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Expanding Primary Care to Pharmaceutical Patient Care in Diabetes Mellitus Type 2 through the European Union's Community Pharmacies, between 2008 and 2018: A Systematic Review

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Keywords
Diabetes mellitus type 2 · Community pharmacy services · Outcome sets monitoring · European Union

Abstract
Background: The analysis of the European Union (EU28) health systems' intervention for type 2 diabetes mellitus (T2DM) reports an insufficient combination of legal support, prevention, and early diagnosis. This fact compromises the patient's health outcomes. The inclusion of pharmacy services oriented to T2DM (PS-T2DM) in strategic primary care network's programs could be a solution. However, the different regulatory frameworks that include good pharmaceutical practices and clinical guidelines for T2DM in each EU28 country may be a limitation. Health systems need to know the evolution of these community services and to analyze their operational and regulatory base, both in time and space. ***Methods:*** A systematic review was carried out on a qualitative and quantitative approach to the expansion and upgrading of PS-T2DM provided in EU28 pharmacies between 2008 and 2018. ***Results:*** The implementation of PS-T2DM in EU28 has increased sharply since 2009 and 2010. Diabetes mellitus (DM) is regulated in 5 countries (Bulgaria, Spain, Italy, Lithuania, and Portugal) and T2DM in 3 (Austria, Latvia, and Romania). Also, in 3 countries (Latvia, Poland, and Spain), pharmacists are involved in implementing guidelines for DM and T2DM, but there is no evidence on the regulation of PS-T2DM. Twenty-two countries showed detailed studies for the PS-T2DM's provision. The type of PS-T2DM implemented in the highest number of EU28 countries was "promoting the rational use of medicines," and the specific subtype T2DM-related more commonly reported was the "glucose measurement." ***Discussion/Conclusion:*** Pharmacy disease-oriented services contributed to improving the accessibility, proximity, and equity of primary care for T2DM provided in community pharmacies across the EU28 in recent decades. This promising strategy for improving health outcome sets may be a call to the action of health systems due to its impact consistent with some objectives of universal health coverage for the eradication of DM and T2DM.

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Expandindo os cuidados de saúde para os cuidados farmacêuticos na diabetes mellitus tipo 2 através das farmácias comunitárias da União Europeia, entre 2008 e 2018: Revisão Sistemática

Palavras Chave
Diabetes mellitus tipo 2 · Cuidados farmacêuticos · Monitorização dos resultados de saúde · União Europeia

Resumo
Introdução: A análise da intervenção dos sistemas de saúde da União Europeia (UE28) para a diabetes mellitus tipo 2 (T2DM) relata uma combinação insuficiente em termos de apoio jurídico, prevenção e diagnóstico precoce da doença, o que compromete os resultados de saúde. A inclusão de serviços de cuidados farmacêuticos orientados para a T2DM (PS-T2DM) nos programas estratégicos da rede de cuidados de saúde primários pode ser uma solução. No entanto, a diferente estrutura reguladora, que inclui as boas práticas farmacêuticas e as diretrizes clínicas para T2DM de cada país da UE28 podem ser uma limitação. Os sistemas de saúde devem conhecer a evolução conjunta desses serviços e analisar a sua base operacional e regulatória, tanto no tempo quanto no espaço. ***Métodos:*** Foi realizada uma revisão sistemática, numa abordagem qualitativa e quantitativa, da expansão e atualização da prestação de PS-T2DM nas farmácias comunitárias da UE28 entre 2008 e 2018. ***Resultados:*** Houve um aumento do número e tipo de PS-T2DM na UE28 desde 2009-2010. A *diabetes mellitus* (DM) encontra-se regulada em 5 países (Bulgária, Espanha, Itália, Lituânia e Portugal) e a T2DM em 3 (Áustria, Letônia e Romênia). Além disso, em 3 países (Letônia, Polônia e Espanha) os farmacêuticos estão envolvidos na implementação das *guidelines* para a DM e T2DM, embora não haja evidências sobre a regulamentação dos PS-T2DM. Vinte e dois países mostraram estudos concretos para a prestação de PS-T2DM. O tipo de PS-T2DM implementado num maior número de países da UE28 foi "promoção do uso racional de medicamentos" e o subtipo específico para a T2DM mais comumente relatado foi a "medição de glicose". ***Discussão / Conclusão:*** A crescente contribuição para a melhoria da acessibilidade, proximidade e equidade dos cuidados primários para T2DM prestados em farmácias comunitárias em toda a UE28 nas últimas décadas deve-se à disponibilidade crescente de serviços orientados para a doença. Essa estratégia promissora do melhoramento dos resultados de saúde mostrou a possibilidade de ter um impacto positivo e consistente com alguns objetivos da cobertura universal de saúde para a erradicação da DM e da T2DM, assim como atuar como um apelo à ação dos sistemas de saúde.

Introduction

Diabetes mellitus (DM) is a complex heterogeneous metabolic disorder considered to be one of the world's worst noncommunicable diseases (NCDs) [1, 2]. DM was the leading cause of hospitalization in the European Union (EU) in 2015. Current global data estimates that there are around 463 million adults with DM (2019), and it will increase to 700 million in 2045 (20–79 years old) [2, 3]. Also, around 232 million cases of DM are undiagnosed, and the annual global expenditure on DM is estimated at 760 billion – regarding its treatment and prevention of complications, around 150 billion EUR were spent in total and about 4.6 billion EUR per adult/year [2–5]. The most heterogeneous and common type of DM is the "type 2" (T2DM), which corresponds to about 90% of DM cases worldwide [2]. It is characterized to manifest chronic hyperglycemia that can damage blood vessels and nerves, causing long-term irreversible complications that represent >50% of the mortality in people with T2DM [6, 7]. Also, the other disorder closely related to DM is "prediabetes" which signifies a risk of the future development of T2DM and its complications. This is a term increasingly used to designate the impaired glucose tolerance (IGT) and the impaired fasting glucose (IFG) [2, 3]. In order to respond to the DM burden's grow in a global health perspective, world health systems have been working together over the last decades, expressing common concerns about DM eradication and seeking to implement effective interventions to reduce its impact, mainly on the economic and social level [4, 5, 8–11]. In 2008, the World Health Organization (WHO) developed an action plan focused on reducing the global burden of 4 chronic diseases that included DM [10, 12, 13] and its latest report – the *WHO Global Report on DM (2016)* – declared that DM should be included in all NCD's policies [13]. In parallel, some of the most influential international health entities and pharmaceutical sciences organizations from most EU countries (International Federation of Pharmacists, Pharmaceutical Group of European Union [PGEU], Pharmaceutical Care Network Europe, professional associations, and pharmacy associations) have taken joint initiatives

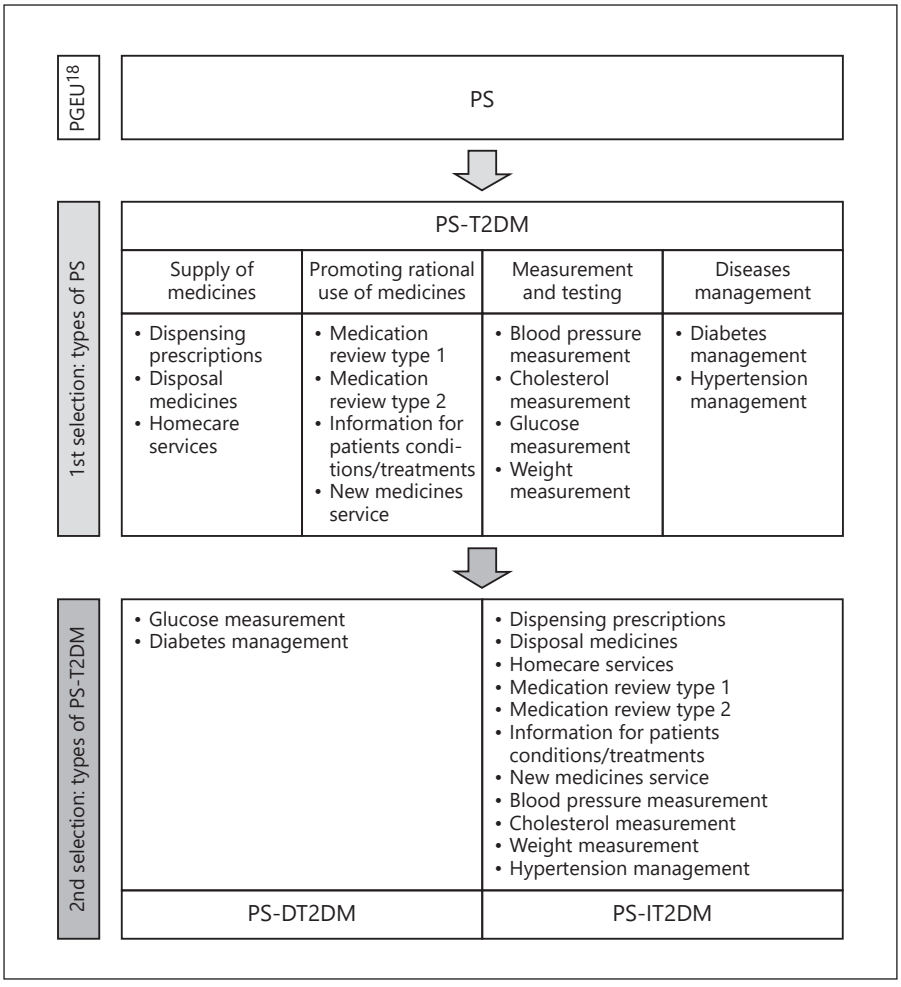

Fig. 1. Short diagram: selected PS-T2DM-oriented (PS-T2DM) by type, subtype and category. PGEU, Pharmaceutical Group of European Union.

to make the community pharmacy and the pharmaceutical care practitioners (the community pharmacist, CPH) more collaborative with primary care and involved in its networks and projects, beyond the dispensing of medicines to the community (started in 1950) and the practice of handling pharmacy (started in 1910–1920). Thus, today, community pharmacy and CPH are centered on clinical pharmacy practice and primary care. CHP is focused on disease management, giving priority to making early diagnosis and pharmacovigilance. This kind of pharmaceutical patient care is realized through services that are called "pharmacy services" (PS) [11, 14]. The study aimed to explore evidence of implementing pharmaceutical care in T2DM in EU28 community pharmacies over 10 years (2008–2018). Besides, it sought to explore the diversity, complexity, and the existence of regulation for PS-T2DM.

