¹ onde demonstraram que as intervenções multifacetadas e ativas são as mais eficazes.

¹ Arnold SR, Straus SE, Arnold S: Interventions to improve antibiotic prescribing practices in ambulatory care. *Cochrane Database Syst Rev* 2005, 4(4):CD003539.

CAPÍTULO 9

CONCLUSÕES E IMPLICAÇÕES

9 CONCLUSÕES E IMPLICAÇÕES

A revisão sistemática permitiu-nos concluir que existe uma grande heterogeneidade no desenho dos estudos publicados, demonstrando, no entanto, que intervenções educativas ativas e multifacetadas têm um impacto bastante positivo na redução do consumo de antibióticos, assim como na qualidade da prescrição. Esta revisão permitiu evidenciar a importância de realizar intervenções educativas para melhorar o uso de antibióticos e a necessidade de desenhar estudos controlados aleatórios que permitam uma melhor comparação de resultados.

O estudo qualitativo permitiu concluir que os farmacêuticos têm a percepção que as resistências bacterianas são um importante problema de saúde pública, sendo que atribuem a responsabilidade a outros. A causa de possível dispensa sem receita médica é atribuída as causas externas e à complacência com o doente.

Construiu-se um instrumento válido para identificação de atitudes e conhecimentos dos farmacêuticos em relação às resistências bacterianas e ao uso de antibióticos a partir da informação obtida de um estudo qualitativo na forma de grupos focais. Este instrumento poderá ser utilizado em outros países, sendo contudo necessário proceder à sua validação na população em estudo.

As atitudes dos farmacêuticos estão relacionadas com a sua propensão para dispensar antibióticos sem receita médica. A atribuição da responsabilidade a outros, a complacência com o doente e a precaução ou medo são atitudes que influenciam a propensão dos farmacêuticos para dispensar antibióticos sem receita médica.

As intervenções educativas dirigidas a farmacêuticos focando as atitudes identificadas como influenciando o seu comportamento durante a dispensa contribuem para melhorar o uso de antibióticos na população.

Intervenções educativas conjuntas em farmacêuticos e médicos com intervenções ativas e envolvendo também os doentes e a população em geral, com divulgação de informação, têm um impacto estatisticamente significativo na redução do consumo de antibióticos na população.

O problema das resistências bacterianas parece um problema sem resolução próxima, devido à falta de desenvolvimento de novos antibióticos e devido à pressão seletiva que existe sobre as bactérias associada ao mau uso de antibióticos. Desta forma é muito importante o desenvolvimento de intervenções que melhorem o uso de antibióticos, sendo que a intervenção educativa aqui apresentada pode ser facilmente reproduzida em outras regiões. O consumo de

antibióticos em cuidados de saúde primários em Portugal continua muito elevado comparando com outros países europeus, e os níveis de resistência também são bastante elevados, revelando a necessidade de intervir para diminuir este flagelo. Apesar das medidas governamentais, aprovadas em 2013 para reduzir o consumo de antibióticos, parece-nos importante associar-lhes intervenções educativas dirigidas aos profissionais de saúde e à população geral, de forma a terem um maior impacto, como evidenciado pelas diferenças de consumo de antibióticos obtidas no nosso estudo entre o grupo intervenção e o grupo controlo.

CAPÍTULO 10

TRABALHOS EM DESENVOLVIMENTO E PERSPETIVAS DE
INVESTIGAÇÃO FUTURA

10 TRABALHOS EM DESENVOLVIMENTO E PERSPETIVAS DE INVESTIGAÇÃO FUTURA

Com o objetivo de avaliar a necessidade de intervenção no âmbito do consumo de antibióticos, na formação dos futuros profissionais de saúde, está a ser desenvolvido o estudo “Avaliação do perfil de consumo de antibióticos pelos estudantes de cursos superiores da área da saúde”. Os objetivos específicos deste projeto são:

- Avaliar o perfil de consumo de antibióticos pelos estudantes inscritos em cursos superiores da área da saúde.
- Identificar se os estudantes tomam antibióticos sem receita médica.
- Avaliar a perceção dos jovens em relação à facilidade de aquisição de antibióticos diretamente nas farmácias sem receita médica.
- Avaliar se o comportamento em relação à toma de antibióticos é diferente entre os estudantes do primeiro ano e os estudantes dos últimos anos de formação.

Com base numa revisão bibliográfica, construiu-se um questionário para recolha de informação. Está a ser realizado um estudo transversal através da aplicação do questionário aos estudantes dos cursos de Ciências Farmacêuticas, Enfermagem, Farmácia e Medicina da Universidade da Beira Interior e do Instituto Politécnico da Guarda.

O consumo de antibióticos em contexto hospitalar é também um tema importante de investigação e estudo. Assim, está a ser desenvolvido um estudo transversal para avaliar as atitudes e conhecimentos dos farmacêuticos hospitalares em relação às resistências bacterianas e ao consumo de antibióticos. Após análise dos resultados obtidos será avaliada a necessidade de intervenção neste grupo profissional em meio hospitalar.

LISTA DE PUBLICAÇÕES

Publicações em revistas científicas internacionais com revisão por pares incluídas na tese

- **Roque F**, Herdeiro MT, Soares S, Teixeira Rodrigues A, Breitenfeld L, Figueiras A. Educational interventions to improve prescription and dispensing of antibiotics: a systematic review. BMC Public Health. 2014 Dec 15;14:1276. doi: 10.1186/1471-2458-14-1276.
- **Roque F**, Soares S, Breitenfeld L, Figueiras A, Herdeiro MT. Influence of community pharmacists' attitudes on antibiotic dispensing behavior: a cross-sectional study in Portugal. Clin Ther. 2015 37(1):168-77. doi: 10.1016/j.clinthera.2014.11.006.
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ANEXOS

Anexo I - Autorização da Comissão Nacional de Proteção de Dados



Proc. N.º: 3154/2013 | 1



AUTORIZAÇÃO Nº 2866/13 12013

I. Do Pedido

O Centro de Biologia Celular da Universidade de Aveiro notificou à CNPD um tratamento de dados pessoais com a finalidade de realização de um estudo observacional subordinado ao tema “Intervenção educativa para melhorar o uso de antibióticos nos profissionais de saúde portugueses: ensaio controlado aleatório por *cluster*”.

O estudo terá como objetivo, por um lado, identificar as atitudes e conhecimentos dos profissionais de saúde – médicos e farmacêuticos – relativamente à prescrição/dispensa de antibióticos e resistência microbiana e, por outro, realizar um ensaio controlado aleatório por *clusters*, cujo objetivo é melhorar a utilização de antibióticos, através de uma intervenção educativa dirigida aos médicos e farmacêuticos na região definida pela Administração Regional de Saúde do Centro, IP (ARS-Centro), com seguimento durante doze meses após a intervenção.

Serão incluídos no estudo todos os médicos e farmacêuticos a exercer atividade nos centros de saúde e nas farmácias comunitárias da área adstrita à ARS Centro, bem como os farmacêuticos hospitalares e os médicos a exercer atividade nos serviços de medicina interna dos centros hospitalares da região centro.

O estudo qualitativo, através de grupos focais para identificação de atitudes e conhecimentos relevantes, irá incidir sobre grupos de discussão de seis a oito farmacêuticos de uma região abrangida pela ARS-Norte – de modo a evitar a contaminação da amostra – implicando a gravação das discussões que serão posteriormente transcritas.

Em seguida, serão elaborados questionários de acordo com a revisão bibliográfica e informação recolhida nos grupos focais, que serão aplicados a farmacêuticos e médicos. Estes questionários de autopreenchimento serão remetidos aos potenciais



participantes por correio, acompanhados de um envelope pré-pago para a sua devolução aos investigadores.

Já no que respeita à segunda fase do estudo, os médicos e farmacêuticos da ARS-Centro que aceitem participar no estudo realizarão uma intervenção educativa quanto à prescrição de antibióticos.

Os participantes no estudo serão acompanhados durante doze meses, para avaliação da eficácia da intervenção.

O investigador que modera as reuniões solicitará o consentimento aos participantes no estudo, que conservará em local de acesso reservado.

Aos titulares dos dados é assegurado o direito de conhecer e corrigir os dados que lhes respeitem.

A segurança das informações é garantida pela manutenção dos dados em local de acesso reservado.

II. Da Análise

Porque em grande parte referentes à vida privada, os dados recolhidos pela requerente têm a natureza de sensíveis, razão pela qual o respetivo tratamento só pode basear-se no consentimento expresso, esclarecido e livre dos titulares dos dados, ou dos seus legais representantes nos termos do disposto no n.º 2 do artigo 7.º da Lei nº 67/98, de 26 de outubro (Lei de Protecção de Dados - LPD).

