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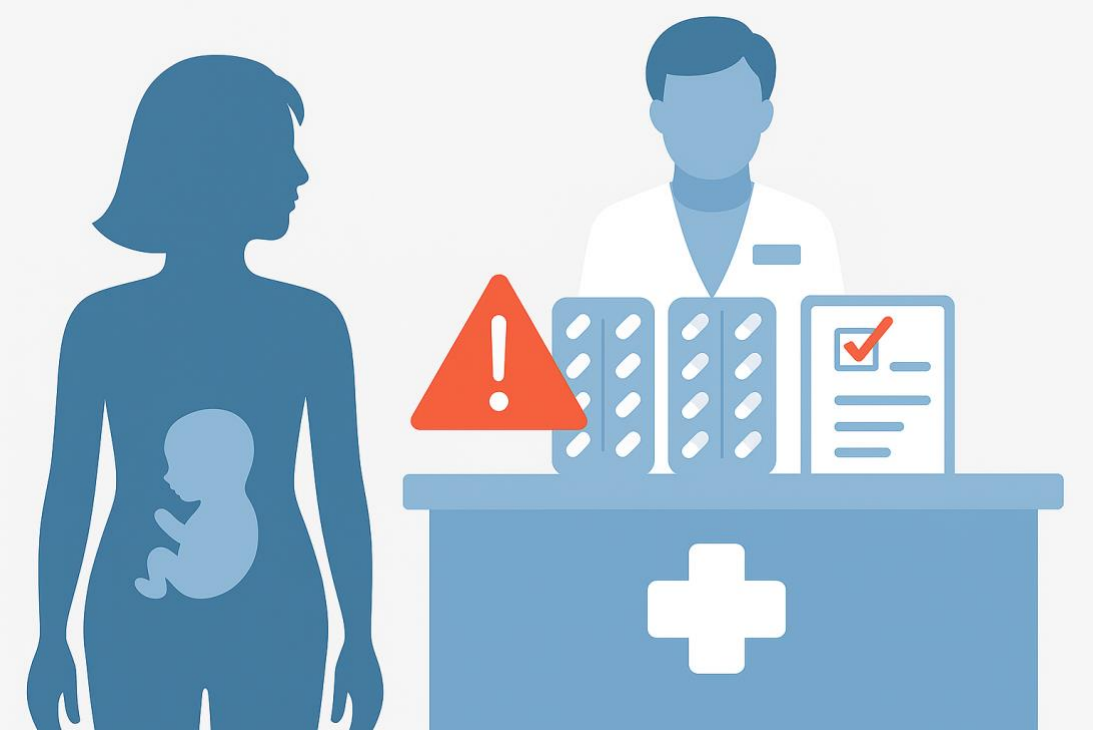
Besvarelsesinformationer

Titel: Bevidsthed om og overholdelse af graviditetsforebyggelsesprogrammet (PPP) blandt farmakonomer ved udlevering af orale retinoider og valproat i Danmark - Et kvantitativt studie
Titel, engelsk: The Awareness of and Adherence to the Pregnancy Programme (PPP) among Pharmacy Technicians for dispensing Oral Retinoids and Valproate in Denmark - A quantitative study
Tro og love-erklæring: Ja
Indeholder besvarelsen fortroligt materiale: Nej

UNIVERSITY OF COPENHAGEN
FACULTY OF HEALTH AND MEDICAL SCIENCES
DEPARTMENT OF PHARMACY

The Awareness of and Adherence to the Pregnancy Prevention Programme (PPP) among Pharmacy Technicians for dispensing Oral Retinoids and Valproate in Denmark – A quantitative study



Master Thesis

Jasmin Hosseinzadeh (tzf440)

Supervisor: Ramune Jacobsen

Submitted June 14th, 2025

Preface

This Master thesis project was carried out at the University of Copenhagen from February 1st to June 14th, 2025, and accounts for 30 ECTS credits in total.

This thesis is structured into three independent parts: Part I, Part II, and Part III.

- **Part I** is the core of the thesis. It represents a quantitative scientific article that assesses Danish pharmacy technicians' awareness of and adherence to the Pregnancy Prevention Programme (PPP) for dispensing oral retinoids and valproate in community pharmacies.
- **Part II** is a qualitative report exploring the pharmaceutical, clinical, regulatory and social aspects of valproate and oral retinoids, including findings from the European Medicinal Agency (EMA).
- **Part III** is a systematic literature review focusing on pharmacy technicians' knowledge, attitudes, and practices regarding prescription medicines in community pharmacies worldwide.

Each part is written as an independent report. Part II and III are supplementary papers that support and complement the main thesis in Part I.

I would like to thank my supervisor, Ramune Jacobsen from the Social and Clinical Pharmacy Research Group, for her expert guidance, support and valuable input throughout this project. I also want to thank Kristin Rose Primdahl for her help in connecting this project with the Network for the Development of Pharmacy Practice (Netværk for Udvikling af Apotekspraksis, NUAP). Her initiative made it possible to distribute the questionnaires nationwide through project-affiliated community pharmacies, which greatly improved the study's reach and participant recruitment.
Lastly, I want to express my heartfelt gratitude to my family and friends for their constant support and encouragement throughout this project.

University of Copenhagen, Faculty of Health and Medical Sciences Copenhagen, June 14th, 2025

Jasmin Hosseinzadeh

Resume – Part I

Formål: Formålet med denne undersøgelse var at vurdere danske farmakonomers viden, opmærksomhed og efterlevelse af Det Europæiske Lægemiddelagenturs (EMA) graviditetsforebyggelsesprogram (PPP) for valproat og orale retinoider. Undersøgelsen belyste også deres brug af informationsmateriale samt rådgivningspraksis i forbindelse med udlevering af disse lægemidler til kvinder i den fødedygtige alder på danske apoteker.

