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THELMA ONOZATO

FATORES QUE INFLUENCIAM A IMPLEMENTAÇÃO DE SERVIÇOS CLÍNICOS FARMACÊUTICOS EM HOSPITAIS: IDENTIFICAÇÃO E ANÁLISE PELO *FRAMEWORK* APOTECA

SÃO CRISTÓVÃO

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Tese de Doutorado apresentada ao Programa de Pós-Graduação em Ciências da Saúde da Universidade Federal de Sergipe como requisito para obtenção do grau de Doutor em Ciências da Saúde.

Orientador: Prof. Dr. Divaldo Pereira de Lyra Júnior

Linha de pesquisa: Formação de recursos humanos em saúde

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Aprovado em:__/__/__

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Orientador: Prof. Dr. Divaldo Pereira de Lyra Júnior

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Examinador 4: Prof. Dr. Marcos Cardoso Rios

PARECER

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Dedico este trabalho aos meus pais, Toneo e Rita, com quem aprendi o valor do estudo e do trabalho.

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"Health care is a sacred mission [...] a moral enterprise and a scientific enterprise but not fundamentally a commercial one. We are not selling a product. […]Ultimately, the secret of quality is love. You have to love your patient, you have to love your profession, you have to love your God. If you have love, you can then work backward to monitor and improve the system".

(Avedis Donabedian, 1919-2000)

RESUMO

FATORES QUE INFLUENCIAM A IMPLEMENTAÇÃO DE SERVIÇOS CLÍNICOS FARMACÊUTICOS EM HOSPITAIS: IDENTIFICAÇÃO E ANÁLISE PELO *FRAMEWORK* APOTECA. Thelma Onozato, 2018.

Introdução. A implementação de Serviços Clínicos Farmacêuticos (SCF) é uma ação estratégica para otimizar a farmacoterapia de pacientes hospitalizados. Embora muitos estudos relatem resultados benéficos dos SCF, ainda não há padronização dessa prática em hospitais, inclusive no Brasil. Conhecer os fatores que influenciam a implementação de SCF e identificar onde atuam é o primeiro passo para adoção bem-sucedida destes serviços. **Objetivo**. Identificar os fatores que afetam a implementação da SCF no ambiente hospitalar e analisá-los utilizando os domínios Apoteca. **Metodologia**. O estudo foi realizado em cinco etapas. (1) *Desenvolvimento de um framework de determinantes para análise de fatores que influenciam a implementação de SCF*. Para isso, foram realizadas observações sistemáticas durante experiências de implementação de SCF conduzidas pelos pesquisadores e análise de modelos conceituais fundamentados em observações da realidade. (2) *Revisão sistemática da literatura para identificar fatores que influenciam a implementação de SCF em ambiente hospitalar*. Seis bases de dados foram pesquisadas até janeiro de 2018. A estratégia de busca foi desenvolvida usando termos relacionados a: "farmácia clínica", "fatores influenciadores", "implementação" e "hospital". Dois revisores selecionaram artigos originais, extraíram os dados e avaliaram a qualidade dos estudos. Após a síntese de *framework* e categorização dos fatores em grupos de interesse e domínios Atitudinais, Políticos, Técnicos e Administrativos (Apoteca), uma abordagem diagramática foi utilizada para apresentar os resultados. (3) *Grupo focal com farmacêuticos e entrevistas com gerentes hospitalares para conhecer as percepções acerca dos fatores que poderiam influenciar a implementação de SCF no hospital do estudo*. (4) *Intervenção estruturada,* com abordagens atitudinais, políticas, técnicas e administrativas. (5) *Entrevistas com os farmacêuticos e gerentes ligados aos SCF para conhecer as percepções acerca dos fatores que influenciaram efetivamente a implementação de SCF no hospital do estudo*. Depois de coletar as informações, os registros de áudio foram transcritos e analisados usando análise de *framework* e os domínios Apoteca. **Resultados**. Foram propostos quatro domínios para análise dos fatores influenciadores da implementação de SCF: Atitudinal, Político, Técnico e Administrativo - *framework* Apoteca. Na revisão foram identificados 53 fatores em 21 estudos incluídos. Os fatores mais citados foram uniformemente distribuídos nos quatro domínios Apoteca, em termos de grupos de interesse, o "farmacêutico" teve a maior concentração de fatores. O fator mais citado foi "Habilidades e conhecimento clínico", seguido de "Tempo para implantar SCF". No estudo de intervenção, farmacêuticos relataram 19 barreiras e gerentes perceberam 16. Cerca de metade das barreiras citadas foram consideradas superadas ou não-concretizadas na segunda entrevista. Gerentes e farmacêuticos mencionaram um número menor de facilitadores quando comparados às barreiras (onze e dez, respectivamente), e os segundos só conseguiram percebê-los após a intervenção. Em relação à classificação Apoteca, a maioria das barreiras foi administrativa e dos facilitadores foi político. **Conclusão**. Os resultados obtidos mostraram a natureza multifatorial do processo de implementação de SCF e que farmacêuticos e gerentes anteciparam mais barreiras e menos facilitadores quando comparados aos fatores efetivamente experimentados. Esses achados sugerem que a implementação estruturada, considerando os quatro domínios Apoteca podem auxiliar na implementação bem-sucedida de SCF em hospitais.

Palavras-chave: Farmácia clínica; Farmacêutico; Pesquisa de implementação; Fatores influenciadores; Barreiras; Facilitadores; Hospital.

ABSTRACT

FACTORS INFLUENCING THE IMPLEMENTATION OF CLINICAL PHARMACY SERVICES IN HOSPITALS: IDENTIFICATION AND APOTECA FRAMEWORK ANALYSIS. Thelma Onozato, 2018.

Introduction. The implementation of Clinical Pharmacy Services (CPS) is a strategic action to optimize the pharmacotherapy of hospitalized patients. Although many studies have shown beneficial results for CPS, they are not uniformly established in hospitals worldwide, including in Brazil. To know the factors that influence CPS deployment and to identify where they act is the first step toward successful adoption of these services in hospitals. **Aim.** To identify the factors that affect the CPS implementation in the hospital setting and to analyze them using the Apoteca domains. **Methods.** The study was carried out in five stages. (1) *Framework development to analyze factors that influence the implementation of SCF*. For this, systematic observations were made during SCF implementation experiences conducted by the researchers and analysis of conceptual models based on observations of reality were performed. (2) *Systematic review of the literature to identify factors that influence the implementation of CPS in the hospital setting*. Six databases were searched until January 2018. The search strategy was developed using terms related to: "clinical pharmacy", "influencing factors", "implementation" and "hospital". Two reviewers selected original articles, extracted data and assessed the quality of the studies. After the framework synthesis and categorization of the factors in groups of interest and Attitudinal, Political, Technical and Administrative domains (Apoteca), a diagrammatic approach was used to present the results. (3) *Focus group with pharmacists and interviews with hospital managers were carried out to know the perceptions about the factors that could influence the implementation of CPS in the hospital studied*. (4) *Structured implementation intervention* with attitudinal, political, technical and administrative approaches. (5) *Interviews were carried out with the pharmacists who performed the CPS and managers, to know the participants' perceptions of the factors that actually influenced the CPS implementation in the hospital*. After collecting the information, the audio records were transcribed and analyzed using framework analysis and the Apoteca domains, in order to compare the perceptions before and after the structured SCF implementation. **Results.** Four domains were proposed to analyze the factors influencing the SCF implementation: Attitudinal, Political, Technical and Administrative – the Apoteca framework. Fifty-three factors were identified in the 21 studies included in the review. The most cited influencing factors were uniformly distributed in the four Apoteca domains, but in terms of interest groups, the "pharmacist" had the highest concentration of factors. "Clinical skills and knowledge" was the most cited factor, followed by "Time to implement CPS". In the intervention study, pharmacists reported 19 obstacles in total, while managers perceived 16 different barriers. About half of the barriers cited were considered to have been overcome or not-met in the second interview. Managers and pharmacists mentioned fewer facilitators when compared to barriers (eleven and ten, respectively), and the latter were only able to perceive them after the intervention. Regarding the Apoteca classification, most of the barriers were administrative and the majority of the facilitators were political. **Conclusion.** The results showed the multifactorial nature of the CPS deployment process and that pharmacists and managers anticipated more barriers and less facilitators when compared to the factors actually experienced. Those findings suggest that a structure implementation, considering the four Apoteca domains, can help in planning strategies to enable the successful implementation of CPS in a hospital setting.

Keywords: Clinical pharmacy; Pharmacists; Implementation research; Influencing factors; Barriers; Facilitators; Hospital.

SUMÁRIO

INTRODUÇÃO

1 **INTRODUÇÃO**

A morbimortalidade relacionada a medicamentos é um problema de saúde pública prevalente em todo o mundo (CHAN et al., 2016; MOUTON et al., 2016; OSCANOA; LIZARASO; CARVAJAL, 2017; PARIHAR et al., 2017). Embora medicamentos proporcionem benefícios terapêuticos - cura, controle da evolução ou alívio de sintomas de doenças - seu uso não é isento de riscos (CURTIN; SCHULZ, 2011). Assim, parte dos pacientes obtém o máximo benefício com o uso de medicamentos, enquanto outros sofrem danos, por vezes, evitáveis. Além disso, o uso subótimo dos medicamentos pode resultar no aumento de custos para os sistemas de saúde por meio, por exemplo, de hospitalizações causadas por erros de prescrição ou morbidade por baixa adesão à farmacoterapia (FARIA et al., 2014).

Angamo et al. (2016), em revisão de 43 estudos observacionais realizada em 21 países, mostram que a prevalência de admissões hospitalares e mortalidade relacionadas às reações adversas a medicamentos variam de 0,2 a 54,5 %, e de 0 a 10%, respectivamente. No ambiente hospitalar, outra revisão sistemática observou que as taxas de prevalência de erros de prescrição relacionados a medicamentos de alta vigilância variam entre 0,24 e 89,6 erros por 100 prescrições desses medicamentos (ALANAZI; TULLY; LEWIS, 2016). Ademais, Salmasi et al. (2015) reportam, em revisão sistemática, que a taxa de prevalência de erros de administração de medicamentos em hospitais do Sudeste Asiático varia entre 15,2 e 88,6%.

Neste cenário, o farmacêutico tem atuado de maneira relevante na prevenção de erros e eventos adversos relacionados a medicamentos, bem como, na otimização da farmacoterapia para a promoção da saúde dos pacientes (STEED et al., 2014; WEANT et al., 2014; WIMMER; NEUBERT; RASCHER, 2015). Desde a década de 1960, com a reorientação da prática farmacêutica para o paciente e desenvolvimento do conceito de Farmácia Clínica, houve expansão das atividades do farmacêutico, da preparação e fornecimento de medicamentos para a avaliação e o gerenciamento das necessidades farmacoterapêuticas das pessoas, como também maior integração e interação com outros profissionais de saúde por meio dos serviços clínicos farmacêuticos (SCF) (CIPOLLE; STRAND; MORLEY, 2012; PEARSON, 2007; SCHINDEL et al., 2017).

A literatura aponta que tais serviços otimizam os resultados em saúde dos pacientes (JOKANOVIC et al., 2016; ROTTA et al., 2015). Holh et al. (2017), em estudo quase-randomizado com 10.807 pacientes de alto risco (grupo intervenção=6.416; grupo controle=4.391), reportaram que um serviço clínico farmacêutico reduziu em 0,48 dias a média de dias de internação (IC=0,00 a 0,96; p=0,058) em três hospitais no Canadá, quando

comparado ao controle. Uma revisão sistemática com meta-análise avaliou a efetividade de programas de conciliação de medicamentos realizadas por farmacêuticos e verificou que pacientes que receberam esses serviços tiveram redução de eventos adversos relacionados a medicamentos (EAM) causados por reinternações (RR 0,33; 95% CI 0,20 to 0,53), visitas a pronto-atendimento por todas as causas (RR 0,72; 95% CI 0,57 to 0,92) e readmissões hospitalares por todas as causas (RR 0,81; 95% CI 0,70 to 0,95) (MEKONNEN; MCLACHLAN; BRIEN, 2016).

Apesar da expansão das atribuições do farmacêutico e das evidências da literatura sobre os benefícios quando os pacientes são acompanhados por este profissional, os serviços clínicos farmacêuticos ainda não estão consolidados de maneira uniforme pelo mundo (DOLORESCO; VERMEULEN, 2009; LEBLANC; SEOANE-VAZQUEZ; DASTA, 2007; PANDE et al., 2013; WORLD HEALTH ORGANIZATION; INTERNATIONAL PHARMACEUTICAL FEDERATION, 2006). Assim, em países desenvolvidos como Estados Unidos e Inglaterra estes serviços são consolidados (JACOBI et al., 2016). Por outro lado, em países subdesenvolvidos e em desenvolvimento, incluindo o Brasil, a implementação desses serviços é uma realidade recente (ALBEKAIRY et al., 2015; BILAL et al., 2016; IQBAL; ISHAQ, 2017; REIS et al., 2015; SHANIKA et al., 2017).

O referencial teórico mais utilizado pelos pesquisadores para a avaliação e implementação de serviços de saúde com qualidade, incluindo os serviços de Farmácia Clínica, é o preconizado por Avedis Donabedian (1966). Para tanto, o referido autor, absorveu da teoria de sistemas a noção de indicadores de estrutura, processo e resultado, adaptando-os aos serviços de saúde (modelo SPO). O componente *estrutura* se refere às características relativamente estáveis e necessárias ao processo assistencial, os *processos* se relacionam às interações e procedimentos envolvendo profissionais de saúde e pacientes e os *resultados* correspondem à alteração no estado de saúde atribuível à intervenção, também às mudanças relacionadas a conhecimentos e comportamentos, assim como à satisfação do usuário ligada ao recebimento dos cuidados.

Este modelo pode ser utilizado como norteador tanto para a avaliação, quanto para a implementação de serviços de saúde qualificados, como a Farmácia Clínica (SCHOENMAKERS et al., 2015). Neste contexto, a avaliação possibilita a identificação das condições existentes e das mudanças necessárias para garantir a implementação de SCF com qualidade (AGUIAR et al., 2013; RADEMAKERS; DELNOIJ; DE BOER, 2011). No Brasil, a carência de dados sobre implementação e avaliação da qualidade dos SCF no âmbito hospitalar justifica a pesquisa sobre o tema, podendo contribuir para a promoção da segurança e do

cuidado ao paciente internado (ANDRADE et al., 2011; ANDRADE et al., 2015; MAGEDANZ; SILLIPRANDI; DOS SANTOS, 2012; REIS et al., 2013).

Nos Estados Unidos e Canadá, além da abordagem relativa à qualidade, estudos denominados Pesquisa de Implementação *(Implementation Research)* tiveram início na década de 1990, seu objetivo era preencher a lacuna entre o conhecimento gerado pelas evidências científicas e a utilização desses conhecimentos em prol da população (FIXSEN, 2005; PETERS et al., 2013). Para isso são considerados vários aspectos do processo, incluindo fatores que o influenciam, o processo em si e os resultados da implementação. O foco da pesquisa de implementação pode ser identificar problemas comuns do processo, compreender os fatores que dificultam ou facilitam o acesso a intervenção, desenvolver e testar soluções para superar barreiras no processo de incorporação, do uso em larga escala e da sustentabilidade das inovações. A intenção é compreender o quê, por quê e como as intervenções (políticas públicas, programas ou práticas profissionais) ocorrem no "mundo real" e testar abordagens para aprimorá-las (FIXSEN et al., 2005; PETERS et al., 2013).

Dentre os aspectos do processo de implementação, a identificação de barreiras e facilitadores é uma das principais etapas do processo de implementação em serviços de saúde, inclusive farmacêuticos (MOULLIN; SABATER-HERNÁNDEZ; BENRIMOJ, 2016a). A maioria dos estudos sobre o tema relatam fatores que influenciam a implementação de serviços clínicos farmacêuticos em farmácias comunitárias (DOSEA et al., 2015; FAKEYE et al., 2017; KENNELTY et al., 2015; MOULLIN; SABATER-HERNÁNDEZ; BENRIMOJ, 2016b; NIK et al., 2016; SMITH; SPIGGLE; MCCONNELL, 2017), incluindo uma revisão sobre facilitadores (ROBERTS et al., 2006). Entretanto, até o presente momento, são poucos os trabalhos que exploraram esta temática no âmbito hospitalar.

No contexto nacional, os serviços clínicos farmacêuticos no âmbito hospitalar ganharam impulso nos últimos anos. As publicações de normativas como a Resolução CFF 585/ 2013 que regulamenta as atribuições clínicas do farmacêutico (CONSELHO FEDERAL DE FARMÁCIA, 2013a), a Portaria GM/MS nº 529/2013 que institui o Programa Nacional de Segurança do Paciente (BRASIL, 2013a) e a Portaria GM/MS nº 3.390, de 30 de dezembro de 2013 que institui a Política Nacional de Atenção Hospitalar (BRASIL, 2013b), bem como a disseminação dos programas de residência multiprofissional em saúde, que inclui o farmacêutico como um dos integrantes da equipe, contribuíram para expansão desses serviços nos hospitais. Porém, essa ainda não é uma realidade estabelecida de maneira uniforme em todo território nacional (MELO et al., 2017).

Em países como o Brasil em que os SCF ainda não estão consolidados, conhecer os fatores que influenciam a incorporação de práticas clínicas na rotina do farmacêutico hospitalar pode ser fundamental para planejar o processo de implementação e garantir a sustentabilidade de tais serviços (HOFSTEDE et al., 2013; HUIJG et al., 2014; MOUSAVI et al., 2014). Para tanto, a elaboração de *modelos de categorização* que considerem as características principais dos fatores, bem como a influência exercida nos grupos de interesse, podem contribuir para a efetiva implementação de serviços clínicos farmacêuticos e a disseminação desses serviços no país.

1.1 ESTRUTURA DA TESE

Esta tese foi estruturada em fundamentação teórica, seguida de três artigos distribuídos em capítulos. O eixo central é composto pelo desenvolvimento e aplicação de um *framework* de determinantes da implementação de SCF em hospitais, os artigos que compõem esta tese seguem as normas dos periódicos científicos aos quais foram submetidos ou previsto para submissão. Segue apresentação das seções desta tese:

REVISÃO DA LITERATURA – consiste em uma revisão narrativa sobre o panorama histórico e conceitual da implementação de SCF em hospitais e os fatores que influenciam esse processo.

CAPÍTULO 1 – apresenta o desenvolvimento do *framework* Apoteca (fatores atitudinais, políticos, técnicos e administrativos), utilizando a abordagem fenomenológica. Esse artigo descreve as experiências de implementação e leituras que culminaram na proposição do *framework*. O artigo **"Apoteca: construindo um *framework* para auxiliar na implementação de serviços clínicos farmacêuticos",** será submetido ao periódico *RESEARCH IN SOCIAL AND ADMINISTRATIVE PHARMACY* (fator de impacto 2,315. Qualis B1), na seção *Proposed models*.

CAPÍTULO 2 – apresenta os resultados de uma revisão sistemática cujo objetivo foi identificar fatores que influenciam a implementação de SCF em hospitais. As análises foram realizadas utilizando a classificação Apoteca e um formato gráfico inovador, que considera as características dos fatores e o nível de implementação que estes influenciam. O artigo "**Factors influencing the implementation of clinical pharmacy services for hospitalized patients: A mixed-methods systematic review,**" foi submetido ao periódico *RESEARCH IN SOCIAL AND ADMINISTRATIVE PHARMACY* (fator de impacto 2,315. Qualis B1).

CAPÍTULO 3 – o terceiro artigo é um estudo qualitativo que visa compreender os fatores que influenciaram a implementação de SCF em um hospital de alta complexidade do Nordeste do Brasil. Os dados foram coletados em dois momentos, antes e depois do processo de implementação estruturada, e foram consideradas as perspectivas de farmacêuticos e gerentes da instituição. O artigo **"Factors influencing clinical pharmacy implementation at a Brazilian hospital: a qualitative study"** foi submetido ao periódico *QUALITATIVE HEALTH RESEARCH* (fator de impacto 2,413 Qualis B1).

REVISÃO DA LITERATURA

2 **REVISÃO DA LITERATURA**

2.1 MORBIMORTALIDADE ASSOCIADA À FARMACOTERAPIA NO AMBIENTE HOSPITALAR

Levando em consideração a História da humanidade, a ideia do hospital como um local de recuperação da saúde é recente, avanços tecnológicos e o aparecimento da medicina científica no final do século XVIII revolucionaram o papel e as funções do hospital de um lugar para se morrer, para um local destinado a curar. A partir desse momento, tem-se o desenvolvimento do modelo atual de instituições hospitalares (CATÃO, 2011).

Segundo o Ministério da Saúde do Brasil (2013b),

> os hospitais são instituição complexas, com densidade tecnológica especifica, de caráter multiprofissional e interdisciplinar, responsável pela assistência aos usuários com condições agudas ou crônicas, que apresentem potencial de instabilização e de complicações de seu estado de saúde, exigindo-se assistência contínua em regime de internação e ações que abrangem a promoção da saúde, a prevenção de agravos, o diagnóstico, o tratamento e a reabilitação.

Atualmente, esta instituição é o centro de referência encarregado pela recuperação da saúde e o responsável por devolver o indivíduo à sociedade em melhores condições físicas e psicológicas. Neste ambiente são realizados procedimentos de alta complexidade tecnológica e inovação que envolve o aumento dos riscos com a terapia empregada, elevando os custos e exigindo segurança, qualidade, efetividade e responsabilidade (MALAGÓN-LODOÑO; MORERA; LAVERDE, 2010).

Pacientes hospitalizados utilizam medicamentos praticamente de maneira obrigatória, quer seja em processos diagnósticos, de reabilitação da saúde ou prevenção de doenças. Apesar desta tecnologia em saúde proporcionar inúmeros benefícios para os seus usuários, quando utilizados de forma inadequada os medicamentos trazem consigo aumento na morbimortalidade associada à farmacoterapia, além de consequente elevação de custos, principalmente no ambiente hospitalar (CABELLO et al., 2016; OSCANOA et al., 2017; PARIHAR et al., 2017).

A partir da década de 1990, a discussão sobre a segurança e a qualidade no cuidado ao paciente se intensificou em todo o mundo. Em 1999, o *Institute of Medicine* dos Estados Unidos estimou que os erros relacionados aos cuidados de saúde causavam a morte de 44.000 a 98.000 norte-americanos anualmente, sendo que os erros de medicação seriam os responsáveis por mais de 7.000 mortes anuais e ocasionavam 2% dos eventos adversos em pacientes

hospitalizados, incrementando os gastos em saúde em bilhões de dólares todos os anos (KOHN et al., 2000).

Dados mais recentes sugerem que este relatório pode ter subestimado a prevalência de mortes por erros relacionados aos cuidados de saúde. James (2013), em um artigo de revisão, estimou que eventos adversos preveníveis seriam os responsáveis pela morte de 210.000 a 400.000 pacientes hospitalizados por ano nos Estados Unidos. Makary e Daniel (2016) extrapolaram os dados de estudos anteriores para o número de pacientes hospitalizados no ano de 2013, e chegaram a uma estimativa de aproximadamente 251.000 mortes anuais por eventos adversos preveníveis, colocando esses erros como a terceira causa de morte nos Estados Unidos, naquele ano.

Dentre os eventos adversos com maior incidência estão àqueles relacionados ao uso de medicamentos. Em um estudo realizado em 24 hospitais espanhóis, com uma amostra de 5.624 prontuários, 37,4% dos eventos adversos estavam associados a medicamentos (ARANAZ-ANDRÉS et al., 2008). Em uma revisão sistemática sobre o assunto, incluindo 74.485 prontuários de pacientes hospitalizados, os eventos relacionados a medicamentos foram o segundo tipo de evento mais frequente (15,1%) (DE VRIES et al., 2008). Mais recentemente, Rutberg e colaboradores (2014) analisaram 960 prontuários de pacientes de um hospital sueco, entre os anos de 2009 e 2012, e verificaram que 24% dos eventos adversos que acometeram os pacientes não-cirúrgicos eram relacionados a medicamentos.

Eventos adversos a medicamentos podem causar graves prejuízos para pacientes e também para as instituições hospitalares. Em um estudo recente, Parihar e colaboradores (2017) verificaram que as admissões hospitalares devido a eventos adversos relacionados a antidepressivos aumentaram de maneira significativa nos Estados Unidos, de 17.375 admissões em 2001 para 20.588 admissões em 2011. A média do tempo de internação também teve um incremento de 2,18 dias para 2,81 dias ($p<0,01$) e a média dos gastos hospitalares mais que dobrou, de US$ 8.456,2 para US$ 21.572,5 ($p<0,01$). Em outro estudo, realizado em um hospital terciário espanhol, foram analisados 1.388 prontuários de pacientes que foram a óbito em um período de 22 meses. Medicamentos foram suspeitos de provocar 146 óbitos e de contribuir para a morte de outros 110 pacientes, comorbidades e/ou polifarmácia foram identificados como fatores de risco para óbitos relacionados a medicamentos (CABELLO et al., 2016).

No contexto nacional, dados sobre a morbimortalidade de medicamentos são escassos. Uma recente revisão sistemática verificou alta prevalência de consumo de medicamentos entre adultos brasileiros, 12 estudos mediram o consumo de medicamentos entre adultos nos 15 dias

anteriores à coleta de dados e foi encontrada prevalência de 49,1% (IC95%: 48,5-49,6%; I2 =100%) (GOMES; SILVA; GALVÃO, 2017). Os dados mais recentes divulgados pelo Sistema Nacional de Informações Tóxico-Farmacológicas, referentes ao ano de 2014, mostram que os medicamentos foram responsáveis por 22.144 casos de intoxicação, resultando em 41 óbitos. Os motivos mais frequentes de intoxicação por medicamentos foram: acidente individual (36%), tentativa de suicídio (31%), erros de administração (11%) e uso terapêutico (11%).

No Brasil, embora não existam dados nacionais para prevalência de eventos adversos, Mendes et al. (2009) observaram em três hospitais do Rio de Janeiro que a incidência de eventos adversos ficou próxima a média internacional de 7,6% de pacientes acometidos. Nesse sentido, órgãos governamentais brasileiros, baseando-se na experiência de outros países, começaram a se empenhar na criação de programas e projetos com objetivos de melhorar os serviços prestados e prevenir possíveis agravos (ADAMI, 2000).

2.1.1 **Estratégias para prevenção de eventos adversos**

Na tentativa de diminuir os danos causados pelos serviços de saúde, algumas iniciativas foram instituídas. Uma das primeiras foi a acreditação hospitalar, conceituada como a avaliação desenvolvida para criar a cultura de qualidade e segurança no interior dos serviços de saúde, os quais devem se aperfeiçoar continuamente nos processos de cuidado ao paciente a fim de obter os melhores resultados (MANZO; BRITO; CORREA, 2012). Dentre os critérios avaliados pelas organizações acreditadoras a questão da segurança do paciente e a qualidade do tratamento estão intimamente relacionados com os serviços realizados pela Farmácia, incluindo os SCF, como indicadores de qualidade da assistência prestada (CIPRIANO, 2009).

Além da acreditação hospitalar, podemos citar ações preconizadas pelas políticas públicas brasileiras, como a Política Nacional de Assistência Farmacêutica que envolve um conjunto de ações voltadas à promoção, proteção e recuperação da saúde, garantindo os princípios da universalidade, integralidade e equidade (BRASIL, 2004). Especificamente no âmbito hospitalar, o Ministério da Saúde do Brasil, baseado nos princípios e diretrizes do Sistema Único de Saúde e na Política Nacional de Assistência Farmacêutica, aprovou em 2010 a portaria 4.283 que institui as diretrizes e estratégias para organização, fortalecimento e aprimoramento das ações e serviços da assistência farmacêutica no âmbito hospitalar, com o intuito de assegurar o acesso da população a serviços farmacêuticos de qualidade nessas instituições (BRASIL, 2010).

Dentre as diretrizes propostas estão àquelas relacionadas a ações assistenciais desenvolvidas, preferencialmente, no contexto multidisciplinar e privilegiando a interação direta dos farmacêuticos com os usuários. Segundo as diretrizes, o cuidado farmacêutico tem como objetivos "contribuir para a promoção da atenção integral à saúde, à humanização do cuidado e à efetividade da intervenção terapêutica, além de promover o uso seguro e racional de medicamentos e reduzir custos decorrentes do uso inadequado da farmacoterapia" (BRASIL, 2010).