Por esta razão é necessário o «consentimento expresso do titular», entendendo-se por consentimento qualquer manifestação de vontade, livre, específica e informada, nos termos da qual o titular aceita que os seus dados sejam objeto de tratamento, o qual deve ser obtido através de uma “declaração de consentimento informado” onde seja utilizada uma linguagem clara e acessível.



A handwritten mark or signature in the top right corner of the page.

Nos termos do artigo 10.º da LPD, a declaração de consentimento tem de conter a identificação do responsável pelo tratamento e a finalidade do tratamento, devendo ainda conter informação sobre a existência e as condições do direito de acesso e de retificação por parte do respetivo titular.

Os titulares dos dados, de acordo com a declaração de consentimento informado junta aos autos, apõem as suas assinaturas na mesma, deste modo satisfazendo as exigências legais.

O fundamento de legitimidade é o consentimento dos titulares dos dados.

A informação tratada é recolhida de forma lícita (cfr. alínea a) do n.º 1 do artigo 5.º da LPD), para finalidades determinadas, explícitas e legítimas (cfr. alínea b) do mesmo artigo).

III. Da Conclusão

Em face do exposto, a Comissão Nacional de Protecção de Dados (CNPD) autoriza o tratamento de dados pessoais *supra* apreciado, nos termos do n.º2 do artigo 7.º, da alínea a) do n.º1 do artigo 28.º e do n.º 1 do artigo 30.º da LPD, consignando-se o seguinte:

Responsável pelo tratamento: Centro de Biologia Celular da Universidade de Aveiro

Finalidade: Estudo observacional subordinado ao tema “Intervenção educativa para melhorar o uso de antibióticos nos profissionais de saúde portugueses: ensaio controlado aleatório por *cluster*”.

Categoria de Dados pessoais tratados:

- dos participantes nas discussões de grupo: dados demográficos (género, idade, anos de experiência profissional), atividade que desempenha, opiniões sobre a prescrição de medicamentos, designadamente antibióticos e voz;



- dos farmacêuticos inquiridos: idade, sexo, anos de experiência profissional, atividade que desempenha, número de medicamentos que dispensa por dia (média), número de antibióticos que dispensa por dia (em média), quantos funcionários trabalham na farmácia;

- dos médicos inquiridos: idade, sexo, especialidade, tipo de atividade que desempenha, realiza serviço de atendimento de urgência, quantos doentes vê por dia (em média), quantos doentes vê por semana em contexto de urgência (em média) e quanto tempo dedica a cada doente em contexto de urgência (em média).

Entidades a quem podem ser comunicados: Não há.

Formas de exercício do direito de acesso e retificação: Junto da responsável pelo tratamento dos dados.

Interconexões de tratamentos: Não há.

Transferências de dados para países terceiros: Não há.

Prazo de conservação dos dados: Os dados pessoais e as gravações devem ser destruídos um mês após o fim do estudo.

Lisboa, 09 de abril de 2013

Ana Roque, Helena Delgado António, Carlos Campos Lobo (Relator), Luís Barroso, Luís Paiva de Andrade, Vasco Almeida

Filipa Calvão (Presidente)

Anexo II - Registo do protocolo de estudo no *Clinical Trials*

ClinicalTrials.gov
Protocol Registration System



Protocol Registration Receipt
06/23/2014

An Educational Intervention to Improve the Use of Antibiotics in Portuguese Health Professional

This study has been completed.

Sponsor:	Aveiro University
Collaborators:	Fundação para a Ciência e a Tecnologia
Information provided by (Responsible Party):	Maria Teresa Herdeiro, Aveiro University
ClinicalTrials.gov Identifier:	

► Purpose

This is a cluster randomised controlled trial covering all general practitioners working in the National Health System (SNS) and all pharmacists working in community pharmacies in the area covered by the Health Region Administration of Center (ARS-C) . A specific educative intervention, designed from gaps detected in knowledge and attitudes with respect to antibiotics and resistance, will be carried out on the intervention group. The control group will not receive any specific intervention.

Hypotheses:

1. The attitudes and knowledge towards antibiotics generate habits of prescription by physicians
2. The attitudes and knowledge towards antibiotics generate propensity to dispense antibiotics without prescription by pharmacists
3. The identification of the attitudes, knowledge and factors that generate habits of inadequate prescription will allow the design of specific educative interventions to improve the use of antibiotics
4. The identification of the attitudes, knowledge and factors that generate propensity to dispense antibiotics without prescription will allow the design of specific educative interventions to antibiotic use
5. The interventions designed from gaps detected in knowledge and attitudes with respect to antibiotics and resistance will improve the prescription and dispensation of antibiotics by physicians and pharmacists, respectively.

6. The intervention will collaborate in the control of the bacterial resistance.

Condition	Intervention	Phase
Antibiotics Misuse	Multidisciplinary and multifaceted educational intervention.	N/A

Study Type: Interventional

Study Design: Single Group Assignment, Open Label, N/A

Official Title: An Educational Intervention to Improve the Use of Antibiotics in Portuguese Health Professional: Cluster-randomized Trial

Further study details as provided by Maria Teresa Herdeiro, Aveiro University:

Primary Outcome Measure:

- Reduction from Baseline antibiotic consumption at 18 months, in primary care [Time Frame: up to 18 months] [Designated as safety issue: Yes]

Enrollment: 2300

Study Start Date: May 2013

Primary Completion Date: October 2013

Arms	Assigned Interventions
<p>Experimental: Educational multifaceted intervention</p> <p>Multidisciplinary and multifaceted educational intervention about antibiotic prescription and dispense, in physicians and pharmacists.</p>	<p>Multidisciplinary and multifaceted educational intervention.</p> <p>Outreach visits (40 minutes) which included a PowerPoint presentation and impress materials: poster; flyers; participation certificate and articles mentioned in the presentation. This outreach visit aimed to change the knowledge-attitudes previously identified in a previous study as being associated with poor prescribing of antibiotics in the case of physicians and propensity to dispense antibiotics without medical prescription in the case of pharmacists.</p>

The intervention will consist of group outreach visits (40 minutes), and will be targeted at changing the knowledge-attitudes previously found to be associated with poor prescribing of antibiotics in the case of physicians and propensity to dispense antibiotics without medical prescription in the case of pharmacists.. An observational cohort study of a sample of 1100 primary care physicians and 1200 community pharmacists will be carried out to identify knowledge-attitudes associated with inappropriate prescribing of antibiotics. The independent variables (knowledge-attitudes) will be assessed by a self-administered postal questionnaire and dependent variables are some quantity and quality indicators of the prescribing antibiotics, and consumption data.

Eligibility

Genders Eligible for Study: Both

Inclusion Criteria:

- All general practitioners working during the period of the study in the National System of Health (SNS) All pharmacists working during the period study in the community pharmacies.

Exclusion Criteria:

-

More Information

Responsible Party: Maria Teresa Herdeiro, Prof, Aveiro University

Study ID Numbers: PTDC/SAU-ESA/105530/2008

Health Authority: Portugal: Data Protection Agency

Anexo III - Consentimento informado

Título do estudo: Intervenção educativa para melhorar o uso de antibióticos nos profissionais de saúde portugueses: ensaio controlado aleatório por clusters.

Investigador principal: Maria Teresa Ferreira Herdeiro da Universidade de Aveiro.

Moderador: Maria de Fátima dos Santos Marques Roque do Instituto Politécnico da Guarda.

Esta primeira fase consiste num estudo qualitativo. Se decidir participar, formará parte de um grupo de 6 a 8 farmacêuticos, dirigido por um moderador, em que haverá um debate sobre infecções, antibióticos e resistências antimicrobianas. A sessão irá decorrer durante 60 minutos. As sessões serão gravadas, uma vez que é uma parte fundamental para análise dos resultados na investigação qualitativa e mantida a confidencialidade.

O estudo, recolha, tratamento e comunicação dos dados, será de acordo com a Lei 67/98 - Lei de Protecção de Dados Pessoais.

Eu (nome completo)

.....

Fui informado dos objectivos do estudo e aceito participar no mesmo. Dou o meu consentimento para a gravação da sessão em que vou participar

Assinatura do participante

Assinatura do moderador

Data:

Data

Anexo IV - Carta de apresentação do estudo piloto (1º envio)



Aveiro, 19 de Maio de 2011

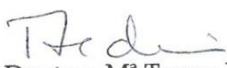
Cara colega


Vimos pela presente, dar conhecimento de um estudo que estamos a realizar na Universidade de Aveiro, intitulado “Intervenção educativa para melhorar o uso de antibióticos nos profissionais de saúde portugueses: ensaio controlado aleatório por cluster” e solicitar desde já a vossa colaboração.