Metoder: Undersøgelsen blev gennemført som en kvantitativ, online tværsnitsundersøgelse i april 2025 med fokus på danske farmakonomers viden, opmærksomhed og praksis i relation til EMA's graviditetsforbyggende tiltag (PPP) for valproat og orale retinoider. Der blev udviklet to separate spørgeskemaer med 22 spørgsmål hver: ét med fokus på valproat og ét på orale retinoider. Spørgsmålene var inddelt i tre temaer: demografiske oplysninger, faglig praksis og erfaring, samt håndtering, rådgivning og kendskab til PPP-materiale ved udlevering af de pågældende lægemidler til kvinder i den fødedygtige alder.
Respondenterne blev rekrutteret via sociale medier, faglige netværk og direkte kontakt til danske apoteker. Undersøgelsen inkluderede både farmakonomer og farmakonomstuderende. Spørgeskemaerne blev distribueret via distribueret via SurveyXact, og data blev analyseret med deskriptiv statistik i Microsoft Excel (version 16.89.1).

Resultater: I alt gennemførte 80 respondenter spørgeskemaet om orale retinoider, og 41 gennemførte spørgeskemaet om valproat. Bevidstheden om den teratogene risiko var højere for orale retinoider end for valproat. 55% af deltagerne angav, at de havde været bekendt med risikoen ved orale retinoider i over 5 år, mens det kun gjaldt 26,8% for valproat. Anvendelsen af PPP-materiale var generelt begrænset for begge lægemidler, men advarselsmærkerater på medicinpakningen blev hyppigst benyttet. Rådgivningspraksis varierede betydeligt og forekom sjældnere i forbindelse med valproat sammenlignet med orale retinoider.

Konklusion: Undersøgelsen viser, at danske farmakonomer har varierende viden og en uensartet anvendelse af materiale og rådgivning relateret til PPP for valproat og orale retinoider. Resultaterne peger på et behov for målrettet efteruddannelse og tydeligere faglige retningslinjer. Dette kan styrke farmakonomernes kompetencer og bidrage til en mere sikker anvendelse af teratogene lægemidler blandt kvinder i den fødedygtige alder.

Resume – Part II

Formål: Formålet med denne opgave var at foretage en kritisk vurdering af de teratogene risici forbundet med valproat, isotretinoin og acetretin, samt at undersøge, i hvilken grad de nuværende regulatoriske strategier – særligt graviditetsforebyggende programmer (Pregnancy Prevention Programme, PPP) – har været effektive til at minimere fosterudsættelse i Europa. Opgaven havde til hensigt at:

- Opsummere den aktuelle videnskabelige viden om fosterskader relateret til disse lægemidler, baseret på observationsstudier, kliniske indberetninger og erfaringer fra bivirkningsovervågning (pharmacovigilance).
- Undersøge implementeringen, efterlevelsen og de praktiske udfordringer ved PPP'er i forskellige europæiske sundhedssystemer.
- Analysere faktorer, der påvirker overholdelsen af PPP'er, herunder lægers adfærd, patienters bevidsthed, alder, socioøkonomisk status og strukturelle forhold i sundhedssystemet.
- Identificere mangler i klinisk praksis og foreslå forbedringer inden for patientuddannelse, sundhedsprofessionelles træning og håndhævelse af gældende politikker.

Denne opgave er udarbejdet med det formål at danne et solidt grundlag for og understøtte den videnskabelige artikel præsenteret i del I.

Resume – Part III

Formål: Formålet med dette studie var at gennemføre et systematisk litteraturstudie med henblik på at identificere, undersøge og vurdere eksisterende forskning om farmakonomers viden og holdninger til receptpligtig medicin i apotekssektoren på globalt plan.

Metoder: Der blev foretaget en systematisk litteratursøgning i PubMed for studier publiceret i perioden 2017 til 2025. Inklusionskriterierne omfattede engelske kvantitative tværsnitsstudier og kvalitative studier, der fokuserede på farmakonomers viden og holdninger til receptpligtig medicin i apotekspraksis verden over.

Resultater: Litteratursøgningen identificerede 10 artikler fra ni lande fordelt på fire globale regioner: Europa, Afrika, Asien og Sydamerika. Studierne giver samlet set et bredt indblik i farmakonomers viden, holdninger og praksis i relation til receptmedicin. Centrale temaer inkluderede betydningen af uddannelse, oplæring, lovgivningsmæssige rammer og arbejdskultur. Der blev observeret markante regionale forskelle, hvor studier fra vestlige lande generelt rapporterede højere vidensniveauer sammenlignet med studier fra Afrika og Asien.

Konklusion: Det systematiske litteraturstudie fremhævede centrale faktorer, der påvirker farmakonomers viden og holdninger til receptpligtig medicin i apotekssektoren globalt. Forståelsen af disse faktorer giver sundhedsorganisationer mulighed for at udvikle og implementere strategier, der forbedrer farmakonomers viden, holdninger og praksis (KAP). Der er behov for yderligere forskning for at udvikle evidensbaserede interventioner, der kan styrke KAP, fremme fastholdelse i faget og bidrage til bedre sundhedsresultater på verdensplan.

Abbreviations:

CHMP: Committee for Medicinal Products for Human Use

CMDh: Coordination Group for Mutual Recognition and Decentralised Procedures – Human

DHCP: Direct Healthcare Professional Communication

EMA: European Medicines Agency

EU: European Union

GP(s): General Practitioner(s)

HCP: Healthcare Professional

KAP: Knowledge, Attitude, Practice

MAH(s): Marketing Authorisation Holder(s)

NMRA: National Medicines Regulatory Authority

PPP: Pregnancy Prevention Programme

PRAC: Pharmacovigilance Risk Assessment Committee

Table of content

Part I

The Awareness of and Adherence to the Pregnancy Prevention Programme (PPP) among Pharmacy Technicians for dispensing Oral Retinoids and Valproate in Denmark:

A quantitative cross-sectional study

Scientific Article

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Abstract

Background: Valproate and oral retinoids are effective therapeutic agents but pose serious teratogenic risks when used by women of childbearing potential. To mitigate these risks, the European Medicines Agency (EMA) introduced a revised Pregnancy Prevention Programme (PPP) in 2018. While pharmacists' awareness of and adherence to PPP for valproate and oral retinoids have been studied, little is known about how pharmacy technicians engage with these measures.

Objective: This study aimed to assess Danish pharmacy technician's knowledge, awareness, and adherence to the PPP for valproate and oral retinoids, including their use of educational materials and counseling practices in community pharmacies.