Ademais, como parte dessa série de medidas tomadas para melhorar a qualidade da assistência à saúde hospitalar no âmbito do Sistema Único de Saúde, foram instituídas a Política Nacional de Atenção Hospitalar (BRASIL, 2013b)- que visa organizar o componente hospitalar na Rede de Atenção à Saúde e qualificar estes serviços – e a Política Nacional de Segurança do Paciente (BRASIL, 2013a) - que propõe a implementação de protocolos com foco nos problemas de maior incidência, incluindo a segurança na prescrição, uso e administração de medicamentos e a comunicação entre profissionais de saúde, ações estas desempenhadas por meio dos SCF, como elemento fundamental para garantir a segurança dos usuários de serviços de saúde.

Mais recentemente, a Organização Mundial de Saúde (2017) lançou o terceiro "Desafio Global para Segurança do Paciente – Uso Seguro de Medicamentos (*Medication without harm*)". Lançado em março de 2017, esse desafio tem como objetivo geral reduzir em nível mundial 50% dos danos severos e evitáveis relacionados a medicamentos, nos próximos cinco anos. Para isso, o documento propõe melhoras em cada etapa do processo de uso do medicamento (incluindo prescrição, dispensação, administração, monitoramento e utilização) e tem como temas prioritários situações relacionadas a pacientes hospitalizados, a saber: situações de alto risco (pacientes internados, crianças pequenas e idosos, pacientes portadores de enfermidades renais ou hepáticas), polifarmácia (uso de quatro ou mais medicamentos concomitantemente) e transição de cuidado (entre instituições, setores e profissionais de saúde).

Embora os SCF estejam incluídos em políticas institucionais, públicas ou de organizações não-governamentais internacionais, a prática e a publicação de estudos sobre SCF no Brasil são ainda incipientes, quando comparadas aos de países desenvolvidos. Assim, o desenvolvimento da prática clínica do Farmacêutico juntamente com a pesquisa e a publicação de estudos sobre o tema pode auxiliar sobremaneira na melhora da qualidade dos serviços de saúde e a segurança de seus pacientes.

2.2 QUALIDADE EM SERVIÇOS DE SAÚDE

Como abordado anteriormente, os serviços e sistemas de saúde tem se deparado com uma série de desafios nas últimas décadas: o alto custo relacionado à incorporação de novas tecnologias em saúde, o envelhecimento populacional, a mudança do perfil epidemiológico com a presença de múltiplas doenças crônicas, além de recursos limitados para a saúde (HUSSEY; WERTHEIMER; MEHROTRA, 2013; ZULMAN et al., 2014). Para atender às necessidades dos usuários e enfrentar esses desafios, as instituições de saúde têm buscado a mais alta qualidade técnica dos serviços ofertados, com o menor custo. Logo, a avaliação da qualidade em saúde tem ganhado destaque entre profissionais e gestores da área, pois estes precisam responder à demanda da população que exige cuidado seguro e de qualidade (CHUN; BAFFORD, 2014).

2.2.1 **Breve histórico sobre a qualidade em serviços de saúde**

O conceito ocidental de qualidade em saúde começou a ser desenvolvido no início da década de 1850, com o trabalho da enfermeira Florence Nightingale. Em 1854, ela foi enviada à Turquia para cuidar dos soldados britânicos feridos na Guerra da Crimeia. As condições precárias das instalações de saúde e a alta mortalidade dos soldados levaram Nightingale e sua equipe a empreender um projeto de melhora da qualidade, baseados em ações de saneamento e higiene. Seis meses após essas intervenções, a taxa de mortalidade caiu de 42,7% para 2,2%, resultados que só puderam ser apresentados graças à documentação meticulosa de todos os processos e desfechos, que geraram medidas estatísticas da qualidade do serviço prestado (NEUHAUSER, 2003; SHEINGOLD; HAHN, 2014).

Por volta de 1910, o cirurgião americano Ernest Codman, iniciou os primeiros trabalhos sobre a necessidade de garantir a qualidade das intervenções e procedimentos médicos. Em 1913, juntamente com o também médico Edward Martin, co-fundou o *American College of Surgeons* que estabeleceu o Comitê de Padronização Hospitalar, liderado pelo próprio Ernest Codman. Em 1917, esta instituição adotou seu sistema de "desfechos finais" (*end result system*) para o seu Programa de Padronização Hospitalar, definindo um conjunto de padrões mínimos hospitalares para garantir a qualidade da assistência prestada aos pacientes (DONABEDIAN, 1989; ROBERTS; COALE; REDMAN, 1987).

Em 1952, o *American College of Physicians*, a *American Hospital Association*, a *American Medical Association* e a *Canadian Medical Association*, juntaram-se ao *American*

College of Surgeons para formar a *Joint Commission on Accreditation of Healthcare Organizations*, uma organização independente e sem fim lucrativos, que desde janeiro de 1953 desenvolve atividades de acreditação hospitalar, baseada em avaliação, educação e consultoria para instituições interessadas em oferecer cuidado de qualidade aos pacientes (CHUN; BAFFORD, 2014; ROBERTS; COALE; REDMAN, 1987).

No final da década de 1980, a *Joint Commission* implementou um rigoroso conjunto de padrões de acreditação, que refletiam os conceitos de avaliação da qualidade em cuidados de saúde, apresentadas pelo médico Avedis Donabedian no artigo "Evaluating the Quality of Medical Care" (CHUN; BAFFORD, 2014; DONABEDIAN, 1966). Assim, o movimento pela qualidade, amplamente difundido no setor industrial, foi incorporado aos cuidados com a saúde, inicialmente nas instituições hospitalares e ao longo dos anos vem ganhando destaque nos vários cenários de prática dos sistemas de saúde pelo mundo (MORRIS et al., 2002).

2.2.2 **Definição de qualidade em serviços de saúde**

Definir e medir qualidade em saúde não é uma tarefa fácil, a natureza complexa do cuidado, os distintos tipos de serviços de saúde, os interesses e as perspectivas individuais dos participantes envolvidos no cuidado contribuem para que não haja uma definição única, universalmente aceita para este termo (MOSADEGHRAD, 2014).

Uma das primeiras definições de qualidade em serviços de saúde foi formulada por Avedis Donabedian, referência mundial na área. Segundo o autor, a qualidade em saúde corresponderia "a aplicação da ciência e tecnologia médica de uma forma que maximize seu benefício para a saúde sem aumentar o risco de forma correspondente" (DONABEDIAN, 1980 apud MOSADEGHRAD, 2014).

Na década seguinte, o *Institute of Medicine* dos Estados Unidos definiu qualidade em saúde como "o grau em que os serviços de saúde para indivíduos e populações aumentam a probabilidade de desfechos de saúde desejados e são consistentes com o conhecimento profissional corrente", sendo esta definição uma das mais comumente utilizadas (LOHR, 1990).

Posteriormente, a *Agency for Healthcare Research & Quality* (1997) dos Estados Unidos definiu qualidade como "estar fazendo a coisa certa, no momento certo, da maneira certa, para a pessoa certa e alcançar os melhores resultados possíveis". Diante dessas várias definições, verifica-se que o foco da qualidade em saúde evoluiu dos aspectos técnicos do cuidado para o atendimento das necessidades dos pacientes e da sociedade (BUSARI, 2012).

Além dessas definições sintetizadas, alguns autores definiram a qualidade em saúde por meio de seus atributos (CAMPBELL; ROLAND; BUETOW, 2000). Um exemplo é a definição mais recente da Organização Mundial da Saúde (2017) que descreve a qualidade em saúde como "a medida em que os serviços de saúde prestados aos indivíduos e às populações melhoram os desfechos de saúde desejados. Para conseguir isso, os cuidados de saúde devem ser seguros, eficazes, oportunos, eficientes, equitativos e centrados nas pessoas".

Donabedian (1990), também elencou atributos específicos, denominados por ele de sete pilares da qualidade, a saber: eficácia, efetividade, eficiência, otimização, aceitabilidade, legitimidade e equidade. O estabelecimento desses atributos tem importância para o campo da Pesquisa de Qualidade em Saúde, pois além de servirem para a definição do termo, também servem como indicadores de qualidade na avaliação do cuidado.

2.2.3 **Avaliação da qualidade em serviços de saúde**

Apesar de existirem vários modelos teóricos utilizados para a avaliação da qualidade em serviços de saúde, como o *framework* de comportamento de Andersen (ANDERSEN, 1995) e o *framework* de planejamento organizacional (GITTELL; WEISS, 2004), o modelo SPO (*structure - process - outcome*) proposto por Donabedian (1966, 1988) é o referencial mais utilizado mundialmente, pois fornece uma maneira conceitual, simples, intuitiva e flexível para avaliar, categorizar e priorizar medidas de qualidade de saúde (MCDONALD et al., 2007; SEIBERT et al., 2015). Para tanto, Donabedian absorveu da teoria de sistemas a noção de indicadores de estrutura, processo e resultado adaptando-os para a avaliação da qualidade em serviços de saúde (D'INNOCENZO; ADAMI; CUNHA, 2006):

- O eixo *estrutura* corresponde às características mais estáveis da assistência à saúde e compreende os fatores organizacionais do sistema de saúde onde o serviço é prestado. Neste eixo estão incluídos recursos físicos (instalações e equipamentos), humanos (número e capacitação dos indivíduos que prestam a assistência) e estrutura organizacional (organização, métodos de avaliação, modalidades de financiamento e instrumentos normativos técnico-administrativos) (DONABEDIAN, 1988). Em suma, ao avaliar a estrutura, deve-se analisar quais recursos estão disponíveis e como eles estão organizados (CAMPBELL; ROLAND; BUETOW, 2000).

- Os *processos*, por sua vez, são definidos como as interações e procedimentos envolvendo profissionais de saúde e pacientes, e inclui o reconhecimento de problemas, métodos diagnósticos e os cuidados prestados. (DONABEDIAN, 1988). Portanto, refere-se à

aplicação das evidências científicas na resolução de um problema de saúde, bem como a elementos que compõe a interação entre os profissionais de saúde e os usuários, incluindo habilidades, como a comunicação com o paciente (CAMPBELL; ROLAND; BUETOW, 2000).

- O eixo r*esultados* corresponde às consequências da assistência realizada, refletindo as alterações observadas no estado de saúde do paciente e da população. Incluem a melhora do conhecimento, as mudanças de comportamento e o grau de satisfação do paciente (DONABEDIAN, 1966; DONABEDIAN, 1988). Como mencionado anteriormente, a avaliação de resultados foi uma das primeiras medidas de qualidade da saúde, em 1917 o *American College of Surgeons* já adotava o sistema de "desfechos finais" de Codman para avaliar e garantir a qualidade da assistência prestada aos pacientes, visto que desfechos favoráveis são considerados o objetivo último do cuidado em saúde (DONABEDIAN, 1989).

Embora o componente *resultados* seja o mais importante a ser avaliado do ponto de vista técnico, algumas características ressaltam a importância de uma avaliação holística, considerando os três eixos do modelo SPO. Para certos procedimentos ou condições, as medidas de resultados podem ser bastante evasivas, muitos não podem ser medidos com precisão por meio de testes físicos ou exames de imagem; nestes casos, a avaliação baseia-se em instrumentos que avaliam a percepção dos pacientes sobre seus sintomas e melhorias funcionais. Além disso, certas complicações (resultados negativos), podem demorar muitos anos para se manifestar, tornando difícil para os avaliadores determinar a eficácia das intervenções, a menos que os pacientes sejam seguidos por muitos anos (CHUNG; SHAUVER, 2009).

Essas dificuldades levaram os analistas da saúde a se voltarem para a estrutura e o processo para medir a qualidade do cuidado. A maioria dos indicadores de estrutura e processo podem ser avaliados com relativa facilidade e rapidez. Para fins de exemplificação, podem ser citadas a informação sobre o volume do procedimento de uma instituição ou a prática da administração de antibióticos pré-operatórios que estão prontamente disponíveis ou podem ser obtidas por meio de bancos de dados de pacientes, sem nenhuma dificuldade. Portanto, devido à sua natureza direta, elas são geralmente consideradas como medidas de qualidade adequadas. Existem, no entanto, inconvenientes. Em alguns casos, apesar do mau desempenho nos indicadores de estrutura e processo, os resultados nem sempre são comprometidos. Nestas situações, é preciso ter o cuidado de não confundir a falta de resultados negativos com boa qualidade de atendimento (CHUNG; SHAUVER, 2009).

Diante desse contexto, é importante ressaltar que a avaliação em saúde deve considerar critérios nos três eixos (estrutura, processo e resultados) e não deve perder de vista a eficácia,

efetividade, eficiência, otimização, aceitabilidade, legitimidade e equidade relacionadas ao cuidado do paciente (DONABEDIAN, 1988). Apesar do modelo SPO proposto por Donabedian ser o mais conhecido e utilizado em estudos de avaliação da qualidade em saúde, este possui limitações destacadas pelo próprio autor: i) a validade da abordagem depende da relação causal entre os domínios da tríade; ii) a interrelação entre os domínios nem sempre está presente na prática clínica; iii) avaliação separada de qualquer eixo gera dados inconsistentes, sendo necessário utilizar indicadores representativos dos três domínios do modelo; iv) há reunião de indicadores com características muito distintas em um mesmo domínio; v) o modelo não inclui aspectos emocionais e éticos do cuidado (AYANIAN; MARKEL, 2016; DONABEDIAN, 1966; 1992; 2002).

Mesmo com essas limitações, o modelo SPO se tornou o principal norteador de programas de avaliação e de melhora da qualidade, inclusive em serviços clínicos farmacêuticos (MARQUES, 2015; SANTOS JÚNIOR, 2015; SHIYANBOLA; MOTT; CROES, 2016), pois a compreensão dos aspectos de qualidade, de acordo com este modelo, pode contribuir na formação de farmacêuticos aptos para atender as necessidades de pacientes e sociedade, bem como auxiliar na mensuração do impacto de seus serviços clínicos (MULLINS; BALDWIN; PERFETTO, 1996).

2.2.4. **Avaliação da qualidade em serviços farmacêuticos**

No setor farmacêutico, a preocupação com a avaliação da qualidade dos serviços prestados iniciou-se na década de 1930, com a criação do Comitê de Farmácia da *American Hospital Association*. Em 1936 foram adotados os Padrões Mínimos para Farmácias em Hospitais e, em 1937, foi publicado o primeiro relatório sobre a situação das farmácias hospitalares americanas. A partir desses resultados, foi verificada a necessidade de melhoras no setor e de avaliações periódicas para garantir a qualidade do serviço (ZELLMER, 2010).

Em 1975 foi publicado, o que pelo nosso conhecimento seria, o primeiro estudo sobre avaliação da qualidade dos serviços farmacêuticos utilizando o modelo SPO de Donabedian. Neste trabalho, Mikeal e colaboradores analisaram os componentes de estrutura e processos de serviços farmacêuticos ofertados em 112 hospitais americanos. Os resultados obtidos mostraram que quanto maior o número de leitos do hospital, melhor a qualidade da estrutura dos serviços farmacêuticos. No caso da qualidade do processo, além do número de leitos, a localização urbana também tinha relação positiva. Por fim, nas instituições com maior número

de farmacêuticos trabalhando em tempo integral era maior a percepção de qualidade do cuidado (MIKEAL et al., 1975).

Para ilustrar a utilização do modelo SPO na estruturação de serviços farmacêuticos de qualidade, Brito (2015) reporta que o farmacêutico tem dificuldades em fornecer serviços clínicos sem insumos estruturais importantes, como prontuários de pacientes. Do mesmo modo, as ações do farmacêutico são inviabilizadas caso não haja rotinas estabelecidas para o manejo da farmacoterapia e de orientação ao paciente sobre o tratamento. Os resultados, como a melhora nos padrões clínicos, satisfação dos pacientes e redução dos custos, são o produto final da assistência prestada e mostram o sucesso das intervenções ou o alerta para necessidade de adequações das etapas anteriores, estruturais ou de processos.

Posteriormente à proposta de Donabedian, estudos sobre a avaliação de resultados da prática farmacêutica apresentaram um modelo para avaliação e planejamento das ações denominado "modelo ECHO" (resultados econômicos, clínicos e humanísticos). Que quando utilizado em conjunto com o modelo SPO, pode oferecer aos farmacêuticos uma possibilidade para melhor conhecer e avaliar os resultados de suas intervenções (CHENG et al., 2013; KOZMA; REEDER; SCHULZ, 1993).

Ao longo do tempo, várias associações (ZELLMER, 2010), sociedades (HAAS et al., 2013; SOCIEDADE BRASILEIRA DE FARMÁCIA HOSPITALAR E SERVIÇOS DE SAÚDE, 2017; TAYLOR et al., 2013) e sistemas de acreditação (JOINT COMMISSION INTERNATIONAL, 2013) vêm aprimorando os padrões de avaliação dos serviços farmacêuticos para garantir a qualidade e a segurança dos pacientes atendidos. Além disso, estudos sobre o tema da qualidade e segurança do paciente no setor farmacêuticos também têm crescido nas últimas décadas (SANTOS-JUNIOR et al., 2015; SILVESTRE et al., 2017 a; SILVESTRE et al., 2017 b; SMITH, 2009).

Neste contexto, a implementação de serviços clínicos farmacêuticos com qualidade pode ser determinante para a prevenção de erros e promoção do uso seguro de medicamentos nos diversos cenários de prática, incluindo os hospitais.

2.3 SERVIÇOS CLÍNICOS FARMACÊUTICOS NO ÂMBITO HOSPITALAR

2.3.1 **Contextualização histórica dos serviços clínicos farmacêuticos hospitalares**

Desde os primórdios da humanidade, a Farmácia se desenvolveu de forma paralela à Medicina, escritos sobre substâncias e preparações utilizadas para cura de doenças foram

reportados pelos povos sumérios, egípcios e chineses da Antiguidade. Na cultura greco-romana surgiram os primeiros centros de aconselhamento médico, prognóstico e cura, os templos dedicados ao deus *Asklepios*, considerados as primícias das instituições hospitalares. A separação das artes do boticário e do médico foi iniciativa do povo árabe, estabelecendo em Bagdá no final do século VIII as primeiras farmácias de propriedade privada. (KREMERS; SONNEDECKER, 1986).

Em 1495 foi fundada a primeira Farmácia Hospitalar ocidental no *Hôtel-Dieu* de Paris, onde os medicamentos eram preparados e distribuídos por religiosos e em 1752 foi criada a primeira Farmácia Hospitalar nos moldes próximos aos atuais, no Hospital da Pensilvânia, nos Estados Unidos (MESLER, 1991). No Brasil, ainda na época da Colônia, foram instaladas as primeiras farmácias hospitalares nas Santas Casas de Misericórdia e Hospitais Militares. Nestas chamadas boticas públicas, o farmacêutico manipulava os medicamentos dispensados aos pacientes internados, obtidos de um ervanário do próprio hospital (ROSA, 1997).

A industrialização nas décadas de 1920 a 1930 teve impacto em todas as atividades desenvolvidas pelo farmacêutico. Muitos medicamentos que o farmacêutico era capaz de produzir individualmente podiam ser fabricados pela indústria a um menor custo e com qualidade superior, ademais a indústria passou a assumir a responsabilidade pela qualidade do medicamento, que era tradicionalmente um papel do farmacêutico (MESLER, 1991).

As mudanças nas atividades deste profissional, que deixava de ser responsável pela coleta, preservação e composição das drogas para ser o dispensador de fórmulas preparadas pela indústria, iniciaram no século XIX e foram intensificadas no século XX (MESLER, 1991). Em vários países desenvolvidos, a solução para essa crise foi voltar à atenção para atividades clínicas hospitalares nas áreas de estabilidade de medicamentos industrializados, farmacocinética e farmacodinâmica, passando o Farmacêutico a ser um *expert* em medicamentos e recuperando a relação médico-farmacêutico e farmacêutico-paciente. A sua principal habilidade passou a ser a informação (ROSA, 1997).

Neste contexto, a filosofia da Farmácia Clínica surgiu em meados da década de 1960, no ambiente hospitalar dos Estados Unidos, caracterizada como a atividade farmacêutica desenvolvida em função do paciente, visando a maior eficácia do farmacoterapia (FRANCKE, 2007; SMITH, 1967). Esta nova filosofia se desenvolveu a partir das inquietudes de farmacêuticos que haviam perdido sua função de preparo dos medicamentos, quando do surgimento das indústrias farmacêuticas, permitindo novamente a esses profissionais participar da equipe de saúde e contribuir com seus conhecimentos para melhorar o cuidado ao paciente.

Esses conceitos e práticas foram paulatinamente difundidos e incorporados pelos farmacêuticos no mundo todo. No Brasil, porém, a solução encontrada para a crise da profissão foi a busca de novos caminhos de atuação, dando ênfase principalmente às análises clínicas. Consequência disso, a arte farmacêutica da orientação, manipulação e conhecimento sobre medicamentos, ficou relegada ao segundo plano (LYRA JÚNIOR, 2005; ROSA, 1997).

Na América Latina, a Farmácia Clínica foi incorporada no programa de graduação dos farmacêuticos da Universidade do Chile em 1972 e, desde 1977 esta universidade tem realizado o Curso Latinoamericano de Farmácia Clínica, que capacitou os primeiros farmacêuticos clínicos a atuarem no Brasil (WITZEL, 2008). Em 1979 foram criados o primeiro serviço de Farmácia Clínica e o primeiro Centro de Informações de Medicamentos brasileiros, no Hospital das Clínicas do Rio Grande do Norte, hoje Hospital Universitário Onofre Lopes (ANGONESI, SEVALHO, 2010). Porém, o reduzido número de farmacêuticos clínicos para as dimensões continentais do país, somado à formação voltada para áreas tecnológicas em detrimento das disciplinas clínicas contribuíram para a lenta disseminação desta prática profissional pelo Brasil (MELO et al, 2017)

Mais recentemente, as resoluções do Conselho Federal de Farmácia números 585 e 586 (CONSELHO FEDERAL DE FARMÁCIA, 2013a; CONSELHO FEDERAL DE FARMÁCIA, 2013b), que versam sobre as atribuições clínicas e a prescrição de farmacêuticos, a Lei federal 13.021 (BRASIL, 2014), que dispõe sobre o exercício das atividades farmacêuticas, juntamente com novas diretrizes curriculares (BRASIL, 2017) que trazem mais disciplinas voltadas para o cuidado, tem impulsionado a implementação de serviços clínicos farmacêuticos no âmbito hospitalar. Apesar desses esforços, os serviços clínicos farmacêuticos ainda não estão amplamente consolidados no contexto hospitalar brasileiro (MELO et al., 2017)

2.3.2 **Definição e competências para o desenvolvimento de serviços clínicos farmacêuticos**

Farmácia clínica é um termo comumente utilizado na prática e literatura farmacêutica, cujas definições mais amplamente referidas são descritas a seguir. A *European Society of Clinical Pharmacy* define farmácia clínica como: “uma especialidade de saúde que descreve as atividades e serviços do farmacêutico clínico para desenvolver e promover o uso racional e apropriado de medicamentos e dispositivos”. Ademais, o conceito ressalta: “o termo inclui todos os serviços realizados por farmacêuticos que trabalham em hospitais, farmácias comunitárias, lares de idosos, serviços de cuidados domiciliares, clínicas e qualquer outro

ambiente onde medicamentos são prescritos e utilizados" (EUROPEAN SOCIETY OF CLINICAL PHARMACY, 2017).

O *American College of Clinical Pharmacy* (2008) define que:

> Farmácia clínica é uma disciplina das Ciências da Saúde na qual farmacêuticos proveem cuidados aos pacientes que otimizem a farmacoterapia e promova a saúde, o bem – estar e a prevenção de doenças. A prática da farmácia clínica engloba a filosofia da atenção farmacêutica, associa uma orientação para o cuidado com conhecimento terapêutico especializado, experiência e discernimento, objetivando garantir ótimos resultados para o paciente. Como uma disciplina, a farmácia clínica também tem uma obrigação de contribuir para a geração de novos conhecimentos que melhorem a saúde e a qualidade de vida.

Diferenças são percebidas ao comparar as duas definições: a europeia denomina farmácia clínica como especialidade de saúde e enfatiza os cenários de prática do farmacêutico, enquanto que a definição americana, a trata como disciplina e inclui também a pesquisa (geração de novos conhecimentos) como um atributo a ser desenvolvido pelo farmacêutico clínico.

Dentre as atividades clínicas desenvolvidas por farmacêuticos é possível citar: aconselhamento ao paciente; dispensação; programas de rastreio de doenças; elaboração de programas de educação sanitária; informação e suporte à equipe de saúde; conciliação de medicamentos; revisão da farmacoterapia; acompanhamento farmacoterapêutico; detecção e notificação de eventos adversos a medicamentos; participação em rondas clínicas; monitorização terapêutica de medicamentos (farmacocinética clínica); aconselhamento de alta; participação em comissões clínicas multidisciplinares; participação em projetos de pesquisa (ensaios clínicos e estudos de utilização de medicamentos) e prescrição independente (CONSELHO FEDERAL DE FARMÁCIA, 2016; ROTTA et al., 2015; STOTT, 2001)

Para prestar qualquer um desses serviços de cuidado e ser responsável pela qualidade dos resultados do tratamento, o farmacêutico precisa desenvolver competências clínicas (conhecimentos, habilidades e atitudes), a fim de orientar os pacientes de maneira acessível e compreensível quanto ao uso seguro dos medicamentos (FUENTES; AZIZE-VARGAS, 2007; VAN, 2005). Assim, em 2008, o *American College of Clinical Pharmacy* publicou cinco domínios de competências do farmacêutico clínico, que estabeleceram os conhecimentos e habilidades necessários para os profissionais envolvidos na prática de SCF, a saber: solução de problemas clínicos, julgamentos e tomada de decisão; comunicação e educação; avaliação e gerenciamento de informação em saúde; manejo de pacientes em uma população; conhecimento terapêutico (BURKE et al., 2008).

Em 2017, foi publicada uma atualização deste documento, que acrescenta mais dois domínios a serem desenvolvidos pelo farmacêutico que deseja se dedicar ao cuidado do paciente: profissionalismo e educação permanente. Ademais, os autores relatam que os farmacêuticos clínicos podem precisar dominar outras áreas de competência à medida que progridem em suas carreiras, como liderança ou pesquisa, mas que estabelecer todas as competências que sejam necessárias para o sucesso em atividades clínicas específicas não é uma pretensão do documento (SASEEN et al., 2017).

2.3.3 **O impacto dos serviços clínicos farmacêuticos no âmbito hospitalar**

Nas últimas décadas, vários estudos têm relatado a contribuição dos SCF desenvolvidos em ambiente hospitalar na minimização dos erros de medicação, diminuição de custos hospitalares e melhora no resultado da farmacoterapia (GALLAGHER; MCCARTHY; BYRNE, 2014; KABOLI et al., 2006).

Em 1986, Hatoum e colaboradores publicaram, o que pelo nosso conhecimento seria, a primeira revisão da literatura sobre o impacto dos SCF nos custos e qualidade do cuidado prestado, bem como, nas atitudes de pacientes e outros profissionais de saúde. A revisão encontrou 305 artigos, publicados entre 1974 e 1984, que reportaram a provisão de SCF para pacientes internados em hospitais para cuidados agudos. Desses, foram incluídos 93 artigos que mostraram resultados de custo (48), melhora da qualidade do cuidado (58) ou aceitação dos SCF (24), a maioria reportando resultados benéficos.

Ao longo dos anos 2000, Bond e colaboradores publicaram uma série de artigos que avaliam a relação entre os SCF e a melhora de processo e resultados clínicos e econômicos em hospitais americanos. Em 2002 Bond, Raehl e Franke verificaram que o aumento no número de farmacêuticos clínicos estaria associado à redução de erros de medicação e, consequentemente, de custos hospitalares. À medida que a equipe de farmacêuticos clínicos/ leito ocupado aumentava do 10º percentil para o percentil 90, os erros de medicação diminuíram de 700,98 (± 601,42) para 245,09 (± 197,38)/ hospital/ ano, uma diminuição de 286%. Em 2006, Bond e Rahel mostraram que os SCF também poderiam contribuir para a redução das reações adversas a medicamentos. Nos hospitais em que não havia monitoramento de reações adversas por farmacêuticos foram reportadas 4.266 reações adversas, 443 mortes e gastos de US$11.745.342 mais que outros com este serviço. Ademais, outro estudo realizado pela mesma dupla de pesquisadores verificou que sete atividades clínicas realizadas por farmacêuticos foram associados a taxas de mortalidade reduzidas, os de maior impacto foram a gestão de protocolo

de uso de medicamentos (18.401 mortes reduzidas, p = 0,017) e o monitoramento de reações adversas (14.518 mortes reduzidas, p = 0,012) (BOND; RAEHL, 2007).