Elaborámos um questionário que pretende recolher informação sobre o conhecimento e procedimentos do farmacêutico em relação à dispensa de antibióticos e resistência microbiana.

Para dar continuidade ao estudo, necessitamos de realizar um teste piloto, no sentido de verificar a reprodutibilidade do referido questionário, pelo que agradecemos que o preencha e faça os comentários que achar convenientes.

Agradecendo antecipadamente a sua colaboração, enviamos os melhores cumprimentos.


Prof. Doutora Mª Teresa Herdeiro
Prof. Auxiliar Convidada
Secção Autónoma das Ciências da Saúde
Universidade de Aveiro


Mestre Fátima Roque
Aluna de Doutoramento
Faculdade de Ciências da Saúde
Universidade da Beira Interior

Anexo V - Carta de apresentação do estudo piloto (2º envio)



Aveiro, 1 de Agosto de 2011

Cara colega,

Estamos a enviar pela segunda vez o questionário que tem por objectivo recolher informação sobre os conhecimentos e procedimentos do farmacêutico em relação à dispensa de antibióticos e resistência microbiana.

Para dar continuidade ao estudo, necessitámos de realizar um teste piloto, no sentido de verificar a fiabilidade e reprodutibilidade do referido questionário, pelo que agradecemos que o preencha novamente.

Faça os comentários que achar convenientes e coloque-o no respectivo envelope.

Agradecendo antecipadamente a sua colaboração, enviamos os melhores cumprimentos.

Prof. Doutora M^a Teresa Herdeiro
Prof. Auxiliar Convidada
Secção Autónoma das Ciências da Saúde
Universidade de Aveiro

Mestre Fátima Roque
Aluna de Doutoramento
Faculdade de Ciências da Saúde
Universidade da Beira Interior



Anexo VI - Questionário



QUESTIONÁRIO N.º: _____

INSTRUÇÕES DE PREENCHIMENTO	totalmente em desacordo	totalmente de acordo
<p>Na coluna da esquerda encontram-se os comentários que serão objecto da sua avaliação e na coluna da direita, à frente de cada afirmação, apresenta-se uma escala gradual na qual deverá marcar com uma X o lugar que, na sua opinião, representa o seu grau de acordo com cada afirmação. Se estiver totalmente em desacordo com a afirmação, deverá marcar a X no extremo esquerdo, da escala e, à medida que aumente o seu grau de concordância com cada afirmação deverá marcar a X sucessivamente mais à direita.</p>	X	100%
	0	100%
	-----X-----	-----X-----
	-----X-----	-----X-----

SOBRE OS ANTIBIÓTICOS E AS RESISTÊNCIAS		
	totalmente em desacordo	totalmente de acordo
1. As resistências a antibióticos são um importante problema de Saúde Pública no nosso meio.	-----	-----
2. O facto de um doente tomar um antibiótico aumenta o risco de desenvolver resistências.	-----	-----
3. Quando se dispensa um antibiótico é fundamental alertar sempre o doente para o cumprimento da terapêutica.	-----	-----
4. Uma importante causa de aparecimento de resistências a antibióticos é a prescrição alargada de novas moléculas.	-----	-----
5. Durante a dispensa, deveriam ser avaliadas as possíveis interações do antibiótico com outros medicamentos que o doente toma.	-----	-----
6. Às vezes dispensa-se um antibiótico sem receita médica porque se sabe que o doente tem dificuldade em obter consulta médica.	-----	-----
7. Duas das principais causas de aparecimento de resistências a antibióticos são a automedicação e o mau uso dos mesmos por parte dos doentes.	-----	-----
8. Por vezes, dispensam-se antibióticos, mesmo sabendo que não são indicados, porque falta tempo para explicar o motivo pelo qual não são úteis.	-----	-----
9. Se um doente acha que precisa de um antibiótico e este não lhe é dispensado, ele consegue facilmente a receita e pode acusar-nos de termos atrasado o tratamento.	-----	-----
10. Estou convicto(a) de que serão desenvolvidos novos antibióticos para solucionar o problema das resistências	-----	-----
11. O uso de antibióticos em animais de consumo é uma causa importante do aparecimento de novas resistências de agentes patogénicos em humanos.	-----	-----
12. Às vezes dispensa-se um antibiótico sem receita médica porque se sabe que o doente não tem tempo e/ou dinheiro para ir ao médico.	-----	-----
13. Se um doente acha que precisa de um antibiótico e este não lhe é dispensado, ele conseguirá obtê-lo facilmente noutra farmácia.	-----	-----
14. A prescrição de antibióticos deveria ser mais controlada.	-----	-----
15. A dispensa de antibióticos sem receita deveria ser mais controlada.	-----	-----
16. O fenómeno da resistência a antibióticos é um problema principalmente do foro hospitalar.	-----	-----

QUANDO SE CONHECE O DOENTE, ÀS VEZES, DISPENSA-SE UM ANTIBIÓTICO, SEM PRESCRIÇÃO MÉDICA, NAS SEGUINTE SITUAÇÕES:





universidade de aveiro

	totalmente em desacordo	totalmente de acordo
Afecções odontológicas (ex. abscessos dentários)	_____	_____
Infecções Respiratórias superiores (ex. otites médias, faringites ...)	_____	_____
Infecções urinárias (cistites)	_____	_____
Qualquer infecção desde que o doente se comprometa a trazer a receita	_____	_____

PARA TERMINAR, ALGUMAS PERGUNTAS DE CARÁCTER GERAL

Que idade tem? ____ anos

Sexo: F M

Anos de experiência profissional em:

Farmácia Hospitalar. Nº de anos ____.

Farmácia Comunitária. Nº de anos ____.

Outra. Qual? ____, Nº de anos ____.

Que tipo de actividade desempenha?

Director Técnico

Farmacêutico Adjunto

Farmacêutico

Aproximadamente, quantos medicamentos dispensa, em média, por dia? _____

Aproximadamente, quantos antibióticos, dispensa, em média por dia? _____

Quantos funcionários trabalham na farmácia?

- Farmacêuticos _____

- Técnicos de farmácia _____

- Ajudantes Técnicos de farmácia _____

- Outros _____. Quais? _____

TEM ALGUMA SUGESTÃO QUE GOSTARIA DE FAZER SOBRE ANTIBIÓTICOS E RESISTÊNCIAS?

MUITO OBRIGADO PELA SUA COLABORAÇÃO

Anexo VII - Carta do Presidente da Secção Regional do Centro da Ordem dos Farmacêuticos enviada com os questionários



Secção Regional de Coimbra

Setembro de 2011

Assunto: Colaboração em estudo de investigação sobre resistências aos antibióticos

Cara(o) Colega,

A resistência microbiana aos antibióticos é um fenómeno que tem vindo a assumir proporções preocupantes, sendo hoje reconhecido como um grave problema de saúde pública a nível mundial.

O farmacêutico, enquanto profissional de saúde, tem uma responsabilidade acrescida não somente na tentativa de conter a propagação do fenómeno, através da sua prática profissional, como promovendo e apoiando todo o trabalho e todos os estudos que visem a caracterização das causas subjacentes ao problema, bem como à sua contenção.

Neste sentido, tendo em consideração a relevância desta problemática e a importância da colaboração dos farmacêuticos, a Secção Regional de Coimbra decidiu apoiar um estudo promovido por investigadores da Universidade de Aveiro acerca dos factores que influenciam o aparecimento das resistências microbianas aos antibióticos, concretamente promovendo a recepção de um questionário desenvolvido pela equipa de investigação, a todos os farmacêuticos inscritos nesta Secção Regional.

Informação mais detalhada poderá ser consultada em anexo.

Na expectativa da melhor atenção dos Colegas, subscrevemo-nos com os melhores cumprimentos,

O Presidente da Direcção Regional de Coimbra da OF

Paulo Moreira da Fonseca

Anexo VIII - Carta de apresentação do estudo transversal



Setembro 2011

Caro colega,

Está a ser desenvolvido, na Universidade de Aveiro, um estudo financiado pela FCT intitulado “Intervenção educativa para melhorar o uso de antibióticos nos profissionais de saúde portugueses: ensaio controlado aleatório por *cluster*”. Projecto-PTDC/SAU-ESA/105530/2008.

Para dar continuidade ao projeto desenvolvemos um questionário que tem como objetivo identificar as atitudes e conhecimentos dos farmacêuticos, em relação à dispensa de antibióticos e resistência microbiana. Neste sentido vimos solicitar a sua colaboração no projeto através do preenchimento voluntário do questionário que enviamos, desenhado a pensar num rápido e fácil preenchimento.