Methods: Two descriptive, cross-sectional surveys were conducted using convenience, purposive, and random sampling strategies. Participants were recruited through Facebook groups, professional networks, and direct contact with pharmacies. Pharmacy technicians were asked about their knowledge of teratogenic risks, frequency of dispensing and counseling, and familiarity with PPP materials. Data were analyzed using descriptive statistics in Microsoft Excel.

Results: A total of 80 respondents completed the oral retinoids survey and 41 completed the valproate survey. Awareness of teratogenic risks was higher for oral retinoids, with 55% of technicians reporting they had known about the risks for over five years, compared to 26.8% for valproate. Use of PPP materials was generally limited across both drug types, though warning labels were the most frequently used tools. Counseling practices varied and were notably less frequent for valproate. A significant number of respondents expressed willingness to incorporate PPP tools into future practice.

Conclusion: Danish pharmacy technicians demonstrated varying levels of knowledge and inconsistent use of PPP materials and counseling practices. There is a need for targeted training, and clearer professional guidance may serve as a valuable platform to strengthen technician's competencies in supporting the safe use of valproate and oral retinoids.

1. Introduction

Medicinal products such as valproate and oral retinoids are widely used across Europe for the treatment of neurological and dermatological conditions. Valproate is primarily prescribed for epilepsy and bipolar disorder, while oral retinoids – such as isotretinoin, acitretin, and alitretinoin – are used for severe dermatologic diseases including acne and psoriasis (1), (2). Despite their therapeutic efficacy, both drug classes are associated with significant teratogenic risks. Exposure during pregnancy may lead to congenital malformations and long-term neurodevelopmental disorders, which has prompted the introduction of regulatory risk minimisation strategies.

In response to ongoing concerns regarding pregnancy exposure, the European Medicines Agency (EMA) implemented a revised Pregnancy Prevention Programme (PPP) in 2018 (3), (4). This programme aims to ensure that women of childbearing potential are adequately informed and protected. The PPP includes educational materials, such as healthcare professional (HCP) guides, patient reminder cards, warning labels, and formal risks acknowledgment procedures. However, studies have shown that awareness and adherence to these measures among both healthcare professionals and patients remain limited, and pregnancies exposed to teratogenic substances still occur (5).

Community pharmacy professionals – particularly pharmacy technicians in Denmark – play a central role in the dispensing and counseling of these medicines. Yet, limited research has explored their awareness, knowledge, and practices related to the PPP in the context of their daily work. Most studies focus primarily on pharmacists, with pharmacy technicians only occasionally included under broader terms such as “pharmacy staff” or “pharmacy professionals”, making it difficult to draw conclusions specific to technicians (6). Understanding how pharmacy technicians engage with PPP measures is critical for improving the safe use of these medications and enhancing reproductive health protection.

This study therefore aimed to assess Danish pharmacy technician’s knowledge, awareness, and practices concerning the PPP for valproate and oral retinoids. Using two descriptive surveys, the study investigates the extent to which pharmacy technicians are familiar with teratogenic risks, utilise PPP materials, and provide counselling related to contraception and pregnancy prevention.

2. Aim

The study aimed to achieve several objectives:

1. Assess pharmacy technicians' awareness and knowledge of the teratogenic risks associated with valproate and oral retinoids.
2. Investigate the frequency and consistency of counseling practices provided by pharmacy technicians when dispensing valproate and oral retinoids.
3. Examine the use, familiarity, and intended future use of Pregnancy Prevention Programme (PPP) educational materials among pharmacy technicians.
4. Identify gaps and differences in awareness, adherence, and counseling practices between the two medicines (valproate and oral retinoids).

3. Methods

3.1 Study design

Two descriptive surveys were conducted to assess Danish pharmacy technician's knowledge, attitudes, and practices regarding valproate and oral retinoids for women of reproductive age. The surveys explored how familiar pharmacy technicians were with the pregnancy-related risks associated with these medications. The questionnaires used in this study were adapted from a version originally developed and tested in an international project targeting pharmacists. For this study, the content was modified to specifically address pharmacy technicians. Questions were organized into four domains: demographic information, knowledge of teratogenicity, use of Pregnancy Prevention Programme (PPP) materials, and counseling practices.

Participants were asked about their age, gender, professional role, and years of experience in community pharmacy. Questions also covered their knowledge of the teratogenic risks associated with valproate and oral retinoids – when they first became aware of these risks and through which sources. Additional questions assessed their familiarity and engagement with PPP tolls, such as the healthcare professional (HCP) guide, warning signs on outer packaging, patient reminder cards, checklists, and Direct Healthcare Professional Communication (DHPC) letters.

The survey also examined how frequently participants dispensed valproate and oral retinoids to women of reproductive age, as well as how often they provided counseling related to contraception, pregnancy testing and situations where pregnancy might be suspected.

Finally, the surveys included questions on perceived changes in counseling practices since the implementation of the PPP in 2018, along with perceptions of how counseling and PPP material usage have evolved in daily pharmacy practice.

The questionnaires were designed in Danish and pilot-tested with a sample of practicing pharmacy technicians to ensure clarity, comprehension, and content validity. Final adjustments were then made before launching the surveys digitally via the online survey platform, SurveyXact.

3.2 Sampling and recruitment

A combination of three sampling strategies was used to recruit participants: convenience sampling, purposive sampling, and random sampling.

Convenience sampling was carried out through posts and reminders in large, public Facebook groups relevant to Danish pharmacy technicians, including *"Farmakonomer på privat apotek"*, *"Farmakonom",* and *"Farmakonomer alt mellem himmel og jord*", which together included thousands of members.

Purposive sampling targeted a closed professional network associated with the NUAP project. The questionnaires were shared via email and through a private Facebook group consisting of both pharmacists and pharmacy technicians.

For random sampling, every second pharmacy listed in a publicly available national registry was selected. Invitations were sent to their official email addresses, followed by one reminder. In total, emails were sent to 246 addresses.

This combined approach ensured broad outreach across different professional settings and geographic regions.

Recruitment took place from April to May 2025, with one follow-up reminder sent during the data collection period to help increase the response rate.

3.3 Data analysis

All data were analyzed using Microsoft Excel (version 16.89.1). Descriptive statistics were used to summarize respondents' characteristics and their answers to the survey questions. Frequencies and percentages were calculated for categorical variables, such as gender, professional experience, and use of PPP materials.