Kaboli e colaboradores (2006) encontraram resultados que corroboraram os achados descritos anteriormente, ao realizar uma revisão da literatura sobre o impacto de intervenções de farmacêuticos clínicos nos processos e resultados dos cuidados de pacientes adultos internados. Foram revisados artigos publicados entre 1985 e 2005, sendo incluídos 36. Estes verificaram que eventos adversos a medicamentos ou erros de medicação foram reduzidos (em 7 de 12 estudos); adesão, informação e adequação da farmacoterapia melhoraram (em 7 de 11 estudos) e houve redução de dias de internação (em 9 de 17 estudos). Nenhuma intervenção causou piora dos resultados clínicos.

Mais recentemente, estudos têm confirmado o impacto positivo dos SCF em hospitais. Os benefícios relatados incluem melhoras nos processos, como a redução de erros preveníveis em pacientes hospitalizados infectados pelo HIV (EGINGER et al., 2013) ou a diminuição do tempo para o tratamento do acidente vascular cerebral isquêmico (RECH, BENNETT, DONAHEY, 2017), bem como melhores resultados clínicos. Uma revisão sistemática sobre o efeito das intervenções de transição de cuidados apoiadas pela equipe de Farmácia sugeriu a redução de mais de 30% na probabilidade de readmissões em 30 dias quando comparado com os cuidados habituais (RODRIGUES et al., 2017). Em relação aos resultados econômicos, uma revisão sistemática de estudos publicados entre 2001 e 2005 sobre o impacto econômico dos SCF revelou que a maioria dos trabalhos foi realizada em ambiente hospitalar e em 69% dos estudos com avaliação econômica completa foram observados benefícios econômicos associados aos SCF. Entre os estudos que reportaram dados necessários para o cálculo da razão custo-benefício, verificou-se que em média, para cada dólar gasto houve redução direta ou indireta de custos de US$4,81 (PEREZ et al, 2009).

Em 2014 foi publicada uma atualização desta revisão que incluiu 25 estudos publicados entre 2006 e 2010. O cenário hospitalar continuava o mais comum nos estudos (36%). Somente três pesquisas forneceram dados para o cálculo do custo- benefício, que variaram de US$1,05: US$1 a US$25,95: US$1. Os autores concluíram que, na maioria dos casos, os SCF proporcionaram boa relação custo- benefício ou custo-efetividade (TOUCHETTE et al., 2014). No mesmo ano, Gallagher, McCarthy e Byrne publicaram uma revisão sistemática sobre análise de custos relacionadas a SCF que incluiu 20 artigos, publicados entre 2008 e 2012. Esta revisão apontou que a maioria dos estudos analisados apresentou economia relacionados aos cuidados de saúde, incluindo gastos com medicamentos e internação. Apesar de não ter sido possível determinar a intervenção mais vantajosa, verificou-se que a prevenção de eventos adversos a

medicamentos foi responsável por parte das economias geradas pelos SCF. É importante ressaltar que entre essas duas últimas revisões, houve o incremento de estudos em países da Ásia (China, Taiwan, Malásia), Oriente Médio (Líbano) e América Latina (Brasil), além de países europeus de língua não-inglesa (Alemanha, Suécia e Holanda), o que reflete a recente expansão de serviços clínicos farmacêuticos pelo mundo, e o consequente aumento de pesquisas sobre tema nesses países.

Outro estudo realizado em um hospital francês avaliou o serviço de Revisão da Farmacoterapia para pacientes adultos, hospitalizados, diagnosticados com câncer. Foram avaliadas 4393 prescrições de 489 pacientes, 12,6% das prescrições apresentaram algum problema relacionado a medicamentos e 552 intervenções farmacêuticas foram realizadas, 96% delas foram aceitas e implementadas pela equipe de saúde (DELPEUCH et al., 2015). Zhai et al. (2016), em estudo com 15.197 pacientes (pré-intervenção=5.703 pacientes; pós-intervenção=9.494 pacientes), reportaram redução significativa das taxas de mortalidade por todas as causas em uma unidade de cardiologia de um hospital universitário na China após intervenções de um serviço de farmácia clínica (1,5% vs 0,9%, p=0,0005).

Outros estudos realizados em hospitais da Arábia Saudita (ASSIRI et al., 2017), Egito (SABRY; ABBASSI, 2014) e Etiópia (MEKONNEN et al., 2013) também mostraram efeitos benéficos para melhora dos processos e desfechos clínicos de pacientes internados. Dentre esse grupo de países, pode-se incluir o Brasil, que vem aumentando as pesquisas sobre o tema, mas ainda com publicações sobre SCF incipiente, quando comparada aos países desenvolvidos.

Estudo realizado no Instituto Nacional de Traumatologia e Ortopedia, no Rio de Janeiro, quantificou e analisou as intervenções realizadas pelos farmacêuticos residentes junto a equipe de saúde. Os problemas foram detectados principalmente pelos próprios farmacêuticos. Dos problemas identificados, 84,1% correspondiam a erros, dos quais 49,5% foram prevenidos com as intervenções. Das intervenções realizadas, 70% foram aceitas, sendo este percentual de 60% quando relacionada à prescrição (NUNES et al., 2008).

Posteriormente, um estudo realizado na unidade de primeiro atendimento de um hospital em São Paulo avaliou 3.542 prescrições médicas, que demandaram 1.238 intervenções farmacêuticas, classificadas em 17 tipos. As de maior incidência foram relativas à dose (35%), diluição (9,77%), via de administração (8,48%), tempo de infusão (6,13%) e frequência (5,89%) (MIRANDA et al., 2012). No estudo de Magedanz, Silliprandi e dos Santos (2012) foi reportada a economia de cerca de US$8.000,00 mensais nos gastos com antibióticos quando o farmacêutico foi incluído como parte da equipe multidisciplinar de um programa de gestão de antimicrobianos, em um hospital brasileiro especializado em cardiologia.

Outro estudo realizado em um hospital universitário do Paraná analisou as intervenções farmacêuticas em unidade de terapia intensiva e cardiologia. Durante o estudo, 6.438 prescrições foram avaliadas e 933 intervenções farmacêuticas foram realizadas. A aceitação das intervenções foi de 76,32%. Os dados mostraram que 14,6% das prescrições revisadas apresentaram algum problema relacionado a medicamentos e que as intervenções do farmacêutico clínico promoveram mudanças benéficas em sete de cada dez prescrições com algum problema (REIS et al., 2013).

Mais recentemente, Ferracini e colaboradores (2017) publicaram um estudo que avaliou as intervenções farmacêuticas para pacientes com câncer, internados em um hospital ensino de Campinas, São Paulo. Foram avaliadas 1874 prescrições de 248 pacientes, 283 erros de prescrição foram identificados, a maioria destes referente à interação medicamentosa. 294 intervenções farmacêuticas foram realizadas, com alta aceitação de 73,5%.

Em Sergipe, estudos publicados sobre a influência dos SCF na prevenção dos erros de medicação apresentaram alto índice de erros e problemas nas prescrições de pacientes internados no setor de cardiologia (SIQUEIRA et al., 2011) e de pacientes idosos internados (SIQUEIRA et al., 2012), eventos que poderiam ser evitados com a instituição de SCF estruturados (LYRA JR. et al., 2010).

No atual contexto brasileiro, as regiões Sul e Sudeste concentram o maior número de SCF implementados e, em consequência, maior número de estudos sobre o tema, evidenciando assim, a falta de uniformidade na implementação de tais serviços pelos hospitais do país (MELO et al, 2017). Diante desse cenário, verifica-se a necessidade de mais investigações sobre os fatores que influenciam a implementação de serviços clínicos farmacêuticos em ambientes complexos, como os hospitalares, a fim de contribuir para implementação de serviços sustentáveis, avaliação da qualidade do serviço ofertado e disseminação da prática clínica farmacêutica em hospitais que desejem garantir a qualidade e a segurança de seus pacientes.

2.4 PESQUISAS SOBRE IMPLEMENTAÇÃO DE SERVIÇOS DE SAÚDE

Tradicionalmente, o sucesso profissional dos pesquisadores da área de saúde tem se apoiado na realização de estudos descritivos, orientados a mecanismos de ação ou estudos de intervenção em populações altamente selecionadas e publicados em periódicos acadêmicos, idealmente de alto fator de impacto. Para a maioria desses pesquisadores tradicionais da área de saúde não havia preocupação em verificar se os resultados dos estudos se traduziam em impacto na saúde pública (BAUER et al., 2015).

Nas últimas décadas este paradigma para o sucesso acadêmico tem sido alvo de críticas. Estudos sobre práticas baseadas em evidências estimam que são necessários em média 17 anos para que os resultados das pesquisas sejam incorporados à prática clínica e que apenas cerca de metade delas atingem o uso clínico generalizado (BAUER et al., 2015; MORRIS, WOODING, GRANT, 2011). Ademais, a diminuição do financiamento para pesquisa em todo o mundo levou a debates sobre as vantagens entre investir em projetos mais conservadores com resultados previsíveis *versus* pesquisas mais inovadoras, incluindo projetos envolvendo mais amostras do "mundo real" que poderiam resultar em maior impacto na saúde pública (ALBERTS et al., 2014).

Diante desse cenário, na década de 1990 nos Estados Unidos e Canadá, tiveram início pesquisas que englobavam estudos com características muito diversificadas, mas que tinham em comum o fato de terem os serviços de saúde como objeto privilegiado e uma utilidade potencial do conhecimento produzido nos processos de decisão de sistemas e serviços, denominadas Pesquisas em Serviços de Saúde. Dentre esses estudos, destacam-se os de Pesquisa de Implementação, que visam preencher a lacuna entre as evidências geradas pelas pesquisas científicas e a utilização desses conhecimentos em prol da população (ECCLES; MITTMAN, 2006; NOVAES, 2004; PETERS et al., 2013).

2.4.1 **Definição e características da Pesquisa de Implementação**

A ciência de implementação pode ser definida como "o estudo científico de métodos para promover a incorporação sistemática de resultados de pesquisa e outras práticas baseadas em evidências na prática clínica rotineira e, portanto, melhorar a qualidade e eficácia dos serviços de saúde" (ECCLES; MITTMAN, 2006). Este campo incorpora um escopo mais amplo do que a pesquisa clínica tradicional em saúde, focando não apenas no paciente, mas também no provedor de cuidado, nas organizações e nas políticas públicas (BAUER et al, 2015).

No Reino Unido e Europa os termos *Implementation Science* e *Research Utilization* são comumente utilizados para designar os estudos de implementação, no Canadá os termos *Knowledge Translation e Knowledge Transfer and Exchange* também são referidos na literatura e nos Estados Unidos da América usa-se também os termos *Knowledge Transfer and Uptake* e *Dissemination and Diffusion, Research Use* (STRAUS; TETROE; GRAHAM, 2009).

Na língua portuguesa, as palavras parônimas Implantar e Implementar são muitas vezes tomadas por sinônimas e utilizadas de forma indistinta. Porém, de acordo com o Dicionário Houaiss (2009), a palavra implantar é originada do Latim IN, "em", e PLANTARE, o mesmo

que “empurrar para dentro do solo com o pé; significa portanto, “iniciar, desenvolver, estabelecer, fixar”. Por outro lado, implementação vem de IMPLERE do Latim, com o sentido de “encher, satisfazer, completar”, e em português seu significado é “colocar em execução”. Na língua inglesa, não há esta confusão, pois *implant* refere-se à “ação de inserir um dispositivo ou tecido no corpo humano”, e *implement* é “ato de colocar um plano em ação” (CAMBRIDGE UNIVERSITY PRESS, 2018). Considerando esta particularidade da língua, na presente Tese utilizamos o termo implementação para designar todo o processo que leva à prática efetiva dos SCF.

Para estudar esse processo, os pesquisadores de implementação buscam responder uma variedade de questões, incluindo a forma como as evidências da pesquisa são traduzidas para a prática e como as novas intervenções são adotadas, entregues e se mantém em sistemas do “mundo real” (PROCTOR, 2014). O objetivo final da pesquisa de implementação é construir uma base de evidências sobre os processos e estratégias mais eficazes para melhorar a qualidade dos cuidados. Importante ressaltar que ela deve ser precedida por pesquisas de efetividade. Neste sentido, a pesquisa de implementação, seria o passo seguinte, que procura descobrir como promover essas intervenções baseadas em evidências em cenários específicos, estendendo sua disponibilidade, alcance e benefícios para pacientes e comunidades.

O processo de implementação corresponde à ação de colocar em prática ou integrar inovações envolvendo a avaliação das estratégias e os efeitos de uma intervenção clínica sobre resultados relevantes (MOULLIN et al., 2015). Os conceitos sobre implementação englobam o processo operacional, os domínios (grupos ou níveis de influências) e mais três elementos: os fatores (também chamados de barreiras e facilitadores ou determinantes), as estratégias e as avaliações.

Para isso são considerados vários aspectos do processo, incluindo fatores que o influenciam, o processo em si e os resultados da implementação (FIXSEN et al., 2005; PETERS et al., 2013). Dessa maneira, o foco deste tipo de pesquisa pode ser identificar problemas comuns do processo, compreender os fatores que dificultam ou facilitam o acesso à intervenção, desenvolver e testar soluções para superar barreiras do processo, introduzir inovações em sistemas de saúde ou promover seu uso em larga escala e promover sustentabilidade das intervenções. A intenção é compreender o que, por que e como as intervenções (políticas públicas, programas ou práticas profissionais) ocorrem no “mundo real” e testar abordagens para aprimorá-las. É amplamente aceito que a implementação não é um evento único, mas um processo longo e complexo. Moullin (2016) destaca que esse processo é delineado em numerosos arranjos e diferentes denominações dos estágios, identificados na literatura como:

- implantação/ desenvolvimento/ identificação/ criação de conhecimento/ detecção de problemas;
- comunicação: difusão (comunicação passiva natural, não direcionada e não controlada) ou disseminação (abordagem ativa de comunicação para um público alvo, por meio de canais determinados e usando estratégias planejadas);
- exploração/ conscientização/ conhecimento e persuasão/ processo de decisão sobre a inovação;
- preparação/ adoção;
- implementação/ aplicação/ operação;
- sustentabilidade/ institucionalização/ implementação completa/ melhora da prática/ confirmação/ estabilização/ manutenção/ pós-implementação;
- utilização em larga escala/ replicação/ propagação.

Neste contexto de definição e caracterização, é importante diferenciar a pesquisa de implementação de outros tipos de pesquisas, como estudos de efetividade de inovação baseada em evidência, estudos em sistemas de saúde e pesquisas translacionais, pois seus objetivos estão voltados para os efeitos das inovações implementadas (novo tratamento, prática profissional ou política pública) em sistemas de saúde e organizações, e não no processo, influências e resultados da implementação em si (BAUER et al., 2015; REMME et al., 2010). Diante disso, é importante conhecer os métodos de pesquisas mais adequados para atender os objetivos da pesquisa de implementação.

2.4.2 **Métodos de pesquisa utilizados em estudos de Implementação**

Como em outros tipos de estudos em sistemas de saúde, a pergunta de pesquisa é a norteadora de todo processo da pesquisa de implementação e a partir destas são determinados os métodos a serem utilizados nas investigações. Uma descrição mais detalhada da pergunta de pesquisa é fundamental para que pesquisadores e profissionais de saúde possam determinar quais os métodos de pesquisa que devem ser utilizados. A relação entre os principais objetivos da pesquisa de implementação, suas perguntas de pesquisa e metodologias mais apropriadas são apresentadas no Quadro 1 (PETERS et al., 2013).

Quadro 1 - Tipos de objetivo de pesquisa de implementação, pergunta de implementação e métodos de pesquisa.

Objetivo	**Descrição**	**Pergunta de implementação**	**Métodos de pesquisa e abordagens de coleta de dados**
Explorar	Explorar uma ideia ou fenômeno para gerar hipóteses ou generalizações de exemplos específicos	Quais são os possíveis fatores e agentes responsáveis pela implementação bem-sucedida de uma intervenção de saúde? Para melhorar ou expandir uma intervenção de saúde?	Métodos qualitativos: teoria fundamentada em dados (*grounded theory*), etnografia, fenomenologia, estudos de caso e abordagens narrativas; entrevistas com informantes-chave, grupos focais, análises históricas
			Métodos quantitativos: análise de rede, estudos transversais
			Métodos mistos: combinando métodos qualitativos e quantitativos
Descrever	Identificar e descrever o fenômeno e seus correlatos ou possíveis causas	Como é o contexto em que a implementação ocorre? Quais os principais fatores que influenciam a implementação em um determinado contexto?	Métodos quantitativos: estudos transversais (descritivos), análise de rede
			Métodos qualitativos: etnografia, fenomenologia, estudos de caso e abordagens narrativas; entrevistas com informantes-chave, grupos focais, análises históricas
			Métodos mistos: inquérito qualitativo e quantitativo com convergência de dados e análises
Influenciar	Testar se uma intervenção produz um resultado esperado		
Com adequação	Com confiança suficiente de que a intervenção e os resultados estão ocorrendo	A cobertura de uma intervenção de saúde está mudando entre os beneficiários da intervenção?	As séries prévias ou temporais apenas em receptores de intervenção; pesquisa de ação participativa
Com plausibilidade	Com maior confiança de que o resultado é devido à intervenção	O resultado de saúde é plausível devido à intervenção implementada e não a outras causas?	Ensaios de agrupamento simultâneos, não aleatorizados: intervenção em saúde implementada em algumas áreas e não em outras; estudo prévio ou transversal em beneficiários do programa e não beneficiários; estudos típicos de melhoria da qualidade
Com probabilidade	Com uma probabilidade elevada (calculada) de que o resultado se deve à intervenção	É um resultado de saúde devido à implementação da intervenção?	Ensaios parcialmente controlados: ensaios clínicos randomizados e pragmáticos; intervenção de saúde implementada em algumas áreas e não em outras; implementação híbrida de eficácia

Fonte: Peters et al, 2013.

Quadro 1 - Tipos de objetivo de pesquisa de implementação, pergunta de implementação e métodos de pesquisa. Continuação.

Objetivo	Descrição	Pergunta de implementação	Métodos de pesquisa e abordagens de coleta de dados
Explicar	Desenvolver ou expandir uma teoria para explicar a relação entre conceitos, os motivos da ocorrência de eventos e como eles ocorreram	Como e por que a implementação da intervenção leva a efeitos sobre comportamento, serviços ou status de saúde em todas as suas variações?	Métodos mistos: inquérito qualitativo e quantitativo com convergência de dados e análises
			Quantitativo: medidas repetidas de contexto, atores, profundidade e amplitude de implementação em subunidades; identificação de rede; pode usar desenhos para inferências confirmatórias; implementação híbrida de eficácia
			Métodos qualitativos: estudos de caso, abordagens fenomenológicas e etnográficas com entrevistas com informantes-chave, grupos focais, análises históricas
			Pesquisa-ação participativa
Prever	Usar conhecimentos prévios ou teorias para prever eventos futuros	Qual é o curso provável da futura implementação?	Quantitativo: modelo baseado em agente; modelagem de simulação e previsão; extrapolação de dados e análise de sensibilidade (análise de tendências, modelagem econométrica)
			Qualitativa: exercícios de construção de cenários; técnicas Delphi com opinião de líderes

Fonte: Peters et al., 2013.

Além das metodologias de pesquisa, é importante conhecer os desfechos mensurados nas pesquisas de implementação. Proctor e colaboradores (2011) definiram os desfechos da implementação como "os efeitos de ações deliberadas e intencionais para implementar novos tratamentos, práticas e serviços", cujos objetivos seriam: servir como indicadores do sucesso da implementação, como indicadores proximais dos processos de implementação e como desfechos intermediários (substitutos) em relação a pesquisas em sistema de saúde, pesquisas clínicas e pesquisa de qualidade de cuidados. A seguir são descritos alguns desfechos de implementação (PETERS et al., 2013; PROCTOR et al., 2011):

- Aceitabilidade: a percepção entre *stakeholders* (consumidores, provedores de cuidado, gerentes, políticos) que uma intervenção é aceitável, satisfatória.
- Adoção: a intenção, decisão inicial ou ação para tentar empregar nova intervenção.
- Adequação: o ajuste ou relevância percebida da intervenção para um cenário específico, um determinado público-alvo (provedor ou consumidor) ou problema.
- Viabilidade: a medida em que uma intervenção pode ser realizada em um determinado cenário ou organização.

- Fidelidade: o grau em que uma intervenção foi implementada conforme foi projetado em um protocolo, plano ou política inicial.
- Custo de implementação: o custo incremental da estratégia de implementação ou o custo total da implementação, que pode incluir o custo da própria intervenção.
- Cobertura: o grau em que a população que é elegível para se beneficiar de uma intervenção realmente a recebe.
- Sustentabilidade: a medida em que uma intervenção é mantida ou institucionalizada em um determinado contexto.

2.4.3 **Teorias, modelos e *frameworks* que norteiam a Pesquisa de Implementação**

Os termos teoria, modelo e *frameworks* são frequentemente utilizados na literatura científica de forma intercambiável e imprecisa, apesar de se referirem a abordagens distintas (BAUER et al., 2015). Para definir e diferenciar esses termos Nilsen (2015) realizou uma revisão narrativa de literatura para identificar modelos, teorias e *frameworks* utilizados em Pesquisas de Implementação e conceitua essas diferentes abordagens como se segue:

- A *teoria* pode ser definida como um conjunto de princípios ou afirmações analíticas destinadas a estruturar a observação, compreensão e explicação do mundo. Uma teoria é constituída por definições de variáveis, um domínio em que se aplica, um conjunto de relações entre variáveis e estimativas específicas. No campo da Implementação, a teoria implica alguma capacidade preditiva, com tentativas de explicar os mecanismos causais do processo, ou seja, deve fornecer uma explicação clara de como e por que relações específicas levam a eventos específicos.

- O *modelo* normalmente envolve uma simplificação deliberada de um fenômeno ou um aspecto específico de um fenômeno e pode ser descrito como uma teoria com um escopo de explicação mais definido. A diferença entre o modelo e a teoria é que o primeiro é geralmente explicativo, usado para descrever ou orientar o processo de tradução da pesquisa para a prática, enquanto a segunda é explicativa e descritiva, ou seja, pode prever ou analisar quais fatores influenciam os resultados da implementação. Assim, a teoria pode ser operacionalizada por meio de um modelo.

- O *framework* geralmente representa uma estrutura, visão geral, esquema, sistema ou plano consistindo em várias categorias descritivas, como conceitos, constructos ou variáveis, e as relações entre eles que se presume serem responsáveis por um fenômeno. Os *frameworks*

não fornecem explicações, apenas descrevem fenômenos empíricos ajustando-os a um conjunto de categorias. Na pesquisa de implementação estes tem um propósito descritivo, apontando para fatores que podem influenciar ou influenciam de fato, os resultados da implementação.

Todas essas abordagens teóricas utilizadas na pesquisa de implementação podem ser classificadas nas seguintes categorias (MOULLIN et al., 2015; NILSEN, 2015):

- *Modelos ou frameworks de processo*: seu objetivo é descrever e orientar o processo de transferência dos resultados das pesquisas para a prática profissional. Para isso, são especificadas as etapas (passos, fases) de todo processo, desde o resultado da pesquisa até a plena implementação da prática profissional, serviço ou política pública. Exemplos: *ACE Star Model of Knowledge Transformation* (STEVENS, 2013), *Generic Implementation Framework* (GIF) (MOULLIN et al., 2015) *Framework for the Implementation of Services in Pharmacy* (FISpH) (MOULLIN; SABATER-HERNÁNDEZ; BENRIMOJ, 2016a).
- *Frameworks de determinantes da implementação*: especifica os tipos (classes ou domínios) de determinantes da implementação (fatores de implementação), que atuam como barreiras ou facilitadores e influenciam os resultados da implementação, podendo também especificar relações entre os fatores. O objetivo geral é compreender e explicar influências sobre os desfechos da implementação, como prever resultados ou interpretar os resultados retrospectivamente. Exemplos: *Consolidated Framework for Implementation Research* (CFIR) (DAMSCHRODER et al., 2009), *Theoretical Domains Framework* (TDF) (MICHIE; VAN STRALEN; WEST, 2011), *Tailored Implementation for Chronic Diseases* (TICD) (FLOTTORP et al., 2013).
- *Teorias clássicas:* teorias que se originam de disciplinas externas à ciência de implementação, como a psicologia, sociologia e teoria organizacional, que podem ser aplicadas para fornecer compreensão ou explicação de aspectos do processo de implementação. Exemplo: *Theory of Diffusion* (ROGERS, 1995), teorias de redes sociais, teorias organizacionais (NILSEN, 2015).
- *Teorias de implementação:* teorias que foram desenvolvidas por pesquisadores de implementação (a partir do zero ou adaptando teorias e conceitos existentes) para fornecer compreensão ou explicação de aspectos de implementação. Exemplos: *Organizational Readiness* (WEINER, 2009), *Normalization Process Theory* (MAY; FINCH, 2009).

- *Frameworks de avaliação:* especifica aspectos da implementação que possam ser avaliados para determinar o seu sucesso. Exemplos: Ex: *Reach, Effectiveness, Adoption, Implementation, and Maintenance framework* (RE-AIM) (GLASGOW; VOGT; BOLES, 1999), *framework* de Proctor et al. (2011).

2.4.4 **Pesquisa de Implementação e os serviços farmacêuticos**

Por ser uma área de estudo recente são poucos os trabalhos sobre implementação de serviços farmacêuticos, sendo que a maioria dos estudos tem como objetivo avaliar dados referentes à estrutura, processo ou resultados dos serviços implementados em instituições de longa permanência para idosos (SILVA et al., 2015), farmácias comunitárias (AGUIAR; BALISA-ROCHA; LYRA-JR, 2013; KEMPEN et al. 2014; ROCHA et al., 2015), serviços ambulatoriais (ANDERSON et al., 2013; MANZOOR et al., 2017; SANTOS-JÚNIOR et al., 2015) e da assistência farmacêutica nos sistemas de saúde (BARRETO, GUIMARÃES, 2010; SOUZA et al., 2017), muitas vezes analisando a intervenção e não o processo de implementação em si.

Neste contexto, vários serviços farmacêuticos tiveram sua efetividade clínica (ROTTA et al., 2015) e benefícios econômicos (GALLAGHER; MCCARTHY; BYRNE, 2014) demonstrados, embora a exequibilidade de alguns serviços esteja sendo questionada, visto que muitos não conseguiram ser totalmente implementados com sucesso (PATWARDHAN; AMIN; CHEWNING, 2014; ROTTA et al., 2015). Porém, poucos estudos relatam fatores que influenciam a implementação de SCF em hospitais (BRAZINHA; FERNANDEZ-LLIMOS, 2014; PENM et al., 2014).

As pesquisas atuais sobre serviços farmacêuticos focam principalmente nas fases iniciais de definição do serviço e avaliação clínica e de custos (PATWARDHAN; AMIN; CHEWNING, 2014). Todavia, para garantir a efetividade dessas práticas clínicas na "vida real", as investigações devem ser estendidas para compreensão e melhora da introdução e integração desses serviços em um contexto real, pois mesmo sendo desenvolvidos, testados, prontos para serem aceitos e mesmo remunerados, muitas vezes acabam interrompidos em uma ou mais etapas do processo de implementação. (MAKOWSKY et al., 2013; MOULLIN; SABATER-HERNÁNDEZ; BENRIMOJ, 2016a).

Os resultados das pesquisas de implementação também têm mostrado que a utilização de estratégias de implementação únicas ou voltadas para um único fator geralmente não são suficientes para a implementação bem-sucedida e com sustentabilidade (GRIMSHAW et al.,

2001; SCOTT et al., 2012). Em outras palavras, fatores como motivação, conhecimento prévio, remuneração ou treinamento por si só não são suficientes para garantir a implementação bem-sucedida de SCF (MOULLIN, 2016). Na prática, acreditava-se que a remuneração e o treinamento seriam suficientes para impulsioná-la, porém a partir das experiências em países como Austrália é possível observar que estes fatores não são suficientes para assegurar a qualidade do serviço implementado. Dentre outros fatores, o modo desarticulado das estratégias adotadas nesse país pode ser uma das explicações (LINGAM, 2013; MOULLIN, 2016).

Em 2006, Roberts e colaboradores publicaram uma revisão de modelos e *frameworks* para a implementação de SCF em farmácias comunitárias e verificaram, que até aquele momento, poucos estudos sobre o tema focavam no processo de implementação em si, a maioria dos modelos encontrados davam muita ênfase nas habilidades, conhecimento e atitudes dos farmacêuticos e presumiam que desenvolvendo esses domínios, automaticamente haveria uma mudança de prática bem sucedida. Baseados nesses achados, os autores sugeriram que elementos organizacionais também deveriam ser considerados nestes modelos para que a mudança da prática profissional farmacêutica fosse efetiva e sustentável. Dentre os modelos identificados, destacamos o "modelo de implementação do Cuidado Farmacêutico (PIPC model)" de Odedina e colaboradores (1997) e o "modelo de mudança da prática" de Holland e Nimmo (1999).