O universo deste estudo é formado pelos farmacêuticos comunitários a trabalhar na área abrangida pela ARS-Centro. Do ponto de vista metodológico, é fundamental que haja uma participação completa e com uma elevada qualidade das respostas. Garantimos a confidencialidade absoluta dos dados. O código numérico do questionário utilizar-se-á mantendo a confidencialidade, para resolver o problema das “não respostas”. A informação recolhida só será apresentada de maneira agrupada e utilizada unicamente para fins científico-académicos.

No cabeçalho do questionário, encontrará as instruções para o seu correto preenchimento, que agradecemos leia atentamente.

Quando terminar de preencher o questionário, agradecemos que o coloque dentro do envelope franquiado e pré-preenchido e nos envie pelo correio.

Agradecendo antecipadamente a sua colaboração, enviamos os melhores cumprimentos.

Prof. Doutora Maria Teresa Herdeiro
Prof. Auxiliar Convidada
Secção Autónoma das Ciências da Saúde
Universidade de Aveiro

Mestre Fátima Roque
Aluna de Doutoramento
Faculdade de Ciências da Saúde
Universidade da Beira Interior



Anexo IX - Poster

MENOS ANTIBIÓTICOS, MAIS SAÚDE!



<http://www.stockfreemages.com/3671676/Cute-monochrome-boy.html>

Consumo excessivo de antibióticos não tem vantagens para a saúde.

Antibióticos não curam nem melhoram os sintomas de Grippes e Constipações virais.

Quando não são necessários, os antibióticos podem ser prejudiciais.

RISCO PARA A SAÚDE DAS GERAÇÕES FUTURAS!

Patrocínio Científico

Colaboração

GOVERNO DE PORTUGAL
MINISTÉRIO DA SAÚDE

ARISC ADMINISTRAÇÃO REGIONAL DE SAÚDE DO CENTRO, L.P.

COMPETE CENTRO DE OPERACIONALIDADE EM RECURSOS HUMANOS

FCT Fundação para a Ciência e a Tecnologia

Este trabalho é financiado por fundos FEDER através do Programa Operacional Factores de Competitividade – COMPETE e por Fundos Nacionais através da FCT – Fundação para a Ciência e a Tecnologia no âmbito do projecto PTDC/SAU-ESA/12553/2009.

Anexo X - Flyer

a ter em consideração:



Antibióticos não curam gripes ou constipações.



Muco de cor verde não significa necessidade de antibiótico.



Antibióticos podem provocar reações alérgicas e destruição da flora bacteriana.



Incentive a adoção de medidas não farmacológicas.

Antibióticos: SÓ quando necessário!

Patrocínio Científico



Colaboração



Ilustrações: [Mário Correia Barra](#) | Imagens: <http://www.stockfreeimages.com/>

Este trabalho é financiado por Fundos FEDER através do Programa Operacional Factores de Competitividade - COMPETE e por Fundos Nacionais através da FCT - Fundação para a Ciência e a Tecnologia no âmbito do projecto PTDC/SAU-ESA/10558Q/2006.



Menos Antibióticos, Mais Saúde.




Problemática Mundial,



Aumento dos custos associados aos cuidados de saúde.

Aumento da morbidade e mortalidade.

Dificuldade no controlo de infeções.

Risco de retorno à era Pré-antibiótica.

que afeta Portugal,

Portugal apresenta elevados níveis de resistência para algumas bactérias.
A resistência do *Staphylococcus aureus* à meticilina ultrapassa os 50%*

Os antibióticos são prescritos, na sua maioria, em Cuidados Primários. Revela a importância dos cuidados primários nesta problemática.

Verifica-se um elevado consumo de antibióticos na região centro.
Desde 2000 que o consumo total de antibióticos nesta região é superior à média em Portugal Continental.

devendo destacar-se:

Consumo de antibióticos induz o desenvolvimento de resistências.
A introdução de antibióticos no mercado tem sido acompanhada por um aumento gradual das resistências bacterianas.

Consumo excessivo de antibióticos não apresenta vantagens clínicas.
Nos países onde se verifica um maior consumo de antibióticos, não se observam maiores benefícios clínicos para os doentes.

Diminuição dos antibióticos disponíveis em clínica.
Verifica-se uma perda de efetividade dos antibióticos disponíveis, bem como uma diminuição do desenvolvimento de novas moléculas.

Anexo XI - Cartaz de divulgação das intervenções educativas

MENOS ANTIBIÓTICOS, MAIS SAÚDE!



http://www.sxcodirectimages.com/3571876/cute-manufacture-baby.html

Formação dirigida a Farmacêuticos.

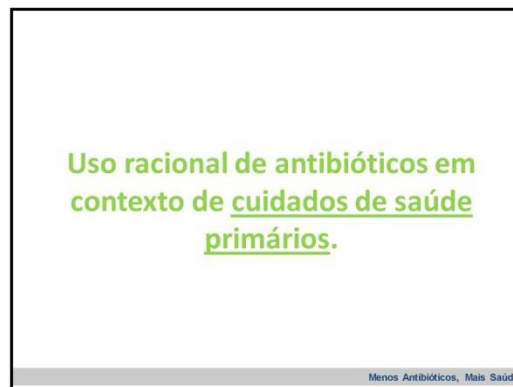
- **Covilhã** - Faculdade Ciências da Saúde da UBI: 30 de maio de 2013 (14h00); 3 de Junho (14h00 e 16h30)
- **Castelo Branco** - Centro de Saúde de S. Miguel: 5 de junho de 2013 (14h00 e 16.30)
- **Guarda** – Escola Superior de Saúde do IPG: 13 de junho de 2013 (15h00 e 16h30)



Escolha a sua sessão e inscreva-se para froque@ipg.pt



Anexo XII - Material educativo da intervenção “Menos Antibióticos Mais Saúde”



Consequências do desenvolvimento de Resistências Microbianas

- Morbilidade e Mortalidade
- Dificulta o controlo de infeções
- Retorno à era Pré-antibiótica




Menos Antibióticos, Mais Saúde

Consequências do desenvolvimento de Resistências Microbianas

- Morbilidade e Mortalidade
- Dificulta o controlo de infeções
- Retorno à era Pré-antibiótica
- Aumento dos custos em Saúde




Menos Antibióticos, Mais Saúde

Consequências do desenvolvimento de Resistências Microbianas

- Morbilidade e Mortalidade
- Dificulta o controlo de infeções
- Retorno à era Pré-antibiótica
- Aumento dos custos em Saúde
- Arrisca ganhos em Saúde





Menos Antibióticos, Mais Saúde

Consequências do desenvolvimento de Resistências Microbianas

- Morbilidade e Mortalidade
- Dificulta o controlo de infeções
- Retorno à era Pré-antibiótica
- Aumento dos custos em Saúde
- Arrisca o ganho em Saúde
- Ameaça à escala global




Menos Antibióticos, Mais Saúde

Factos sobre a resistência microbiana aos antibióticos



- Prevalência das Resistências Microbianas.
- Consumo de antibióticos e Resistências microbianas.
- Papel dos cuidados primários de saúde.
- Consumo excessivo de antibióticos.
- Realidade Portuguesa.
- Qual o futuro dos Antibióticos?




Menos Antibióticos, Mais Saúde

Factos sobre a resistência microbiana aos antibióticos

A maioria dos antibióticos é prescrito em contexto de cuidados primários!

Menos Antibióticos, Mais Saúde

Factos sobre a resistência microbiana aos antibióticos

 **A maioria dos antibióticos é prescrito em contexto de cuidados primários!**



Menos Antibióticos, Mais Saúde

Factos sobre a resistência microbiana aos antibióticos

 **O consumo de antibióticos está na base do desenvolvimento de resistências microbianas!**

Menos Antibióticos, Mais Saúde

Factos sobre a resistência microbiana aos antibióticos

 **O consumo de antibióticos está na base do desenvolvimento de resistências microbianas!**


THE LANCET

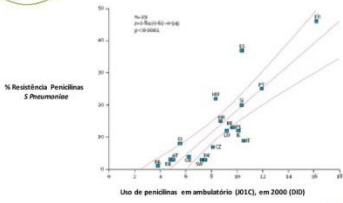
Outpatient antibiotic use in Europe and association with resistance: a cross-national database study

Simon Cassels, Helen Firth, Adam Valleron, Stéphanie Hingray, Benjamin J. Gold, et al. *Lancet* 2015; 385: 1112-19

Menos Antibióticos, Mais Saúde


Factos sobre a resistência microbiana aos antibióticos

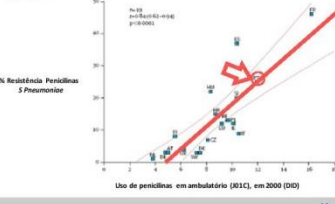
 **O consumo de antibióticos está na base do desenvolvimento de resistências microbianas!**