Methods

The main objective of this study was to analyze the implementation of pharmaceutical care in T2DM in community pharmacies of EU28 countries, as pharmacy services, with the evidence available between 2008 and 2018. The research question was elaborated based on the methodology Participants, Interventions, Control, Outcomes, Study design [15], and it was as follows: *What type of pharmacy services for T2DM has been implemented in EU28 community pharmacies between 2008 and 2018 and which guidelines were supporting this?*

A systematic review of the literature was the research methodology selected because it is a precise and reliable way that allows synthesizing a substantive set of information with scientific evidence. Then, the *Prisma statement® methodology* followed the elaboration instructions referred by Liberati et al. [16]. According to the PGEU Annual Report 2010 [17] and 2017 [18], all types of PS (4) selected to be studied, and its subtypes (13) were summarized in Figure 1 to organize the research and its results. The 4 types of PS were designated as "pharmacy services T2DM-oriented" (PS-T2DM) and divided into 2 categories. These categories are: (i) "pharmacy services directly oriented toward T2DM" (PS-DT-

Table 1. Eligibility criteria checklist for the research [16, 92]

Rated item	
Internal validity	Is the objective clear and appropriate? Is the study clearly defined?
External validity	Do the study results apply to people who do not participate in it? Do the study results apply to other countries (out of EU) which do not participate in it?
Bias	*Selection bias* Were the results of interest in the study? Case-control studies: Are enough participants to minimize the effect of chance? Are groups and inclusion criteria well and clearly defined? Cohort studies: Are enough participants to minimize the effect of chance? Are exposure factors clearly defined? *Measurement bias* Is there evidence of a change in the classification of the condition of interest during the study period?
Confounding variables	Are the main confounding variables identified and taken into account in study design and data analysis (e.g., use of matching randomization OR stratification)?
Results	Are the results accurate (check confidence interval, risk estimation)?

EU, European Union.

2DM), which includes 2 PS subtypes: (a) *glucose measurement*, that consists of the measurement of plasma glucose levels and can be calculated either in fasting or in postprandial phase and (b) *diabetes management,* that consists of a pharmaceutical patient consultation to manage health status and monitoring health outcomes (T2DM or prediabetes); and "pharmacy services indirectly oriented towards T2DM" (PS-IT2DM), which includes the following 11 subtypes of PS related to DM's treatment adherence and parameters monitoring, and the management of its risk factors: (a) *dispensing prescriptions*, that consists of checking the medication in terms of dose and dosage, frequency, form, treatment duration, and appropriated instruction for each patient; (b) *disposal of medicines*, that consists of a service for the safe disposal of expired or unused medicines; (c) *hope care services/homecare services*, that consists of a support for patients with chronic diseases in tertiary care, in their homes; (d) *medication review type 1*, that consists of a mandatory dispensing process (checking the medication, dose and dosage, frequency, form, treatment duration, and appropriated instruction for each patient); (e) *medication review type 2*, that consists of structured and private consultation between the pharmacist and patient, where the "medication review type 1" happens simultaneously with the verification of treatment adherence and the safe, effective, and rational use of medicines; (f) *information to patients on conditions/treatments*, whose information is related to the disease and the current treatment prescribed to patients; (g) *new pharmacy service*, also known as "new medicines service" that consists of a medication review specifically provided to patients starting a new medication which aims to support adherence in the first month(s) of treatment; (h) *blood pressure measurement*; (i) *weight measurement*, which may or may not include comparison with height and it results in the calculation of "body mass index"; (j) *cholesterol measurement*, by standard measurement of total cholesterol; and (k) *hypertension management*, which consists of a pharmaceutical patient consultation to monitoring the blood pressure values obtained at rest, over time, of the person whose disease (arterial hypertension) was diagnosed previously [17, 18].

The identification of the relevant literature followed 2 ways. It was based on a search in the PubMed, Web of Science, B-On, Health Policy, The Lancet and IndeX databases (R1); and by Google Scholar, other official documents of health (national and international) repositories, pharmaceutical legislation, and health and statistical data (R2). The research descriptors were limited to the variables resulting from the research question referred to above, which was as follows: "pharmacy services" OR "pharmaceutical care," "community pharmacy" OR other expressions associated with pharmaceutical sciences (community pharmacist OR pharmacy), DM (diabetes mellitus type 2 OR diabetes type 2 OR T2DM), pharmaceutical legislation (clinical guidelines/guidelines for pharmaceutical care for diabetes/DM/diabetes type 2/T2DM), health policies for DM (public health diabetes/DM/T2DM-related), protocols for the implementation of pharmaceutical care for diabetes/DM/T2DM management in community pharmacies, pharmaceutical care in community settings, European Union, Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, The Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, and United Kingdom.

The search started exploring the PubMed database according to the *Medical Subject Headings*. The same strategy was subsequently done in other databases. Studies conducted in the last 12 years (period January 2008 – February 2020) were written in English, Portuguese, French, German, and Spanish. The selection of studies was made in 2 stages: screening and an evaluation of the quality of the studies. The screening was carried out through a checklist of the research question elaboration criteria – Intervention (exposure): pharmacy services for management of T2DM Control (group of): EU28 countries (Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, The Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, and United Kingdom); and Study design: ecological time-series study. Then, it was evaluated the quality of the studies also applying a PRISMA checklist [16] that met the eligibility criteria (Table 1, online suppl. Table S1; see www.karger.com/doi/10.1159/000506261 for all online suppl. material). Also, a validated tool (ROBIN-I, online suppl. Table S2) is used to assess some bias in the selected studies of the way research R1 could be seen on online supplementary Table S3.

"Introduction" and "Methods" were written with the support of the literature found between 2001 and 2020, to approach the theme from a temporal perspective. From the totality of the stud-

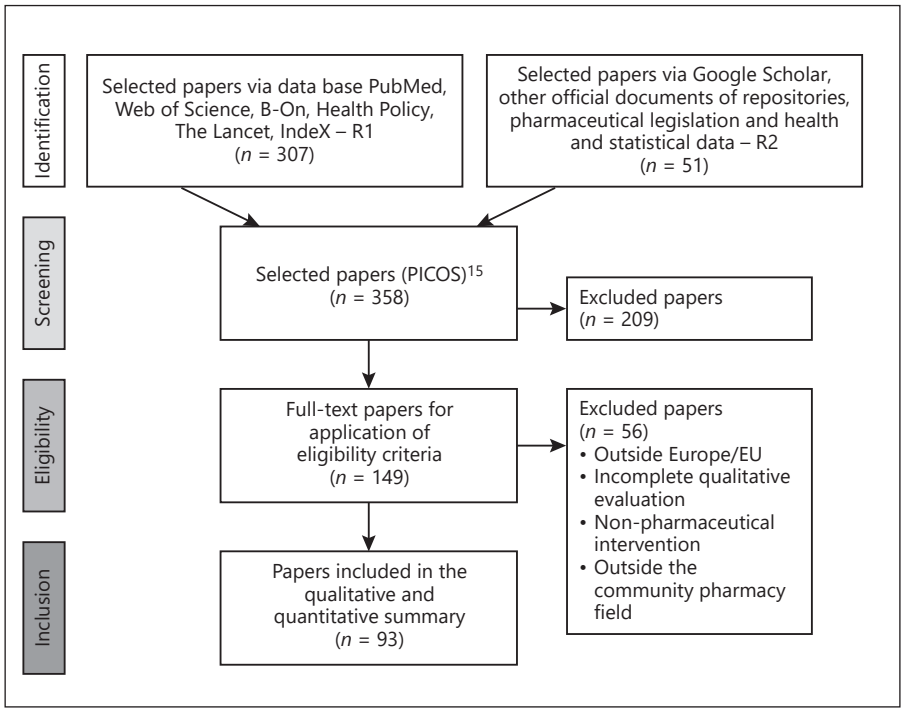

Fig. 2. Flow diagram: studies selection and methodology used. PICOS, Participants, Interventions, Control, Outcomes, Study design; EU, European Union.

ies, the inclusion criteria were: empirical study reports referring to all interventions focused on the provision of PS to people with DM or T2DM, with available references, published in scientific and indexed databases; studies that included individuals aged 18 years or more; full-text articles with a clear theme and objective related to the research question. Exclusion criteria refer to studies with animals, not adults (<18 years old), specific studies for DM type 1 or gestational DM, studies related to other non-diabetes complications, studies not related to EU countries, studies inconclusive and lack of access to the full text of the studies. Studies that dealt with the subject but had variations, such as studies in a hospital/hospital pharmacy environment, were also excluded. The selection of the studies considered eligible included 2 stages: screening and non-categorical evaluation of study quality. In the first stage, the criteria for the elaboration of the research question were validated: participants/countries, interventions/community pharmacy and health systems, results and study design; in the second step, the full text of the articles considered relevant, using the same criteria, was analyzed to determine their eligibility for inclusion in the review. The total of documents collected was tracked following the 2 research paths mentioned above, R1 and R2. These studies were selected after repeated studies, and they were excluded in the 2 series (R1 and R2). The inclusion and exclusion criteria were applied and read in full. The data collected were systematized in tables, which included all the most relevant elements of each study, namely: year, country, PS, PS-T2DM, PS-DT2DM, and PS-IT2DM, and guidelines and legal framework for DM/T2DM in each EU country, when available.

The analysis of the studies was predominantly interpretive and qualitative with a comparative approach. The final set of studies selected should describe pharmacy services not specific for T2DM, but applicable to T2DM and DM-related varying from country to country, and therefore differing in terms of social and demographic context, not considered as variables in the present study. A systematic review of the literature helped us to organize data/information found accurately, synthetically, and with evidence, because it was very dispersed either in R1 either in R2. Figure 2 illustrates the dynamics of the identification and selection process of articles for analysis.