Mais recentemente, *frameworks*, modelos conceituais e teorias têm sido aplicados em pesquisas sobre implementação de práticas farmacêuticas inovadoras em vários cenários, a maioria desses em farmácias comunitárias e serviços ambulatoriais, dentre os quais é possível citar: RE-AIM *framework* (MOTT et al., 2014); teoria do comportamento planejado (DEMIK et al., 2013;); difusão de inovações (KAAE; CHRISTENSEN, 2012; TEETER et al., 2014); CFIR (MURPHY et al., 2014; MOULLIN; SABATER-HERNÁNDEZ; BENRIMOJ, 2016b; SHOEMAKER et al., 2017); TDF e *Behavioural Change Wheel* (BCW) (MURPHY et al., 2014); Ecological model (HOSSAIN et al., 2017); e FISpH (MOULLIN; SABATER-HERNÁNDEZ; BENRIMOJ, 2016a).

No âmbito hospitalar poucos estudos utilizam modelos conceituais para análise de implementação de SCF, a saber: Six-sigma (KUMAR; KWONG, 2011), difusão de inovações (MAKOWSKY et al., 2013), teoria da mudança organizacional de Borum, teoria da rede social e modelo organizacional de Leavitt (BRAZINHA; FERNANDEZ-LLIMOS, 2014; PENM et al., 2014). Desses trabalhos, os três últimos utilizaram modelos para analisar fatores de implementação.

Os escassos modelos conceituais específicos para serviços de farmácia foram desenvolvidos ou adaptados considerando os cenários de prática da farmácia comunitária (MOULLIN; SABATER-HERNÁNDEZ; BENRIMOJ, 2016a) ou de cuidados primários (BLANCHARD et al., 2017; SHOEMAKER et al, 2017), e apresentam contexto diverso em relação ao ambiente hospitalar. Além disso, modelos genéricos adaptados para aplicação no contexto de implementação de SCF em hospitais podem não alcançar resultados satisfatórios. Em um estudo recente sobre o CFIR adaptado à implementação de SCF em farmácias comunitárias, vários fatores poderiam tanto facilitar quanto dificultar a implementação, restringindo sua categorização nos constructos do CFIR (SHOEMAKER et al., 2017).

2.4.5 **Pesquisa de Implementação e o Laboratório de Ensino e Pesquisa em Farmácia Social (LEPFS/ UFS)**

Estabelecido em 2007, o Laboratório de Ensino e Pesquisa em Farmácia Social da Universidade Federal de Sergipe – Brasil (LEPFS/UFS) desenvolve atividades relacionadas ao ensino, pesquisa e extensão nas diversas vertentes da Farmácia Social. Coordenado pelo professor Dr. Divaldo Pereira de Lyra Júnior, o LEPFS/UFS tem como missão inovar e formar para o cuidado ao paciente e para promoção do uso racional de medicamentos.

Ao longo desses dez anos de existência, as atividades de pesquisas e extensão do LEPFS/ UFS se concentraram em três grandes áreas de interesse: *educação farmacêutica*, com foco na comunicação; *avaliação da qualidade de serviços farmacêuticos*, baseada na tríade estrutura, processos e resultados (DONABEDIAN, 1966); e *pesquisa de implementação de serviços clínicos farmacêuticos*. A farmácia comunitária, a instituição de longa permanência para idosos, o ambulatório e o hospital são os cenários mais frequentes das atividades.

Os primeiros trabalhos sobre implementação de serviços farmacêuticos do grupo foram realizados no ambulatório de um hospital universitário. Em 2011 as atividades do Serviço de Cuidados Farmacêuticos foram iniciadas a convite de professores do curso de Medicina, ainda com um foco na avaliação da qualidade de serviços de saúde, foram originados deste projeto duas Dissertações de mestrado - de Genival Araújo dos Santos Júnior (SANTOS JÚNIOR, 2013) e de Rafaella Oliveira Santos Silva (SILVA, 2017) -, além da Tese de doutorado de Tatiane Cristine Marques (MARQUES, 2015), em que foram avaliados diferentes aspectos dos indicadores de qualidade necessários para implementação do serviço de Revisão da Farmacoterapia em um ambulatório-escola.

Em 2012, o LEPFS/UFS foi convidado pela coordenação da Fundação Estadual de Saúde de Sergipe (Funesa-SE) a iniciar um projeto de implementação de SCF numa rede de farmácias comunitárias públicas. Para tanto, foram realizados um estudo transversal para avaliar a estrutura (física e recursos humanos), um estudo longitudinal descrevendo o processo e os resultados da implementação dos serviços, e dois estudos qualitativos que permitiram conhecer as percepções dos farmacêuticos sobre o processo de implementação (DOSEA et al., 2015; HERMANSYAH; SAINSBURY; KRASS, 2018; HINDI; JACOBS; SCHAFHEUTLE, 2018). Estes trabalhos, que fizeram parte da Tese de doutorado de Gisele de Carvalho Brito (BRITO, 2015), e da Dissertação de mestrado de Aline Santana Dosea (DOSEA, 2015), foram os primeiros do LEPFS/ UFS a avaliar aspectos quali-quantitativos da implementação de serviços, seguindo uma tendência de pesquisa internacional (CURRAN; SHOEMAKER, 2017).

Diante desses resultados, os farmacêuticos de um hospital público de grande porte se interessaram em firmar parceria com esta equipe de pesquisadores, a fim de replicar no hospital o sucesso da implementação de serviços descrita anteriormente. Em 2013, a convite dos gestores da assistência farmacêutica da instituição, foram iniciadas as atividades do projeto de implementação da Farmácia Clínica no hospital. Este projeto, além de gerar os resultados desta Tese de doutorado, também originou a Dissertação de mestrado (ALCÂNTARA, 2016) e o projeto de doutorado (em andamento) de Thaciana dos Santos Alcântara. Na Dissertação foram apresentados os resultados da avaliação diagnóstica da estrutura (física e recursos humanos), bem como as percepções antecipadas referente ao processo de implementação de SCF na instituição (ALCÂNTARA et al., 2018). O projeto de Doutorado pretende avaliar o processo de implementação de um serviço de conciliação de medicamentos no setor de pediatria do referido hospital. Por fim, esta Tese desenvolveu o *framework* Apoteca de implementação (cap. 1), avaliou os fatores que influenciaram a implementação de SCF no hospital, em momentos diferentes do processo, e sob a ótica de dois grupos distintos: farmacêuticos e gestores (cap. 3), além de incluir os resultados de uma revisão sistemática sobre o assunto utilizando a categorização Apoteca (cap. 2).

Mais recentemente, de julho de 2015 a março de 2016, foi firmada uma parceria entre o Ministério da Saúde do Brasil, Secretaria Municipal de Saúde de uma metrópole brasileira e os pesquisadores do LEPFS/UFS para implementar SCF na Rede de Atenção à Saúde de uma metrópole do Nordeste brasileiro e avaliar esse processo. Os resultados desse estudo fazem parte da Tese de Doutorado de Genival Araújo dos Santos Júnior defendida em 2018 (SANTOS-JÚNIOR, 2018), e compreende a descrição e avaliação do processo e dos resultados

de implementação dos serviços (SANTOS-JÚNIOR et al., 2018), além das percepções dos farmacêuticos sobre fatores e estratégias que influenciaram o processo (RAMOS et al., 2018.

A inclusão deste modelo de pesquisa nas linhas temáticas de editais do Programa Pesquisa para o SUS: Gestão Compartilhada em Saúde (PPSUS 2017) de estados como Pernambuco (GOVERNO DO ESTADO DE PERNAMBUCO, 2017), Ceará (GOVERNO DO ESTADO DO CEARÁ, 2017) e Goiás (FUNDAÇÃO DE AMPARO À PESQUISA DO ESTADO DE GOIÁS, 2017), além da edição especial temática de setembro-outubro de 2017 do periódico *Research in Social and Administrative Pharmacy*, fator de impacto 2,196, dedicado à Ciência da Implementação (CURRAN; SHOEMAKER, 2017) evidenciam a demanda de investigações sobre o tema e o alinhamento das pesquisas do LEPFS/ UFS com as tendências nacionais e internacionais.

OBJETIVOS

3 **OBJETIVOS**

3.1 OBJETIVO GERAL

- Analisar os fatores que afetam a implementação de Serviços Clínicos Farmacêuticos (SCF) no ambiente hospitalar.

3.2 OBJETIVOS ESPECÍFICOS

- Desenvolver um *framework* de determinantes da implementação de SCF.
- Identificar os fatores que afetam a implementação da SCF no ambiente hospitalar, relatados na literatura científica.
- Conhecer as expectativas sobre a implementação de SCF em um hospital público de alta complexidade, percebidos por farmacêuticos e gestores.
- Identificar os fatores que influenciaram a implementação de SCF em um hospital público de alta complexidade, percebidos por farmacêuticos e gestores.
- Testar a proposta de *framework* desenvolvido (Apoteca) a partir de determinantes da implementação de SCF.

RESULTADOS

CAPÍTULO 1

4.1 CAPÍTULO 1 - Apoteca: construindo um *framework* para auxiliar na implementação de serviços clínicos farmacêuticos

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RESUMO

Vários trabalhos têm relatado a contribuição dos serviços clínicos farmacêuticos (SCF) na melhora das condições clínicas de pacientes e na diminuição de custos relacionados à farmacoterapia, apesar disso, essa ainda não é uma prática consolidada nos países em desenvolvimento. No intuito de auxiliar na identificação e compreensão de fatores que influenciam os desfechos do processo de implementação de SCF, este artigo propõe um *framework* de determinantes de implementação. Este *framework* emergiu de discussões entre os autores, baseada nas observações sistemáticas dos pesquisadores e suas experiências de implementação de SCF. Modelos conceituais fundamentados em observações da realidade, como o modelo de avaliação da qualidade em saúde de Donabedian e o modelo de mudança da prática de Holland e Nimmo, também inspiraram os autores. Após a análise de todos os aspectos relativos aos determinantes da implementação de SCF, foram propostos os seguintes fatores: Atitudinais, Políticos, Técnicos e Administrativos (Apoteca), que já foram utilizados como referencial para três pesquisas de implementação e uma pesquisa de integração de serviços clínicos farmacêuticos, mostrando seu potencial para uso no planejamento de intervenções, na identificação e avaliação retrospectiva de fatores determinantes para a implementação, além de referencial teórico para pesquisas sobre o tema.

Descritores: implementação, serviços clínicos farmacêuticos, *framework*.

INTRODUÇÃO

A ciência da implementação pode ser definida como "o estudo científico de métodos para promover a incorporação sistemática de resultados de pesquisa e outras práticas baseadas em evidências na prática clínica rotineira e, portanto, melhorar a qualidade e eficácia dos serviços de saúde"[2]. Nos estudos são considerados vários aspectos da implementação, incluindo fatores que o influenciam, o processo em si e o impacto dos resultados na realidade onde estão inseridos. A intenção é compreender o que, por que e como as intervenções (políticas públicas, programas ou práticas profissionais) ocorrem no "mundo real" e testar abordagens para aprimorá-las [3,4].

Por ser uma área de estudo recente são poucos os estudos sobre implementação de serviços clínicos farmacêuticos (SCF), sendo que a maioria visa relatar dados referentes a estrutura, processo ou resultados dos serviços implementados em instituições de longa permanência para idosos [5], farmácias comunitárias[6,7] e serviços ambulatoriais [8–10], muitas vezes avaliando a intervenção e não o processo de implementação em si.

Na prática, as pesquisas atuais sobre SCF têm focado principalmente nas fases iniciais de definição do serviço e avaliação clínica e de custos [11]. Todavia, para garantir a sustentabilidade dessas práticas clínicas no "mundo real", as investigações devem ser alicerçadas e construídas a partir da compreensão desses serviços em um contexto real, pois mesmo sendo desenvolvidos, introduzidos, testados e mesmo remunerados, muitas vezes são interrompidos em uma ou mais etapas do processo de implementação[12,13]. Situação verificada principalmente em países em desenvolvimento da América Latina, Ásia, África e Oriente Médio, onde os SCF ainda não estão consolidados[14].

Nesses estudos, é possível observar que a integração dos serviços é prejudicada pela falta de uniformidade nos métodos e dos poucos modelos específicos para a implementação dos SCF, limitando comparações e deixando pesquisadores, gestores e farmacêuticos sem referência. Assim, este estudo teve como objetivo propor a construção de um *framework* de determinantes de implementação que pode auxiliar na identificação e compreensão de fatores que influenciam os desfechos do processo de implementação de SCF.

DESENVOLVIMENTO DO *FRAMEWORK* APOTECA

Nos últimos 15 anos, a profissão farmacêutica evoluiu no Brasil, com legislação apropriada, mudanças curriculares e maior visibilidade para os serviços clínicos realizados em diversos cenários de prática[15]. Todavia, os pesquisadores envolvidos neste trabalho, na interface entre o ambiente acadêmico e profissional, tem observado uma transição paradigmática morosa e sem uma linha condutora definida nas instituições de saúde do país. Esta situação instigou o questionamento: "Por que, apesar de evidências mostrando os benefícios proporcionados pelos SCF, estes ainda não estão consolidados no Brasil?"

Para compreender melhor esta questão, foi proposto um *framework* de determinantes simples, lógico e de base empírica que pode ser usado para classificar e caracterizar os fatores que influenciam a implementação de SCF, auxiliando na compreensão desses fatores, gerando *insights* sobre estratégias para consolidar esses serviços e orientar futuras pesquisas. Assim, o *framework* Apoteca emergiu de uma série de discussões entre os autores, a partir de uma abordagem fenomenológica, ao considerar as observações sistemáticas do grupo de pesquisa (LEPFS/ UFS) e suas vivências de implementação de SCF nos vários cenários do sistema de saúde brasileiro.

Estabelecido em 2007, o Laboratório de Ensino e Pesquisa em Farmácia Social da Universidade Federal de Sergipe – Brasil (LEPFS/UFS) tem desenvolvido atividades relacionadas ao ensino, pesquisa e extensão, participando da elaboração de legislações, políticas e práticas inovadoras no país[16] . Ao longo de mais de dez anos de existência, as atividades de pesquisas e extensão do LEPFS/ UFS se concentram em três grandes áreas de interesse: *educação farmacêutica*, com foco na comunicação; *avaliação da qualidade de serviços farmacêuticos*, baseada na tríade estrutura, processos e resultados [17]; e *pesquisa de implementação de serviços clínicos farmacêuticos*. Os cenários mais frequentes das atividades são a farmácia comunitária, instituições de longa permanência para idosos, unidades de saúde pública e hospitais.

Os primeiros trabalhos sobre implementação de serviços farmacêuticos do grupo foram realizados no ambulatório de um hospital universitário. Em 2011 as atividades do Serviço de Cuidados Farmacêuticos foram iniciadas a convite de professores do curso de Medicina, ainda com um foco na avaliação da qualidade de serviços de saúde, em que foram avaliados diferentes aspectos dos indicadores de qualidade necessários para implementação do serviço de revisão da farmacoterapia em um ambulatório-escola [10].

Em 2012, o LEPFS/UFS foi convidado a iniciar um projeto de implementação de SCF em uma rede de farmácias comunitárias públicas. Para tanto, foram realizados um estudo transversal para avaliar a estrutura (física e recursos humanos), um estudo longitudinal descrevendo o processo e os resultados da implementação dos serviços[18], e um estudo qualitativo que permitiram conhecer as percepções dos farmacêuticos sobre o processo de implementação[19]. Estes foram os primeiros estudos a avaliar aspectos quali-quantitativos da implementação de serviços, seguindo a tendência de pesquisa internacional[20].

Diante desses resultados, foi firmada uma parceria com farmacêuticos de um hospital público de alta complexidade, a fim de replicar o modelo de implantação empregado em projetos anteriores. Em 2013, foram iniciadas as atividades do projeto de implementação de SCF na instituição com a avaliação diagnóstica da estrutura (física e recursos humanos)[21], bem como das percepções antecipadas referentes ao processo de implementação de SCF na instituição[22]. Além disso, foram avaliados os fatores que influenciaram a implementação de SCF no hospital, em momentos diferentes do processo e sob a ótica de dois grupos distintos: farmacêuticos e gestores (cap. 3 desta Tese).

Entre julho de 2015 a março de 2016, ocorreu mais um projeto de implementação de SCF, mediante parceria entre o Ministério da Saúde do Brasil, Secretaria Municipal de

Saúde de uma metrópole no Nordeste do país e o LEPFS/UFS. Este trabalho teve o objetivo de implementar e propor integração de SCF na Rede de Atenção à Saúde municipal[23,24]. Os resultados obtidos neste projeto-piloto possibilitaram que pesquisadores do LEPFS/ UFS auxiliem gestores e farmacêuticos na implementação de SCF em outros municípios brasileiros.

Além das vivências citadas, modelos conceituais fundamentados em observações da realidade, como o "modelo SPO de avaliação da qualidade em saúde" de Donabedian (1966)[17] e o "modelo de mudança da prática" de Holland e Nimmo (1999)[25] serviram de inspiração para a construção desse novo *framework*. Donabedian (1966)[17] propôs a avaliação da qualidade do cuidado médico, fundamentado em suas experiências profissionais e na revisão da literatura pertinente sobre o tema, considerando três fatores: a estrutura, os processos e os resultados. Holland e Nimmo (1999)[25], por sua vez, combinaram seus conhecimentos e percepções, com resultados de pesquisas científicas e propuseram um modelo "intuitivo", composto por três conjuntos de condições que devem ser simultaneamente satisfeitas para que a mudança da prática profissional seja implementada, a saber: recursos para aprendizagem, cenário de prática e estratégias motivacionais.

Pesquisas empíricas já mostraram que, fatores como motivação, conhecimento prévio, remuneração ou treinamento por si só não são suficientes para garantir a implementação bem-sucedida de SCF[26]. Na prática, acreditava-se que a remuneração e o treinamento seriam suficientes para impulsioná-la, porém a partir das experiências relatadas em países como Austrália foi possível observar que estes fatores não são suficientes para assegurar a qualidade do serviço implementado. Dentre outros fatores, o modo desarticulado das estratégias adotadas pode ser uma das explicações[26,27]. Ao considerar esse *background*, o pesquisador sênior DPLJ observou ao longo da execução dos projetos citados anteriormente, que a implementação de serviços é afetada por múltiplos fatores que se repetiram nos cenários trabalhados e que a compreensão desses fatores foi fundamental para o sucesso das iniciativas. Outros estudos corroboram que a utilização de estratégias de implementação únicas ou voltadas para um único fator geralmente não são suficientes para a implementação bem-sucedida e sustentável[28,29].

Dentre os fatores analisados, os políticos, técnicos e administrativos pareciam ser determinantes para implementações exitosas. Porém, com as observações realizadas durante a execução do projeto no hospital, aliada a discussões entre os autores e a leitura

de textos sobre a temática, TO propôs agregar um novo fator relacionado a motivação e atitudes dos farmacêuticos, que seria transversal aos outros três antes identificados.

Após a análise de todos os aspectos relativos aos determinantes da implementação de SCF, foram propostos os seguintes fatores: Atitudinais, Políticos, Técnicos e Administrativos, cujas inicias coincidentemente formaram o acrônimo Apoteca, muito próximo da palavra latina *apothēca*, que deu origem à palavra inglesa *apothecary* e, com algumas variações, atualmente significa Farmácia em alemão, holandês, em línguas eslavas, escandinavas, entre outras. Assim, os quatro domínios do *framework* Apoteca foram definidos da seguinte forma:

Fatores atitudinais: relacionados ao comportamento, ação ou reação, e motivados por um sentimento ou opinião em relação a um fato ou pessoa particular. Também relacionados à motivação interna e externa.

Fatores políticos: relacionados aos relacionamentos dentro de um grupo ou organização que permitem que determinados indivíduos ou grupos influenciem os outros (apoio e suporte).

Fatores técnicos: relacionados às características do SCF implementado, bem como as habilidades e conhecimentos necessários para realizá-los.

Fatores administrativos: relacionados aos processos administrativos (organização e gerenciamento) necessários para execução dos SCF.

A compreensão desses fatores possibilita uma implementação sustentável dos SCF, sendo assim o *framework* Apoteca é representado pela Figura 1, apoiada em três pilares fundamentais e independentes (políticos, técnicos e administrativos), porém interligados pelos fatores atitudinais que auxiliam os profissionais a erguerem e sustentarem os SCF a serem implementados. Deste modo, o *framework* Apoteca pode auxiliar na compreensão da influência desses fatores no processo de implementação de SCF e ser o ponto de partida necessário à sua implementação adequada e sustentável, com consequente elevação da qualidade dos serviços de saúde para atender demandas individuais e coletivas de pacientes, profissionais e sistemas de saúde.

Figura 1. Imagem ilustrativa do *Framework* Apoteca.

APLICABILIDADE DO *FRAMEWORK* APOTECA

Desde o seu desenvolvimento, o *framework* Apoteca foi utilizado como referencial para três pesquisas de implementação[23, cap. 2 e cap. 3 desta Tese] e uma pesquisa de integração de serviços clínicos farmacêuticos[24] do grupo de pesquisa LEPFS/ UFS, mostrando seu potencial para uso no planejamento de intervenções, na identificação e avaliação retrospectiva de fatores determinantes para a implementação, além de referencial teórico para pesquisas sobre o tema.

É importante ressaltar que o desenvolvimento e aplicação deste *framework* tiveram como cenário principal o sistema de saúde brasileiro, por isso não é possível generalizar os resultados das análises que utilizaram o *framework* Apoteca. Porém, é provável que iniciativas conduzidas em países que tenham condições semelhantes ao Brasil possam se beneficiar da utilização deste *framework*, vide a aplicação do instrumento em uma revisão sistemática que incluiu 21 estudos conduzidos na América, Europa, Ásia, Oceania e África [(cap. 2 da Tese)].

Ademais deve-se considerar que o uso de modelos conceituais complementares para analisar o processo de implementação de SCF (triangulação de métodos) pode auxiliar na identificação de fatores determinantes com mais precisão, bem como na geração de *insights* sobre estratégias para superar barreiras e promover facilitadores. Assim, a intenção do presente *framework* não é refutar modelos e quadros conceituais

propostos anteriormente, mas dar suporte e contribuir para uma compreensão abrangente do processo de implementação de SCF.

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CAPÍTULO 2

4.2 CAPÍTULO 2 - Factors influencing the implementation of clinical pharmacy services for hospitalized patients: a mixed-methods systematic review

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Abstract

Background: Despite the evidence of benefits, clinical pharmacy services (CPS) are not uniformly implemented across healthcare institutions. Understanding the influencing factors and identifying the domains in which they act is the first step to a successful implementation. **Objective:** To identify the factors that affect the implementation of CPS for inpatients and to categorize them. **Methods:** Cochrane Library, Embase, CINAHL, IPA, Medline/PubMed, and Lilacs databases were researched up until January 2018. The search strategy was developed using text words or MESH terms related to the following four domains: "clinical pharmacy," "influencing factors," "implementation," and "hospital." Two reviewers selected original research articles that reported the factors influencing the implementation of CPS in hospitals, extracted data, and assessed the quality of the studies. After framework synthesis and categorization of the factors, a diagrammatic approach was used to present the results. **Results:** Fifty-three factors were identified in the 21 studies that were included in this review. The most cited influencing factors were uniformly distributed across the following four domains: Attitudinal, POlitical, TEChnical and Administrative (Apoteca domains). However, in terms of level (pharmacist, healthcare team, patient, institution, and national organization), the "pharmacist" group had the highest concentration of factors. "Clinical skills and knowledge" was the most frequently cited implementation factor, followed by "time to implement CPS." **Conclusion:** Our findings showed the multifactorial nature of CPS implementation process. We suggest that factors from all four Apoteca domains need to be fully considered and strategies need to be addressed for all five groups of interest to successfully implement CPS in hospitals. Future studies on the influence of implementation stages, interrelationships of implementing factors, and strategies to

overcome barriers could accelerate the successful adoption of these services. Registration: PROSPERO register CRD42016050140.

Keywords: clinical pharmacy; pharmacists; implementation research; barriers; facilitators; hospital.

Introduction

Clinical pharmacy is defined by the American College of Clinical Pharmacy (ACCP) as "a health science discipline in which pharmacists provide patient care that optimizes medication therapy and promotes health, wellness, and disease prevention" [1]. A variety of clinical pharmacy services (CPS) can be offered, such as patient education and counseling, medication review, medication therapy management, and pharmacist's prescriptions, to serve patients with different health needs and levels of complexity [2].

The studies that evaluated CPS in the hospital setting have shown that their implementation leads to demonstrable clinical [2–5] and economic benefits [6–9]. A systematic review of studies conducted in Europe found that CPS can have a positive effect in older inpatients, in general, and, on the appropriateness of medicinal use and reduction in medication errors, adverse drug reactions, and drug-related problems, in particular. Moreover, all studies that evaluated costs favored this intervention [10].

Another systematic review and meta-analysis demonstrated that multi-disciplinary teams that involve pharmacists might improve prescribing appropriateness in geriatric hospitalized patients, with a reduction in the Medication Appropriateness Index score by 7.45 points (from admission to discharge) in the intervention group [11].

The economic outcomes of CPS have been assessed by the ACCP since 1988. Most of the services analyzed were performed in the hospital setting, and all reviews have

shown that, generally, CPS provides a return on investment by providing good benefit-cost ratio or a cost-effective service [6–9].

However, despite the evidence of benefits when patients are followed up by the pharmacists, CPS is not uniformly incorporated across healthcare institutions [12–14]. There is, therefore, a need to systematically delineate and evaluate the obstacles and enablers for the implementation of CPS.

It is widely known that most research studies on the benefits of CPS are conducted in a controlled setting and for a limited time [15,16]. When such evidence is translated into the "real world," the same results are not always achieved, because context plays a key role in the uptake and sustainability of the interventions that are tested. Implementation research is an emerging field in health research that is aimed at identifying the common problems of process and bridging the gap between research findings, as well as their delivery in the real world [17].

Identifying these problems may help in understanding the factors that hinder or enable the intervention, the development of solutions to overcome process barriers, the introduction of innovations in health systems, or the promotion of their use on a large scale and their sustainability [17]. In countries where CPS are not established, implementation research may constitute a fundamental strategy to assure the successful adoption and sustainability of these processes [18–20].

Understanding the influencing factors and identifying where they act is the first step. Thereafter, it is possible to develop the strategies and the assessment tools that are specific to each problem and process level [20,21]. Although there are generic models for categorizing the factors that influence the implementation of health services, such as Consolidated Framework for Implementation Research (CFIR) [18] and the Tailored

Implementation for Chronic Diseases (TICD) [22], few studies report specific models being applied to pharmaceutical services [19,20].

Most of the available literature on the implementation of CPS reports quality indicators of structure, process, or outcomes (SPO) of the implemented services in nursing homes [23], community pharmacies [24,25], and ambulatory care services [26,27]. Few studies have been published on the factors that influence the implementation of CPS, most of which have been conducted in community pharmacies [28–31], including a systematic review in Australia [32] and a review of facilitators [33]. To the best of our knowledge, no reviews have been conducted that explore these factors in the hospital setting.

Given the above, this systematic review primarily aimed to answer the question "What factors influence the implementation of CPS for hospitalized patients?" and secondarily to categorize the identified factors.

Methods

This systematic review was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [34], as well as with the Enhancing Transparency in Reporting the Synthesis of Qualitative Research (ENTREQ) statement [35].

Search strategy

Studies were located through a comprehensive literature search up until January 2018 in the following six databases: Cochrane Library, Embase, CINAHL, IPA, Medline/PubMed, and Lilacs. The search strategy was designed to match the following research question: "What factors influence the implementation of CPS for hospitalized patients?"

- The phenomenon of interest: “implementation” of “clinical pharmacy”;
- Evaluation: “influencing factors”;
- Setting/sample: “hospital”.

Free-text words and database-controlled vocabulary were used to determine the four domains of the search strategy. The search terms were generated for each domain by examining the terminology used in the papers related to the review theme and database-controlled vocabulary thesaurus. No limits were applied to the search. The fully executed Medline/PubMed search strategy can be found in the supplementary material (S1 Text). The protocol of this systematic review was registered in the PROSPERO database (registration number: CRD42016050140).

Study selection

The study´s inclusion and exclusion criteria are described in Table 1.

Table 1. Inclusion and exclusion criteria for study selection.

Inclusion criteria
i) Studies report an assessment of factors (barriers or facilitators) that influence the implementation of CPS (as defined by the ACCP, 2008)[1] provided by pharmacists for the hospitalized patients. ii) Full-text journal articles in English, Spanish, French, or Portuguese languages. iii) Original research results, with no restrictions on the types of study design (mixed methods, qualitative studies or quantitative cross-sectional opinion surveys were eligible). iv) Study participants included pharmacy personnel (pharmacists, pharmacy technicians, pharmacy residents), hospital managers/administrators, patients, or other healthcare professionals (nurses, medical doctors).