Menos Antibióticos, Mais Saúde

Factos sobre a resistência microbiana aos antibióticos

 **O consumo de antibióticos está na base do desenvolvimento de resistências microbianas!**

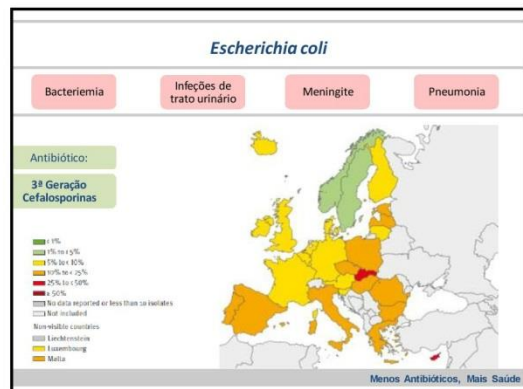
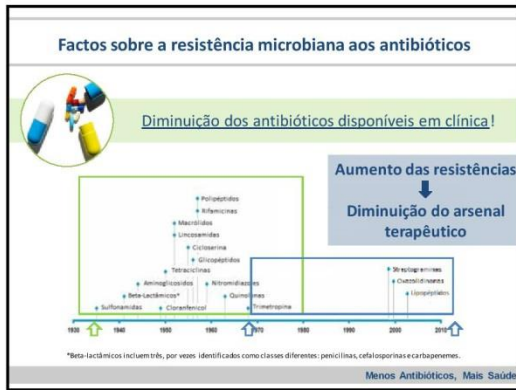


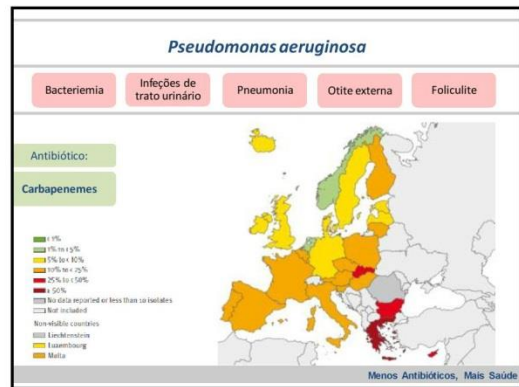
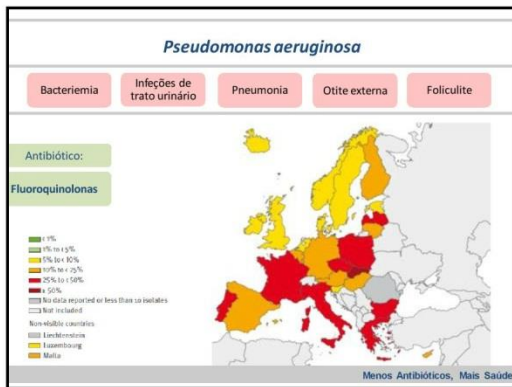
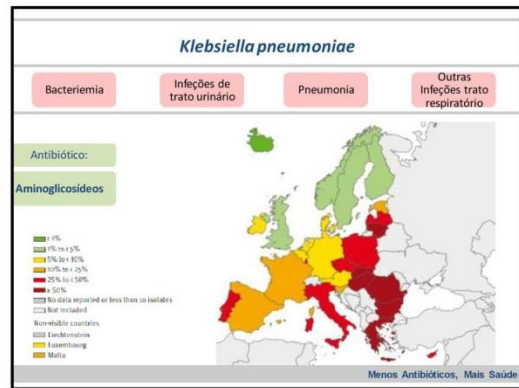
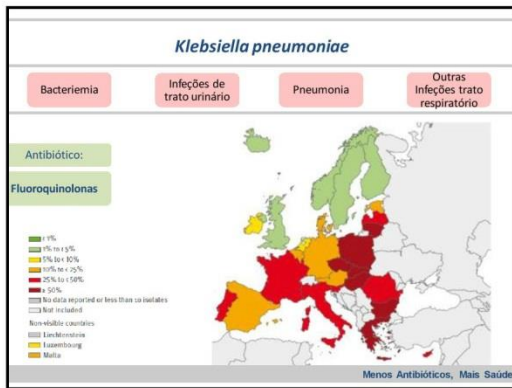
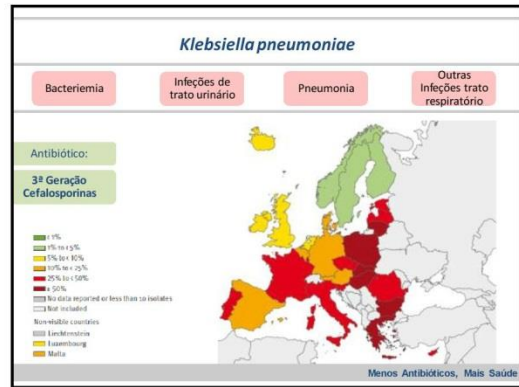
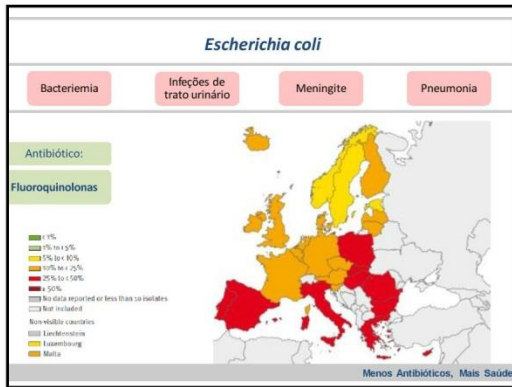
Menos Antibióticos, Mais Saúde

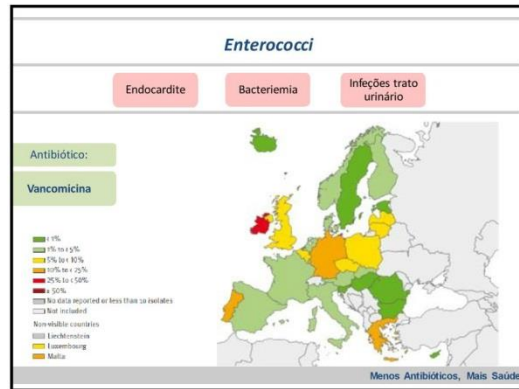
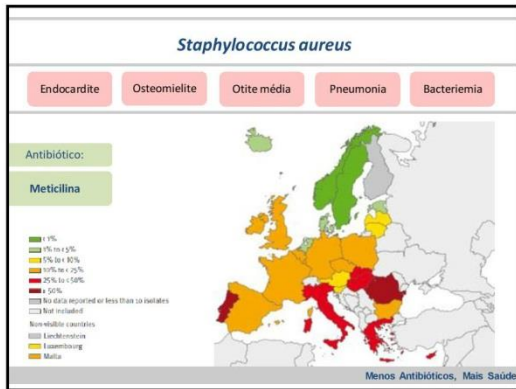
Factos sobre a resistência microbiana aos antibióticos

 **Consumo excessivo de antibióticos não apresenta vantagens clínicas!**

Menos Antibióticos, Mais Saúde







Factos sobre a resistência microbiana aos antibióticos

Em Portugal, a Região Centro é a que apresenta maior consumo de antibióticos.

Menos Antibióticos, Mais Saúde

Factos sobre a resistência microbiana aos antibióticos

Em Portugal, a Região Centro é a que apresenta maior consumo de antibióticos.

A Evolução do Consumo de Antibióticos em Ambulatório em Portugal Continental 2000-2009

Evolution of Outpatient Antibiotic Use in Mainland Portugal 2000-2009

Isabel RAMALHÃO, Mariana RIBEIRINHO, Isaura VIEIRA, José CABRITA
Acta Med Port 2012; 25(1):20-28

Menos Antibióticos, Mais Saúde

Factos sobre a resistência microbiana aos antibióticos

Em Portugal, a Região Centro é a que apresenta maior consumo de antibióticos.

	2000	2001	2002	2003	2004	2006	2008	2007	2008	2009	Var.(%)
Norte	23,69	23,95	24,06	24,15	22,48	23,75	22,00	22,19	21,43	21,95	-7,26
Centro	25,20	24,74	24,99	25,53	23,88	25,73	23,48	22,19	22,49	22,56	-10,48
Lisboa e V. Tejo	24,62	23,56	23,71	24,05	22,78	24,59	22,74	21,42	21,44	21,73	-9,53
Alentejo	23,06	22,21	22,77	23,41	22,01	24,37	21,92	20,78	21,59	21,78	-5,56
Algarve	23,08	23,66	22,09	23,88	22,06	24,03	23,76	22,51	22,08	22,48	-2,83
Centroeste	24,12	22,82	24,03	24,40	22,89	24,56	22,88	21,99	21,72	22,93	-8,85

F=3,286, p<0,001

Menos Antibióticos, Mais Saúde

Factos sobre a resistência microbiana aos antibióticos

Em Portugal, a Região Centro é a que apresenta maior consumo de antibióticos.