For continuous variables, including age, the mean, standard deviation (SD), and range were reported. No interferential statistical analyses were conducted, as the aim of the study was to provide a descriptive overview of pharmacy technician's knowledge, use of educational materials, and counseling practices related to valproate and oral retinoids.

4. Results

4.1 Participant overview and response flow

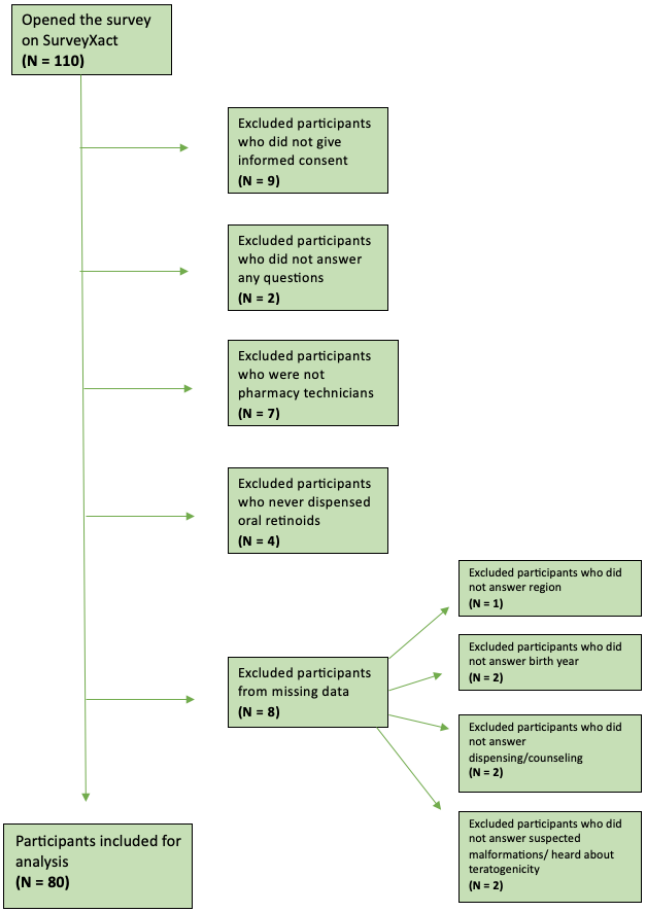

Figure 1: An inclusion/exclusion flowchart illustrating how many participated in the oral retinoid survey.

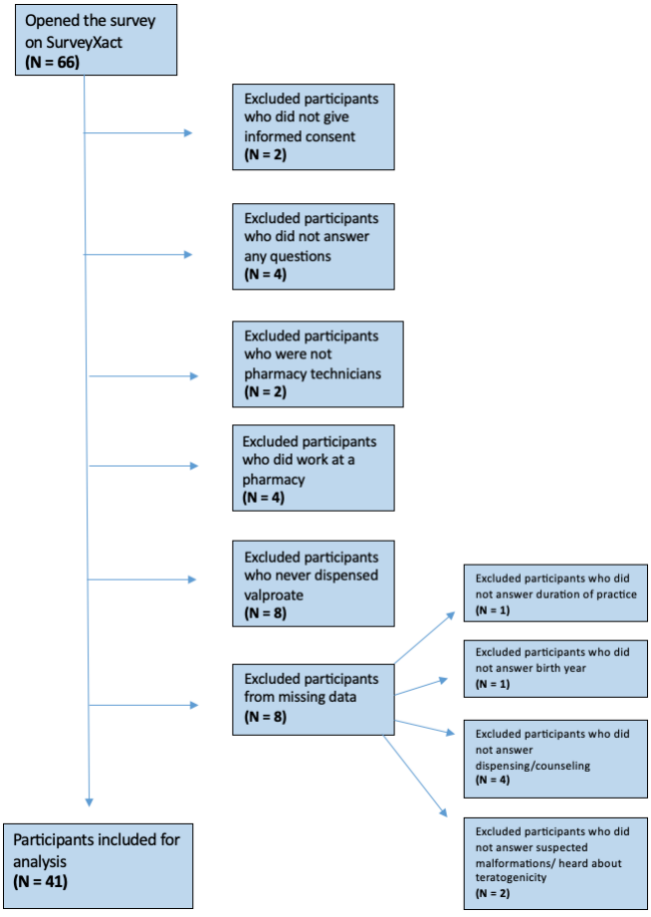

Figure 2: An inclusion/exclusion flowchart illustrating how many participated in the valproate survey.

For the oral retinoids survey, 110 individuals accessed the questionnaire via SurveyXact. Of these, 30 participants were excluded for various reasons: not providing informed consent, not answering any questions, not being pharmacy technicians, not having dispensed oral retinoids, or missing key information such region, birth year, counseling practices, or awareness of teratogenicity. After these exclusions, 80 pharmacy technicians were included in the final analysis (see Figure 1).

In the valproate survey, 66 individuals opened the questionnaire. A total of 25 responses were excluded due to lack of consent, unanswered questions, ineligibility (e.g. not being a pharmacy technician or not working in a pharmacy), not having dispensed valproate, or missing data such as years of practice, birth year, counseling practices, or awareness of teratogenic risks. This resulted in a final analytical sample of 41 pharmacy technician respondents (see Figure 2).

4.2 Demographic and professional characteristics: Valproate and Oral retinoids

Table 1: The demographic characteristics of the respondents and frequency in dispensing and counseling both valproate and oral retinoids for women of reproductive age.