Exclusion criteria
i) The services were provided exclusively for patients in ambulatory care settings, even if they were a part of a hospital. Outpatients present more stable health conditions when compared with inpatients. Because of that, hospitalized patients need assistance from an intensive health care team. These particularities may influence the perceptions of barriers and facilitators for implementing CPS and justifying the choice of the authors of focusing this review on inpatients. ii) Data from CPS offered for the inpatients could not be analyzed separately. iii) The study only evaluated clinical, economic, and humanistic outcomes of CPS implementation. iv) The study was a summary of the literature for the purpose of gathering information or commentary, an editorial, or a discussion paper.

Data extraction

Titles, abstracts, and full-text screenings were conducted independently by two researchers, considering the inclusion and exclusion criteria. Consensus decided the outcome of disagreements, and, if they persisted, a third impartial evaluator resolved them. The primary outcomes were defined as factors that influenced the implementation of CPS in hospitalized patients, including anticipated evaluations of barriers or facilitators during the pre-implementation or planning phases.

The extracted information included authors and date of publication, country, study design, setting, number and characteristics of the participants, data collection, data analysis, implementation phase, type and characteristics of the service implemented, barriers and facilitators to the implementation, strategies to overcome barriers (suggested

or carried out) and factor relationships. Two researchers extracted the data independently. Discrepancies were identified and resolved through consensus.

Data analysis and synthesis

Considering the research question, the nature of data managed, and the willingness to produce an output directly applicable to pharmacists, hospital administrators, and researchers, the framework synthesis [36,37] was the method chosen to analyze the data that was generated by this systematic review.

An integrated approach was used to combine the data from very heterogeneous study designs [38]. The quantitative data was converted into themes, codified, and then analyzed with qualitative data.

Apoteca framework

Following multiple readings of the papers to achieve familiarization, the researchers decided to propose a simple, logical, and empirically-based categorization framework that could be used to classify and report the influencing factors of CPS implementation for inpatients.

Therefore, the Apoteca framework was designed to assist in understanding the factors that influence the implementation of CPS, in generating insights on strategies to consolidate these services, and guiding empirical research. The intention of the present framework is not to disprove previous tools, but rather to support them and to contribute to a comprehensive understanding of the CPS implementation process.

The conceptual framework has emerged from a series of discussions, led by the senior researcher, based on the systematic observation of the authors and our research group (Laboratory of Teaching and Research in Social Pharmacy, Brazil) through the

experiences of implementing CPS in several organizations within the Brazilian health system (see Reflexivity section). Conceptual models, such as the SPO model of healthcare quality assessment [39] and the Holland–Nimmo practice change model [40], have also inspired the authors.

Initially, the following four domains were developed: Attitudinal, POlitical, TEChnical and Administrative (Apoteca). They were defined as follows:

Attitudinal factors: related to behavior, action, or reaction, and motivated by a feeling or opinion toward or of a particular fact or person. Also, internal and external motivation.

Political factors: related to the relationships within a group or organization that allow particular individuals or groups to influence others (support).

Technical factors: related to the CPS' own characteristics as well as the skills and knowledge needed to perform them.

Administrative factors: related to the administrative processes (organization and management) that are required to perform CPS.

Coding

The studies were manually coded, line by line, and the subsequent articles were coded considering previous concepts; new ones were created when necessary. This process was performed by one of the authors and independently reviewed by a second investigator to confirm the comprehensiveness and reliability of the findings.

Because barriers and facilitators are dynamic elements (as they can switch positions depending on the context and phase of the implementation process), a neutral term, such as an implementation factor, may be more appropriate for better analyzing them. In this case, the neutral element may moderate the process, either positively or

negatively [41]. Therefore, the denominations of the implementation factors were developed by the researchers from the barriers and facilitators that were identified. Afterward, the factors were analyzed according to their characteristics and causes and categorized according to the framework domains.

The denominations, analysis, and categorization of the implementation factors were performed by two or more researchers, and the final results were reached by consensus.

As the data analysis proceeded, the following novel insight was generated: the importance of stratifying the results by five levels of implementation according to their responsibilities over the factors identified: pharmacist, healthcare team, patients, institution (hospital), and national organizations.

Charting data in the framework matrix

The coded data (implementation factors) were transferred to the matrix to aid analysis. However, as the traditional table format, largely used to present systematic reviews' data, could not provide a comprehensive and clear visualization of the results, the researchers opted for a diagrammatic approach, which has been used in some studies to present complex results in a clear, visual way [42,43]. The concentric squares, representing the levels of implementation, and the positioning of the domains on the figure's sides facilitate insight into the main results and their relations.

Interpretation

Characteristics of the data were identified, the frequency of data citation on the primary studies was considered, connections between categories to explore relationships

and/or causality were mapped by two or more researchers independently, and the final results were reached by consensus.

Quality assessment

Two researchers independently assessed the quality of the included studies using the CASP Qualitative Research Checklist [44], Critical Appraisal of a Case Study [45], and the Critical Appraisal Checklist for Cross-Sectional Study (Survey) [46]. The mixed methods studies were assessed according to the methodology that was used to report or analyze the implementation factors.

The articles were classified as high/moderate/low quality based on the modified classification of Gan et al. (2016) [47]. A point was allocated for each element fulfilled, up to a maximum of 10 for the "qualitative" and "case study" checklists and 12 for the "cross-sectional study" tool. The articles considered to be of high methodological quality had ≥8 and 10 points; moderate = (7–5) and (9–6) points, and low ≤ 5 and 6 points, respectively.

Scoring disagreements were infrequent and were resolved through consensus. Two researchers independently inferred the study designs from the articles that did not report them. Disagreements were also infrequent and were resolved through consensus. No studies were excluded based on quality alone.

Reflexivity

The data were interpreted based on the authors' professional experiences who had worked as pharmacists and tutors of CPS implementation process in several organizations within the Brazilian health system. It is also noteworthy that the authors have studied and worked in a professional atmosphere of pharmacy practice transition, from a product-focused to a patient-centered care model.

These experiences may facilitate the identification of the factors and the interpretation of findings, but simultaneously, they may highlight the value of some aspects over others. This information may help the readers of this article to gain a better understanding of how data have been managed and interpreted.

Results

Search results and study characteristics

A total of 2,439 citations were identified from our literature search. After the exclusion of duplicates and title assessment, 385 abstracts were evaluated, which yielded 60 studies for full-text reading. At the end of the selection process, 21 articles [48–68] met the specific inclusion criteria. Fig 1 describes the steps involved in the search and selection process.

<Insert Figure 1: Flowchart with study steps adapted from Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).>

The study characteristics of the selected articles are listed in Table 2. The included articles were published between 2006 and 2018. The studies were conducted in America, with the largest number of published studies [50,57,59,61–65,68], followed by Europe [49,52,58,60], Asia [48,54,56,66], Oceania [53,67], and Africa [51]. One of the studies was conducted in countries of Asia and Oceania [55].

Most of the selected articles used qualitative methods for data collection and evaluation. The main services implemented were as follows: medication reconciliation [48,57,58,62,65] and pharmacist prescribing activities [49,52,67,68]. Considering the phase of data

collection, most of the studies did not define the stage of implementation, i.e., they reported information from both pre- and post-implemented services [52,54,55,59–63,66,68].

Regarding the quality of the studies, the majority were classified as moderate quality [48,53–55,57,58,63,67]. All high-quality articles have a qualitative study design [49,51,56,60,66,68].

Table 2. Characterization of the studies (n = 21) included in this systematic review.

Authors/ year	Location	Design	Participants	Hospital characteristics	Data collection	Data analysis	Implementation phase	CPS implemented	Quality rating
Al-Hashar et al. (2015)	Oman	Cross - sectional Survey	143 physicians, 47 pharmacists and assistant pharmacists and 274 nurses	450 bed, academic, tertiary care hospital	Survey	Descriptive statistics	Pre-implementation	Medication reconciliation	Moderate
Auta et al. (2015)	England	Qualitative study	22 pharmacists and 6 pharmacy technicians	Not reported	Semi-structured interviews	Thematic analysis	Post-implementation	Extended clinical roles, including pharmacist prescribing.	High
Brazinha; Fernandez-Llimós (2014)	Portugal	Qualitative study	20 practicing hospital pharmacists	20 hospitals. The majority was public and < 500 beds	Semi-structured, face-to-face interviews	Thematic analysis	Pre- and post-implementation	Medication follow-up	High
Clay et al. (2008)	United States of America	Cross - sectional Survey	295 attendees of the 2006 Society of Hospital Medicine National Meeting	Academic tertiary center (71) Community teaching hospital (84) Non-academic hospital (139)	Survey tool	Descriptive statistics	Pre- and post-implementation	Medication reconciliation	Low
Dezia et al. (2017)	United States of America	Case report	1 pharmacy resident, 2 clinical pharmacists, 1 staff pharmacist, 1 anesthesiologist	1,070-bed, private, nonprofit, tertiary academic hospital	Authors report	Not reported	Pre- and post-implementation	Pharmacist-led patient-controlled analgesia dosing service	Moderate
Gilmore et al. (2015)	United States of America	Case report	Not reported	The Johns Hopkins Hospital	Authors report	Not reported	Post-implementation	Transitions-of-care services	Low
Greenwald et al. (2010)	United States of America	Qualitative study	Participants of an invitation-only meeting	Not reported	Facilitated discussion groups and focus groups	Not reported	Not reported	Medication reconciliation	Low

Table 2. Characterization of the studies (n = 21) included in this systematic review (continued).

Authors/ year	Location	Design	Participants	Hospital characteristics	Data collection	Data analysis	Implementation phase	CPS implemented	Quality rating
Katoue; Al-Taweel (2016)	Kuwait	Qualitative study	7 senior total parenteral nutrition pharmacists of Kuwait	Six governmental hospitals and one private hospital. Beds: 180 - 857	Face-to-face semi-structured interviews	Thematic analysis	Pre- and post-implementation	Pharmaceutical care	High
Khoo; Bajorek (2006)	Australia	Mixed-methods	9 clinical pharmacists and 1 acute/post-acute care team pharmacist	Teaching hospital	Audit of pharmacist interventions (quanti). Focus group and interview (quali).	Thematic analysis	Pre-implementation	Prescribing in the area of warfarin management	Moderate
Makowsky et al. (2013)	Canada	Qualitative study	38 pharmacists	Not reported	Brief questionnaire and semi-structured telephone interview	Interpretive description	Pre- and post-implementation	Pharmacist prescribing	High
Marr et al. (2018)	United States of America	Mixed-methods	3 clinical pharmacists; 10 pharmacy residents, and 3 pharmacy students	803-bed, tertiary, teaching institution	Survey and semi-structured interview	Thematic coding	Post-implementation	Comprehensive medication management	Low
Mekonnen et al. (2013)	Ethiopia	Qualitative study	20 participants: Pharmacy students and heads of nurse, pharmacy, medical and administration	Public, teaching, referral hospital. 450 beds.	Semi-structured interviews	Thematic analysis	Not reported	Clinical pharmacy practice	High
Mulholland (2015)	United Kingdom	Cross-sectional Survey	45 pharmacists, members of the Neonatal and Paediatric Pharmacists Group	Not reported	Electronic survey	Not reported	Pre- and post-implementation	Supplementary and independent prescribing	Low

Table 2. Characterization of the studies (n = 21) included in this systematic review (continued).

Authors/ year	Location	Design	Participants	Hospital characteristics	Data collection	Data analysis	Implementation phase	CPS implemented	Quality rating
Padhye et al. (2012)	Australia	Qualitative study	4 accredited pharmacists, 8 hospital pharmacists, 4 community pharmacists, 4 hospital doctors, 3 general practitioners	Not reported	Face-to-face semi-structured interviews	Thematic analysis	Post-implementation	Medication review	Moderate
Pawluk et al. (2014)	Qatar	Cross-sectional survey	60 pharmacists that participated in an Antimicrobial Stewardship workshop	Not reported	Survey	Descriptive statistics	Pre- and post-implementation	Antimicrobial stewardship	Moderate
Penm et al. (2014)	China	Qualitative study	24 pharmacy directors, 53 clinical pharmacists, 47 dispensing pharmacists, and 6 hospital administrators	29 hospitals. The majority was public, tertiary, > 500 beds	Interviews face to face	Framework analysis	Not reported	Clinical pharmacy	High
Penm et al. (2015)	31 countries from Asia and Oceania	Cross-sectional Survey	Not reported	726 hospitals. The majority was public and > 500 beds	Online survey	Multivariate logistic and linear regressions	Pre- and post-implementation	Clinical pharmacy services	Moderate
Rabi et al. (2007)	United States of America	Case report	01 pharmacy resident	Tertiary hospital	Authors report	Not reported	Post-implementation	Medication reconciliation	Moderate
Somers et al. (2016)	Belgium	Case report	14 pharmacists and 3 pharmacy technicians	Academic, publicly funded hospital, with 1062 beds	Authors report	Not reported	Post-implementation	Medication reconciliation, medication review, ward round participation and outpatient activity.	Moderate

Table 2. Characterization of the studies (n = 21) included in this systematic review (continued).

Authors/ year	Location	Design	Participants	Hospital characteristics	Data collection	Data analysis	Implementation phase	CPS implemented	Quality rating
Thomas 3rd et al. (2006)	United States of America	Cross-sectional Survey	318 pharmacy directors	315 hospitals. The majority was short-term general and other special, <100 beds, private (nonprofit)	Pretested survey instrument	Descriptive statistics	Pre- and post-implementation	Collaborative drug therapy management	Low
Uema et al. (2008)	Argentina	Cross-sectional descriptive study	90 pharmacists	Not reported	Semi-structured and self-administered questionnaire	Descriptive statistics and ‘‘difficulty score’’	Pre- and post-implementation	Pharmaceutical care	Low

Perceived factors affecting implementation of CPS in the hospital setting

The framework synthesis of the perceived factors that affect the implementation of CPS in hospital settings is presented as a summary of the findings (Table 3), as the frequency of citation greatly influences the Apoteca framework. However, it is important to mention that the fact that an implementation factor was cited more often does not necessarily imply that it takes precedence over the others that are less cited.

Fifty-three factors were identified in this review. Of the 21 studies included, 14 reported enablers of the process [48–53,55,56,58,59,62,64,67,68] and 20 mentioned barriers for the implementation of CPS [48–54,56–68] (Table 3).

Table 3. Factors influencing implementation of clinical pharmacy services (CPS) in the hospital setting. Apoteca categorization.

Apoteca Domains	Levels	Implementing Factors*	Barriers	Facilitators
At	Ph	**Confidence (pharmacist)**	Pharmacist's lack of confidence [50, 52, 56, 64]	Pharmacist confidence [49, 56, 63]
At	Ph	**Motivation (pharmacist)**	Pharmacist's lack of motivation [50, 59, 67]	Pharmacist motivation [49, 59, 63, 67]
At	H	**Interest (medical doctor)**	Disinterest from medical doctors [66]	Requests from medical chief and medical doctors [59, 66]
At	Ph	**Medicolegal responsibility (pharmacist)**	Fear of medicolegal responsibility [56, 57, 64]	–
At	H	**Resistance (medical doctor)**	Resistance from medical doctors [49, 50]	–
At	Pa	**Interest (patients)**	Patient's disinterest [61, 65]	–
At	Ph	**Resistance towards change (pharmacist)**	Pharmacist's resistance towards change [50]	–
At	Ph	**Proactive approach (pharmacist)**	–	Pharmacist's proactive approach [61]
At	Ph	**"Key individuals"/ "champions of change" (pharmacist)**	–	"Key individuals"/ "Champions of change" [49]
At	H	**Expectations (medical doctor)**	–	Physician's positive expectations [63]
At	Pa	**Expectations (patient)**	–	Patient's positive expectations [63]
Pol	Na	**Support (governmental)**	Lack of governmental support [50, 64, 67]	Government support (funding and appropriate policies and legislation) [49, 60, 63, 64, 66]
Pol	H	**Support (healthcare team)**	Lack of support from medical doctors [67]	Healthcare team support [61, 63, 57, 53, 49, 60, 67]

*Factors organized by domain, from the most to the least cited. Abbreviations: Domains – At = attitudinal, Pol = political, Tech = technical, Adm = administrative. Levels – Ph = pharmacist, Pa = patients, I = institution (hospital), H = health team, Na = national organizations. CPS = clinical pharmacy services; MD = medical doctor.

Table 3. Factors influencing implementation of clinical pharmacy services (CPS) in the hospital setting. Apoteca categorization (continued).

Apoteca Domains	Levels	Implementing Factors*	Barriers	Facilitators
Pol	I	**Support (managers)**	Lack of support from administrators [50, 67]	Support from hospital administrators [63, 64, 67]
Pol	Na	**Support (pharmaceutical organizations)**	Lack of support from pharmaceutical organizations [50, 55, 64]	_
Pol	I	**Autonomy (pharmacist)**	Pharmacist's lack of autonomy [55, 57]	_
Pol	Ph	**Support (peer pharmacists)**	Lack of peer support [50, 55]	_
Pol	Pa	**Support (patients)**	_	Support from patients [63]
Pol	H	**Recommendation to CPS**	_	Medical doctors' recommendation of clinical pharmacists to other colleagues [49]
Pol	Na	**High-income countries**	_	High-income countries [63]
Pol	I	**Institutional policies**	Pharmacist's lack of autonomy due to institutional policies [57]	_
Tech	Ph	**Clinical skills and knowledge (pharmacist)**	Insufficient clinical skills and knowledge [50-53, 56, 59, 60, 62, 64, 66]	Pharmacists' clinical training [49, 58, 66, 67]
Tech	Ph; H	**CPS process**	Inadequate CPS process (bureaucratic, takes too long, not worth effort) [50- 52, 57]	More streamlined process [61] Model flexibility [58] Detailed workflow and practice guideline [58]
Tech	Ph; Pa; H	**Communication (pharmacist, patient, health team, MD)**	Lack of effective communication with healthcare providers and patients [48, 50, 51, 62]	Good communication , quick access to medical doctors [58]

*Factors organized by domain, from the most to the least cited. Abbreviations: Domains – At = attitudinal, Pol = political, Tech = technical, Adm = administrative. Levels – Ph = pharmacist, Pa = patients, I = institution (hospital), H = health team, Na = national organizations. CPS = clinical pharmacy services; MD = medical doctor.

Table 3. Factors influencing implementation of clinical pharmacy services (CPS) in the hospital setting. Apoteca categorization (continued).

Apoteca Domains	Levels	Implementing Factors*	Barriers	Facilitators
Tech	Pa	**Awareness about the CPS (patient)**	Patient's unawareness about the CPS [48, 51, 61, 64, 65]	_
Tech	Ph; H	**Relationship with healthcare team**	_	Collaborative relationship with healthcare team [57, 61, 66, 67]
Tech	Ph	**Awareness about the CPS (pharmacist)**	Pharmacist´s unawareness about the CPS [50, 51, 64]	_
Tech	H	**Awareness about the CPS (healthcare team, MD)**	Healthcare team's unawareness about the CPS [61, 64, 66]	_
Tech	H	**Previous experiences with CPS (health team, MD)**	_	Healthcare professional's prior positive experiences with pharmacists [59, 61, 66]
Tech	Ph	**Previous experiences with CPS (pharmacist)**	_	Pharmacist's legitimization of previous practice [56, 57]
Tech	Ph	**Research (pharmacist)**	_	Research on CPS area performed by the hospital pharmacists [66] Research studies documenting benefits [67]
Adm	Ph	**Time (pharmacist)**	Lack of time [48, 50, 53-55, 58, 61, 67, 68]	_
Adm	I	**Number of pharmacists**	Insufficient pharmacists [52, 58, 60] Shortage of pharmacists [49, 64, 67]	Appropriate number of pharmacists [63]
Adm	I	**Access to patients' information**	Restricted access to patients' clinical information [48, 50, 51, 56, 66]	Access to patient information [57, 66]

*Factors organized by domain, from the most to the least cited. Abbreviations: Domains – At = attitudinal, Pol = political, Tech = technical, Adm = administrative. Levels – Ph = pharmacist, Pa = patients, I = institution (hospital), H = health team, Na = national organizations. CPS = clinical pharmacy services; MD = medical doctor.

Table 3. Factors influencing implementation of clinical pharmacy services (CPS) in the hospital setting. Apoteca categorization (continued).

Apoteca Domains	Levels	Implementing Factors*	Barriers	Facilitators
Adm	Ph	**Workload (pharmacist)**	Pharmacists' high workload [50, 52, 55, 56, 61, 65]	_
Adm	I	**Source of information on medicines and treatment guidelines**	Lack of a reliable source of information on medicines and treatment guidelines [50, 55, 64,67]	Treatment protocols [67]
Adm	I	**Pharmacy staff (technician)**	Insufficient pharmacy staff [50, 55, 62]	_
Adm	I	**Costs to implement CPS**	Associated costs to implement CPS [49, 53, 54, 67]	_
Adm	I	**Information technology**	_	Information technology, computer system, electronic medical record [48, 58, 67]
Adm	I	**Material resources**	Lack of resources [48, 53]	Appropriate resources [63]
Adm	I	**Working facilities**	Lack of adequate working facilities [50]	Appropriate structure [63]
Adm	I	**Focus on logistical activities (hospital)**	Organizations focus the role of pharmacists on logistical activities [50, 59]	_
Adm	I	**Pharmacist practice location**	Pharmacists practice away from patients/ healthcare team [50, 55]	_
Adm	I	**Remuneration (pharmacist)**	Hospital pharmacist's low remuneration [50, 64]	_
Adm	I	**Profit on the sales of medicines (hospital)**	Clinical pharmacist interventions may reduce hospitals profit on the sales of medicines [64]	_

*Factors organized by domain, from the most to the least cited. Abbreviations: Domains – At = attitudinal, Pol = political, Tech = technical, Adm = administrative. Levels – Ph = pharmacist, Pa = patients, I = institution (hospital), H = health team, Na = national organizations. CPS = clinical pharmacy services; MD = medical doctor.

Table 3. Factors influencing implementation of clinical pharmacy services (CPS) in the hospital setting. Apoteca categorization (continued).

Apoteca Domains	Levels	Implementing Factors*	Barriers	Facilitators
Adm	H	**Profit on the sales of medicines (medical doctors)**	Clinical pharmacist interventions may reduce medical doctors' profit on the sales of medicines [64]	_
Adm	I	**Career pathway (pharmacist)**	_	Clinical career pathway for hospital pharmacists [49]
Adm	I	**Antibiotic stewardship**	_	Antibiotic stewardship [66]
Adm	I	**Hospital accreditation**	_	Hospital accreditation [66]
Adm	I	**Pharmacy and Therapeutics Committee**	_	Effective and proactive Pharmacy and Therapeutics Committee [66]
Adm	I	**Public hospital**	_	Public hospital [64]
Adm	I	**Residents and graduate students**	_	Include residents and graduate students in the CPS process [58]
Adm	I	**Teaching hospital**	_	Teaching hospital [51]

*Factors organized by domain, from the most to the least cited. Abbreviations: Domains – At = attitudinal, Pol = political, Tech = technical, Adm = administrative. Levels – Ph = pharmacist, Pa = patients, I = institution (hospital), H = health team, Na = national organizations. CPS = clinical pharmacy services; MD = medical doctor.

Attitudinal factors

Regarding the level of implementation, all the factors allocated in this domain were at the following internal levels: pharmacist, healthcare team, and patients (Fig 2). "Pharmacist´s confidence" [49,55,56,60,63,67] and "Pharmacist motivation" [49,51,55,59,60] were the most frequently mentioned factors of this domain (Table 3).

<Insert Figure 2. Factors influencing the implementation of clinical pharmacy services (CPS) in the hospital setting. Apoteca categorization.>

Interactions between attitudinal factors and the other three Apoteca domains have been identified throughout the data analysis. Hospital pharmacists in Portugal considered that lack of adequate "remuneration," lack of "support from colleagues" and "hospital managers," and lack of "interest from physicians" influence the pharmacists' "motivation to implement CPS" [60]. The quote below illustrates the influence of remuneration on a pharmacist's motivation as follows [60]:

''In the hospital pharmacist career, where people have the same salary as that of their entry year, and the Government increases the salary just by the rate of inflation without any other compensation, what kind of stimulus do I have to invest in my training?''—Pharmacist (without experience in CPS)

"Medical doctors' resistance" was considered to be the cause of difficulties in "communication" and "relationship with the health team" [60]. However, this barrier could be overcome with a more streamlined "CPS process," "previous experiences with CPS," and a "proactive approach" from pharmacists [53].

Political factors

The political domain comprised 10 factors (Table 3), mostly at the following external levels: three at the "institution" level and three at the "national organizations" level (Fig 2). "Support from the government" was the most frequently mentioned factor

in this domain [49,52,55,56,58–60], followed by "support from the healthcare team" [49,52,53,55,59,64,68] (Table 3).

Interrelations between political and administrative factors have been reported in the following primary studies: in Portugal, lack of support from the government for CPS implementation is supposed to generate "*scarce human and technological resources, pressure on cost containment, and the lack of a motivational professional and functional career*" [60]. On the other hand, in England, several documents and legislations were reported as key drivers, providing a better career structure for hospital pharmacists and promoting the retention of experienced clinical staff [49].

Moreover, "support from hospital administrators" was perceived as enabling the following other four domains: "clinical skills and knowledge (pharmacist)" [56], "workload" [48], "pharmacist motivation" [60], and "quantity of pharmacists" [56]. This was expressed by a Chinese director of the pharmacy [56] as follows:

> *"The number of clinical pharmacists is quite large in this hospital, all because we have the support of the hospital director."*—Pharmacy director

Technical factors

Amongst the 10 technical factors identified in this systematic review, the following three were considered to operate on multiple levels: "Communication"—pharmacist, healthcare team. and patients—"CPS process" and "relationship with the healthcare team"—pharmacist and healthcare team. None of the factors were at the external levels of "institution" and "national organizations" (Fig 2). "Clinical skills and

knowledge (pharmacist)" was the most frequently cited factor of this domain [49–52,54,56,58–60,63,64,67], followed by "CPS process" [50,53,60,62,63,68] (Table 3).

Along the data analysis, some interactions between implementation factors from different domains have been identified, particularly between technical and attitudinal domains. "Clinical skills and knowledge (pharmacist)" was considered to affect other implementation factors. Brazinha & Fernandez-Llimós (2014) associated lack of "clinical skills and knowledge" with "unawareness of CPS process" [60]. In a study in the United Kingdom (UK), the authors reported that changes in "clinical skills and knowledge" led to an increase in "confidence" and a decrease in "resistance towards change" [49]. In China, lack of "confidence" was perceived as a consequence of poor "clinical skills and knowledge," as stated by a clinical pharmacist [56]:

"We currently do not have that much clinical knowledge, so we do not have any confidence when we are on patient rounds to answer a question the doctor may have."—Clinical pharmacist

Administrative factors

Administrative factors were the most frequently reported by the included studies. As expected, the great majority of administrative factors were at the "institutional" level (19 factors) (Fig 2). However, the most frequently cited implementation factor of this domain was at the "pharmacist" level as follows: "Time to provide CPS" [48,50,53,59–61,64–66], followed by "number of pharmacists" [49,50,52,55,56,59,63] and "access to patient's clinical information" [48,58,60,62,67,68] (Table 3). The following quotes from hospital pharmacists illustrate the following barriers:

‘‘*Then, at the hospital, (…) it is due to the lack of workforce and lack of time for so much bureaucracy that we end up being unavailable for patient-related tasks’’*—Pharmacist (with experience in CPS) [60]

“I used to go to the wards myself to check patients’ medical charts, but now because of the overwhelming load that we have and lack of time, I review patients’ lab results with their TPN orders at the TPN unit.”—TPN pharmacist [66]

It is noteworthy that the factor “time to implement CPS” is, apparently, an effect rather than the cause of an implementation problem. Some of the studies included in this review have highlighted the following relations: “lack of time” was perceived as a consequence of “high workload,” mostly bureaucratic [53,57,60] and “insufficient workforce” (pharmacists and pharmacy technicians) [49,60,61,66].

Brazinha & Fernandéz-LLimós (2014) suggested that other possible causes for the “lack of time to develop CPS” were the main focus of the hospital pharmacist practice on logistic and administrative tasks and a poor attitude toward the delegation of some activities to pharmacy technicians and the administrative staff [60].

Discussion

The current review was the first, to the best of our knowledge, that identified factors influencing the implementation of CPS for inpatients and categorized them in the Apoteca domains.