	1º 2000	1º 2001	1º 2002	1º 2003	1º 2004	1º 2006	2º 2006	2º 2007	1º 2008	1º 2009	Var.(%)
Norte	23,69	23,95	24,06	24,15	22,48	23,75	22,00	22,19	21,43	21,95	-7,26
Centro	25,20	24,74	24,99	25,53	23,88	25,73	23,48	22,19	22,49	22,56	-10,48
Lisboa e V. Tejo	24,62	23,56	23,71	24,05	22,78	24,59	22,74	21,42	21,44	21,73	-9,53
Alentejo	23,06	22,21	22,77	23,41	22,01	24,37	21,92	20,78	21,59	21,78	-5,56
Algarve	23,08	23,66	22,09	23,88	22,06	24,03	23,76	22,51	22,08	22,48	-2,83
Centroeste	24,12	22,82	24,03	24,40	22,89	24,56	22,88	21,99	21,72	22,93	-8,85

F=3,286, p<0,001

Menos Antibióticos, Mais Saúde



Factos sobre a resistência microbiana aos antibióticos

Portugal apresenta elevados níveis de resistência para algumas bactérias.

Consumo de antibióticos induz o desenvolvimento de resistências.

Os antibióticos são prescritos, na sua maioria, em Cuidados Primários.

Consumo excessivo de antibióticos não apresenta vantagens clínicas.

O maior consumo de antibióticos verifica-se na Região Centro.

Diminuição dos antibióticos disponíveis em clínica.

Menos Antibióticos, Mais Saúde

Intervenções para melhorar a utilização de antibióticos

Snort. Sniffle. Sneeze. No Antibiotics Please.

Treat colds and flu with care. Talk to your healthcare provider.

GET SMART

Menos Antibióticos, Mais Saúde

Intervenções para melhorar a utilização de antibióticos

You are Smart! You've learned a great thing: taking medicines — and giving medicines to children. But there is a problem. Many people take antibiotics when they do not need them. Antibiotics do not work for every illness.

What is an antibiotic? An antibiotic is a medicine that destroys harmful bacteria. It does not work for viruses and other illnesses.

For more information talk with your healthcare provider. Call 1-800-4-A-DRUG for more information.

BE SMART

Menos Antibióticos, Mais Saúde

Intervenções para melhorar a utilização de antibióticos

Remember

When you do need them, make sure you take antibiotics responsibly.

- Antibiotics won't work in the case of a cold or the flu.
- Take antibiotic responsibility and only when they are prescribed by your doctor.
- Keeping antibiotics effective is everybody's responsibility.

Antibiotic Awareness Keep Antibiotics Effective

Menos Antibióticos, Mais Saúde

Intervenções para melhorar a utilização de antibióticos

LEMBRE-SE

antibióticos a mais saúde a menos

aconselhe-se com o seu médico

PRESEERVE OS ANTIBIÓTICOS - CAMPANHA DE SENSIBILIZAÇÃO DO CENADIC

Menos Antibióticos, Mais Saúde

Intervenções para melhorar a utilização de antibióticos



Menos Antibióticos, Mais Saúde

A imprensa no mundo



Chief Medical Officer Dame Sally Davies:
Resistance to antibiotics risks health
'catastrophe' to rank with terrorism and climate
change

Menos Antibióticos, Mais Saúde

A imprensa em Portugal



Sociedade

Resistência a antibióticos pode
gerar crise sanitária

Menos Antibióticos, Mais Saúde

A imprensa em Portugal



Governo quer disciplinar prescrição de antibióticos



Menos Antibióticos, Mais Saúde

Resistência Microbiana aos Antibióticos

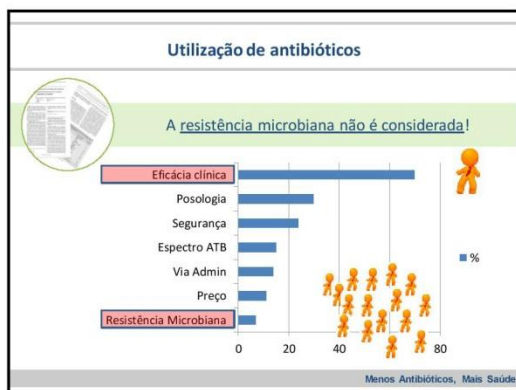
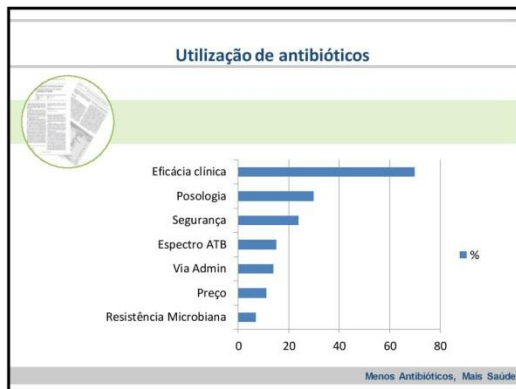


Combat Drug Resistance: No action today, no cure tomorrow!

Menos Antibióticos, Mais Saúde

Fatores que influenciam o
consumo de Antibióticos

Menos Antibióticos, Mais Saúde



Fatores que influenciam o consumo de antibióticos

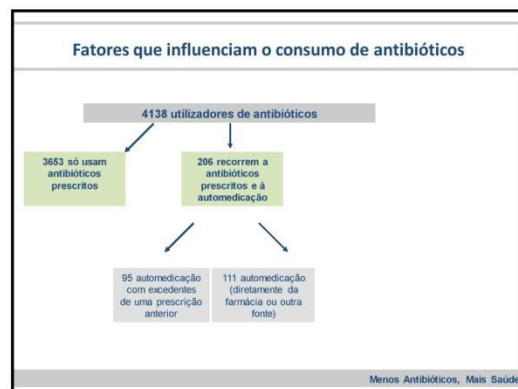
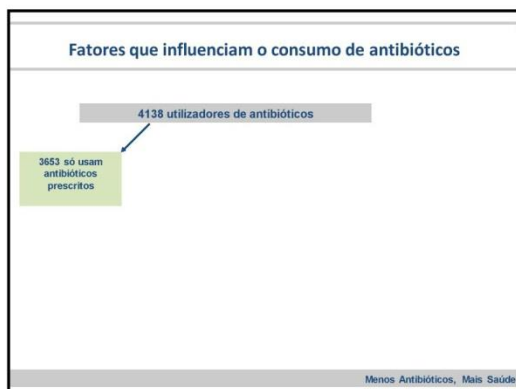
Journal of Antimicrobial Chemotherapy (2007), 59, 152-156
doi:10.1093/jac/dk167
Advance Access publication 22 November 2006

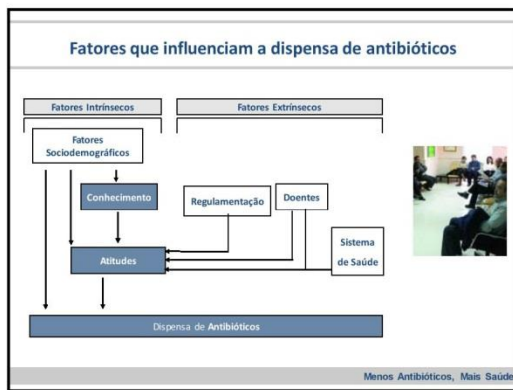
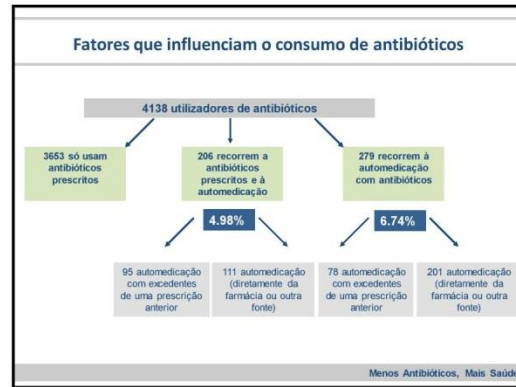
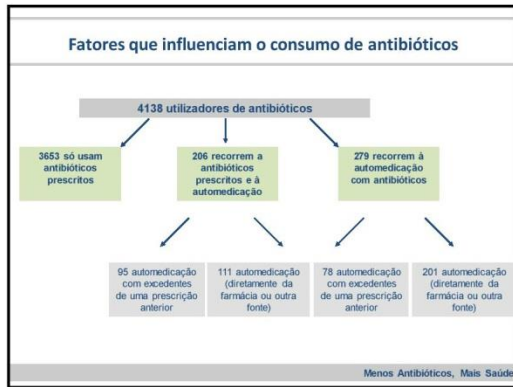
JAC

Is self-medication with antibiotics in Europe driven by prescribed use?