		Valproate, N = 41	**Oral retinoids, N = 80**
Characteristics			
Age	Mean (SD) Median (IQR) Range of age	33.1 (9.21) 29 (26.5-41.0) 21-58	37.3 (12.16) 33.00 (28.00-46.75) 19-69
Gender N (%)	Female Male Rather not say	2 (4.9%) 37 (90.2%) 2 (4.9%)	76 (95.0%) 2 (2.5%) 2 (2.5%)
Professional category, N (%)	Pharmacy technician Pharmacy technician student	33 (80.5%) 8 (19.5%)	68 (85.0%) 12 (15.0%)
Practice (N%)			
Period practicing current profession, N (%)	0-5 years 6-10 years 11-20 years Over 20 years	25 (61.0%) 7 (17.1%) 3 (7.3%) 6 (14.7%)	43 (53.8%) 13 (16.3%) 15 (18.8%) 9 (11.3%)
Frequency of dispensing oral retinoids for women of reproductive age, N (%)	Once a week or more A few times a month Once a month or less frequently	3 (7.3%) 10 (24.4%) 28 (68.3%)	22 (27.5%) 35 (43.8%) 23 (28.7%)
Frequency of providing information to women of	Once a week or more A few times a month	0 (0.0%) 4 (9.8%)	21 (26.3%) 33 (41.3%)

reproductive age about oral retinoids, N (%)	Once a month or less frequently	31 (75.6%)	25 (31.3%)
	Never	6 (14.6%)	1 (1.3%)

Valproate

A total of 41 pharmacy technicians completed the valproate survey. The mean age of respondents was 33.1 years (SD = 9.21), with an age range of 21 to 58 years. The majority were male (n = 37, 90.2%), while 2 participants (4.9%) were female and 2 (4.9%) preferred not to disclose their gender. Most respondents (80.5%) were certified pharmacy technicians, and 19.5% were students in training.

Regarding professional experience, 61.0% had worked in the profession for 0-5 years, 17.1% for 6-10 years, and 14.7% had more than 20 years of experience.

In terms of dispensing frequency, 7.3% of respondents reported dispensing valproate once a week or more, 24.4% did so a few times per month, and the majority (68.3%) dispensed it once a month or less. Counseling frequency was generally low: 75.6% provided counseling once a month or less, 9.8% a few times per month, and none reported counseling weekly or more frequently. Notably, 14.6% stated they never provide counseling when dispensing valproate.

Oral retinoids

A total of 80 pharmacy technicians completed the oral retinoids survey. The mean age of participants was 37.3 years (SD = 12.16), with an age range of 19 to 69 years. The majority were female (n = 76, 95.0%), while 2 participants (2.5%) were male and 2 (2.5%) preferred not to disclose their gender. Most respondents (85.0%) were certified pharmacy technicians, and 15.0% being students.

Regarding professional experience, 53.8% has worked in the field for 0-5 years, 16.3% for 6-10 years, and 11.3% for more than 20 years.

In terms of dispensing frequency, 43.8% dispensed oral retinoids a few times per month, 28.7% once a month or less, and 27.5% once a week or more. Counseling frequency followed a similar pattern: 41.3% provided counseling a few times per month, 31.3% once a month or less, and 26.3%

once a week or more. Only 1.3% reported that they never provide counseling when dispensing oral retinoids.

Full demographic and professional characteristic for respondents of both surveys are presented in Table 1.

4.3 Awareness of teratogenic risks and information sources

Table 2: Pharmacy technicians' reported timeframe for first learning about teratogenic risks of valproate and oral retinoids, and their primary sources of information (Note: Participants could select more than once source of information).

	Valproate (N = 41)	**Oral retinoids (N = 80)**
Timeframe (N%)		
Within the last 2 years	6 (14.6%)	17 (21.3%)
Within the last 5 years	12 (29.3%)	17 (21.3%)
More than 5 years ago	11 (26.8%)	44 (55.0%)
Just know, when answering the questionnaire	12 (29.3%)	2 (2.5%)
Information source		
Health Authorities	4 (9.8%)	16 (20.0%)
Danish Medicines Agency	6 (14.6%)	20 (25%)
Professional Societies	2 (4.9%)	6 (7.5%)
Colleagues	9 (22.0%)	31 (38.8%)
Professional Journals	4 (9.8%)	4 (5.0%)
Manufacturers	6 (14.6%)	19 (23.8%)
Internet	3 (7.3%)	8 (10.0%)
Symposia/conferences	1 (2.4%)	0 (0.0%)
Academic/professional studies	18 (43.9%)	43 (53.8%)
Post-academic training	1 (2.4%)	4 (5.0%)
Other Sources	1 (2.4%)	8 (10.0%)

Valproate

Awareness of valproate's teratogenic risks varied among respondents (see Table 2). Notably, 29.3% reported that they became aware of the risks when completing the questionnaire, while

another 29.3% had learned about them within the past five years. A further 26.8% had known about the risks for more than five years.

The most cited source of information was academic or professional studies (43.9%). Other reported colleagues (22.0%), Danish Medicines Agency and Manufacturers (14.6%). Fewer respondents mentioned the internet (7.3%). A small proportion (2.4%) selected "Other sources".

Oral retinoids

Most respondents reported having been aware of the teratogenic risks associated with oral retinoids for some time (see Table 2). Over half (53.8%) indicated they had learned about the risks more than five years ago, while 21.3% had done so within the last five years. 2.5% became aware of the risks while completing the questionnaire.

Academic or professional studies were the most frequently reported source of information (53.8%), followed by colleagues (38.8%), Danish Medicines Agency (25.0%) and manufacturers (23.8%). Fewer respondents cited professional societies (7.5%) or professional journals (5.0%), while 10.0% selected the internet and "Other sources".

4.4 Use of educational materials, counseling practices, and reported changes after PPP implementation

Table 3: Pharmacy technicians' reported use of educational materials related to the Pregnancy Prevention Program (PPP) for valproate and oral retinoids, including current use, likelihood for future use, and awareness of specific tools (e.g. HCP guides, warning signs, DHPCs). Valproate: N = 31, Oral retinoids: N = 62

Use of educational materials	**Check list for pharmacy staff**	**HCP guide**	**Warning sign on the outer package**	**Patient reminder card**	**DHCP**
Yes (valproate)	1 (3.2%)	6 (19.4%)	1 (3.2%)	1 (3.2%)	1 (3.2%)
Yes (oral retinoids)	4 (6.5%)	3 (4.8%)	34 (54.0%)	1 (1.6%)	2 (3.2%)
Not sure/No (valproate)	30 (96.8%)	25 (80.6%)	30 (96.8%)	30 (96.8%)	30 (96.8%)
Not sure/No (oral retinoids)	58 (93.6%)	59 (95.2%)	29 (45.9%)	61 (98.4%)	60 (96.8%)

If no, likely to use in the future (valproate)	16 (51.6%)	20 (67.7%)	13 (41.9%)	12 (38.7%)	16 (51.6%)
If not, likely to use in the future (oral retinoids)	12 (19.4%)	14 (22.6%)	23 (36.5%)	12 (19.4%)	15 (24.2%)
If no, unlikely to use in the future (valproate)	5 (16.1%)	2 (6.5%)	8 (25.8%)	6 (19.4)	5 (16.1%)
If no, unlikely to use in the future (oral retinoids)	20 (32.3%)	23 (37.1%)	3 (4.8%)	25 (40.3%)	21 (33.9%)

4.4.1 Use of educational materials

Valproate

The use of Pregnancy Prevention Programme (PPP) educational materials related to valproate was limited among the respondents (see Table 3). Only one pharmacy technician (3.2%) reported using each of the specific materials, including checklists for pharmacy staff, patient reminder cards, and Direct Healthcare Professional Communications (DHCP). The most frequently acknowledged material was the healthcare professional (HCP) guide, used by six respondents (19.4%).