Results

Our study tracked 358 documents, 307 articles by R1, and 51 by R2. After a new selection, 93 articles were retained in total. This set was the study's documentary core. Forty-nine studies related to the implementation of PS-T2DM in EU28, were selected and then organized in Table 2 by country, by type, and subtype of PS-T2DM.

The PGEU Annual Report 2010 [17] and PGEU Annual Report 2017 [18] were the most noteworthy documents found by R2, in terms of results' integrity, informative cooperation, and feasibility of data collection. Both documents classify pharmaceutical care as community pharmacy services. The PGEU Annual Report 2010 data supported the first phase of the research. In this document, it found 3 levels of pharmacy services' classification: "core services," "basic services," and "advanced services." The other reports (PGEU 2013– PGEU 2017) have

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Table 2. Studies of the implementation of PS-T2DM-oriented in each of the EU22 case countries and EU28: by type and by subtype (2009–2018)

Types of PS-DM2 subtypes of PS-DM2	Supply of medicines services			Promoting rational use of medicines				Measurement and testing services				Diseases management	
	dispensing prescriptions (study year)	disposal medicines (study year)	homecare services (study year)	medication review type 1 (study year)	medication review type 2 (study year)	information to patients on conditions/ treatments (study year)	new medicines service (study year)	blood pressure measurement (study year)	cholesterol measurement (study year)	glucose measurement (study year)	weight measure-ment (study year)	diabetes management[1] (study year)	hypertension management (study year)
GE	WHO 2014 [44], EphEU 2019 [51]	WHO 2014 [44]	WHO 2014 [44]	WHO 2014 [44], EphEU 2019 [51]	WHO 2014 [44], EphEU 2019 [51]	WHO 2014 [44], EphEU 2019 [51]	WHO 2014 [44], EphEU 2019 [51]	PGEU 2014 [20]	PGEU 2014 [20]	PGEU 2014 [20]	PGEU 2014 [20]	PGEU 2014 [20]	PGEU 2014 [20]
AU	Langer et al. 2018 [52]	No data	No data	Lemmens-Gruber et al. 2012 [53], Langer et al. 2018 [52]	No data	Lemmens-Gruber et al. 2012 [53], Langer et al. 2018 [52]	No data	Lemmens-Gruber et al. 2012 [53], Langer et al. 2018 [52]	Langer et al. 2018 [52]	Langer et al. 2018 [52]	Langer et al. 2018 [52]	Lemmens-Gruber et al. 2012 [53]	Lemmens-Gruber et al. 2012 [53]
BE	No data	Martins et al. 2015 [54]	Martins et al. 2015 [54]	OPHACO 2017 [55]	OPHACO 2017 [55]	Martins et al. 2015 [54]	No data	Martins et al. 2015 [54]	Martins S et al. 2015 [54]	Martins et al. 2015 [54]	Martins et al. 2015 [54]	OPHACO 2017 [55]	OPHACO 2017 [55]
BU	Petkova et al. 2017 [56]	No data	No data	Martins et al. 2015 [54], Petkova et al. 2017 [56]	No data	Martins et al. 2015 [54]	No data	No data	No data	No data	No data	No data	No data
CR	Jonjić et al. 2010 [57], Meštrović et al. 2012 [58], EphEU 2019 [59]	Jonjić et al. 2010 [57], Martins et al. 2015 [54]	No data	Meštrović et al. 2012 [58], EphEU 2019 [59]	No data	Jonjić et al. 2010 [57], EphEU 2019 [59]	No data	Jonjić et al. 2010 [57]	No data	No data	Jonjić et al. 2010 [57]	No data	No data
DK	Deloitte 2016 [60]	Martins et al. 2015 [54], Deloitte 2016 [60]	Martins et al. 2015 [54]	Haugbølle 2009 [61], Martins et al. 2015 [54], Deloitte 2016 [60], Søndergaard et al. 2018 [62]	Deloitte 2016 [60]	Martins et al. 2015 [54], Deloitte 2016 [60], Søndergaard et al. 2018 [62]	No data	Deloitte 2016 [60], Søndergaard et al. 2018 [62]	Deloitte 2016 [60]	Søndergaard et al. 2018 [62]	Deloitte 2016 [60]	Søndergaard et al. 2018 [62]	Søndergaard et al. 2018 [62]
SL	Horvat et al. 2015 [63]	No data	No data	Horvat et al. 2011 [64], Horvat et al. 2015 [63], Gmeiner et al. 2017 [65]	No data	Horvat et al. 2011 [64]	No data	Gmeiner et al. 2017 [65]	No data	Gmeiner et al. 2017 [65]	No data	Gmeiner et al. 2017 [65]	Gmeiner et al. 2017 [65]
SP	No data	Martins et al. 2015 [54]	No data	Olave Quispe 2011 et al. [66], Martins et al. 2015 [54], Deloitte 2016 [60]	Olave Quispe 2011 et al. [66], Deloitte 2016 [60]	Olave Quispe 2011 et al. [66], Deloitte 2016 [60]	No data	Deloitte 2016 [60]	Deloitte 2016 [60]	Deloitte 2016 [60]	Deloitte 2016 [60]	Deloitte 2016 [60]	Deloitte 2016 [60]
ES	Sepp 2015 [67]	No data	No data	Sepp 2015 [67]	No data	Sepp 2015 [67]	No data	Sepp 2015 [67]	Sepp 2015 [67]	Sepp 2015 [67]	Sepp 2015 [67]	Sepp 2015 [67]	No data
FI	No data	No data	No data	Leikola et al. 2012 [68]	Leikola et al. 2012 [68], Svensberg et al. 2015 [69]	No data	No data	No data	No data	No data	No data	No data	No data
FR	No data	No data	No data	Supper et al. 2017 [70]	No data	No data	No data	Supper et al. 2017 [70]	Supper et al. 2017 [70]	Supper et al. 2017 [70]	Supper et al. 2017 [70]	Supper et al. 2017 [70]	Supper et al. 2017 [70]
HU	No data	Martins et al. 2015 [54]	Martins et al. 2015 [54]	Martins et al. 2015 [54]	No data	Martins et al. 2015 [54]	No data	No data	No data	No data	No data	No data	No data
IR	Deloitte 2016 [60]		Deloitte 2016 [60]	Deloitte 2016 [60]	No data	Deloitte 2016 [60]	No data	Deloitte 2016 [60]	Deloitte 2016 [60]	Deloitte 2016 [60]	Deloitte 2016 [60]	Deloitte 2016 [60]	Deloitte 2016 [60]
IT	No data	Martins et al. 2015 [54]	Martins et al. 2015 [54]	Martins et al. 2015 [54]	No data	Martins et al. 2015 [54]	No data	No data	No data	No data	No data	No data	No data
LT	No data	No data	No data	Urbonas et al. 2010 [71]	No data	Urbonas et al. 2010 [71]	No data	No data	No data	No data	No data	No data	No data

Table 2 (continued)