Larissa Grigoryan¹*, Johannes G. M. Burgerhof², Flora M. Haaijer-Ruskamp¹, John E. Degener³, Reginald Dwechepo⁴, Dominique L. Monnet⁵, Antonella Di Matteo⁶, Elizabeth A. Sckina⁷, Ana-Claudia Bara⁸, Cecilia Ståhlby Lundborg⁹ and Joan Bikki¹⁰ on behalf of the SAR group

Menos Antibióticos, Mais Saúde





Fatores que influenciam a dispensa de antibióticos

Fatores considerados como as principais causas de resistências:

Int J Clin Pharm
DOI 10.1007/s11426-013-0134-4
RESEARCH ARTICLE

Attitudes of community pharmacists to antibiotic dispensing and microbial resistance: a qualitative study in Portugal

Fátima Borges · Sara Soares · Luísa Revolta-Mil · Ana Luísa Soares · João Filipeiros · Maria Teresa Hordido

Received: 14 May 2012 / Accepted: 22 January 2013
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Menos Antibióticos, Mais Saúde

Fatores que influenciam a dispensa de antibióticos

Fatores considerados como as principais causas de resistências:

1. Automedicação com antibióticos prescritos para situações clínicas anteriores, em que não foi concluída a terapêutica e/ou aquisição de antibióticos sem prescrição médica nalgumas farmácias

Menos Antibióticos, Mais Saúde


Fatores que influenciam a dispensa de antibióticos

Fatores considerados como as principais causas de resistências:

1. Automedicação com antibióticos prescritos para situações clínicas anteriores, em que não foi concluída a terapêutica e/ou aquisição de antibióticos sem prescrição médica em determinadas farmácias
2. Não cumprimento da terapêutica de acordo com a dosagem prescrita

Menos Antibióticos, Mais Saúde

Fatores que influenciam a dispensa de antibióticos



Fatores considerados como as principais causas de resistências:

1. Automedicação com antibióticos prescritos para situações clínicas anteriores, em que não foi concluída a terapêutica e/ou aquisição de antibióticos sem prescrição médica em determinadas farmácias
2. Não cumprimento da terapêutica de acordo com a dosagem prescrita
3. **Prescrição em excesso/inadequada**

Menos Antibióticos, Mais Saúde

Fatores que influenciam a dispensa de antibióticos



Fatores considerados como as principais causas de resistências:

1. Automedicação com antibióticos prescritos para situações clínicas anteriores, em que não foi concluída a terapêutica e/ou aquisição de antibióticos sem prescrição médica em determinadas farmácias
2. Não cumprimento da terapêutica de acordo com a dosagem prescrita
3. Prescrição em excesso/inadequada
4. **Uso excessivo de antibióticos em animais para consumo humano**

Menos Antibióticos, Mais Saúde

Fatores que influenciam a dispensa de antibióticos



Int J Clin Pharm
DOI 10.1007/s11426-013-9533-4
RESEARCH ARTICLE


Attitudes of community pharmacists to antibiotic dispensing and microbial resistance: a qualitative study in Portugal

Fátima Roque · Sara Soares · Luísa Reinkenfeldt · Ana Lopes-Duarte · António Figueiredo · Maria Teresa Herdeiro

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Menos Antibióticos, Mais Saúde


Fatores que influenciam a dispensa de antibióticos



1. **Unidades prescritas insuficientes para completar o tratamento**

Menos Antibióticos, Mais Saúde


Fatores que influenciam a dispensa de antibióticos



1. Unidades prescritas insuficientes para completar o tratamento
2. **Prescrição através do telefone**

Menos Antibióticos, Mais Saúde


Fatores que influenciam a dispensa de antibióticos



1. Unidades prescritas insuficientes para completar o tratamento
2. Prescrição através do telefone
3. **Doente conhecido/história clínica conhecida, como amigdalite recorrente (doente traz a prescrição mais tarde)**

Menos Antibióticos, Mais Saúde


Fatores que influenciam a dispensa de antibióticos



1. Unidades prescritas insuficientes para completar o tratamento
2. Prescrição através do telefone
3. Doente conhecido/história clínica conhecida, como amigdalite recorrente (doente traz a prescrição mais tarde)
- 4. Tratamento de infeções específicas, tais como infeções dentárias e urinárias (sabem que o médico irá prescrever)**

Menos Antibióticos, Mais Saúde

Fatores que influenciam a dispensa de antibióticos



1. Unidades prescritas insuficientes para completar o tratamento
2. Prescrição através do telefone
3. Doente conhecido/história clínica conhecida, como amigdalite recorrente (doente traz a prescrição mais tarde)
4. Tratamento de infeções específicas, tais como infeções dentárias e urinárias (sabem que o médico irá prescrever)
- 5. Atitudes e conhecimentos**


Menos Antibióticos, Mais Saúde

Estratégias para melhorar a utilização de antibióticos

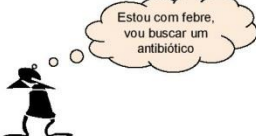
Problema	Solução
 Expectativas e pressão do doente	
 Uso de antibióticos em animais	
 Guidelines de seguimento farmacoterapêutico	

Menos Antibióticos, Mais Saúde

Estratégias para melhorar a utilização de antibióticos




Problema




Expectativas do doente

Menos Antibióticos, Mais Saúde

Estratégias para melhorar a utilização de antibióticos




Problema




Expectativas do doente

Menos Antibióticos, Mais Saúde

Estratégias para melhorar a utilização de antibióticos



Problema



Expectativas do doente

Menos Antibióticos, Mais Saúde

Estratégias para melhorar a utilização de antibióticos

Problema

Vou à farmácia, eles conhecem-me...

Expectativas do doente

Menos Antibióticos, Mais Saúde

Estratégias para melhorar a utilização de antibióticos

Qual o papel do farmacêutico?

RESEARCH ARTICLES

Dispensing of antibiotics without prescription in Greece, 2008: another link in the antibiotic resistance chain

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 & 1st Department of Internal Medicine, University of Athens, Medical School, Athens, Greece

Menos Antibióticos, Mais Saúde

Estratégias para melhorar a utilização de antibióticos

Problema

Já que nas outras farmácias dispensam... Eu também vou dispensar...

Pressão do doente

Menos Antibióticos, Mais Saúde

Estratégias para melhorar a utilização de antibióticos

Problema

Já que nas outras farmácias dispensam... Eu também vou dispensar...

Responsabilidade de outros

Pressão do doente

Menos Antibióticos, Mais Saúde

Estratégias para melhorar a utilização de antibióticos

Problema

Já que nas outras farmácias dispensam... Eu também vou dispensar...

Não é por eu dispensar um antibiótico que vai haver mais resistências!

Responsabilidade de outros

Pressão do doente

Menos Antibióticos, Mais Saúde

Estratégias para melhorar a utilização de antibióticos

Problema

Já que nas outras farmácias dispensam... Eu também vou dispensar...

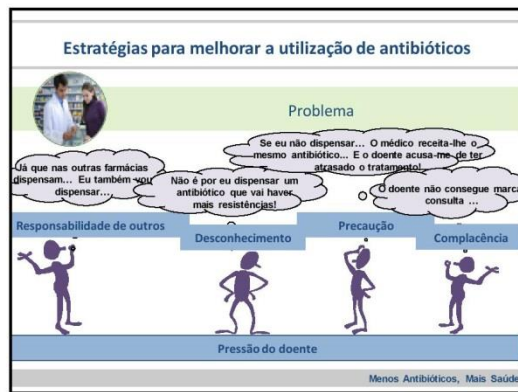
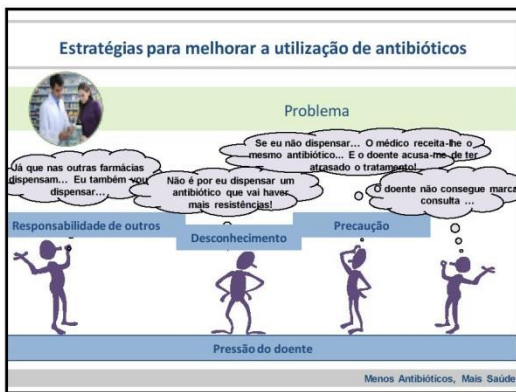
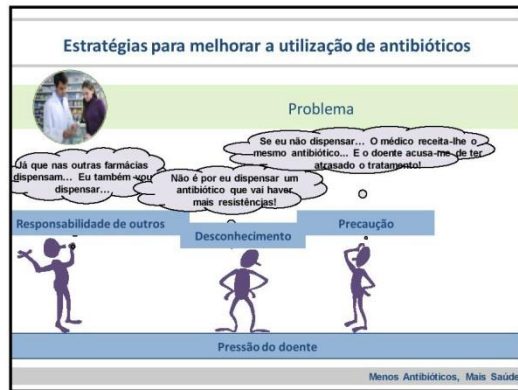
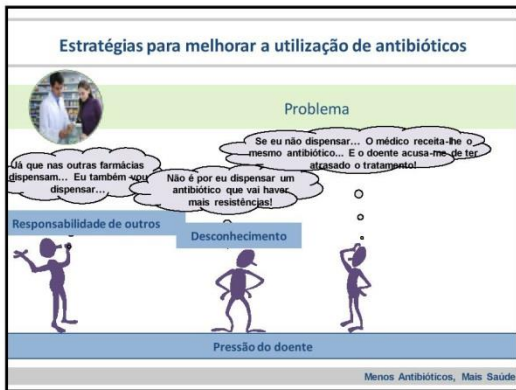
Não é por eu dispensar um antibiótico que vai haver mais resistências!