Among those not currently using PPP materials, many expressed a willingness to use them in the future – especially for the HCP guide (67.7%), as well as the checklist and DHCP (51.6%). However, some respondents indicated they were unlikely to use certain tools in the future practice, particularly the warning sign on outer package (25.8%) and patient reminder cards (19.4%),

Oral retinoids

Use of PPP materials for oral retinoids was similarly limited (see Table 3). Out of 62 respondents, 3-4 individuals (4.8%-6.5%) reported using specific tools such as check list for pharmacy staff and HCP guides. The most widely recognized material was the warning sign on the outer packaging,

with 34 respondents (54.0%) indicating awareness. The least reported material was the patient reminder card acknowledged by one pharmacy technician (1.6%).

The intention to use PPP materials in the future was relatively high, particularly for the warning label on the outer packaging (36.5%) and the DCHP (24.2%). However, a notable proportion of respondents remained unsure or expressed reluctance to use some of the materials. This included the patient reminder card (40.3%), HCP guide (37.1%), DHCP (33.9%), and staff checklist (32.3%).

4.4.2 Dispensing and counseling practices

Table 4: Frequency of counseling practices reported by pharmacy technicians when dispensing valproate (N = 29) and oral retinoids (N = 58) to women of reproductive age.

Practices while dispensing	Always/often	Never/seldom
Inform about effective contraception (valproate)	13 (44.8%)	16 (55.2%)
Inform about effective contraception (oral retinoids)	42 (72.4%)	16 (27.6%)
Advice stopping treatment when pregnant (valproate)	8 (27.6%)	21 (72.4%)
Advice stopping treatment when pregnant (oral retinoids)	21 (36.2%)	37 (63.8%)
Advise to contact doctor when suspect a pregnancy (valproate)	18 (62.1%)	11 (37.9%)
Advise to contact doctor when suspect a pregnancy (oral retinoids)	33 (56.9%)	25 (43.1%)
Inform about pregnancy testing before/during/after treatment (valproate)	9 (31.0%)	20 (69.0%)

Inform about pregnancy testing before/during/after treatment (oral retinoids)	31 (53.4%)	27 (56.3%)

Valproate

Counseling practices related to valproate showed variation in consistency (see Table 4). Fewer than half of respondents (44.8%) reported regularly informing patients about effective contraception, and 27.6% frequently advised patients to stop treatment if they became pregnant. Counseling was more common when a pregnancy was suspected, with 62.1% advising patients to contact their doctor. 31.0% reported consistently informing patients about the need for pregnancy testing before, during or after treatment. Conversely, 72.4% stated they never or rarely advice patients to stop treatment if pregnant, and 69.0% rarely or never informed patients about pregnancy testing before, during or after treatment.

Oral retinoids

Counseling practices related to oral retinoids were generally more consistent than for valproate (see Table 4). A majority of respondents (72.4%) stated they regularly informed women of reproductive age about effective contraception. Additionally, 36.2% consistently advised stopping treatment if a patient became pregnant.

More than half (56.9%) said they routinely advised patients to contact their doctor if pregnancy was suspected, and 33.4% regularly informed patients about pregnancy testing. On the other hand, 63.8% said they never or seldom advised stopping treatment when pregnant, and 56.3% rarely or never mentioned pregnancy testing before, during, or after treatment.

4.4.3 Reported changes in dispensing

Table 5: Change of dispensing valproate and oral retinoids since the implementation of PPP in 2018 and the impact of the educational materials on dispensing valproate and oral retinoids.

	Valproate	**Oral retinoids**
Change of dispensing after implementation (N%)		

	Valproate (N = 26)	Oral retinoids (N = 54)
Yes	8 (30.7%)	9 (16.7%)
Not sure	11 (42.3%)	27 (50.0%)
No	7 (26.9%)	18 (33.4%)
Educational materials impacting the change most		
	Valproate (N = 8)	Oral retinoids (N = 9)
Check list for community pharmacists		2 (22.2%)
HCP guide	3 (37.5%)	2 (22.2%)
Warning sign in the outer package	6 (75.0%)	8 (88.9%)
Patient reminder card	2 (25.0%)	1 (11.1%)
DHPC	2 (25.0%)	1 (11.1%)

Valproate

When asked whether the implementation of the PPP had changed their dispensing practices for valproate, 42.3% of the 26 respondents stated they were unsure (see Table 5). Among the educational materials, the warning sign on the outer packaging was reported as having the most impact (75.0%). Fewer respondents recalled using the patient reminder card or DHCP materials (25.0%).

Oral retinoids

Among the 54 pharmacy technicians who answered the question about changes in dispensing, 50.0% reported being unsure whether the PPP influenced their practice (see Table 5). Recognition of specific PPP materials was relatively low: 22.2% mentioned the check list for community pharmacists and the HCP guide, while 11.1% reported using the patient reminder card and DHCP. The warning sign on the outer packaging was most frequently cited as impactful, acknowledged by 88.9% respondents.

5. Discussion

This study investigated Danish pharmacy technicians' knowledge, awareness, and implementation of the Pregnancy Prevention Programme (PPP) when dispensing valproate and oral retinoids to

women of reproductive age. While general awareness of teratogenic risks was moderate – particularly for oral retinoids – the use of specific PPP materials and adherence to counseling guidelines were suboptimal. Awareness and implementation appeared stronger for oral retinoids than for valproate. A significant proportion of respondents, especially in the valproate group, reported first learning about these risks while completing the survey. Many participants expressed uncertainty about changes in practice since PPP was introduced, and actual use of educational tools was low, although future intent to use them was higher.