Types of PS-DM2 subtypes of PS-DM2	Supply of medicines services			Promoting rational use of medicines				Measurement and testing services				Diseases management	
	dispensing prescriptions (study year)	disposal medicines (study year)	homecare services (study year)	medication review type 1 (study year)	medication review type 2 (study year)	information to patients on conditions/ treatments (study year)	new medicines service (study year)	blood pressure measurement (study year)	cholesterol measurement (study year)	glucose measurement (study year)	weight measurement (study year)	diabetes management[i] (study year)	hypertension management (study year)
MA	Vella et al. 2009 [72]	No data	No data	No data	No data	Vella et al. 2009 [72]	No data	Wirth et al. 2010 [73]	No data	Wirth et al. 2010 [73]	No data	Wirth et al. 2010 [73]	Wirth et al. 2010 [73]
NL	Van Geffen et al. 2011 [74]	Martins et al. 2015 [54]	Hugtenburg et al. 2009 [75], Martins et al. 2015 [54]	Hugtenburg et al. 2009 [75], Van Geffen et al. 2011 [74], Martins et al. 2015 [54], Deloitte 2016 [60]	Van Geffen et al. 2011 [74], Deloitte 2016 [60]	Hugtenburg et al. 2009 [75], Van Geffen et al. 2011 [74], Martins et al. 2015 [54]	Deloitte 2016 [60]	No data	No data	No data	No data	Van Geffen et al. 2011 [74]	Van Geffen et al. 2011 [74]
PT	No data	No data	No data	Martins et al. 2013 [76]	No data	Martins et al. 2013 [76]	No data	Martins et al. 2013 [76]	Martins et al. 2013 [76]	Martins et al. 2013 [76]	Martins et al. 2013 [76]	Martins et al. 2013 [76]	Martins et al. 2013 [76]
CZ	Nachtigal et al. 2017 [77]	No data	Nachtigal et al. 2017 [77]	Nachtigal et al. 2017 [77]	Nachtigal et al. 2017 [77]	Nachtigal et al. 2017 [77]	No data	Nachtigal et al. 2017 [77]	No data	Nachtigal et al. 2017 [77]	No data	No data	No data
UK	Taylor et al. 2012 [78], Twigg et al. 2013 [79], Twigg et al. 2013 [80], Morton et al. 2015 [81]	Martins et al. 2015 [54], Deloitte 2016 [60]	Longley et al. 2012 [82], Twigg et al. 2013 [79], Martins et al. 2015 [54], Deloitte 2016 [60], Andreassen et al. 2016 [84]	Taylor et al. 2012 [78], Lowrie et al. 2012 [85], Twigg et al. 2013 [79], Twigg et al. 2013 [80], Ridge et al. 2014 [86], Morton et al. 2015 [81], Twigg et al. 2015 [83], Andreassen et al. 2016 [84]	Taylor et al. 2012 [78], Longley et al. 2012 [82], Twigg et al. 2013 [79], Twigg et al. 2013 [80], Ridge et al. 2014 [86], Morton et al. 2015 [81], Twigg et al. 2015 [83], Deloitte 2016 [60], Andreassen et al. 2016 [84]	Taylor et al. 2012 [78], Twigg et al. 2013 [79], Twigg et al. 2015 [83], Martins et al. 2015 [54], Deloitte 2016 [60], Andreassen et al. 2016 [84]	Twigg et al. 2013 [79], Twigg et al. 2013 [80], Morton et al. 2015 [81], Deloitte 2016 [60], Andreassen et al. 2016 [84]	Taylor et al. 2012 [78], Lowrie et al. 2012 [85], Twigg et al. 2013 [80], Twigg et al. 2015 [83], Morton et al. 2015 [81], Deloitte 2016 [60], Andreassen et al. 2016 [84]	Taylor et al. 2012 [78], Twigg et al. 2015 [83], Deloitte 2016 [60], Andreassen et al. 2016 [84]	Taylor et al. 2012 [78], Twigg et al. 2013 [80], Ayorinde et al. 2013 [87], Morton et al. 2015 [81], Twigg et al. 2015 [83], Deloitte 2016 [60], Andreassen et al. 2016 [84]	Taylor et al. 2012 [78], Lowrie et al. 2012 [85], Morton et al. 2015 [81], Twigg et al. 2015 [83], Deloitte 2016 [60], Andreassen et al. 2016 [84]	Twigg et al. 2013 [79], Ayorinde et al. 2013 [87], Twigg et al. 2015 [83], Deloitte 2016 [60], Andreassen et al. 2016 [84]	Taylor et al. 2012 [78], Deloitte 2016 [60]
RO	Sandulovici et al. 2018 [88]	No data	No data	Sandulovici et al. 2018 [88]	No data	Sandulovici et al. 2018 [88]	No data	Sandulovici et al. 2018 [88]	Sandulovici et al. 2018 [88]	Sandulovici et al. 2018 [88]	Sandulovici et al. 2018 [88]	No data	No data
SW	Montgomery et al. 2010 [89], Deloitte 2016 [60]	Martins et al. 2015 [54], Deloitte 2016 [60]	Martins et al. 2015 [54], Deloitte 2016 [60]	Montgomery et al. 2010 [89], Deloitte 2016 [60]	Martins et al. 2015 [54], Deloitte 2016 [60]	Montgomery et al. 2010 [89], Martins et al. 2015 [54], Deloitte 2016 [60], PGEU 2016	Deloitte 2016 [60]	Deloitte 2016 [60]	Deloitte 2016 [60]	Deloitte 2016 [60]	Deloitte 2016 [60]	No data	No data
EU28	PGEU 2010 [17], PGEU 2013 [19], PGEU 2015 [21], PGEU 2017 [18], FIP 2017 [90]	PGEU 2010 [17], PGEU 2017 [18], FIP 2017 [90]	PGEU 2010 [17], WHO 2014 [91], PGEU 2015 [21], FIP 2017 [90]	PGEU 2010 [17], PGEU 2013 [19], WHO 2014 [91], PGEU 2015 [21], PGEU 2017 [18], FIP 2017 [90]	PGEU 2017 [18], FIP 2017 [90]	PGEU 2017 [18], FIP 2017 [90]	PGEU 2015 [21], PGEU 2017 [18], FIP 2017 [90]	PGEU 2010 [17], PGEU 2013 [19], WHO 2014 [91], PGEU 2015 [21], Deloitte 2016 [60], PGEU 2017 [18], FIP 2017 [90]	PGEU 2010 [17], PGEU 2013 [19], WHO 2014 [91], PGEU 2015 [21], Deloitte 2016 [60], PGEU 2017 [18]	PGEU 2010 [17], PGEU 2013 [19], WHO 2014 [91], PGEU 2015 [21], Deloitte 2016 [60], PGEU 2017 [18], FIP 2017 [90]	PGEU 2010 [17], PGEU 2013 [19], WHO 2014 [91], PGEU 2015 [21], Deloitte 2016 [60], PGEU 2017 [18]	PGEU 2010 [17], PGEU 2013 [19], WHO 2014 [91], PGEU 2015 [21], Deloitte 2016 [60], PGEU 2017 [18], FIP 2017 [90]	PGEU 2010 [17], PGEU 2013 [19], WHO 2014 [91], PGEU 2015 [21], Deloitte 2016 [60], PGEU 2017 [18], FIP 2017 [90]

The literature consulted does not provide data for inclusion in the review according to the inclusion criteria of the following countries: Cyprus, Slovakia, Greece, Luxembourg, Latvia, Poland; [a] Austria, Belgium, Croatia, Cyprus, Czech Republic, Denmark, Finland, France, Germany, Ireland, Italy, The Netherlands, Poland, Portugal, Slovakia, Slovenia, Spain, Sweden, and the United Kingdom; [b] Belgium, Bulgaria, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Luxembourg, Malta, Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, and the United Kingdom; [c] Austria, Belgium, Bulgaria, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Hungary, Ireland, Italy, Netherlands, Portugal, Slovakia, Slovenia, Spain, Sweden, United Kingdom, and Romania; [d] Austria, Belgium, Bulgaria, Croatia, Denmark, Estonia, Finland, France, Germany, Ireland, Holland, Portugal, Romania, Slovakia, Spain, Sweden, and United Kingdom. AU, Austria; BE, Belgium; BU, Bulgaria; CR, Croatia; CY, Cyprus; CZ, Czech Republic; DK, Denmark; ES, Estonia; FI, Finland; FR, France; GE, Germany; GR, Greece; HU, Hungary; IR, Ireland; IT, Italy; LV, Latvia; LT, Lithuania; MA, Malta; NL, The Netherlands; PO, Poland; PT, Portugal; RO, Romania; SL, Slovakia; SL, Slovenia; SP, Spain; SW, Sweden; UK, United Kingdom; EU, European Union (27 countries at 2010–2012 and 28 countries at 2013–2017); PS-T2DM, pharmacy services type 2 diabetes mellitus.

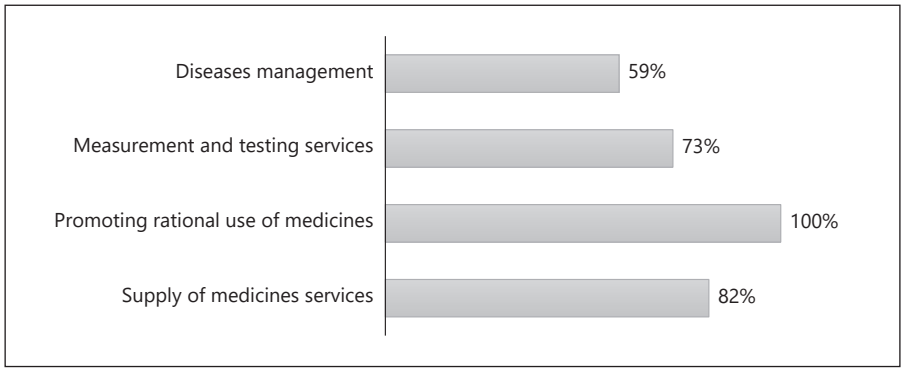

Fig. 3. PS-T2DM-oriented implemented in the EU22 case countries: by type (data 2008–2018).

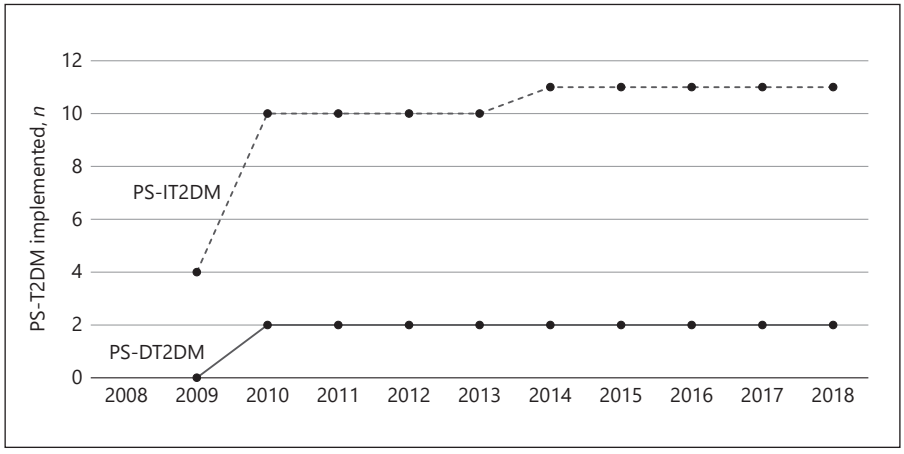

Fig. 4. Evolution of the implementation of PS-T2DM-oriented in EU (22 countries): by category (data 2009–2018). PS-T2DM, pharmacy services T2DM.

the description and the categorization of pharmacy services, as it was mentioned in "Methods" [17–22]. Besides, PGEU recognizes the CPH as the responsible person for the implementation and provision of all these community pharmacy services, as through patient counseling and dispensing medicines and health products (including or not in prescriptions) as pharmacovigilance and referral people with health conditions/diseases to the general practitioner (GP). It was also reported the benefits of a set of PS for disease management to improve health outcomes and the expansion in number and type of PS in EU28 community pharmacies [17–24]. This last fact is also related to the appearance of a new PS – the "new medicines service" – that was highlighted in some PGEU annual reports [18, 25]. However, no accurate records of protocols or guidelines specifics for PS-T2DM's implementation or provision were founded. This fact is an essential barrier to a complete understanding of the strategic planning of health systems in the EU28 for the eradication of T2DM supported by the collaboration of pharmaceutical care in primary care.

Analysis of PS-T2DM Provided in EU22 Countries: By Type, Subtype, and Category

A set of detailed studies for all categories of PS-T2DM was found. They are related to a total of 22 EU countries – the "data set of case countries" (Austria, Belgium, Bulgaria, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Hungary, Ireland, Italy, Lithuania, Malta, Portugal, Romania, Slovenia, Spain, Sweden, The Netherlands, and United Kingdom). Their correspondent studies were organized in Table 2 and reorganized in a quantitative and qualitative approach in Tables 3 and 4, respectively. The remaining countries were excluded from this analysis due to the lack of data related to PS-T2DM implementation and/or provision between 2008 and 2018, and they are Cyprus, Greece, Latvia, Luxembourg, Slovakia, and Poland. The countries that presented the first concrete studies on the existence/implementation/provision of PS-T2DM were Malta, The Netherlands, and Denmark, in 2009. However, the United Kingdom was the country that published more studies about PS-T2DM (12 of 46).