Responsabilidade de outros

Desconhecimento

Pressão do doente

Menos Antibióticos, Mais Saúde



Estratégias para melhorar a utilização de antibióticos

Problema	Solução
Expectativas e pressão do doente	
Uso de antibióticos em animais	
Guidelines de seguimento farmacoterapêutico	

Menos Antibióticos, Mais Saúde

Estratégias para melhorar a utilização de antibióticos

Problema	Solução
Expectativas e pressão do doente	Promoção da comunicação
Uso de antibióticos em animais	
Guidelines de seguimento farmacoterapêutico	

Menos Antibióticos, Mais Saúde

Estratégias para melhorar a utilização de antibióticos

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Menos Antibióticos, Mais Saúde

Estratégias para melhorar a utilização de antibióticos

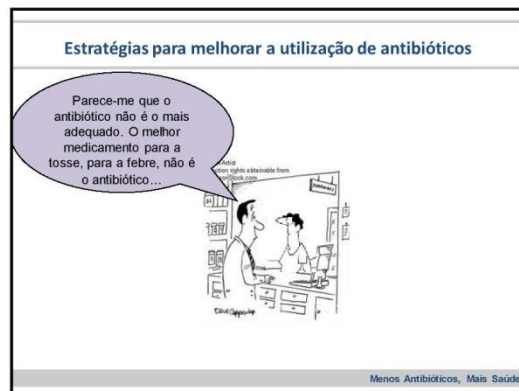
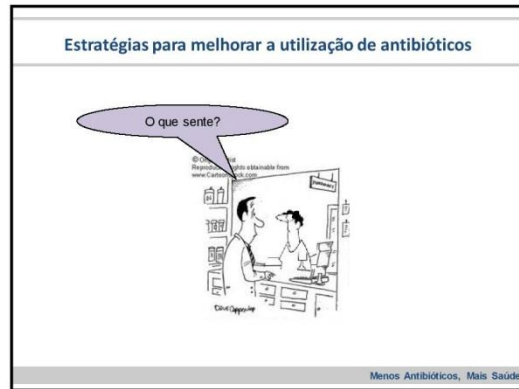
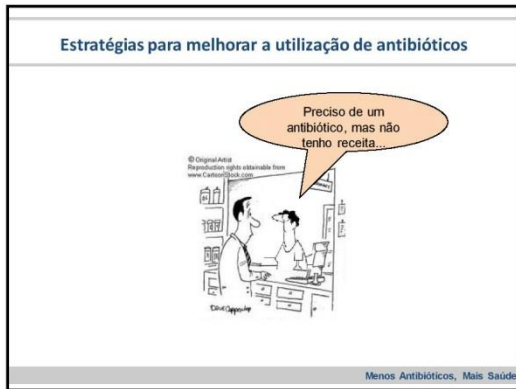
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Menos Antibióticos, Mais Saúde

Estratégias para melhorar a utilização de antibióticos

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Menos Antibióticos, Mais Saúde



Estratégias para melhorar a utilização de antibióticos

Bom dia.
O médico receitou-lhe um antibiótico!
Tem que cumprir o tratamento!
A que horas se levanta? Vamos ver o horário mais adequado para não se esquecer...

Menos Antibióticos, Mais Saúde

Estratégias para melhorar a utilização de antibióticos

Bom dia.
O médico receitou-lhe um antibiótico!
Tem que cumprir o tratamento!
A que horas se levanta? Vamos ver o horário mais adequado para não se esquecer...

Menos Antibióticos, Mais Saúde

Estratégias para melhorar a utilização de antibióticos

Tem mais medicamentos para tomar! Deixe-me ver se há alguma interação entre eles!

Menos Antibióticos, Mais Saúde

Estratégias para melhorar a utilização de antibióticos

Tem mais medicamentos para tomar! Deixe-me ver se há alguma interação entre eles!

Menos Antibióticos, Mais Saúde

Estratégias para melhorar a utilização de antibióticos

Problema	Solução
<p>Expectativas e pressão do doente</p>	Promoção da comunicação
<p>Uso de antibióticos em animais</p>	
<p>Guidelines de seguimento farmacoterapêutico</p>	

Menos Antibióticos, Mais Saúde

Estratégias para melhorar a utilização de antibióticos

Problema


Preciso de um antibiótico para uma ovelha que tenho lá em casa...

Uso de antibióticos em animais: desconhecimento

Menos Antibióticos, Mais Saúde

Estratégias para melhorar a utilização de antibióticos

Problema




Ah! Se é para a ovelha...

Uso de antibióticos em animais: desconhecimento

Menos Antibióticos, Mais Saúde

Estratégias para melhorar a utilização de antibióticos

Problema



Ah! Se é para a ovelha...

Uso de antibióticos em animais: desconhecimento

Menos Antibióticos, Mais Saúde

Estratégias para melhorar a utilização de antibióticos

Problema	Solução
 Expectativas e pressão do doente	Promoção da comunicação
 Uso de antibióticos em animais	
 Guidelines de seguimento farmacoterapêutico	

Menos Antibióticos, Mais Saúde

Estratégias para melhorar a utilização de antibióticos

Problema	Solução
 Expectativas e pressão do doente	Promoção da comunicação
 Uso de antibióticos em animais	Promoção do conhecimento
 Guidelines de seguimento farmacoterapêutico	

Menos Antibióticos, Mais Saúde

Estratégias para melhorar a utilização de antibióticos

Uso de antibióticos em animais é fonte de resistências



Preventive Veterinary Medicine
journal homepage: www.elsevier.com/locate/prevetmed

Evidence of possible methicillin-resistant *Staphylococcus aureus* ST398 spread between pigs and other animals and people residing on the same farm

Larissa J. Pletinsckx^{a,b,c}, Marijke Verbeeghe^{a,d}, Florence Crombé^{e,f}, Jeroen Dewulf^a, Yves De Boeckx^a, Geertuij Raaijmakers^a, Patrick Butaye^{a,g}, Bruno M. Goddeeris^a, Ingrid De Man^a

Menos Antibióticos, Mais Saúde

Estratégias para melhorar a utilização de antibióticos

Problema	Solução
 Expectativas e pressão do doente	Promoção da comunicação
 Uso de antibióticos em animais	Promoção do conhecimento
 Guidelines de seguimento farmacoterapêutico	

Menos Antibióticos, Mais Saúde

Estratégias para melhorar a utilização de antibióticos

Problema	Solução
 Expectativas e pressão do doente	Promoção da comunicação
 Uso de antibióticos em animais	Promoção do conhecimento
 Guidelines de seguimento farmacoterapêutico	Curso Online

Menos Antibióticos, Mais Saúde

Curso Online

Menos Antibióticos, Mais Saúde.










Menos Antibióticos, Mais Saúde

Menos Antibióticos, Mais Saúde.

Obrigada pela atenção!

Maria de Fátima dos Santos Marques Roque
 froque@ipg.pt
 26 de junho de 2013







Menos Antibióticos, Mais Saúde

Anexo XIII - Certificado de Participação



Certificado de Participação

Certifica-se que _____ participou na sessão de formação intitulada

“Menos antibióticos, mais Saúde”, sobre utilização de antibióticos e desenvolvimento de resistências microbianas,

realizada em _____.

Prof.^a Doutora Odete Cruz e Silva

Diretora do Centro de Biologia Celular
Secção Autónoma de Ciências da Saúde
Universidade de Aveiro

Prof.^a Doutora Maria Teresa Herdeiro

Investigadora do Centro de Biologia Celular
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Investigadora do Centro de Investigação em Ciências da Saúde
Faculdade Ciências da Saúde
Universidade da Beira Interior Coimbra