5.1 Awareness of teratogenic risks

Awareness of teratogenic risks was higher for oral retinoids than for valproate. Over half of respondents had known about the risks associated with oral retinoids for more than five years, compared to 26.8% for valproate. Notably, nearly one-third (29.3%) of pharmacy technicians became aware of valproate's risks during the survey. These findings highlight significant gaps in baseline knowledge, particularly regarding valproate. Compared to pharmacists, pharmacy technicians demonstrated similar awareness levels for oral retinoids (7), but lower levels for valproate – where 15.3% of pharmacists reported learning about the risks through a survey (8). The discrepancy may stem from several factors: oral retinoids have historically received more regulatory attention and earlier implementation of risk minimization strategies, dating back to 2003, whereas valproate-specific measure were introduced later, around 2014 (2), (4), (9). Furthermore, the higher teratogenic risk profile of oral retinoids likely contributed to greater public and professional focus on their safe use. Additionally, pharmacy technicians tended to rely more on colleagues and academic studies for information, while pharmacists more often cited official sources such as the

Danish Medicines Agency or pharmaceutical manufacturers (7), (8). This may reflect in differences in access to, or engagement with, formal professional education channels.

5.2 Use of Pregnancy Prevention Programme materials

Use of PPP materials was low across both medications. For valproate, 3.2% of pharmacy technicians reported using each individual tool, such as checklists, DHCP letters, or patient reminder cards. The most frequently used material was the healthcare professional (HCP) guide, reported by 19.4% of respondents.

For oral retinoids, the warning sign on the packaging was the most used tool, acknowledged by 54.0% of respondents. Other materials, such as the patient reminder card of checklist, were rarely used – ranging from 1.6% to 6.5%.

Compared to pharmacists, pharmacy technicians were less likely to currently use PPP materials but reported a stronger intention to use them in the future, particularly for valproate (8). This suggests that although current awareness and integration of PPP tools remain low, there is a relatively high willingness among pharmacy technicians to adopt these tools moving forward. This implies that the low level of current use may stem more from a lack of awareness or training than from resistance or reluctance.

5.3 Dispensing and counseling practices

Counseling practices were inconsistent, with higher frequency reported for oral retinoids compared to valproate. For oral retinoids, 72.4% of pharmacy technicians stated they regularly informed patients about contraception, while 44.8% did so when dispensing valproate. Fewer than one-third of respondents routinely provided information about pregnancy testing or advised patients to stop treatment if pregnant – particularly in relation to valproate.

Compared to pharmacists, pharmacy technicians were generally less consistent in covering most PPP counseling components. However, they were more likely to refer patients to prescribers in suspected pregnancy cases when dispensing valproate (8). This may reflect their central role in patient interaction, but also points to more limited access to formalized clinical guidance.

5.4 Reported changes in practice after PPP implementation

Most pharmacy technicians were unsure whether their dispensing practices have changed following the implementation of the PPP. For valproate, 42.3% responded “not sure”, and this proportion was even higher for oral retinoids (50.0%). The warning label on the outer packaging was the most frequently cited material influencing practice for both medications.

This finding aligns with trends seen among pharmacists, where visual tools such as warning labels were most likely to be noticed and acted upon (7), (8).

However, compared to pharmacists, pharmacy technicians appeared less likely to recognize formal PPP materials – such as DHCP letters or checklist – as influencing practice. This suggests a need for clearer communication and training on the relevance of these tools for all pharmacy staff, not just pharmacists.

5.5 Strengths and limitations

A key strength of this study is its national reach, involving pharmacy technicians from various regions and practice settings across Denmark. The use of multiple sampling strategies enhanced representativeness of the findings. Importantly, the study addresses a significant gap in the literature by focusing specifically on pharmacy technicians – a group often underrepresented in research on teratogenic risk management in pharmacy practice.

However, the study has limitations. The sample size, particularly for the valproate group, was modest and may not fully reflect national practices. Additionally, self-selection bias could have influenced participation, potentially leading to overrepresentation of pharmacy technicians with a personal or professional interest in the topic. The reliance on self-reported data introduces a risk of social desirability bias, especially regarding questions on counseling and guideline adherence. Finally, the study's cross-sectional design does not allow for assessment of changes in behavior over time.

5.6 Implication for practice

The findings highlight a clear need for targeted educational initiatives aimed specifically at pharmacy technicians. Their frontline role places them in a key position to support the implementation of the PPP, but training and educational materials must be tailored to their responsibilities and scope of practice. Resources should be clearly labeled and actively promoted as being relevant to pharmacy technicians – not only pharmacists.

In practice, regular staff meetings in community pharmacies present a valuable opportunity to reinforce PPP principles and promote consistent counseling behaviors.
As noted by Backran et al. (2024), tools such as the pharmacist-specific checklist and patient reminder card were underutilized in Denmark compared to other European countries (7), (8). This points to both a training gap and possible cultural resistance to more formalized risk documentation processes.

Addressing these barriers may require coordinated national initiatives, as well as better integration of PPP content into pharmacy technician training programs. Materials such as checklists, patient

reminder cards, and HCP guides should be made more accessible, more user-friendly, and their relevance clearly communicated to ensure wider adoption in everyday practice.

6. Conclusion

Pharmacy technicians play a vital role in the safe dispensing of teratogenic medications.
This study highlights important gaps in awareness, use of educational materials, and counseling practices among Danish pharmacy technicians in relation to the Pregnancy Prevention Programme (PPP) for valproate and oral retinoids.

Awareness was notably higher for oral retinoids, while significant proportion of respondents reported first learning about valproate's teratogenic risks during the survey itself. Use of PPP materials was limited, although many participants expressed openness to using them in the future – especially if the tools are better tailored to their specific role. Counseling practices also varied, with lower frequencies reported for valproate-related advice.

Strengthening pharmacy technician's involvement in the PPP through targeted training, clearer role definition, and better-designed resources could help improve medication safety and reduce the risk of teratogenic exposure.

Pharmacy technicians are essential contributors to public health and safe medication use. To fully optimize their impact, they must be actively integrated into risk minimization strategies, and supported through accessible, practical tools and ongoing education.