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Table 3. Data table: PS-T2DM-oriented in each of 22 EU case countries: a quantitative approach (data 2009–2018)

Date	Data 2009		Data 2010		Data 2011		Data 2012		Data 2013		Data 2014		Data 2015		Data 2016		Data 2017		Data 2018	
22 EU Countries/ PS-T2DM	DT2DM	IT2DM	DT2DM	IT2DM	DT2DM	IT2DM	DT2DM	IT2DM	DT2DM	IT2DM	DT2DM	IT2DM	DT2DM	IT2DM	DT2DM	IT2DM	DT2DM	IT2DM	DT2DM	IT2DM
Germany	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	●●	●●●●●● ●●●●●	●●	●●●●●● ●●●●●	●●	●●●●●● ●●●●●	●●	●●●●●● ●●●●●	●●	●●●●●● ●●●●●
Austria	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	●●	●●●○○○ ○○○○○	●●	●●●○○○ ○○○○○	●●	●●●○○○ ○○○○○	●●	●●●○○○ ○○○○○	●●	●●●○○○ ○○○○○	●●	●●●○○○ ○○○○○	●●	●●●●●● ●○○○○
Belgium	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	●●●●●● ●○○○○	○○	●●●●●● ●○○○○	●●	●●●●●● ●●●○○	●●	●●●●●● ●●●○○
Bulgaria	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	●●○○○○ ○○○○○	○○	●●○○○○ ○○○○○	○○	●●●○○○ ○○○○○	○○	●●●○○○ ○○○○○
Croatia	○○	○○○○○○ ○○○○○	○○	●●●●●○ ○○○○○	○○	●●●●●○ ○○○○○	○○	●●●●●● ○○○○○	○○	●●●●●● ○○○○○	○○	●●●●●● ○○○○○	○○	●●●●●● ○○○○○	○○	●●●●●● ○○○○○	○○	●●●●●● ○○○○○	○○	●●●●●● ○○○○○
Denmark	○○	●○○○○○ ○○○○○	○○	●○○○○○ ○○○○	○○	●○○○○○ ○○○○○	○○	●○○○○○ ○○○○○	○○	●○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	●●●●●○ ○○○○○	○○	●●●●●● ●●●○○	●●	●●●●●● ●●●○○	●●	●●●●●● ●●●●○
Finland	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	●●○○○○ ○○○○○	○○	●●○○○○ ○○○○○	○○	●●○○○○ ○○○○○	○○	●●○○○○ ○○○○○	○○	●●○○○○ ○○○○○	○○	●●○○○○ ○○○○○	○○	●●○○○○ ○○○○○
France	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	●●	●●●●●○ ○○○○○	●●	●●●●●○ ○○○○○
Slovenia	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	●●○○○○ ○○○○○	○○	●●○○○○ ○○○○○	○○	●●○○○○ ○○○○○	○○	●●○○○○ ○○○○○	○○	●●●○○○ ○○○○○	○○	●●●○○○ ○○○○○	●●	●●●●●○ ○○○○○	●●	●●●●●○ ○○○○○
Spain	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	●●●○○○ ○○○○○	○○	●●●○○○ ○○○○○	○○	●●●○○○ ○○○○○	○○	●●●○○○ ○○○○○	○○	●●●●○○ ○○○○○	●●	●●●●●● ●●○○○	●●	●●●●●● ●●○○○	●●	●●●●●● ●●○○○
Estonia	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	●○	●●●●●● ●○○○○	●○	●●●●●● ●○○○○	●○	●●●●●● ●○○○○	●○	●●●●●● ●○○○○
Hungary	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	●●●●○○ ○○○○○	○○	●●●●○○ ○○○○○	○○	●●●●○○ ○○○○○	○○	●●●●○○ ○○○○○
Italy	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	●●●●○○ ○○○○○	○○	●●●●○○ ○○○○○	○○	●●●●○○ ○○○○○	○○	●●●●○○ ○○○○○
Ireland	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	●●	●●●●●● ●●○○○○○	●●	●●●●●● ●●○○○	●●	●●●●●● ●●○○○
Lithuania	○○	○○○○○○ ○○○○○	○○	●●○○○○ ○○○○○	○○	●●○○○○ ○○○○○	○○	●●○○○○ ○○○○○	○○	●●○○○○ ○○○○○	○○	●●○○○○ ○○○○○	○○	●●○○○○ ○○○○○	○○	●●○○○○ ○○○○○	○○	●●○○○○ ○○○○○	○○	●●○○○○ ○○○○○
Malta	○○	●●○○○○ ○○○○○	●●	●●●●○○ ○○○○○	●●	●●●●○○ ○○○○○	●●	●●●●○○ ○○○○○	●●	●●●●○○ ○○○○○	●●	●●●●○○ ○○○○○	●●	●●●●○○ ○○○○○	●●	●●●●○○ ○○○○○	●●	●●●●○○ ○○○○○	●●	●●●●○○ ○○○○○
The Netherlands	○○	●●●○○○ ○○○○○	○○	●●●○○○ ○○○○○	●●	●●●●●○ ○○○○○	●●	●●●●●○ ○○○○○	●●	●●●●●○ ○○○○○	●●	●●●●●○ ○○○○○	●●	●●●●●● ○○○○○	●●	●●●●●● ●○○○○	●●	●●●●●● ●○○○○	●●	●●●●●● ●○○○○
Portugal	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	●●	●●●●●● ○○○○○	●●	●●●●●● ○○○○○	●●	●●●●●● ○○○○○	●●	●●●●●● ○○○○○	●●	●●●●●● ○○○○○	●●	●●●●●● ○○○○○	●●	●●●●●● ○○○○○
Romania	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	●●●●●● ●○○○○
Czech Republic	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	●●●●●● ●○○○○	○○	●●●●●● ●○○○○
United Kingdom	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○○	○○○○○○ ○○○○○	○●	●●●●●● ●●●○○	●●	●●●●●● ●●●○○	●●	●●●●●● ●●●○○	●●	●●●●●● ●●●●●	●●	●●●●●● ●●●●●	●●	●●●●●● ●●●●●	●●	●●●●●● ●●●●●
Sweden	○○	○○○○○○ ○○○○○	○○	●●●○○○ ○○○○○	○○	●●●○○○ ○○○○○	○○	●●●○○○ ○○○○○	○○	●●●○○○ ○○○○○	○○	●●●○○○ ○○○○○	○○	●●●●●● ○○○○○	○○	●●●●●● ●●●●●	○○	●●●●●● ●●●●●	○○	●●●●●● ●●●●●
EU	○○	○○○○○○ ○○○○	●●	●●●●●● ●●○○○	●●	●●●●●● ●●○○○	●●	●●●●●● ●●○○○	●●	●●●●●● ●●○○○	●●	●●●●●● ●●○○○	●●	●●●●●● ●●●○○	●●	●●●●●● ●●●○○	●●	●●●●●● ●●●●●	●●	●●●●●● ●●●●●

● PS-T2DM implemented; ○ PS-T2DM not implemented. DT2DM: Pharmacy services directly oriented for T2DM – PS-DT2DM: Diabetes management and Glucose measurement. Pharmacy services indirectly oriented for T2DM – PS-IT2DM: Dispensing prescriptions; Disposal medicines; Homecare services; Medication Review type 1; Medication Review type 1; Information to patients on conditions or treatments; New medicines service; Blood pressures measurement; Cholesterol measurement; Weight measurement; Hypertension management. T2DM, type 2 diabetes mellitus; PS-T2DM, pharmacy services type 2 diabetes mellitus; EU, European Union.

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Table 4. Data table: PS-T2DM-oriented in each of EU22 countries: a qualitative approach (data 2009–2018)