Only 21 studies were included in this Systematic Review, which shows that this area has been under-researched. However, all included articles have been published since 2006 and some of them have been published in the last two years [50,58,63,66], suggesting the recent growth of interest in this area. The vast majority of studies are from North America [50,57,59,62–65,68], Western Europe [49,52,58,60], and the Middle East [48,54,66], with only a few of them having been conducted in Oceania [53,55,67], Asia [55,56], Africa [51], and Latin America [61].

Developing countries of Latin America, Africa, Asia, and the Middle East have changed their professional practices more recently and, consequently, few works have been published on the subject. However, there have been a growing number of publications in the recent years [12,14,69–73]. A possible explanation is the publishing of the Institute of Medicine (IOM) reports in the early part of the 2000 decade [74]. The IOM alertness to the problem of patient safety and their recognition of pharmacists as an essential resource in safe medication use may have stimulated the interest in implementing CPS in health care institutions, including hospitals.

Most of the included articles were conducted in developed nations [49,50,52,53,57–60,62–65,67,68], where CPS are well established [75]. In these countries, the main services that were implemented were either more specific, such as medication reconciliation, or more complex, such as pharmacist prescribing activities [76]. A systematic review evaluated the effectiveness of CPS delivered in primary care clinics, and most of the complex and comprehensive interventions, such as physical assessment, monitoring, prescribing, and face-to-face communication with physicians, were carried out in high-income countries [77].

In contrast, many included studies conducted in low- and middle-income nations were not well defined, but were rather more generally denominated as "clinical pharmacy" or "pharmaceutical care" [51,55,56,61,66]. Similar results were found in the

outpatient settings. Pande et al. (2013), in a systematic review of non-dispensing pharmaceutical services in low- and middle-income countries, showed that the most common terminology used in the studies was “pharmaceutical care” and the majority of the interventions involved simple patient education [13].

The most frequently cited influencing factors were uniformly distributed across the four domains Apoteca, with no predominance of one domain over others, evidencing the multifactorial nature of this process [17,41]. They were also perceived by participants regardless of the types of hospitals, CPS implemented, or country.

In terms of level, the “pharmacist” had the highest concentration of the most frequently mentioned factors, which corroborates the results found in the community pharmacy setting [28,33,78,79]. However, in a recent systematic review on patients’, general practitioners’ (GPs), and nurses’ perspectives of the factors influencing the implementation of CPS in Australian community pharmacies, the most cited factors were distributed across the various levels [32]. One possible explanation for this is that the pharmacists were the main participants in the studies included in our review and, consequently, their perception of the process and self-readiness was critical.

Attitudinal factors, such as the pharmacist’s “confidence,” “motivation,” and “resistance towards change” seem to be perceived as an implementation issue as much as, for example, “workload”, “number of pharmacists”, and “communication”. Considering the interrelation between the factors found in this review, along with the other Apoteca domains, the implementation of CPS should strongly consider attitudinal factors as one of the first issues to be tackled.

In their classical series on pharmaceutical professional practice transitions, Holland & Nimmo (1999) have highlighted the attitudes and values as a basic component of their model, especially the intrinsic motivational aspects. According to them, if the

pharmacist is not motivated to choose to change, the change in professional practice does not happen [40]. Brazinha & Fernandéz-Llimós (2014) suggested in their work that change in the pharmacists' mindsets may influence their attitudes toward obstacles that can be easily overcome but had been previously considered to be major barriers [60]. Apparently, strategies such as "clinical education and training" [49,58,64], including coaching techniques [28], "managers support" [55,56], and "key individuals" [49,65] could help to enhance the pharmacists' confidence and motivation to implement CPS in hospitals.

Through appropriate policies and legislation, whether in a mandatory way or by allowing the pharmacist to develop more complex clinical activities, "government support" can be a strong motivator to implement CPS. Contrary to the factor "time to implement CPS," this factor was considered to be a facilitator in five of seven primary studies of this review. The main services implemented in the primary studies, such as medication reconciliation and pharmacist prescribing activities, received governmental and international organizations' support to be implemented in many countries.

The National Institute for Health and Care Excellence (NICE) endorsed policies for medication reconciliation in UK hospitals and recommended that pharmacists should be involved in the process [80]. Pharmacist prescribing received government support in Canada, the United States, and the UK through legislations that permitted this practice [49,81,82]. China and England catalyzed CPS in hospitals due to policies that mandated the need for clinical pharmacists [56] and legislations that enabled hospital pharmacists to modify patients' pharmacotherapy [49].

"Clinical skills and knowledge" was the most frequently cited implementation factor, and it was considered a barrier in eight of ten primary studies. Similar results were found in the community pharmacy scenario [28,78,79]. The insufficient clinical training can be explained by the poor clinical pharmacy *curricula* in most of the countries, which was

virtually all product-oriented until the recent years when the incorporation of clinical disciplines started in pharmacy schools worldwide, particularly in the emerging countries [83].

It is interesting to notice that this factor was also considered an enabler in the studies that were conducted in countries where CPS are established [49,58]. Moreover, this factor seems to stimulate other factors, such as "pharmacists´confidence" [49,56]. Therefore, based on these results, "clinical skills and knowledge" should be one of the first technical factors to be worked with, either as a barrier to be overcome or a facilitator to be encouraged. However, it is important to mention that mitigating this factor alone does not guarantee a successful CPS implementation. A Spanish study showed that continuous training has shifted attitudes toward the provision of pharmacotherapy follow-up, but it has not promoted the implementation of the service [84], suggesting once more that CPS implementation is a multifactorial process in which the other Apoteca domains should be considered.

The most numerous Apoteca domain was "administrative" and, as expected, was present at the "institutional level." Similar results were presented in a review of facilitators in the community pharmacy [33]. In addition, Penm et al. (2014) suggested that administrative support was of greater importance in the hospital setting because of the larger number of human resources and hierarchical levels involved when compared with the community pharmacy [56]. In our analysis, this result reflects the singularity of the administrative process in the various institutions worldwide and the low number of citations from each factor, corroborating this hypothesis.

"Time to implement CPS" was the second most frequently mentioned implementation factor, and it was considered to be a barrier in all studies. Similar results were found in the community pharmacy scenario. A survey in West Virginia, with 174

community pharmacists, revealed that lack of time was the single greatest perceived barrier to the provision of medication therapy management (MTM) services (3.08 ± 1.88) [85]. Another study with 101 community pharmacists from various states of the USA showed that "limited time to devote to the program" was the third most significant potential barrier to implementing personalized medicine services [79].

As "time to implement CPS" is, apparently, an effect rather than the cause of an implementation problem, understanding this causal relationship is important to choose the best strategies to overcome this barrier. Napier et al. (2017) showed that delegating the checking function of dispensing to the pharmacy technicians afforded more time to the pharmacists for developing patient-focused activities. Nevertheless, the reduction in the time spent on dispensing was not always reflected in a corresponding shift to patient-focused activities [86].

Brazinha & Llimós (2014) suggested that, in addition to the lack of workforce, the main focus of the organization on logistic and administrative tasks and the pharmacist's poor attitude toward delegation could be considered to explain the lack of time to develop CPS [60]. These results reinforce the multifactorial aspect of the process and the necessity for a comprehensive root cause analysis of the problem to target it in a multifaceted way [41].

Strengths and limitations

To the best of our knowledge, this study is the first systematic review to identify and categorize the factors that influence CPS implementation perceived in the hospital setting. The classification developed to analyze the data is logical and simple to use, and considered both the characteristics of the factors (Apoteca framework) and the level of

the implementation that they influence. In addition, the graphical format (Fig 2) developed to present the results gives a clear and comprehensive view of the main results.

Nevertheless, there are certain limitations that should be mentioned. The use of other relevant keywords, such as "medication therapy management," "hospitalized," "secondary care" and "quality improvement" may have yielded a larger sample. Grey literature was not considered, and it is not clear how this has influenced our results. Data analysis was reliant upon the descriptions of topics in the primary studies, which, sometimes, were not clearly described. The majority of included studies were classified as moderate or low quality, but as there is no consensus on the literature to exclude studies based on quality assessment only, the authors decided to include them in this systematic review. As with other frameworks, the Apoteca classification depends on one's perceptions and, sometimes, on the factors that are present on the borderline of the two domains.

Agenda for future research

Factors that influence the implementation of CPS can be perceived differently depending on the stage of the process, future studies should stratify the barriers and facilitators by stage of implementation to better understand the process.

Cause–effect interactions between implementing factors have also been identified throughout the data analysis, however, this issue has been poorly explored in the literature [41]. Future studies should analyze factor relationships and root-cause of barriers, to better design effective strategies and improve outcomes of implementation.

Validation of Apoteca framework and their application in primary implementation studies will be considered in future studies.

Conclusion

Fifty-three factors were identified in this review. The most cited factors were uniformly distributed into the Attitudinal, POlitical, TEChnical and Administrative (Apoteca) domains. Our findings lend insight into the attitudinal and political factors that are as important as the pharmacist´s clinical skills to have a successful CPS implementation. With regard to the groups involved, all five have at least one most cited factor, but the "pharmacist" group had the highest concentration of factors. This information allow for practitioners, policy makers and researchers to appreciate the multifactorial considerations for facilitating or hindering the implementation of CPS in hospitals.

Also, these findings may have implications for the sustainability of the implemented service. From this data it is possible to develop the strategies and the assessment tools that are specific to each problem and process level, which could help to move the process forward and enable sustainable services in countries where CPS are not consolidated.

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Figure 1: Flowchart with study steps adapted from Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).

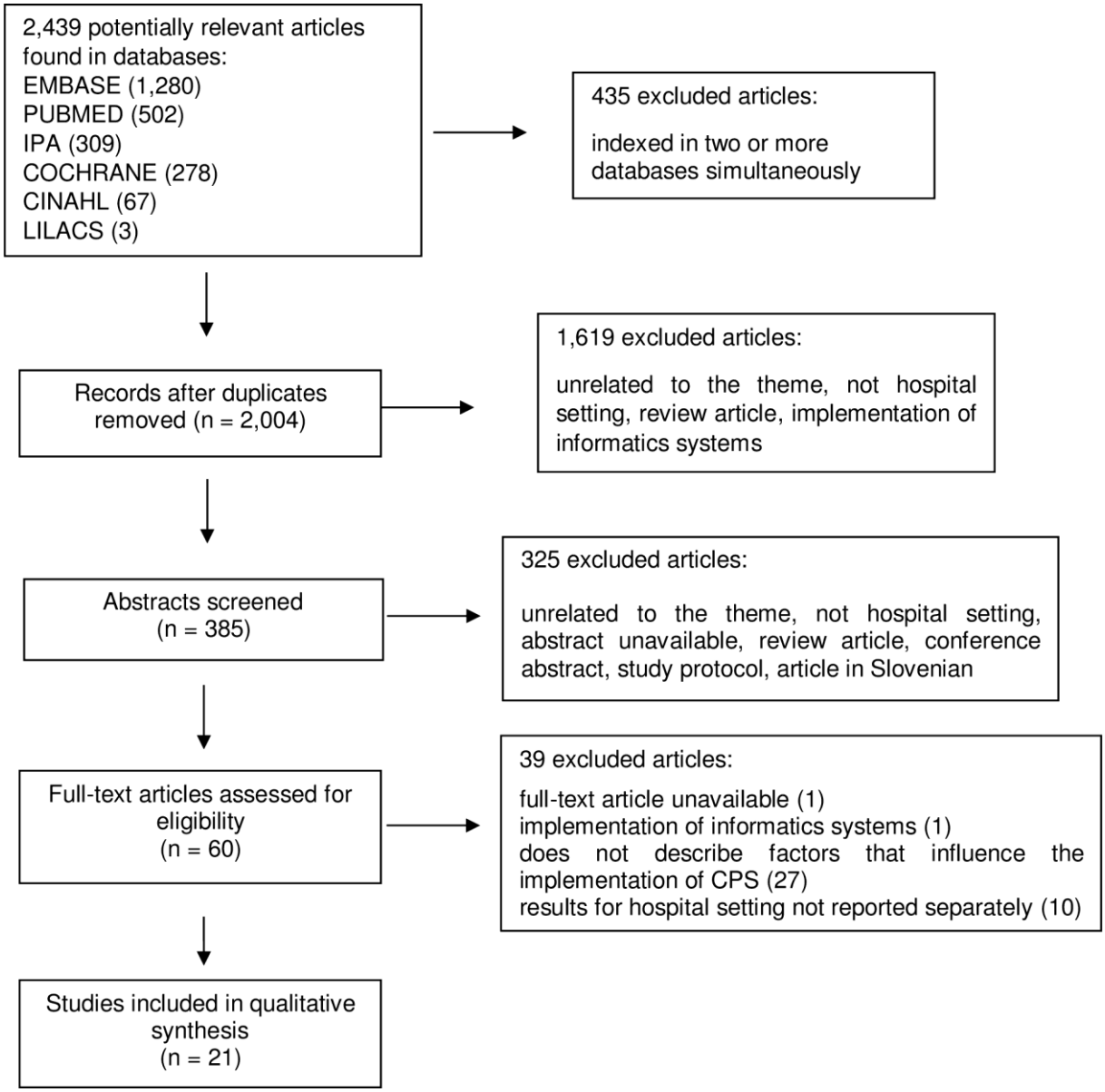
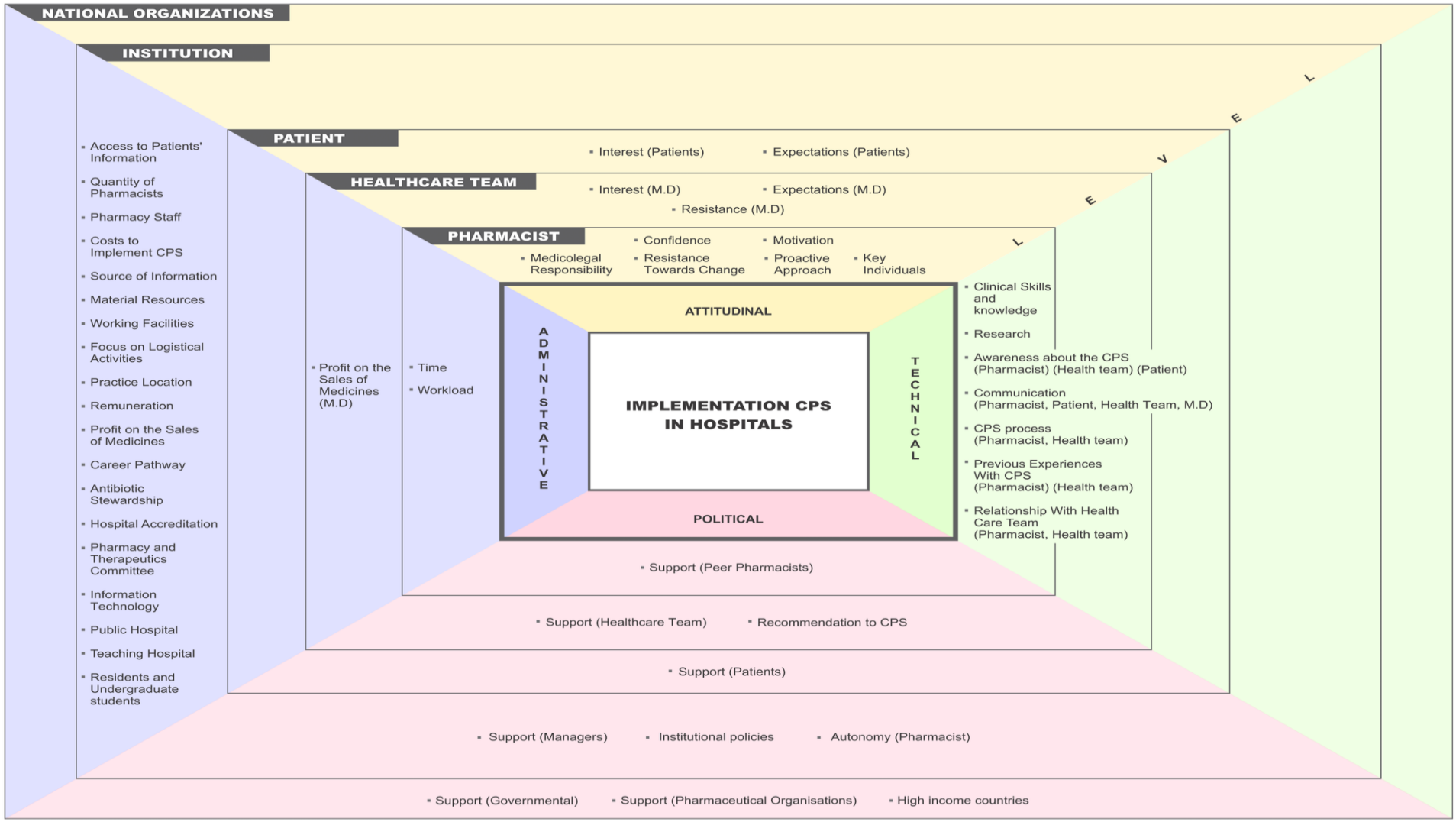


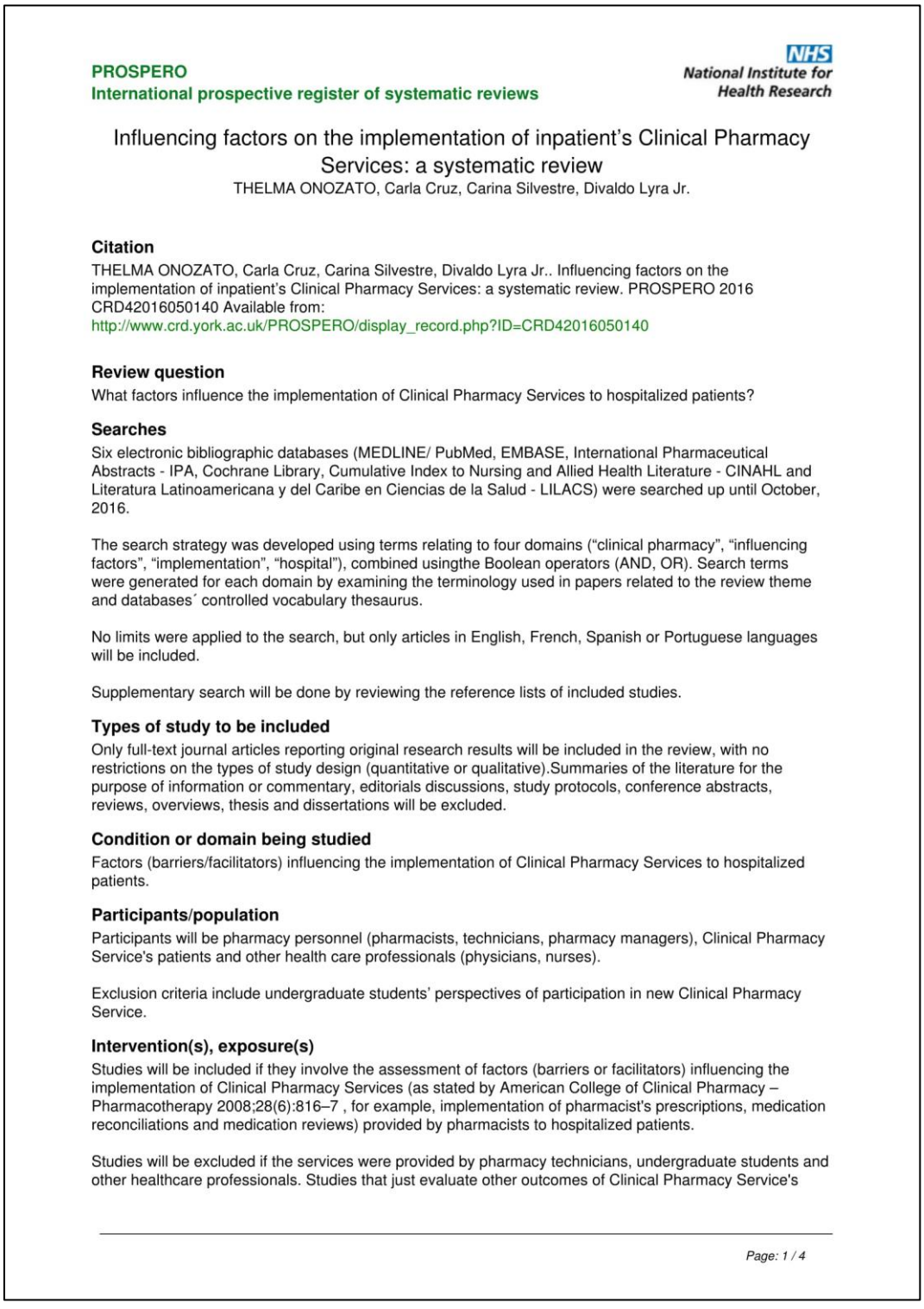
Figure 2. Factors influencing the implementation of clinical pharmacy services (CPS) in the hospital setting. Apoteca categorization



S1 Text. Medline/PubMed search strategy.

Search ((((((((((("pharmacists") OR "pharmacist") OR "pharmacists"[MeSH Terms]) OR “pharmacy practice”) OR “clinical pharmacy”) OR “pharmaceutical care”) OR “pharmaceutical services”) OR “pharmaceutical service”) OR “pharmaceutical services”[MeSH Terms])) AND (("implementation") OR "practice change")) AND ((((((((((((“Barriers”) OR “barrier”) OR “Enablers”) OR “enabler”) OR “Facilitators”) OR “facilitator”) OR “perceptions”) OR “perception”) OR “attitude”) OR “attitudes”) OR “influencing factors”) OR “opinions”) OR “opinion”) OR “attitude”[MeSH Terms]) OR “influencing factor”)) AND (((((((“hospitals”) OR “hospital”) OR “inpatients”) OR “inpatient”) OR “hospitalized patient”) OR “hospitalized patients”) OR “hospitals”[MeSH Terms]) OR “inpatients”[MeSH Terms])

S1 Figure. Prospero´s systematic review protocol



PROSPERO
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NHS National Institute for Health Research

Influencing factors on the implementation of inpatient's Clinical Pharmacy Services: a systematic review

THELMA ONOZATO, Carla Cruz, Carina Silvestre, Divaldo Lyra Jr.

Citation

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http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42016050140

Review question

What factors influence the implementation of Clinical Pharmacy Services to hospitalized patients?

Searches

Six electronic bibliographic databases (MEDLINE/ PubMed, EMBASE, International Pharmaceutical Abstracts - IPA, Cochrane Library, Cumulative Index to Nursing and Allied Health Literature - CINAHL and Literatura Latinoamericana y del Caribe en Ciencias de la Salud - LILACS) were searched up until October, 2016.

The search strategy was developed using terms relating to four domains ("clinical pharmacy", "influencing factors", "implementation", "hospital"), combined usingthe Boolean operators (AND, OR). Search terms were generated for each domain by examining the terminology used in papers related to the review theme and databases´ controlled vocabulary thesaurus.

No limits were applied to the search, but only articles in English, French, Spanish or Portuguese languages will be included.

Supplementary search will be done by reviewing the reference lists of included studies.

Types of study to be included

Only full-text journal articles reporting original research results will be included in the review, with no restrictions on the types of study design (quantitative or qualitative).Summaries of the literature for the purpose of information or commentary, editorials discussions, study protocols, conference abstracts, reviews, overviews, thesis and dissertations will be excluded.

Condition or domain being studied

Factors (barriers/facilitators) influencing the implementation of Clinical Pharmacy Services to hospitalized patients.

Participants/population

Participants will be pharmacy personnel (pharmacists, technicians, pharmacy managers), Clinical Pharmacy Service's patients and other health care professionals (physicians, nurses).

Exclusion criteria include undergraduate students' perspectives of participation in new Clinical Pharmacy Service.

Intervention(s), exposure(s)

Studies will be included if they involve the assessment of factors (barriers or facilitators) influencing the implementation of Clinical Pharmacy Services (as stated by American College of Clinical Pharmacy – Pharmacotherapy 2008;28(6):816–7 , for example, implementation of pharmacist's prescriptions, medication reconciliations and medication reviews) provided by pharmacists to hospitalized patients.

Studies will be excluded if the services were provided by pharmacy technicians, undergraduate students and other healthcare professionals. Studies that just evaluate other outcomes of Clinical Pharmacy Service's

implementation (clinical outcomes, economic evaluations or satisfaction with the service provided) and if any findings relating to factors influencing implementation are not a formal objective of the study will be excluded as well. Furthermore, studies about the implementation of informatics systems will not be included.

Comparator(s)/control

Not applicable.

Context

Studies within hospital settings will be included.

Studies will be excluded if the services were provided to outpatients, including, but not limited to patients of ambulatory care settings (even if it is part of a hospital), clinics, long-term care homes, medical centres, community pharmacies and home-based services.

Primary outcome(s)

Factors influencing the implementation of Clinical Pharmacy Services to hospitalized patients, including anticipated evaluations of barriers or facilitators during the pre-implementation or planning phases.

Secondary outcome(s)

None.

Data extraction (selection and coding)

Titles, abstracts and full-texts screenings will be done independently by two researchers, considering inclusion and exclusion criteria. Disagreements will be decided by consensus and if they persist, a third evaluator will resolve them.

A standardised form will be used to extract data from the included studies for assessment of study quality and evidence synthesis. Extracted information will include:

About the study:

- Authors and date of publication;

- Country;

- Study design;

- Setting;

- Number and characteristics of participants;

- Data collection phase (pre or post-implementation);

- Limitations.

About the implementation:

- Type and characteristics of the service implemented;

- Implementation strategy;

- Assessment methods and tools;

- Outcomes measurements.

About the influencing factors:

- Barriers to the implementation;

- Facilitators of the implementation;

- Assessment methods.

Two researches will extract data independently, discrepancies will be identified and resolved through consensus (with a third evaluator when necessary).

Risk of bias (quality) assessment

Two researchers will independently assess the quality of included studies using the Critical Appraisal Skills Programme (CASP) quality assessment tool for qualitative studies (http://www.caspuk.net/#!casp-tools-checklists/c18f8) and the Critical Appraisal Checklist for Cross-Sectional Study (Survey) for questionnaires (http://www.cebma.org/frequently-asked-questions/what-is-critical-appraisal/).

No overall score or weighting will be applied as the primary purpose of appraisal was to identify weaknesses in study design and how this may affect interpretation of the study findings, rather giving each study an overall score. No studies will be excluded on quality alone.

Disagreements will be resolved by consensus, with involvement of a third evaluator when necessary.

Strategy for data synthesis

We will provide a narrative synthesis of the findings from the included studies, structured around the characteristics of the study, the implementation and the influencing factors. Due to the anticipated inclusion of qualitative data, other methods such as thematic analysis may be considered. The data analysis may be guided by a theoretical framework, such as the Consolidated Framework for Implementation Research (Implementation Science 2009;4:50).

Analysis of subgroups or subsets

By the nature of the review, it is not possible to specify the groups in advance.

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Conflicts of interest
None known

Language
English

Country
Brazil

Stage of review
Ongoing

Subject index terms status
Subject indexing assigned by CRD

Subject index terms
Delivery of Health Care; Hospital Units; Humans; Inpatients; Pharmacists; Pharmacy Service, Hospital; Prescriptions

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Versions
23 November 2016

Stage of review at time of this submission

Stage	Started	Completed
Preliminary searches	Yes	Yes
Piloting of the study selection process	Yes	Yes
Formal screening of search results against eligibility criteria	Yes	No
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No

CAPÍTULO 3

4.3 CAPÍTULO 3 - FACTORS INFLUENCING CLINICAL PHARMACY SERVICES IMPLEMENTATION AT A BRAZILIAN HOSPITAL: A QUALITATIVE STUDY

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ABSTRACT

The aim of this study is to identify the expectations and factors that influenced the implementation of CPS in a Brazilian hospital, through a qualitative study with a before and after design. Initially, a focus group with pharmacists and interviews with hospital managers were carried out. After the structured implementation phase, interviews were conducted with the pharmacists who effectively performed the CPS and the managers. The data were analyzed using the Framework Analysis and the Administrative, Political, Technical and Attitudinal (Apoteca) domains. Most of the expectations were achieved by the points of view of both groups. About half of the barriers cited were considered overcome or not concretized. Managers and pharmacists mentioned the same number of enablers, but pharmacists could not anticipate most of them. In terms of Apoteca domains, most of the barriers were Administrative and most of the facilitators were Political ones.

INTRODUCTION

Over the past 15 years, world organizations have been promoting the safety and prevention of adverse events in health care (Makary & Daniel, 2016). In the hospital setting, many strategies have been proposed and continuously developed to optimize the quality of the services and safety of patients. Among which we can highlight the Clinical Pharmacy Services (CPS) as a key element to prevent errors, in particular, those related to medications (Huynh, Wong, Correa-West, Terry, & McCarthy, 2017; Khuri et al., 2008; Leape, Berwick, & Bates, 2002; Weaver et al., 2013; Wolpaw et al., 2018).