	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Germany						GM, T2DM, DP, DM, HS, M1, M2, IP, NS, BM, CM, WM and HM Start date	GM, T2DM, DP, DM, HS, M1, M2, IP, NS, BM, CM, WM and HM	GM, T2DM, DP, DM, HS, M1, M2, IP, NS, BM, CM, WM and HM	GM, T2DM, DP, DM, HS, M1, M2, IP, NS, BM, CM, WM and HM	GM, T2DM, DP, DM, HS, M1, M2, IP, NS, BM, CM, WM and HM
Austria				T2DM, BM, HM, M1, and IP Start date	T2DM, BM, HM, M1, and IP	T2DM, BM, HM, M1, and IP	T2DM, BM, HM, M1, and IP	T2DM, BM, HM, M1, and IP	T2DM, BM, HM, M1, and IP	GM, DP, CM, T2DM, BM, HM, M1, WM, and IP
Belgium							GM, BM, CM, WM, DM, HS and IP Start date	GM, BM, CM, WM, DM, HS and IP	GM, BM, CM, WM, DM, HS, IP, M1, M2, T2DM and HM	GM, BM, CM, WM, DM, HS, IP, M1, M2, T2DM and HM
Bulgaria							M1 and IP Start date	M1 and IP	DP, M1 and IP	DP, M1 and IP
Croatia		BM, WM, DP, DM, IP Start date	BM, WM, DP, DM, IP	M1, BM, WM, DP, DM, IP	M1, BM, WM, DP, DM, IP	M1, BM, WM, DP, DM, IP	M1, BM, WM, DP, DM, IP	M1, BM, WM, DP, DM, IP	M1, BM, WM, DP, DM, IP	M1, BM, WM, DP, DM, IP
Denmark	M1 Start date	M1	M1	M1	M1	M1	DM, HS, M2, IP and M1	DP, BM, CM, WM, DM, HS, M2, IP and M1	DP, BM, CM, WM, DM, HS, M2, IP and M1	GM, T2DM, HM, DP, BM, CM, WM, DM, HS, M2, IP and M1
Finland				M1 and M2 Start date	M1 and M2	M1 and M2	M1 and M2	M1 and M2	M1 and M2	M1 and M2
France									M1, BM, CM, GM, WM, T2DM and HM *Start date*	M1, BM, CM, GM, WM, T2DM and HM
Slovenia			M1 and IP Start date	M1 and IP	M1 and IP	M1 and IP	DP, M1 and IP	DP, M1 and IP	GM, T2DM, BM, HM, DP, M1 and IP	GM, T2DM, BM, HM, DP, M1 and IP
Spain			M1, M2 and IP Start date	M1, M2 and IP	M1, M2 and IP	M1, M2 and IP	DM, M1, M2 and IP	GM, T2DM, BM, CM, WM, HM, DM, M1, M2 and IP	GM, T2DM, BM, CM, WM, HM, DM, M1, M2 and IP	GM, T2DM, BM, CM, WM, HM, DM, M1, M2 and IP
Estonia							GM, T2DM, DP, M1, IP, BM, CM and WM Start date	GM, T2DM, DP, M1, IP, BM, CM and WM	GM, T2DM, DP, M1, IP, BM, CM and WM	GM, T2DM, DP, M1, IP, BM, CM and WM
Hungary							DM, HS, M1 and IP Start date	DM, HS, M1 and IP	DM, HS, M1 and IP	DM, HS, M1 and IP
Italy							DM, HS, M1 and IP Start date	DM, HS, M1 and IP	DM, HS, M1 and IP	DM, HS, M1 and IP
Ireland								HS, M1, IP, BM, CM, GM, WM, T2DM and HM Start date	HS, M1, IP, BM, CM, GM, WM, T2DM, HM and DP	HS, M1, IP, BM, CM, GM, WM, T2DM, HM and DP
Lithuania		M1 and IP Start date	M1 and IP	M1 and IP	M1 and IP	M1 and IP	M1 and IP	M1 and IP	M1 and IP	M1 and IP
Malta	DP and IP Start date	GM, T2DM, BM, HM, DP and IP	GM, T2DM, BM, HM, DP and IP	GM, T2DM, BM, HM, DP and IP	GM, T2DM, BM, HM, DP and IP	GM, T2DM, BM, HM, DP and IP	GM, T2DM, BM, HM, DP and IP	GM, T2DM, BM, HM, DP and IP	GM, T2DM, BM, HM, DP and IP	GM, T2DM, BM, HM, DP and IP
The Netherlands	HS, M1 and IP Start date	HS, M1 and IP	T2DM, DP, M2, HM, HS, M1 and IP	T2DM, DP, M2, HM, HS, M1 and IP	T2DM, DP, M2, HM, HS, M1 and IP	T2DM, DP, M2, HM, HS, M1 and IP	DM, T2DM, DP, M2, HM, HS, M1 and IP	NS, DM, T2DM, DP, M2, HM, HS, M1 and IP	NS, DM, T2DM, DP, M2, HM, HS, M1 and IP	NS, DM, T2DM, DP, M2, HM, HS, M1 and IP
Portugal				GM, T2DM, M1, IP, BM, CM, WM, HM Start date	GM, T2DM, M1, IP, BM, CM, WM, HM	GM, T2DM, M1, IP, BM, CM, WM, HM	GM, T2DM, M1, IP, BM, CM, WM, HM	GM, T2DM, M1, IP, BM, CM, WM, HM	GM, T2DM, M1, IP, BM, CM, WM, HM	GM, T2DM, M1, IP, BM, CM, WM, HM

Table 4 (continued)

	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Romania										GM, DP, M1, IP, BM, CM and WM Start date
Czech Republic									BM, GM, DP, HS, M1, M2 and IP Start date	BM, GM, DP, HS, M1, M2 and IP
United Kingdom				GM, DP, HS, M1, M2, IP, BM, CM, WM and HM Start date	T2DM, GM, DP, HS, M1, M2, IP, BM, CM, WM and HM	T2DM, GM, DP, HS, M1, M2, IP, BM, CM, WM and HM	DM, NS, T2DM, GM, DP, HS, M1, M2, IP, BM, CM, WM and HM	DM, NS, T2DM, GM, DP, HS, M1, M2, IP, BM, CM, WM and HM	DM, NS, T2DM, GM, DP, HS, M1, M2, IP, BM, CM, WM and HM	DM, NS, T2DM, GM, DP, HS, M1, M2, IP, BM, CM, WM and HM
Sweden		DP,M1 and IP Start date	DP,M1 and IP	DP,M1 and IP	DP,M1 and IP	DP,M1 and IP	DM, HS, M1, M2, DP and IP	GM, NS, BM, CM, WM, DM, HS, M1, M2, DP and IP	GM, NS, BM, CM, WM, DM, HS, M1, M2, DP and IP	GM, NS, BM, CM, WM, DM, HS, M1, M2, DP and IP
European Union[a]		DP, DM, HS, M1, BM, CM, GM, WM, T2DM and HM Start date	DP, DM, HS, M1, BM, CM, GM, WM, T2DM and HM	DP, DM, HS, M1, BM, CM, GM, WM, T2DM and HM	DP, DM, HS, M1, BM, CM, GM, WM, T2DM and HM	DP, DM, HS, M1, BM, CM, GM, WM, T2DM, HM and NS	DP, DM, HS, M1, BM, CM, GM, WM, T2DM, HM and NS	DP, DM, HS, M1, BM, CM, GM, WM, T2DM, HM, NS, M2 and IP	DP, DM, HS, M1, BM, CM, GM, WM, T2DM, HM, NS, M2 and IP	DP, DM, HS, M1, BM, CM, GM, WM, T2DM, HM, NS, M2 and IP

[a] 28EU countries. Pharmacy services directly oriented for T2DM – PS-DT2DM: T2DM, Diabetes management and GM, Glucose measurement. Pharmacy services indirectly oriented for T2DM – PS-IT2DM: DP, Dispensing prescriptions; DM, Disposal medicines; HS, Homecare services; M1, Medication Review type 1; M2, Medication Review type 1; IP, Information to patients on conditions or treatments; NS, new medicines services BM, blood pressure measurement; CM, cholesterol measurement; WM, weight measurement; HM, hypertension management; PS-T2DM, pharmacy services type 2 diabetes mellitus.

An increase of type and number of PD-T2DM, in general, was observed in all 28 case-countries, especially between 2009 and 2010. A strong influence of some countries in the results – Germany and the United Kingdom – was observed. They contribute to the T2DM implementation's growth during the decade studied because they were the only 2 of 28 EU countries that implemented all 13 subtypes of PS-T2DM of the 2 categories (PS-DT2DM and PS-IT2DM). The type of PS-T2DM implemented in all EU22 case-countries was the "promoting rational use of medicines" service, and the least frequent was the "diseases management" service (59%) (Fig. 3). Regarding the implementation of 13 PS-T2DM subtypes, it was observed that: 21 countries implemented the "medication review type 1" service, 20 countries implemented the "information on patients on conditions/treatments" service, 16 countries implemented the "blood pressure measurement" service, 15 countries implemented the "glucose measurement" service, 14 countries implemented the "dispensing of prescriptions" service, 13 countries implemented the "weight measurement" and "diabetes management" services, 12 countries implemented the "cholesterol measurement" service and the "hypertension management" service, 11 countries implemented the "disposal medicines" service, 10 countries implemented the "homecare services" service, 9 countries implemented the "medication review type 2" service, and 4 countries implemented the "new medicines service" service (Fig. 4–6). Thus, between 2009 and 2018, there was an increase in the number of PS-T2DM implemented in the 22 countries, namely the PS-IT2DM (Fig. 6, 7).

Analysis of the Existence of Regulation and Clinical Guidelines for DM or T2DM in EU28

In Table 5, it could be observed that the extent to which the different governments have embraced pharmaceutical care varies between EU countries. In some of them (e.g., Portugal and Spain), pharmaceutical care is officially recognized in the legislation, but it does not mean that pharmaceutical care is understood as an advanced service exclusively provided by CPH. Most of the countries have been involved in the fight against NCDs in the last decade and developed health policies and guidelines for DM and/or T2DM. However, only 3 countries reported regulation for T2DM (Austria, Latvia and Romania). Also, most of the countries (21 out of 28) have an entity attached to the Ministry of Health or equivalent, that was responsible for NCDs. In Belgium, for example, there are specific guidelines for T2DM, adopted from international and relative guidelines for prevention and treatment, applicable at local, regional, and national levels.

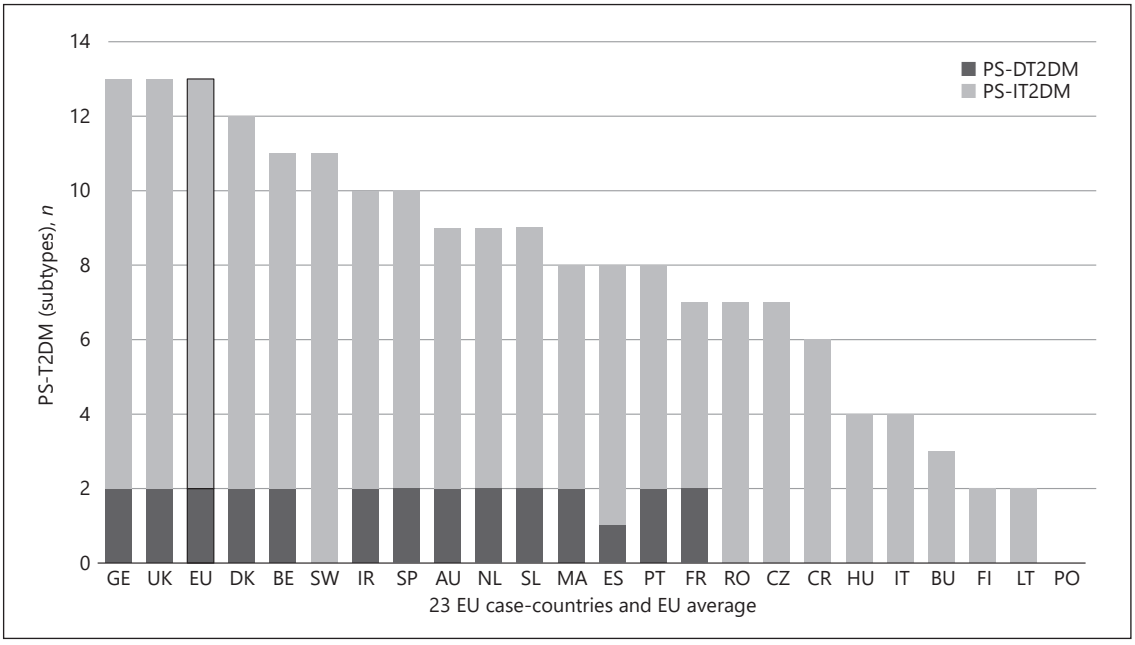


Fig. 5. PS-T2DM-oriented implemented in each of 23 EU countries and EU: by category (data 2009–2018). EU, European Union 23 EU countries and EU - GE: Germany, UK: United Kingdom, DK: Denmark, EU: European Union, SW: Sweden, BE: Belgium, IR: Ireland, SP: Spain, AU: Austria, NL: The Netherlands, SL: Slovenia, MA: Malta, ES: Estonia, PT: Portugal, FR: France, RO: Romania, CZ: C. Republic, CR: Croatia, HU: Hungary, IT: Italy, BU: Bulgaria, FI: Finland, LT: Lithuania, and PO: Poland.