According to the literature, the participation of the clinical pharmacist in the healthcare team can be effective for the prevention or decrease in medication errors, reduction of length of hospital stay, as well as hospital costs (Abdelaziz et al., 2016; Fialová & Desplenter, 2016; Rosenfeld et al., 2018). In the study by Assiri *et al*. (Assiri et al., 2017) pharmacists reduced healthcare costs with hospital discharge interventions by 66.5% in 358 patients with heart problems. A study conducted in the United States showed that clinical pharmacists resolved 467 medication errors of 517 high-risk patients within a month (Buckley et al., 2013).

Although many studies have shown pharmaceutical services beneficial results and the efforts of the World Health Organization (WHO) to promote CPS worldwide, this is still not a well-established practice in developing countries as Brazil (Melo et al., 2017; Pande, Hiller, Nkansah, & Bero, 2013). The implementation process is complex and can be affected by several influencing factors, also known as barriers and facilitators to the implementation of health services (Lau et al., 2016).

Previous studies have shown that there are different behaviors, perceptions, and motivations to change of the pharmacists throughout the CPS implementation process (Moullin, Sabater-Hernández, & Benrimoj, 2016; Zardain et al., 2009). In this regard, it is necessary to understand the perceptions of influencing factors on the various stages of the process, so that

strategies targeted to their causes can be planned and traced successfully (Garcia-Cardenas, Perez-Escamilla, Fernandez-Llimos, & Benrimoj, 2018).

Therefore, the aim of this study is to identify the expectations and perceived factors that influenced the implementation of Clinical Pharmacy services in a public, high-complexity hospital in Brazil, from the perspective of pharmacists and managers.

METHODS

Study design

A qualitative study with a before and after design was carried out from November 2014 to September 2016, with pharmacists and managers who participated in the implementation process of CPS in a Brazilian hospital.

Context

In 1979 the first CPS was implemented in a Brazilian hospital, because of the small number of professionals, the continental size of the country, and the lack of clinical disciplines in the Pharmacy graduation syllabus, expansion and scale-up of CPS occurred only slowly, and even today these services remain fragmented and insufficient in the country (Melo et al., 2017). To change this scenario, more recent initiatives from the Brazilian government, professional associations and institutions have been implemented to foster CPS throughout the country (Alcântara et al., 2018; de Castro & Correr, 2007; Dosea et al., 2017; Magalhaes, Santos, Rosa, & Noblat, 2014; Melo et al., 2017; Santos Júnior et al., 2018).

The study setting was a high-complexity, large, public hospital in the Northeast of Brazil. It has more than 500 beds distributed in adult and children's surgical centers, trauma unit, burn therapy unit, intensive care unit (adult and pediatric), semi-intensive care unit, oncology, pediatrics and other 11 different wards. As in many hospitals in the country, at that time, its Pharmacy Department performed only the logistic, distributive activities.

Data collection

Development of the interview guides and focus group

Semi-structured, open-ended questions about participant´s expectations, as well as difficulties and enablers of the process, were considered to develop the interview guide. The same questions were asked to pharmacists and managers, but given the goal of the study, there were differences between the guides used to collect data in the first and the second phase (Supplementary material).

Procedure

The interviews and focus group were conducted by a moderator represented by one of the researchers (TO in the first phase, DCSAA in the second phase), who had previous experience in this type of data collection. The focus group and interviews have lasted for no more than two hours; the entire discussion has been recorded on video and/or voice recording.

First phase

In November 2014, all the 28 hospital pharmacists of the institution were invited to participate in the focus group with the objective of identifying the perceptions related to the implementation of CPS in the hospital. The project was presented and then the focus group started with the 16 pharmacists that agreed in participating. The other 12 pharmacists did not justify their absences, but it could have been understood as a preference to perform logistical activities, rather than clinical ones, or lack of time to attend the focus group meeting.

Regarding the managers, four professionals who had an overview of the hospital process and influence on the representative determinant classes for the implementation of CPS were interviewed. Therefore, the pharmacist in charge and the chief of the hospital pharmacy, the medical chief of the epidemiological surveillance, and the nurse chief of the risk management division were interviewed face-to-face.

It is noteworthy that the results of the general perception of this first stage were presented previously in the study of Alcântara *et al* .(2018) and that for this article only the data on the perceived barriers, facilitators and expectations were used as a baseline to compare with the data collected after the initial implementation process.

Intervention

In 2014, Pharmacy Department managers from the studied hospital invited the Laboratory of Teaching and Research in Social Pharmacy of the Federal University of Sergipe to collaborate in the implementation of CPS in the hospital. Through a mutual interest and partnership between the institutions, a training program (intervention) was established to implement the service.

The intervention started with a series of meetings to present the proposition to the hospital directors and pharmacists. Then, it was offered 40 hours of theoretical/practical training and six meetings to define the most suitable CPS, the workflows, and the necessary instruments to perform the service in the hospital.

In November 2015, the intervention was presented to the Intensive Care Unit health team and the first pharmaceutical interventions began, supervised by the researchers. Technical and motivational approach, such as “mentoring techniques”, clinical case studies, simulations based on real-life cases, interaction through instant messages groups, and direct supervision of the clinical activities were used in this phase. From June 2016, the institution's pharmacists continued their clinical services without direct supervision.

Second phase

After the implementation of the CPS, in September 2016, individual face-to-face interviews were conducted with the three pharmacists who effectively performed the CPS and three managers who were effectively involved in the implementation process (hospital supplies

manager – which was also responsible for the hospital pharmacy division –, chief of the hospital pharmacy, and the pharmacist in charge).

Only one pharmacist interviewed in the second phase did not participate in the data collection of the initial phase. Two pharmacists and one manager were involved in the two phases, in the respective groups. Two participants were interviewed as a pharmacist in the first phase and as a manager in the second phase.

The purpose of these interviews was to compare the perceived anticipated factors and expectations to the real situation faced by the participants.

Analysis

The audio records were transcribed verbatim and evaluated using the Framework Analysis (Parkinson, Eatough, Holmes, Stapley, & Midgley, 2016), as described in the article by Gale *et al*. (2013) (Gale, Heath, Cameron, Rashid, & Redwood, 2013). The method was chosen considering the comparative aim of the study, with pre-conceived categories, and the willingness to produce results with credibility, directly applicable to hospital pharmacists, managers, and researchers.

After familiarization with the data, the interviews were manually coded, line by line. Subsequent quotes were coded considering previous concepts; new ones were created when necessary. This process was performed independently by two researchers (TSA and TO in the first phase, FCAN and ASD in the second phase), and reviewed by a third investigator (ASD and TO, respectively) to confirm the comprehensiveness and reliability of the findings. Both analyses had an external researcher (ASD) to improve credibility.

To compare the participant´s perceptions before and after the implementation process, the coded data was transferred to the matrix to aid analysis. The *expectations* were subcategorized in “met” and “not met”; *barriers* and *facilitators* were subcategorized in “unreal” (anticipated issues that did not concretize), “real” (anticipated issues that became real),

"overcome" (anticipated issues that were overcome) and "new issues" (real issues that were not anticipated).

Additional framework analysis classified the register units in the following domains: "administrative", "political", "technical" or "attitudinal" factors – the Apoteca framework. This conceptual framework has emerged from a systematic observation and immersion of our research group (LEPFS/ UFS) through the experiences of implementing CPS in several organizations within the Brazilian health system (Santos Júnior *et al*., 2018). The researchers observed that, even in different scenarios, there were four groups of factors that influenced the implementation of CPS:

- Attitudinal factors: related to behavior, action, or reaction, and motivated by a feeling or opinion toward or of a particular fact or person. Including internal and external motivation.
- Political factors: related to the relationships within a group or organization that allow particular individuals or groups to influence others (support).
- Technical factors: related to the CPS' own characteristics, as well as the skills and knowledge needed to perform them.
- Administrative factors: related to the administrative processes (organization and management) that are required to perform CPS.

It is noteworthy that some factors were allocated in more than one category because participants were not always unanimous in their responses.

The data interpretation was performed by two researchers (ASD, FACN), who independently identified the characteristics of the data and map relationships between categories, considering the context of the study. The final results were reached by consensus, with a third researcher (TO).

Reflexivity

The authors of this work have had their Pharmacy undergraduate and working experiences in an atmosphere of professional practice transition, from a product-focused to a patient-centered care model. They have also been working as pharmacists and tutors of CPS implementation process in distinct institutions within the Brazilian health system, including the implementation project in the studied hospital, therefore the data was analyzed based on these perspectives. This background may facilitate the identification of relevant information and the interpretation of findings, although, at the same time, it may highlight the value of some aspects over others.

Availability of data and material

The datasets generated and/or analysed during the current study are not publicly available due the Committee of Ethics in Research precludes the data sharing.

Ethics approval and consent to participate

All participants signed a consent form that allowed video and voice recording and publication of focus group and interviews data. In addition, this study was approved by the Ethics Committee of the Federal University of Sergipe (CAAE: 36927014.4.0000.5546). All participants signed a consent form that allowed publication of focus group and interviews data.

RESULTS

Expectations

15 different expectations were identified, all the interviewees expected a successful CPS implementation, as the “positive impact for the patients” and the “improvement in the medication use process”. Managers expressed more expectations than pharmacists did (12/15 and 7/15, respectively). Pharmacists had a higher expectation for changes in their own practice, while managers also wanted institutional improvements (Table 1).

<Insert Table 1>

Some of these expectations, such as “cost reduction” and “structural adequacy”, were not met throughout the implementation process because they require an extended time to present the results and major financial investments. Notwithstanding, most of them were achieved by the points of view of both groups, such as the “qualification of the pharmacists” and the “recognition of the pharmacist by the healthcare team”.

Pharmacists had only two unmet expectations, while managers had six. One possible explanation is that pharmacists had more technical and attitudinal issues - which may have been well managed by the researchers’ support – while managers expected more administrative resolutions that need more time and financial resources to be achieved.

Barriers

25 different barriers were identified, pharmacists reported 19 obstacles and managers, 16. However, about half of the barriers cited by pharmacists (11/19) and managers (7/16) were considered overcome or not concretized in the second interview (Table 2).

<Insert Table 2>

“Resistance of some health professionals” (including medical doctors) and the “lack of adequate physical structure for CPS implementation” were just anticipated, and they were not perceived as hindering the implementation process. Nevertheless, some barriers were faced by pharmacists and managers, such as “lack of proactive attitude to perform CPS”, “lack of training of the pharmacy assistants”, and the “organization focus the pharmacist’s role on distributive activities”. “Lack of clinical experience and confidence of some pharmacists”, and “difficulties in interacting/communicating with the healthcare team” were perceived as overcome barriers during the implementation process (Table 2).

Conflicting perceptions among pharmacists and managers have emerged. “The lack of staff training” was considered an overcome barrier for pharmacists and a new barrier for managers. A possible explanation is that the pharmacists interviewed in the second phase had

qualified their technician team and the managers, who tend to have a general view of the situation, realized that all technician staff should have been qualified to optimize pharmacist´s time, enabling the implementation of CPS in other units.

Regarding Apoteca classification, participants perceived more administrative (5/14) and attitudinal (4/14) obstacles overcome or just anticipated (14 different hinders, considering only these two categories). The motivational approach developed in the intervention may explain these results, as a motivated pharmacist is capable of realizing that some administrative issues do not interfere in the clinical activities.

About real and new barriers (14 different hinders, considering only these two categories), 9/14 were administrative. These results may reflect the necessity of improvements in structural resources, as well as in the work process, that tend to get a longer time and financial requirements to be resolved (Table 2).

Facilitators

The participants reported 14 different facilitators, which were much lower when compared to the barriers (25). Both groups reported that the "previous clinical experience of some pharmacists" did not facilitate CPS implementation. However, new enablers were reported, as "technical support from researchers" and "support from the trained pharmacy staff" (Table 3).

<Insert Table 3>

The enablers "managers support" and "interest of some pharmacists in providing CPS" were anticipated by the managers, but only reported by the pharmacists in the second interview, probably because of pre-conceived perceptions about the managers and their colleagues. The opposite occurred to another facilitator: the support from the "Drug Information Service at the hospital" was already predicted by pharmacists, who worked directly with the service, but not

by managers, that did not have much knowledge about how this service could enable CPS in the hospital.

It is important to mention that the perception of facilitators has increased over time, especially for pharmacists (4 anticipated and 6 new ones). This change of perception may be attributed to the educational and motivational intervention performed by the researchers, directly with these participants, which allowed them to improve their knowledge about the CPS process and perceive the real situation, including the facilitators of the process.

The same did not occur with the managers, most of the facilitators identified by them in the first phase were perceived as real (7/9), and only 2 new ones were just mentioned in the second phase, showing that, different from the pharmacists, they had a more realistic view of the situation.

In terms of the Apoteca framework, different from the barriers, most of the facilitators were classified as political. After the intervention, pharmacists improved their relationship with managers, healthcare team, and pharmacy staff. The clarification of the pharmacist's role to the team, the mutual trust, and the proximity to the other groups augmented the support perception.

To give the readers of this work the real dimension of the participant's perceptions, some representative quotes were chosen to illustrate their opinions on expectations, barriers, and enablers of CPS implementation (Table 4).

<Insert Table 4>

DISCUSSION

To the extent of our knowledge, this is the first study to compare expectations, barriers, and facilitators of the implementation of CPS in a hospital setting, from the perspective of both pharmacists and managers, before and after a structured deployment intervention.

The expectations that emerged may suggest a relationship between the pharmacist's poor training and the desire to fill this gap. Therefore, the pharmacists saw the implementation of CPS as something new in their practices, and an opportunity for professional evolution and recognition by the healthcare team. Previous studies with hospital pharmacists in England and Jordan had had similar results (Auta, Maz, & Strickland-Hodge, 2015; Hammour, Farha, & Basheti, 2016). However, despite the presence of pharmacists with previous experience in CPS, the expectation that this would be a facilitator was not met. In this sense, studies show that the performance of health professionals is more influenced by personal motivation than previous experiences or educational training (Brazinha & Fernandez-Llimos, 2014; Mak, March, Clark, & Gilbert, 2013; Penm, Moles, Wang, Li, & Chaar, 2014).

Managers, when aware of the importance of CPS to the hospital, also tend to have positive expectations regarding the implementation process, since they want quality improvement in the provision of services and aim to bring positive impact to their patients and the hospital (Parand, Dopson, Renz, & Vincent, 2014). When expectations are met, it can motivate the professionals, as they perceive the feedback of the investment made in the previous stage. It can also encourage managers to participate in other innovative service deployments in any other professional area so that health services can have frequent improvements (Martelli, Lelong, Prognon, & Pineau, 2013).

Regarding the non-met expectations, the adequacy of the structure and recruitment of new pharmacists become a complex issue, due to the bureaucratic and financial difficulties of the Brazilian public health care system (Rios, Cruz, Balisa-Rocha, Brito, & Lyra Jr, 2013; Trivelato, Soares, Rocha, & Faria, 2015). However, it is noteworthy that the lack of adequate structure was not associated with real barriers by some participants (Table 4). Similar results were found in the study of Brazinha and Llimós (2014) (Brazinha & Fernandez-Llimos, 2014), where lack of adequate working facilities and insufficient workforce were frequently reported by Portuguese hospital pharmacists.

In addition, the uncertainty perceived by managers and pharmacists on the sustainability of service may generate insecurity in the professionals. This situation, in turn, may have become a barrier to the service implementation. An expectation when it is not achieved, as the discontinuance of a service, can generate demotivation in health professionals (Thu, Wilson, & McDonald, 2015). In this context, regular *mentoring* sessions can help motivating professionals and planning new strategies when expectations fail, since this method uses motivational elements such as work supervision, autonomy stimulation and feedback to maintain the positive attitudes even in unfavorable situations (Gandhi & Johnson, 2016; Moran et al., 2014; Okello & Gilson, 2015).

Lack of time to manage both logistics and clinical activities was a reported barrier that is often seen in the literature since the pharmacist professional practices are still in transition in many countries (Gubbins et al., 2014; Luetsch, 2017). As in most of the Brazilian hospitals, there are no fixed positions to clinical pharmacists, they need to manage both activities until the institution recognize the importance of a full dedication to patient care. This reality resembles that of countries in Asia (Penm, Moles, et al., 2014), the Middle East (Al-Jedai, Qaisi, & Al-Meman, 2016), Africa (Gray, Riddin, & Jugathpal, 2016), Latin America (Uema, Vega, Armando, & Fontana, 2008) and even Europe (Mil, Boer, & Tromp, 2001). In this regard, studies show that it is necessary to reduce the time of the pharmacist dedicated to distributive issues with delegation of these activities to the pharmacy team (Auta et al., 2015; Zardain et al., 2009) and increase the pharmacy staff capacity (Moullin et al., 2016).

On that subject, lack of training of the pharmacy team becomes a barrier that influences the aforementioned. This situation is illustrated in studies carried out in community pharmacies around the world as a limiting factor of the pharmacist's full dedication to patient care. The untrained staff demands attention from the pharmacists and this situation may overload them, leading the professional to give up the CPS (Austin, Gregory, & Martin, 2010; Mil et al., 2001). The pharmacists' lack of motivation is another barrier widely reported in previous studies, this

situation can emerge from the difficult relationship with the team, insufficient working conditions, and lack of professional training (Brazinha & Fernandez-Llimos, 2014; Dosea et al., 2017; Zardain et al., 2009). To pharmacists and managers, the lack of proactive attitude and collaboration among pharmacists was an actual barrier, which shows that attitude is a poorly developed field among professionals. Unfortunately, some of them do not feel encouraged by managers or peers to develop the clinical skills necessary to implement CPS (El Hajj, AL-Saeed, & Khaja, 2016).

It is important to note that to overcome most of the anticipated barriers it was not necessary a great financial investments or big changes in structure or human resources. Low-cost strategies as educational training and use of motivational techniques, such as mentoring, have been shown to be effective to change the perceptions of participants regarding the challenges to implement CPS. A range of professional training methods to improve self-confidence, knowledge, and autonomy of the pharmacist used in the training sessions of this study has been reported as effective in the literature, such as real-life practice clinical case studies, simulated patient sessions and educational outreach visits (Cairns, O'Brien, Corallo, Guidone, & Dooley, 2017; Dezia, Baccus, Natavio, Conroy, & Hall, 2017; Watkins, Wood, Schneider, & Clifford, 2015; M. C. Watson et al., 2002).

Managers and pharmacists mentioned the same number of enablers but different from managers, pharmacists could not anticipate most of them. As reported by other authors, pharmacists with uncertainty regarding their attitudes and lack of clinical competencies may overestimate barriers and have their ability to perceive facilitators reduced (Brazinha & Fernandez-Llimos, 2014; Zardain et al., 2009).

After the intervention, the support of managers and researchers was a recognized enabler in the interviews. The literature shows that this support can contribute to the quality of the service implemented since it provides assistance in activities including planning process, training, and monitoring (Gubbins et al., 2014; Moullin et al., 2016; V. Watson, Sussex, Ryan,

& Tetteh, 2012). Also, the good relationship among the healthcare team throughout the process is reported in the literature as a facilitator for the implementation of CPS (Auta et al., 2015; Penm, Moles, et al., 2014). Besides being a willingness of supportive managers, the integration of the pharmacist into the clinical activities of the healthcare team generates CPS demands in a continuous way, leading physicians, nurses and other professionals to request the CPS as part of integrated healthcare (Farrell et al., 2013; Mekonnen, Yesuf, Odegard, & Wega, 2013).

In a general view, these results show that there was a similarity between the perceptions of pharmacists and managers about the factors that influenced the implementation of services, although the pharmacist's group had greater perceptions of barriers when compared to the managers. The contrary happened to facilitators and expectations. Both groups anticipated more barriers and fewer facilitators when compared to the factors actually experienced. We hypothesize that this perception's change was influenced by the educational and motivational intervention. Besides, the participants reported that some facilitators can prevent the emergence of new barriers and also that reached expectations can motivate professionals.

Apoteca *framework*

The use of Apoteca categorization brought some interesting insights to this study: political support were the most reported facilitators of the implementation process, both as anticipated factors as well as those perceived only after the beginning of activities. Considering this result, we can suggest that this domain should be one of the first to be considered when implementing CPS in hospitals, as the support of managers, pharmacy staff, and health care team can assist in the operation of the CPS and in overcoming barriers to the implementation of the service.

In England, where CPS is already implemented, government support through legislation and policies was considered the initial key driver for CPS in hospitals (Auta et al., 2015). In a hospital in Belgium, the support of doctors, requiring CPS was reported as one of the drivers

for the implementation of service at this hospital (Somers, Claus, Vandewoude, & Petrovic, 2016).

Regarding the barriers, the administrative ones were the most perceived as real. Studies in other developing countries showed similar results, in Argentina, lack of time, structure, and human resources were perceived as important barriers to the implementation of Pharmaceutical care in the country (Uema et al., 2008). In China, lack of clinical pharmacists and financial incentives were reported as barriers to the implementation process, the authors of this work suggest that the administrative issues are of greater importance in the hospital setting because of the larger number of human and physical resources and hierarchical levels involved, when compared to the community pharmacy (Penm, Moles, et al., 2014).

Attitudinal barriers were one of the most overcome, along with the administrative ones. Studies show that modifying attitudes towards the challenges of implementation may decrease the perception of difficulties faced by pharmacists (Gastelurrutia et al., 2009; Zardain et al., 2009). As aforementioned, strategies such as coaching and mentoring, widely used by junior doctors and nurses (McNamara et al., 2014; Schwellnus & Carnahan, 2014), and the development of clinical skills (Auta et al., 2015) can help in this change of mindset.

In addition, it is important to note that both political and attitudinal strategies do not require significant financial resources, but may help in raising funds for the implementation and improvement of CPS in hospitals, which may consequently reduce the perception of administrative barriers (Penm, Li, et al., 2014; Somers et al., 2016).

Strengths and limitations

To the best of our knowledge, this study is the first to evidence implementation perceptions of both pharmacists and managers in different stages of the CPS implementation, in a hospital setting. To promote the credibility of the results, the researcher's perspective (including an external researcher), the perceptions of the pharmacists and managers, and the Apoteca framework analysis were triangulated. Another strength of this work is to show the

influence of an educational/motivational intervention in changing perceptions of the participants.

Nevertheless, there are certain limitations that should be mentioned: there was a reduction in the number of participants from the first to the second phase of the study, and it was not possible to follow the same participants at the two moments, due to high rotation in managers positions, and because we have prioritized the pharmaceutical managers views in the second phase, as the medical and nurse managers were not so involved throughout the process. Moreover, in the first phase, the focus group was chosen in order to understand the 'collective' pharmacists' perceptions, but in the second stage, the reduced sample did not allow the use of the same technique.

CONCLUSION

Pharmacists and managers anticipated more barriers and fewer enablers when compared to the situations experienced. Moreover, considering the Apoteca analysis, political facilitators were the most perceived in this study. Regarding the barriers, administrative ones were the most perceived as real; attitudinal and technical ones were the most overcome or just anticipated. Those results evidence the multifactorial nature of the implementation process, the usefulness of the Apoteca framework, and the importance of a structured intervention, based on educational and motivational approach, to promote perceptions change and facilitate the initial steps of CPS implementation in the hospital setting.

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DECLARATION OF CONFLICTING INTERESTS

The authors declare that they have no competing interests.

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Table 1. Expectations of pharmacists and managers throughout the implementation of CPS in a high complexity public hospital.

EXPECTATIONS	PHARMACISTS	PHARMACISTS/ MANAGERS	MANAGERS
Met expectations	Positive impact for pharmacists (At) Professional practice focusing on the patients (clinical activities) (T) Support and guidance of the research team (T)	Pharmacist appreciation by the managers (At) Pharmacists qualification (through the implementation project's educational training) (T) Positive impact for patients (P)	Improvement in the communication process among the healthcare team (P) Improvement in the medication use process (T) Recognition and participation of the pharmacist in the healthcare team activities (P/ At)
Not met expectations	NR	CPS sustainability (T)	Adequacy of the physical structure for the service (A) Greater adherence of pharmacists to the CPS (At) Recruitment of new pharmacists (A) Reducing costs and damages caused by misuse of drugs (A/ T) Registration of clinical and economic impacts (T)

Abbreviatio Abbreviations: A = administrative, P = political, T = technical, At = attitudinal, CPS = clinical pharmacy services, NR = not reported.

Table 2. Barriers identified by pharmacists and managers throughout the implementation of Clinical Pharmacy services in a high-complexity public hospital.

BARRIERS	PHARMACISTS	PHARMACISTS/ MANAGERS	MANAGERS
Unreal (just anticipated) barriers	*Drug shortage in the hospital (A) Lack of adequate working facilities to develop CPS (A) *Lack of pharmacist autonomy at work (A)	NR	Lack of standardization of distributive activities (A)
	*Failures of the public health system in Brazil (P)	NR	Changes in the hospital board of directors may hinder the process of CPS implementation (P)
	*Lack of experience and training of pharmacists on clinical practice (T)	*Unawareness of pharmacists' clinical activities by healthcare team and managers (T)	NR
	*Difficulties in interacting/ communicating with the healthcare team (At)	Resistance of some healthcare professionals to CPS (At)	NR
Overcome barriers		Lack of standardization of pharmacist´s work process (A)	
	*Lack of experience and training of pharmacists on clinical practice (T) *Lack of training of pharmacy assistants (T) *Unawareness of pharmacists' clinical activities by healthcare team and managers (T)	NR	NR
	Pharmacists' insecurity, due to poor qualification and experience in clinical practice (At)	*Difficulties in interacting/ communicating with the healthcare team (At)	Lack of integration in the healthcare team activities (collaborative practices) (At)
Real barriers	*Drug shortage in the hospital (A) *Lack of pharmacist autonomy at work (A) Poor workforce management (A) Lack of training of pharmacy assistants, due to high rotation (T)	Insufficient pharmacists to distributive and clinical tasks (A)	High rotation of physicians in the hospital (A) *Insufficient number of pharmacy assistants (A)
	*Failures of the public health system in Brazil/ economic crisis (P)	The organization focus the role of pharmacists on distributive activities (P)	NR
	*Lack of proactive attitude and collaboration among pharmacists (At)	NR	NR

Abbreviations: A = administrative, P = political, T = technical, At = attitudinal, CPS = clinical pharmacy services, NR = not reported.

* Factors have been allocated in more than one category because participants were not unanimous in their responses.

Table 2. Barriers identified by pharmacists and managers throughout the implementation of Clinical Pharmacy services in a high-complexity public hospital. Continued.

BARRIER	PHARMACISTS	PHARMACISTS/ MANAGERS	MANAGERS
New barriers	Impossibility of exclusive dedication to CPS (A) *Insufficient number of pharmacy assistants (A)	Lack of execution of standardized activities (A)	*Drug shortage in the hospital (A) Overload of few pharmacists with the CPS(A)
	Lack of managers support (P)	NR	NR
	NR	NR	*Lack of training of pharmacy assistants (T)
	NR	NR	*Lack of proactive attitude and collaboration among pharmacists (At)

Abbreviations: A = administrative, P = political, T = technical, At = attitudinal, CPS = clinical pharmacy services, NR = not reported.

* Factors have been allocated in more than one category because participants were not unanimous in their responses.

Table 3. Facilitators identified by pharmacists and managers throughout the implementation of Clinical Pharmacy services in a high-complexity public hospital.

FACILITATORS	PHARMACISTS	PHARMACISTS/ MANAGERS	MANAGERS
Unreal (just anticipated facilitators)	NR	NR	Organization of the healthcare team work processes (A)
	NR	Part of the pharmacist's team has experience in CPS (T)	NR
Real facilitators	*Drug Information Service at the hospital (A)	NR	NR
	NR	Support from medical residents (P)	Management support to activities related to patient safety program (P) *Support from healthcare team (P) *Support from the pharmacy staff (P) Support from pharmaceutical residents (P)
	Prior knowledge of other healthcare professionals on CPS (T)	NR	NR
	NR	NR	Good relationship between pharmacists and some healthcare professionals (At) *Interest of some of the pharmacists in providing CPS (At)
New facilitators	Establishment of the Pharmaceutical Assistance working group at the hospital (A)	NR	*Drug Information Service at the hospital (A)
	*Support from the healthcare team (P) Managers support (P) *Support from the trained pharmacy staff (P)	NR	NR
	NR	Technical support from researchers (T)	NR
	*Interest of some pharmacists in providing CPS (At)	NR	NR

Abbreviations: A = administrative, P = political, T = technical, At = attitudinal, CPS = clinical pharmacy services, NR = not reported.

* Factors have been allocated in more than one category because participants were not unanimous in their responses.

Table 4. Selected quotes by thematic categories.