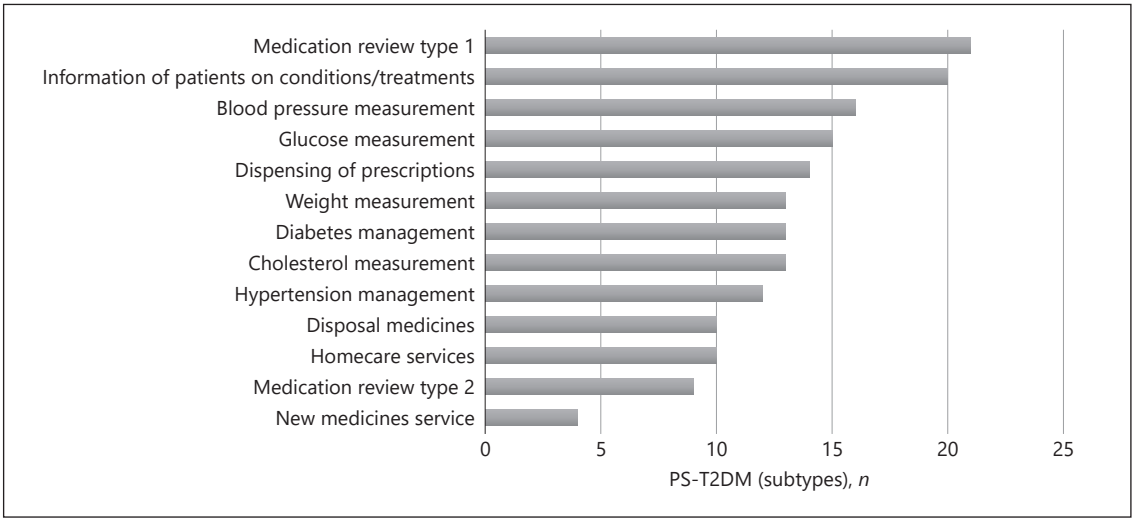
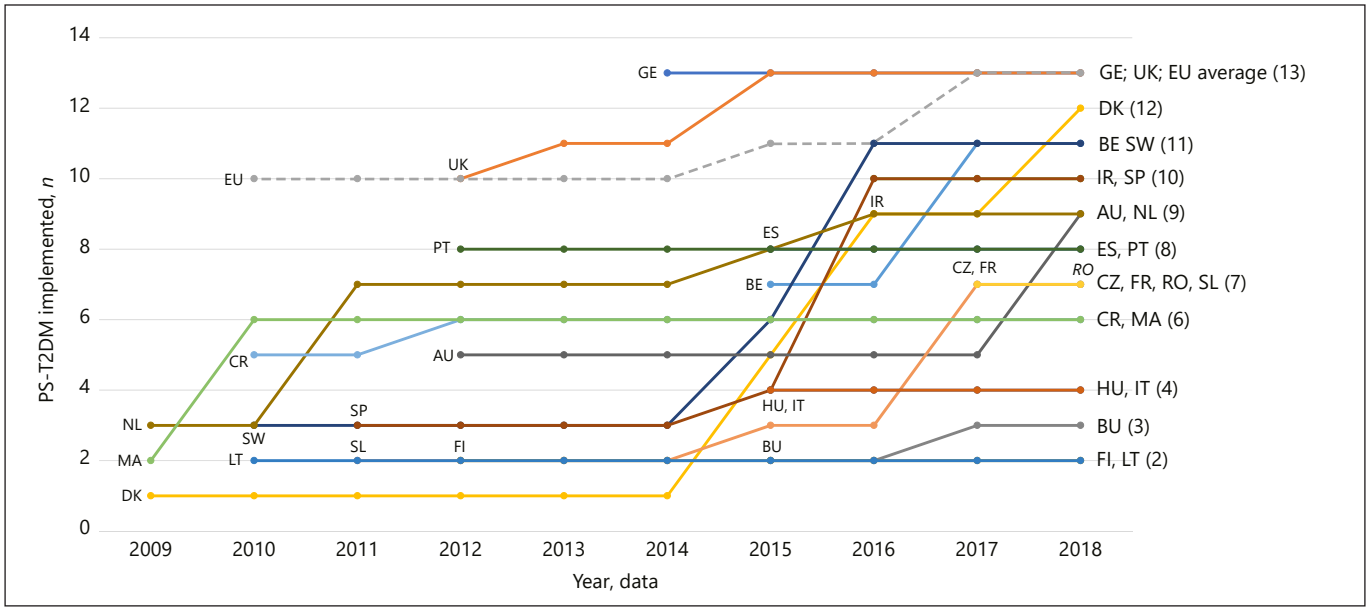


Fig. 6. PS-T2DM implemented in the EU22 case countries: by subtype (data 2008–2018). PS-T2DM, pharmacy services T2DM.

On the other hand, only 8 out of 28 countries have a multisectoral national operational, strategic, or action plan that integrates several NCDs and its associated risk factors. However, in 19 of the 28 countries, it was observed a multisectoral national policy cluster, as well as strategies or action plans, to discourage unhealthy diets and/or promote physical activity. Belgium is again relevant. Latvia as well due to its records of the existence of guidelines for



Color version available online

Fig. 7. Evolution of the implementation of 13 PS-T2DM-oriented in each of EU22 countries: quantitative approach (data 2009–2018) 22 EU countries – GE: Germany, UK: United Kingdom, DK: Denmark, SW: Sweden, BE: Belgium, IR: Ireland, SP: Spain, AU: Austria, NL: The Netherlands, SL: Slovenia, MA: Malta, ES: Estonia, PT: Portugal, FR: France, RO: Romania, CZ: C. Republic, CR: Croatia, HU: Hungary, IT: Italy, BU: Bulgaria, FI: Finland and LT: Lithuania.

T2DM, and its regulation. In addition, in most countries (23 of 28), there were evidence-based national guidelines/protocols/standards for the management of NCDs through a primary care approach. In this case, Latvia and Romania, which have records of the existence of guidelines for T2DM, and their regulation, are relevant. Regarding vigilance and monitoring programs for NCDs that allow the communication of information on the overall NCDs' goals, it is recorded in 7 of the 28 countries, and Latvia is distinguished for the same reasons as mentioned above.

Discussion

Few studies address a concrete interaction between community pharmaceutical services and people with T2DM's health outcome sets monitoring during the study period (2008–2018). The found evidence demonstrated both the benefit of DM management by CPH through these pharmacy services and the success of their implementation in terms of adherence to treatment and correct use of medicines [3, 26–28]. Thus, the application of this close and permanent set of T2DM care services has become an essential model of qualified pharmacy practice for policy considerations [1, 4, 5, 28]. The lack of evidence about the EU as a whole implies the detailed study of each country. Therefore, the European Union's average was not a comparative factor, but only one of the observational units recorded the results in tables and figures.

Community Pharmaceutical Care Services for DM: Operational and Human Resources

The emergence of a new set of pharmacy services has emerged over the last decade to harmonize the different interpretations of its definition – the disease-oriented pharmaceutical care services (e.g., DM treatment, hypertension treatment, and treatment of asthma). Nevertheless, it has raised some questions within European health systems as to whether or not it is ethically permissible to limit pharmaceutical care only to groups of people with specific diseases, as DM [2, 13]. However, studies report that, in the case of DM/T2DM, this care is undisputed and fundamental because it is a disease/set of diseases that needs a specific, close, and permanent assistance to provide: the diagnosis, even early (e.g., undiagnosed cases detection); the optimization of therapy; and monitoring/measurement of biochemical parameters. Moreover, EU community pharmacies have shown that they have invested in implementing these care services to assist health needs like DM [23, 29–31]. Also, CPH is responsible for

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Table 5. Data of legislation, regulation status and clinical guidelines related to DM in each of 28EU case countries (data 2013–2014)

28EU Countries	Existence of an entity linked to the Ministry of Health, or equivalent responsible for NCDs [91]	Existence of a multisectoral national operational policy, strategy or action plan that integrates several NCDs and shared risk factor [91]	Existence of a multisectoral national operational policy, strategy or action plan that integrates several NCDs and shared risk factors [91]	Existence of an operational policy, strategy or plan of action to reduce unhealthy diets and/or promote healthy diets [91]	Existence of evidence-based national guidelines/protocols/ standards for the management of key NCDs through a primary care approach [91]	Existence of a surveillance and monitoring system for NCDs to allow the communication of information on the nine global goals of DNT [91]	Existence of Guidelines for DM [50, 93]
Germany	Yes	No	Yes	Yes	Yes	No	It does not mention specificity for DM or T2DM
Austria	No	No	No	Yes	No	No	T2DM; Regulated; They are not mandatory, they serve only as a basis for decision-making; It does not mention the involvement of pharmacists
Belgium	Yes	No	Yes	Yes	No data	No	T2DM; Adopted from international guidelines; They serve for prevention and treatment; Can operate at local, regional or national level; It does not mention the involvement of pharmacists
Bulgaria	No data	No	No	No	Yes	No	DM; Regulated; Existence of an algorithm that physicians are required to follow; It does not mention the involvement of pharmacists
Croatia	Yes	No	No	Yes	No	No	It does not mention specificity for DM or T2DM
Cyprus	Yes	No data	No data	Yes	No data	No	DM; It does not mention the involvement of pharmacists
Denmark	Yes	No	Yes	Yes	Yes	No	It does not mention specificity for DM or T2DM
Slovakia	No	No	No	Yes	Yes	No	It does not mention specificity for DM or T2DM
Slovenia	Yes	No	No	No	Yes	Yes	DM; Not regulated; regularly use international guidelines; 2003; It does not mention the involvement of pharmacists
Spain	No	Yes	Yes	Yes	Yes	No data	DM; regulated; 2006; It does not mention the involvement of pharmacists
Estonia	Yes	No	Yes	Yes	Yes	No	It mentions specificity for DM or T2DM
Finland	Yes	Yes	Yes	Yes	Yes	No	DM; Not regulated; They aim to improve the quality of care and reduce the different methodologies in the practice of care; DM management; Some for prevention; All for treatment; It does not mention the involvement of pharmacists
France	Yes	No	Yes	Yes	No data	No	It does not mention specificity for DM or T2DM
Greece	Yes	No	Yes	Yes	No data	No	DM; To be started being more based on recommendations; It does not mention the involvement of pharmacists
Hungary	Yes	No data	No	Yes	No	Yes	DM; Not regulated; They emerged in 2011; Non-mandatory use; It does not mention the involvement of pharmacists
Irlanda	Yes	No	Yes	Yes	No	No	DM; Not regulated; There are health care programs; It does not mention the involvement of pharmacists
Italy	Yes	Yes	Yes	Yes	No	Yes	DM; Regulated; It does not mention the involvement of pharmacists
Latvia	Yes	No	Yes	Yes	Yes	Yes	T2DM; Regulated; It emerged in 2010; It does not mention the involvement of pharmacists
Lithuania	Yes	Yes	Yes	Yes	Yes	Yes	DM; Regulated; It emerged in 2008; Used for diagnosis and treatment; It mentions the involvement of pharmacists
Luxembourg	No	No	Yes	Yes	Yes	No	It does not mention specificity for DM or T2DM
Malta	Yes	Yes	Yes	Yes	No	No	It does not mention specificity for DM or T2DM
Netherlands	Yes	No	No	No	Yes	Yes	It does not mention specificity for DM or T2DM

Table 5 (continued)

28EU Countries	Existence of an entity linked to the Ministry of Health, or equivalent responsible for NCDs [91]	Existence of a multisectoral national operational policy, strategy or action plan that integrates several NCDs and shared risk factor [91]	Existence of a multisectoral national operational policy, strategy or action plan that integrates several NCDs and shared risk factors [91]	Existence of an operational policy, strategy or plan of action to reduce unhealthy diets and/or promote healthy diets [91]	Existence of evidence-based national guidelines/protocols/ standards for the management of key NCDs through a primary care approach [91]	Existence of a surveillance and monitoring system for NCDs to allow the communication of information on the nine global goals of DNT [91]	Existence of Guidelines for DM [50, 93]
Poland	No	No	Yes	Yes	No data	Yes	DM; Not regulated; treatment guidelines are formulated by pharmacists (The National Pharmaceutical Policy, 2003); It mentions the involvement of pharmacists
Portugal	Yes	Yes	Yes	Yes	Yes	No	DM; Regulated; Mandatory use; It does not mention the involvement of pharmacists
Czern Republic	Yes	Yes	Yes	Yes	Yes	No	It does not mention specificity for DM or T2DM
United Kingdom	Yes	Yes	Yes	Yes	Yes	No	It does not mention specificity for DM or T2DM
Romania	No	No	No	Yes	Yes	No	T2DM; Regulated; It does not mention the involvement of pharmacists
Sweden	Yes	No	Yes	Yes	Yes	No	It does not mention specificity for DM or T2DM

DM, diabetes mellitus; EU, European Union; T2DM, type 2 DM.

providing this care. PGEU recognized CHP as the responsible person to prevent the reduction of the high risk of nonadherence, especially before and during the start of a new pharmacological treatment. Also, the WHO recognizes his role in pharmacotherapeutic's patient follow-up in cooperation with GP and nurse [17, 25, 32–47].

Community Pharmaceutical Care Services for DM: Legal Resources (Guidelines)

In order to support human and operational resources, the implementation of pharmaceutical care for DM/T2DM depends on legal resources. Some studies and Table 5 show not only the lack of evidence about the existence of guidelines, goals, and strategies for the practice of this care in community pharmacy but also in the primary care field, in general. Moreover, this is important for this discussion, because an effective response by a health system to health needs, considering the predictions of an increased disease burden, requires 2 essential tools: health planning and a robust multifactorial resource structure. In other words, these results led us to conclude that the failure of health systems to solve public severe health problems like DM is not only due to erroneous strategies for the development and implementation of primary health care services but also to planning failures. We found that health goals and strategies varied from country to country, meaning that some countries choose to develop independent policies or strategic plans, others include DM in an integrated NCDs' policy, and other regions choose both.

Community Pharmaceutical Care Services for DM: Implementation in Each EU Country

Only 16 of the EU28 countries implemented the 2 categories of PS-T2DM (PS-DT2DM and PS-IT2DM), and 22 of the EU28 countries implemented 1 subtype of PS-T2DM, at least. That is, all countries have implemented pharmaceutical care for DM in their community pharmacies, although in a service (e.g., medication review type 1) that can be used for other diseases (chronic or acute). Also, it is essential to note that the PS-DT2DM services are implemented in more than half of the countries, and the number of acceding countries has increased over time in the period of study (2008–2018) (Tables 2–4). Furthermore, it could be a future trend of pharmaceutical patient care upgrading in terms of number and quality of the services provided in community pharmacies. It occurs because these services are included in the set of services classified in PGEU as "advanced services" [17]. It signifies an extension and enhancement of primary health care provided for T2DM in community set-

tings. We also observed an increase in the number of countries that implemented PS-T2DM over time, mainly between 2009 and 2010. Germany and the United Kingdom were the only countries that match the EU average, with the implementation of the total of selected PS-T2DM (13 in total) for the study. However, no evidence was found for PS-T2DM guidelines in these countries. In its turn, Lithuania had the lowest number of PS-T2DM implemented. However, it was the only country whose participation of pharmacists is mentioned in the guidelines for the diagnosis and treatment of T2DM besides Poland and Spain, both for DM.

There is a collective political and legal will on some EU countries to develop and implement adequate resources (human, operational, financial, and legal) for the provision of pharmaceutical services in community pharmacies to reduce the disease burden at local, regional, and global level. The contribution for the improvement of the accessibility, proximity, and equity of primary care provided in community pharmacies throughout the EU28 comes up with a new generation of T2DM primary care in community pharmacies – the professional PS-T2DM-oriented. This promising strategy for improvement of health outcome sets showed that they could have a consistent impact with some objectives of universal health coverage for DM/T2DM eradication. This fact was shown through the increase in specificity and number of PS-T2DM that were implemented, developed, and provided in community pharmacies since 2010. Nevertheless, T2DM has prevailed in the last decade at the regional level (EU28), so it is still insufficient to cover health needs related to this disease. So, it is necessary to develop new health policies that contribute to: expand the operational and legal structures of pharmacy services; to include community pharmacy as a mandatory element in primary care; to create an effective connection between the GP/nurse and the patient to perform the primary diagnosis with or without subsequent screening and pharmacotherapeutic follow-up over time; and to promote self-management of health as a way to involve the patient, making him responsible for the evolution of disease. Also, we need further studies to assess the impact of this new generation of pharmacy services on the global burden of this disease and to analyze the feasibility of developing uniformed PS-T2DM protocols/guidelines in harmony with the health care structure of each EU country. In Sweden, for example, health policies are highly focused on health determinants such as social and physical environment of the individual; whereas in The Netherlands and Denmark, priority is given to risk factors such as tobacco and alcohol and serious diseases such as DM and cardiovascular disease [5, 10, 11, 48, 49]. These two countries did not show evidence on the existence of official pharmaceutical care guidelines for T2DM and PS-T2DM, but almost all PS-DT2DM were implemented. Furthermore, here emerges the question, "How is pharmaceutical care implemented without legal support?" [23, 48, 50]. This fact should be part of the future evidence and put in practice by health systems.

Limitations of the Study

The selected studies on the supply of pharmacy services for DM in the EU28 countries between 2008 and 2018 were heterogeneous in several aspects, such as target groups/age groups, health care providers (pharmacists, nurses, and other healthcare providers), disease or target disorder considered in the study, as well as means/strategies to evaluate outcomes and their approach. Also, the studies have shown to be unclear in terms of the organizational and operational strategy of implementing PS (of methodology/protocol/practitioners) and their adaptation to individuals or populations. Besides, the study found that the structure of these PS varies according to the legislation of each health system with regard to community pharmacy, pharmacist, and pharmaceutical care provision. Also, the type of DM of the most of studies explicitly referred to a type of DM, but somewhat generalized to the designation of "diabetes mellitus" or "diabetes." This is one of the main limitations in the selection of study materials, and it implied that the analysis had to be reorganized, in studies with information on the new categories PS-DT2DM and PS-IT2DM.

Conclusions

Type 2 diabetes mellitus implies multimorbidity and polypharmacy, so people with this disease or at risk to develop it (prediabetes) should have a close, frequent, and rigorous monitoring of their health outcomes sets (e.g., parameter values and treatment adherence). EU28 community pharmacy services for T2DM have assumed this role in primary care networks over the last decade. This pharmaceutical patient care has been provided by the CPH. He manages the disease at a core, basic and advanced level. That is, CHP performs the diagnosis, the patient referral to the GP, and the pharmacotherapeutic follow-up at the community pharmacy. This is realized in the form of 13 subtypes of T2DM-oriented pharmacy

services: 2 of them specific for T2DM and 11 for T2DM's risk factors. The present study concluded that the implementation of this pharmaceutical care upgrading was increasing over the period of the study (2008–2018) in 22EU countries, at least. In addition, more evidence was found about these 13 subtypes in the United Kingdom, besides it being the country which gave more recognition to the CPH and pharmacy for the provision of advanced care services ("diabetes management"). However, most EU 28 countries do not have legal support (guidelines, targets, and strategies), and this can condition effective pharmaceutical assistance collaboration in the primary care network.

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Author Contributions

The first author was responsible for all the research and the remaining authors for the review.

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