Category	Quotes
Expectations	Positive impact for pharmacists
	“When I started [the CPS] in the Intensive Care Unit, I felt excited with the clinical activities. I started to see what was missing for me to value my profession. At this moment, I felt that I was enjoying being a pharmacist!” (Pharmacist)
	Valorization by the team
	"We can see that we are becoming more visible because when we are absent from the ambiance they ask´: 'Where's the pharmacist who did not come today?' (...) we got noticed..." (Pharmacist)
	"I think there has been a greater dissemination of pharmacists role in the hospital to all healthcare teams (...) now we are always being invited to participate in some activity, so it is something that other health professionals already understand the need of the pharmacists with them...". (Manager)
	Qualification of pharmacists
	"There was evolution, mainly of the pharmacists that were committed to the process, we notice at our meetings and when we talk to other health professionals, it is noticeable the qualification that they had, the scientific evolution that they had in that process ..." (Manager)
Barriers	Resistance of some health professionals
	"At the beginning of the focus group, what was the greatest difficulty that we have listed? (...) that we would have a lot of resistance (...) from the doctors, and we can see that it really did not happen..." (Pharmacist)
	Unawareness of pharmacists’ clinical activities by the healthcare team
	"Many find it interesting because the pharmacist was never seen on the bedside, together with them [healthcare team]... so they were curious to know what we were doing there, and when we explained, they were fascinated…” (Pharmacist)
	Lack of training and clinical experience
	"We had lack of experience as a major obstacle, but as we were developing the service, we realized that it was not a limiting factor. (...) The problem was just to start, after it started, it worked well ... " (Pharmacist)
	Drug shortage/ Inadequate working facilities
	“The lack of pharmacists, their resistance, the lack of independence of the technician to assume responsibilities in the pharmacy, all this counts… But [inadequate] physical structure? Shortage of drugs? For me all these are pretexts! Excuses not to start the service…” (Pharmacist)
	Reduced number of participating pharmacists
	"The number of pharmacists and pharmacy assistants does not meet the hospital demand, (...) several times we had to interrupt the service or had difficulty in expanding because of this human resource deficiency of the pharmacy department." (Manager)
	Lack of support from pharmacist colleagues
	"Lack of proactivity and collaboration among pharmacists, this was the first [barrier] and until today we suffer with it..." (Pharmacist)
Facilitators	Interest in performing the service
	"I did not know and I still do not know, but it does not stop me from studying ... nowadays I already know something, because I'm going to get it, as I was performing the clinical pharmacy services, I was learning ..." (Pharmacist)
	Drug Information Service
	"I believe that it [drug information service] would be a great ally as a facilitator of the clinical pharmacy, I always believed that it would give the greatest support." (Manager)
	Support from the research team
	"The participation of researchers was a great facilitator. It is so common to have them around that sometimes we forget to mention them and it is important to mention their availability." (Pharmacist)
	Residents' and healthcare team support
	"It was due to residents that she [another pharmacist] was able to collaborate with the infectologist in the ICU, (…) she could develop many interesting activities with him and with the trainee, we had at the time." (Pharmacist)

Abbreviation: ICU = Intensive Care Unit.

SUPPLEMENTARY MATERIAL

The interview guide (phase 1)

1. What are your expectations regarding the implementation of the CPS? (How do you think they will impact your work? What are the benefits for the hospital?)
2. What are the barriers, the difficulties, that you expect to face in the implementation of this services?
3. What does the hospital already have that you think can facilitate the implementation of the CPS?
4. What is your expectation regarding the support of the researchers in the implementation process?

The interview guide (phase 2)

1. What motivated you to persist, to take the implementation of Clinical Pharmacy further? (Only for pharmacists)
2. For you, as a manager, how was the process of Clinical Pharmacy implementation at the hospital? (Only for managers)
3. Looking at the results of the first phase, which anticipated barriers and facilitators do you think actually influenced the implementation of CPS? (Both)
4. Would you have something to add, that has not been quoted previously? (Both)
5. How could we attract more pharmacists to the project and consolidate CPS at the hospital? How could you contribute to this? (Both)

CONSIDERAÇÕES FINAIS

5 CONSIDERAÇÕES FINAIS

5.1 CONCLUSÃO GERAL

A partir da identificação na literatura especializada dos fatores que influenciam a implementação de SCF no ambiente hospitalar foi possível verificar que a efetividade deste processo depende de múltiplos determinantes, que podem ser distribuídos em domínios Atitudinais, Políticos, Técnicos e Administrativos (*framework* Apoteca). Tais domínios são fruto de uma série de análises e discussões realizada pela autora desta Tese e seu orientador, com a colaboração de pesquisadores do Laboratório de Ensino e Pesquisa em Farmácia Social da Universidade Federal de Sergipe (LEPFS/ UFS), baseada em observações sistemáticas de experiências de implementação de SCF em vários cenários do sistema de saúde brasileiro.

Para analisar os dados coletados, foi proposto um *framework* com base empírica, simples, lógico e que pode ser usado tanto para classificar, como para relatar os fatores, pois os modelos existentes não atendiam, de maneira adequada, as necessidades desta pesquisa. A utilização da categorização com os *framework* Apoteca, proposta para análise dos resultados, favoreceu *insights* importantes para a compreensão do processo de implementação de SCF em hospitais:

- os fatores identificados na literatura estavam distribuídos de maneira uniforme pelos quatro domínios, o que sugere a necessidade de um planejamento holístico da implementação, considerando estratégias direcionadas a essas quatro áreas (Fig. 1);
- o domínio Administrativo teve o maior número de fatores citados, tanto na literatura quando nas entrevistas, a maioria deles percebido como barreira;
- quando as barreiras foram avaliadas ao longo do processo de implementação, fatores Atitudinais e Técnicos foram os mais relatados como superados;
- os fatores do domínio Político tiveram o maior número de citações como facilitador.

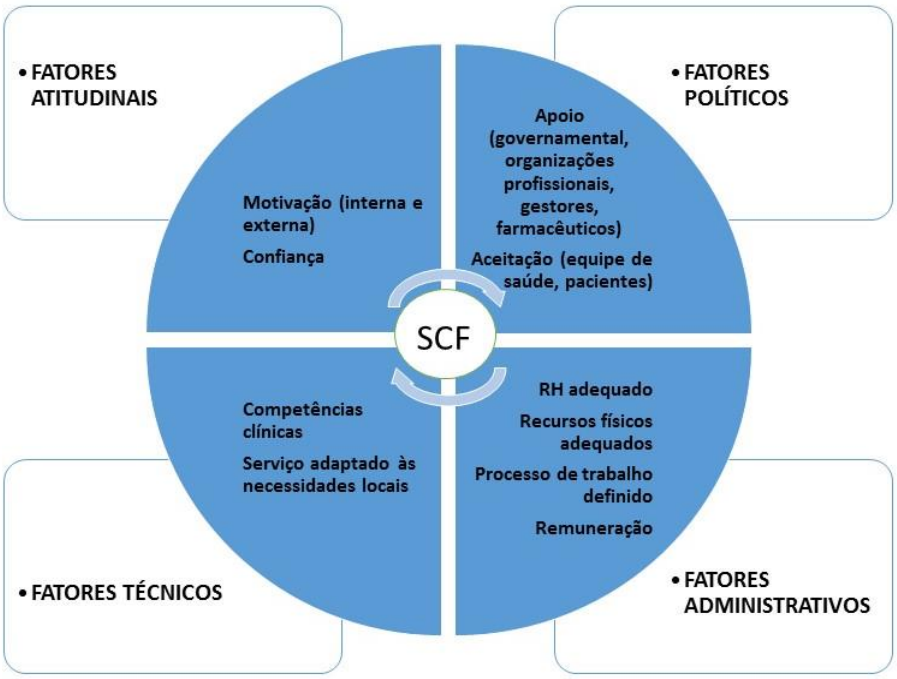

Figura 1. Fatores que influenciam a implementação de SCF identificados nesta Tese. Fonte: da autora.

Adicionalmente, ao longo do processo de implementação de SCF no local do estudo foi possível observar que inicialmente a percepção de barreiras foi superior ao de facilitadores. Porém, após o início das atividades clínicas, tanto gerentes quanto farmacêuticos relataram que a maioria das barreiras previamente referidas não se concretizou ou foi superada. De maneira inversa, a percepção de facilitadores, que era baixa no começo do processo, aumentou após o início das atividades.

Neste contexto, as modificações ocorridas ao longo do processo de implementação de SCF na instituição estudada podem ser atribuídas, em parte, ao projeto de implementação estruturado, que incluiu atividades de capacitação e técnicas motivacionais (incluindo o *mentoring*), para o desenvolvimento de competências clínicas e outras habilidades que permitiram a implantação de SCF no local de estudo.

5.2 PERSPECTIVAS

Espera-se que os resultados do percurso metodológico desenvolvido para identificar e classificar os fatores que influenciam a implementação de SCF em hospitais, descritos nesta tese, possam nortear farmacêuticos e gestores em novos processos de implementação de SCF, com o intuito de melhorar o planejamento e a efetividade do processo em instituições que ainda não possuem esses serviços consolidados. Estas novas perspectivas de uso do *framework* Apoteca poderão gerar evidências adicionais e consistentes sobre as relações entre os domínios e a validação do uso do *framework* proposto na implementação de SCF.

Ademais, os resultados desta Tese, somados ao de outras pesquisas desenvolvidas pelo Laboratório de Ensino e Pesquisa em Farmácia Social (LEPFS/UFS), fazem parte de um modelo de implementação de SCF proposto para nortear farmacêuticos, gestores e pesquisadores da área, no processo de implementação de SCF (Santos Júnior et al, 2018).


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APÊNDICES

7 APÊNDICES

7.1 APÊNDICE A: TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO

TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO

Eu, _____ portador do RG nº _____, comprometo-me a participar do projeto "SERVIÇOS DE FARMÁCIA CLÍNICA EM UM HOSPITAL PÚBLICO DE ALTA COMPLEXIDADE: ANÁLISE DO PROCESSO DE IMPLEMENTAÇÃO", realizado pelo Laboratório de Ensino e Pesquisa em Farmácia Social (LEPFS), localizado na Universidade Federal de Sergipe (SE), mediante entrevista individual e o preenchimento de questionário autoaplicável.

Fui devidamente informado(a) sobre as atividades a serem realizadas, as quais tem como objetivo compreender o processo de Implantação dos Serviços de Farmácia Clínica no Hospital de Urgência de Sergipe. Com consequente, autorizo a utilização dos meus dados e informações prestadas como fonte para elaboração de tese, artigo científico e sua posterior publicação.

Estou ciente de que determinadas perguntas feitas durante a realização das atividades podem me constranger ou incomodar, assim posso escolher não respondê-las. Também estou ciente de que as informações por mim prestadas são confidenciais e minha participação é voluntária, não havendo qualquer tipo de compensação financeira ou funcional por minha participação.

Afirmo ainda que entendi o conteúdo do projeto e fui esclarecido(a) que tenho liberdade de retirar meu consentimento, em qualquer fase da pesquisa, sem penalização alguma e sem qualquer prejuízo.

Firmo o presente,

_____

Aracaju, ____ de _____ de 20__.

Nome da Pesquisadora: Thelma Onozato **Endereço: Cidade Universitária Prof. José Aloisio Campos, Laboratório de Ensino e Pesquisa em Farmácia Social.** **Telefone: (079) 99100-0841**	**Nome do Pesquisador: Divaldo Pereira de Lyra Jr.** **Endereço: Cidade Universitária Prof. José Aloisio Campos, Laboratório de Ensino e Pesquisa em Farmácia Social.** **Telefone: (079) 2105-6844 / 99192-5577**

7.2 APÊNDICE B: TERMO DE CONSENTIMENTO DE USO DE IMAGEM E DEPOIMENTOS

TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO PARA USO DE IMAGENS E DEPOIMENTOS

Eu, _____ portador do RG nº _____, participante do projeto "SERVIÇOS DE FARMÁCIA CLÍNICA EM UM HOSPITAL PÚBLICO DE ALTA COMPLEXIDADE: ANÁLISE DO PROCESSO DE IMPLEMENTAÇÃO", realizado pelo Laboratório de Ensino e Pesquisa em Farmácia Social (LEPFS), localizado na Universidade Federal de Sergipe (SE), fui devidamente informado(a) e autorizo a utilização de imagens e depoimentos feitas durante a participação no projeto supracitado, para fins de elaboração de tese da farmacêutica Thelma Onozato e sua posterior apresentação pública em conferências ou similares, bem como sua publicação na forma de livros e/ou artigos, ficando vedada, no entanto, sua utilização para outros fins.

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Nome da Pesquisadora: Thelma Onozato **Endereço: Cidade Universitária Prof. José Aloisio Campos, Laboratório de Ensino e Pesquisa em Farmácia Social.** **Telefone: (079) 99100-0841**	**Nome do Pesquisador: Divaldo Pereira de Lyra Jr.** **Endereço: Cidade Universitária Prof. José Aloisio Campos, Laboratório de Ensino e Pesquisa em Farmácia Social.** **Telefone: (079) 2105-6844 / 99192-5577**

ANEXOS

8 ANEXOS

8.1 ANEXO A: COMPROVANTE DE SUBMISSÃO DO ARTIGO 2 AO PERIÓDICO RESEARCH IN SOCIAL AND ADMINISTRATIVE PHARMACY

8.2 ANEXO B: COMPROVANTE DE SUBMISSÃO DO ARTIGO 3 AO PERIÓDICO QUALITATIVE HEALTH RESEARCH

8.3 ANEXO C: REGRAS DE PUBLICAÇÃO DO PERIÓDICO *RESEARCH IN SOCIAL AND ADMINISTRATIVE PHARMACY*

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8.4 ANEXO D: REGRAS DE PUBLICAÇÃO DO PERIÓDICO *QUALITATIVE HEALTH RESEARCH*

1. Article types

Each issue of QHR provides readers with a wealth of information — book reviews, commentaries on conceptual, theoretical, methodological and ethical issues pertaining to qualitative inquiry as well as articles covering research, theory and methods.

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- QHR accepts qualitative methods and qualitatively-driven mixed-methods, qualitative meta- analyses, and articles addressing all qualitative methods.
- QHR is a multi-disciplinary journal and accepts articles written from a variety of perspectives including: cross-cultural health, family medicine, health psychology, health social work, medical anthropology, medical sociology, nursing, pediatric health, physical education, public health, and rehabilitation.
- Articles in QHR provide an array of timely topics such as: experiencing illness, giving care, institutionalization, substance abuse, food, feeding and nutrition, living with disabilities, milestones and maturation, monitoring health, and children's perspectives on health and illness.

2. Editorial policies

2.1 Peer review policy

QHR strongly endorses the value and importance of peer review in scholarly journals publishing. All papers submitted to the journal will be subject to comment and external review. All manuscripts are initially reviewed by the Editors and only those papers that meet the scientific and editorial standards of the journal, and fit within the aims and scope of the journal, will be sent for outside review.

QHR adheres to a rigorous double-blind reviewing policy in which the identity of both the reviewer and author are always concealed from both parties. Ensure your manuscript does not contain any author identifying information. Please refer to the editorial on blinding found in the Nov 2014 issue: http://qhr.sagepub.com/content/24/11/1467.full.

QHR maintains a transparent review system, meaning that all reviews, once received, are then forwarded to the author(s) as well as to ALL reviewers.

Peer review takes an average of 6–8 weeks, depending on reviewer response.

2.2 Authorship

Papers should only be submitted for consideration once consent is given by all contributing authors. Those submitting papers should carefully check that all those whose work contributed to the paper are acknowledged as contributing authors.

The list of authors should include all those who can legitimately claim authorship. This is all authors who:

(i) Made a substantial contribution to the concept and design, acquisition of data or analysis and interpretation of data,

(ii) Drafted the article or revised it critically for important intellectual content,
(iii) Approved the version to be published.

Authors should meet the conditions of all of the points above. Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content.
When a large, multicenter group has conducted the work, the group should identify the individuals who accept direct responsibility for the manuscript. These individuals should fully meet the criteria for authorship.
Acquisition of funding, collection of data, or general supervision of the research group alone does not constitute authorship, although all contributors who do not meet the criteria for authorship should be listed in the Acknowledgments section.
Please refer to the International Committee of Medical Journal Editors (ICMJE) authorship guidelines for more information on authorship.

2.3 Acknowledgements

All contributors who do not meet the criteria for authorship should be listed in an Acknowledgements section. Examples of those who might be acknowledged include a person who provided purely technical help, or a department chair who provided only general support.

2.3.1 Writing assistance

Individuals who provided writing assistance, e.g., from a specialist communications company, do not qualify as authors and should only be included in the Acknowledgements section.
Authors must disclose any writing assistance — including the individual's name, company and level of input — and identify the entity that paid for this assistance.

It is not necessary to disclose use of language polishing services.

Please supply any personal acknowledgements separately from the main text to facilitate anonymous peer review.

2.3.2 Funding
QHR requires all authors to acknowledge their funding in a consistent fashion under a separate heading. Please visit the Funding Acknowledgements page to confirm the format of the acknowledgement text in the event of funding. Otherwise, state that: This research received no specific grant from any funding agency in the public, commercial, or not-for- profit sectors.

2.4 Declaration of conflicting interests

It is the policy of QHR to require a declaration of conflicting interests from all authors enabling a statement to be carried within the paginated pages of all published articles. Please ensure that a "'Declaration of Conflicting Interests" statement is included at the end of your manuscript, after any acknowledgements and prior to the references. If no conflict exists, please state that "The Author(s) declare(s) that there is no conflict of interest."
For guidance on conflict of interest statements, please see the ICMJE recommendations here.

2.5 Research ethics and patient consent

Medical research involving human subjects must be conducted according to the World Medical Association Declaration of Helsinki.

Submitted manuscripts should conform to the ICMJE Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals, and all papers reporting animal and/or human studies must state in the methods section that the relevant Ethics Committee or Institutional Review Board provided (or waived) approval. Please ensure that you have provided the full name and institution of the review committee, in addition to the approval number.
For research articles, authors are also required to state in the methods section whether participants provided informed consent and whether the consent was written or verbal.
In terms of patient privacy, authors are required to follow the ICMJE Recommendations for the Protection of Research Participants. Patients have a right to privacy that should not be infringed without informed consent. Identifying information, including patients' names, initials, or hospital numbers, should not be published in written descriptions, photographs, and pedigrees unless the information is essential for scientific purposes and the patient (or parent or guardian) gives written informed consent for publication. Informed consent for this purpose requires that a patient who is identifiable be shown the manuscript to be published. Participant descriptors should not be listed individually. Because qualitative research is descriptive, it is recommended that participant quotations not be linked to identifiers in the manuscript.

2.6 Clinical trials

QHR conforms to the ICMJE requirement that clinical trials are registered in a WHO-approved public trials registry at or before the time of first patient enrolment as a condition of consideration for publication. The trial registry name and URL, and registration number must be included at the end of the abstract.

2.7 Reporting guidelines

The relevant EQUATOR Network reporting guidelines should be followed depending on the type of study. For example, all randomized controlled trials submitted for publication should include a completed Consolidated Standards of Reporting Trials (CONSORT) flow chart as a cited figure, and a completed CONSORT checklist as a supplementary file.

Other resources can be found at NLM's Research Reporting Guidelines and Initiatives.

2.8 Data

SAGE acknowledges the importance of research data availability as an integral part of the research and verification process for academic journal articles.
QHR requests all authors submitting any primary data used in their research articles alongside their article submissions to be published in the online version of the journal, or provide detailed information in their articles on how the data can be obtained. This information should include links to third-party data repositories or detailed contact information for third- party data sources. Data available only on an author-maintained website will need to be loaded onto either the journal's platform or a third-party platform to ensure continuing accessibility. Examples of data types include but are not limited to statistical data files, replication code, text files, audio files, images, videos, appendices, and additional charts and graphs necessary to understand the original research. [The editor(s) may consider limited embargoes on proprietary data.] The editor(s) [can/will] also grant exceptions for data that cannot legally or ethically be released. All data submitted should comply with Institutional or Ethical Review Board requirements and applicable government regulations. For further information, please contact the editorial office at vshannonqhr@gmail.com.

3. Publishing Policies

3.1 Publication ethics

SAGE is committed to upholding the integrity of the academic record. We encourage authors to refer to the Committee on Publication Ethics' International Standards for Authors and view the Publication Ethics page on the SAGE Author Gateway.

3.1.1 Plagiarism

QHR and SAGE take issues of copyright infringement, plagiarism or other breaches of best practice in publication very seriously. We seek to protect the rights of our authors and we always investigate claims of plagiarism or misuse of articles published in the journal. Equally, we seek to protect the reputation of the journal against malpractice. Submitted articles may be checked using duplication-checking software. Where an article is found to have plagiarized other work, or included third-party copyright material without permission, or with insufficient acknowledgement, or where authorship of the article is contested, we reserve the right to take action including, but not limited to: publishing an erratum or corrigendum (correction); retracting the article (removing it from the journal); taking up the matter with the head of department or dean of the author's institution and/or relevant academic bodies or societies; banning the author from publication in the journal or all SAGE journals, or appropriate legal action.

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4. Preparing your manuscript

4.1 Article Format (*see previously published articles in QHR for style*):

- ***Title page:*** Title should be succinct; list all authors and their affiliation; keywords. Please upload the title page separately from the main document.
- ***Blinding:*** Do not include any author identifying information in your manuscript, including author's own citations. Do not include acknowledgements until your article is accepted and unblinded.
- ***Abstract:*** Unstructured, 150 words. This should be the first page of the main manuscript, and it should be on its own page.
- ***Length:*** QHR does not have a word or page count limit. Manuscripts should be as tight as possible, preferably less than 30 pages including references. Longer manuscripts, if exceptional, will be considered.
- ***Methods:*** QHR readership is sophisticated; excessive details not required.
- ***Ethics:*** Include a statement of IRB approval and participant consent. Present demographics as a group, not listed as individuals. Do not link quotations to particular individuals unless essential (as in case studies) as this threatens anonymity.
- ***Results:*** Rich and descriptive; theoretical; linked to practice if possible.
- ***Discussion:*** Link your findings with research and theory in literature, including other geographical areas and quantitative research.
- ***References:*** APA format. Use pertinent references only. References should be on a separate page.

Additional Editor's Preferences:

- Please do not refer to your manuscript as a "paper;" you are submitting an "article."

- The word "data" is plural.

4.2 Word processing formats

Preferred formats for the text and tables of your manuscript are Word DOC or PDF. The text should be double-spaced throughout with standard 1 inch margins (APA formatting). Text should be standard font (i.e., Times New Roman) 12 point.

4.3 Artwork, figures and other graphics

- Figures: Should clarify text.
- Include figures, charts, and tables created in MS Word in the main text rather than at the end of the document.
- Figures, tables, and other files created outside of Word should be submitted separately. Indicate where table should be inserted within manuscript (i.e., INSERT TABLE 1 HERE).
- Photographs: Should have permission to reprint and faces should be concealed using mosaic patches – unless permission has been given by the individual to use their identity. This permission must be forwarded to QHR's Managing Editor.
  - TIFF, JPED, or common picture formats accepted. The preferred format for graphs and line art is EPS.
  - Resolution: Rasterized based files (i.e. with .tiff or .jpeg extension) require a resolution of at least **300 dpi** (dots per inch). Line art should be supplied with a minimum resolution of **800 dpi**.
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- Figures supplied in color will appear in color online regardless of whether or not these illustrations are reproduced in color in the printed version. For specifically requested color reproduction in print, you will receive information regarding the costs from SAGE after receipt of your accepted article.

4.4 Supplementary material

This journal is able to host additional materials online (e.g., datasets, podcasts, videos, images, etc.) alongside the full-text of the article. These will be subjected to peer-review alongside
the article.
Supplementary files will be uploaded as supplied. They will not be checked for accuracy, copyedited, typeset or proofread. The responsibility for scientific accuracy and file functionality remains with the author(s). SAGE will only publish supplementary material subject to full copyright clearance. This means that if the content of the file is not original to the author, then the author will be responsible for clearing all permissions prior to publication. The author will be required to provide copies of permissions and details of the correct copyright acknowledgement.

4.5 Journal layout

In general, QHR adheres to the guidelines contained in the Publication Manual of the American Psychological Association ["APA"], 6th edition (ISBN 10:1-4338-0561-8,

softcover; ISBN 10:1-4338-0559-6, hardcover; 10:1-4338-0562, spiral bound), with regard to manuscript preparation and formatting. These guidelines are referred to as the APA Publication Manual, or just APA. Additional help may be found online at http://www.apa.org/, or search the Internet for "APA format."

4.6 Reference style

QHR adheres to the APA reference style. Click here to review the guidelines on APA to ensure your manuscript conforms to this reference style.

4.7 English language editing services

Articles must be professionally edited; this is the responsibility of the author. Authors seeking assistance with English language editing, translation, or figure and manuscript formatting to fit the journal's specifications should consider using SAGE's Language Services.

4.8 Review Criteria

Before submitting the manuscript, authors should have their manuscript pre-reviewed using the following QHR criteria:

1. Importance of submission: Does it make a meaningful and strong contribution to qualitative health research literature? Is it original? Relevant? In depth? Insightful? Significant? Is it useful to reader and/or practitioner?
2. Theoretical orientation and evaluation: Is it theoretically clear and coherent? Is there logical progression throughout?
3. Methodological assessment: Appropriate to question and/or aims? Approach logically articulated? Clarity in design and presentation? Data adequacy and appropriateness? Evidence of rigor?
4. Ethical Concerns (Including IRB approval and consent):
5. Data analysis and findings: Does the analysis of data reflect depth and coherence? In-depth descriptive and interpretive dimensions? Creative and insightful analysis? Linked with theory? Relevant to practice/discipline?
6. Data analysis and findings: Does the analysis of data reflect depth and coherence? In-depth descriptive and interpretive dimensions? Creative and insightful analysis? Linked with theory?

7. Discussion: Results linked to literature? Contribution of research clear? Relevant to practice/discipline?
8. Manuscript style and format: Please evaluate writing style: Length (as short as possible], organization, clarity, grammar, appropriate citations, etc.); presentation of diagrams/illustrations?

5. Submitting your manuscript

5.1 How to submit your manuscript

QHR is hosted on SAGE Track, a web-based online submission and peer review system powered by ScholarOne Manuscripts.™ Visit http://mc.manuscriptcentral.com/qhr to login and submit your article online. Each component of the manuscript is uploaded separately: Title page, main document, tables, figures, supplemental material.
IMPORTANT: Please check whether you already have an account in the system before trying to create a new one. If you have reviewed or authored for the journal in the past year it is likely that you will have had an account created. For further guidance on submitting your manuscript online please visit ScholarOne.

5.2 Title, keywords and abstracts

Please supply a title, short title, an abstract and keywords to accompany your article. The title, keywords and abstract are key to ensuring readers find your article online through online search engines such as Google. Please refer to the information and guidance on How to Help Readers Find Your Article in the SAGE Journal Author Gateway on how best to title your article, write your abstract and select your keywords.

5.3 Corresponding author contact details

Provide full contact details of the corresponding author including email, mailing address and phone number. Academic affiliations are required for all co-authors. Present these details on the title page, separate from the article main text, to facilitate anonymous peer review.

8.5 ANEXO E: CARTA DE ANUÊNCIA DO LOCAL DE ESTUDO

GOVERNO DE SERGIPE
SECRETARIA DE ESTADO DA SAÚDE

Carta de Anuência

Fundação Hospitalar de Saúde

Declaro para os devidos fins que estamos cientes e de acordo que Thelma Onozato, farmacêutica, realize seu projeto de Doutorado em Ciências da Saúde da UFS, orientado pelo Prof. Dr. Divaldo P. de Lyra Júnior e intitulado: **Implantação da Farmácia Clínica em um hospital público de Sergipe,** junto ao Serviço de Farmácia do Hospital de Urgência de Sergipe – Governador João Alves Filho (HUSE), durante o período de março de 2014 a fevereiro de 2017. Vale ressaltar que durante o estudo, a referida doutoranda terá acesso às informações relacionadas ao tratamento dos pacientes para realizar análise documental necessária ao desenvolvimento de sua Tese. Ademais, deverá ser garantido o sigilo dos dados pessoais dos participantes da pesquisa, sendo que suas informações serão utilizadas apenas para fins científico-acadêmicos.

Sem mais para o momento,

Aracaju, 24 de outubro de 2013.

Michele Santos Menezes
Gerente de Assist. Farmacêutica
CRF/ SE nº 768

Michelle Santos Menezes
Farmacêutica CRF/SE 768
Gerente de Assistência Farmacêutica/ HUSE

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Carolina Samara Lima Franca Bezerra
Farmacêutica CRF/SE 844
Técnica de Referência/ HUSE

8.6 ANEXO F: APROVAÇÃO DO COMITÊ DE ÉTICA EM PESQUISA