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8. Appendices

8.1 Valproate survey

Kære farmakonom,

Som du ved, bliver viden omkring lægemidler ikke kun indsamlet under udviklingen af lægemidlet men også efter lægemidlet er markedsført og bliver brugt af en større gruppe af patienter.
Vores undersøgelse vedrører brugen af medicin der indeholder valproat. Nedenfor er en liste med medicin indeholdende valproat og godkendt i Danmark.
Delepsine, Depakine Retard, Deprakine, Orfiril
Du er inviteret til at udfylde dette spørgeskema, da vi antager at du regelmæssigt ser patienter der bruger valproat eller anden medicin indeholdende valproat.
Vi er især interesserede i at vide mere omkring den information du har modtaget omkring disse lægemidler og hvordan det har påvirket den rådgivning du har givet patienter tidligere og vil give i fremtiden.

Det vil tage ca. 10 min at udfylde spørgsmålene nedenfor. Den information du videregiver bidrager til øget viden omkring forbedret rådgivning af patienter omkring brugen af valproat.
Din deltagelse er frivillig. Svarene registreres anonymt og håndteres i overensstemmelse med den generelle forordning for databeskyttelse (GDPR) (EU) 2016/679 af 27. april 2016.

Jeg giver samtykke til at jeg har læst ovenstående information, at jeg deltager frivilligt og giver tilladelse til at i må bruge mine svar i forskningsøjemed.

- Ja

A. Er du på nuværende tidspunkt ansat på et apotek?
(1) Ja, jeg er ansat på et privatapotek
(2) Ja, jeg er ansat på et sygehusapotek
(3) Ja, jeg er både ansat på et privat- og sygehusapotek
(4) Nej, jeg er ikke ansat på et apotek på nuværende tidspunkt

B. Du er ansat i apoteksregi som:
(1) Farmakonom
(2) Farmaceut

(3) Farmakonom elev

(4) Farmaceutstuderende

(5) Andet

C. I hvilken region ligger det apotek/de apoteker du er ansat på?

(1) Region Nordjylland

(2) Region Midtjylland

(3) Region Syddanmark

(4) Region Sjælland

(5) Region Hovedstaden

(6) Flere af ovenstående (hvis du arbejder på flere apoteker)

(7) Andet (fx Grønland)

(8) Ved ikke

Q1. Hvilket år blev du født? (skriv 4 tal, fx 1970)

Tekstfelt _____

Q2. Hvad er dit køn?

(1) Mand

(2) Kvinde

(3) Ønsker ikke at oplyse

Q4. Hvor længe har du praktiseret i nuværende stilling?

(1) 0-5 år

(2) 6-10 år

(3) 11-20 år

(4) 21-30 år

(5) 31 år eller længere

Q5a. I gennemsnit hvor ofte ekspederer du valproat eller anden medicin indeholdende valproat til kvinder i den fødedygtige alder?

(1) En gang om ugen eller oftere

(2) Et par gange om måneden
(3) En gang om måneden eller sjældnere
(4) Aldrig

Q5b. I gennemsnit hvor ofte rådgiver du kvinder i den fødedygtige alder om valproat eller anden medicin indeholdende valproat når du ekspedere medicinen til de kvinder?
(1) En gang om ugen eller oftere
(2) Et par gange om måneden
(3) En gang om måneden eller sjældnere
(4) Aldrig

Q6. I din praksis har du da mistænkt eller været vidne til misdannelser eller udviklingsdefekter ved nyfødte der kan være forårsaget af brug af lægemidler under graviditet?
(1) Ja
(2) Nej
(3) Jeg er ikke sikker

Q7. Var det relateret til brugen af valproat eller anden medicin indeholdende valproat?
(1) Ja
(2) Nej
(3) Jeg er ikke sikker

Q8. Hvornår har du haft hørt om den teratogene risiko af valproat eller anden medicin indeholdende valproat når de indtages under graviditet?
(1) Lige nu, gennem dette spørgeskema
(2) Indenfor de sidste 2 år
(3) Indenfor de sidste 5 år
(4) Længere end 5 år siden

Q10.Sidste gang du ekspederede valproat eller anden medicin indeholdende valproat til en kvinde i den fødedygtige alder, benyttede du da nogen af de nedenfor listede graviditetsforebyggende tiltag fra 2018? (vælg én mulighed pr. række)

	Ja, jeg benyttede den	Jeg har set den, men benyttede den ikke	Nej, jeg har aldrig set/ benyttet den	Jeg er usikker
Q10a. Læste i "Sundhedspersonalets vejledning"	○	○	○	○
Q10c. Viste en kvinde advarslen om ikke at anvende medicinen under graviditet, udenpå medicinpakningen	○	○	○	○
Q10d. Gav en kvinde et "Patientkort"	○	○	○	○
Q10e. Læste brev med sikkerhedsinformation fra sundhedsmyndigheder eller lægemiddelproducent(DHPC)	○	○	○	○

Q11c. Hvor sandsynligt er det, at du gør kvinden opmærksom på **advarslen om ikke at anvende medicinen under graviditet, udenpå medicinpakningen**, næste gang du ekspederer valproat eller anden medicin indeholdende valproat til kvinder i den fødedygtige alder?

(1) Meget usandsynligt

(2) Usandsynligt

(3) Hverken usandsynligt eller sandsynligt

(4) Sandsynligt

(5) Meget sandsynligt

Q11e. Hvor sandsynligt er det at du læser **brev fra sundhedsmyndigheder eller lægemiddelinstitution med sikkerhedsinformation** (DHPC) om valproat eller anden medicin indeholdende valproat næste gang du ekspederer medicinen?

(1) Meget usandsynligt

(2) Usandsynligt

(3) Hverken usandsynligt eller sandsynligt

(4) Sandsynligt

(5) Meget sandsynligt

Q12. Hvilken alder har kvinder i den fødedygtige alder ifølge dig (vælg alle relevante):

(1) 15-17 år

(2) 18-44 år

(3) 45-50 år

(4) 51-55 år

(5) Andet

Hvis andet, forklar gerne:

Q13a. Vi er interesserede i at vide mere omkring din nuværende praksis, med at rådgive kvinder i den fødedygtige alder omkring valproat eller anden medicin indeholdende valproat. (Et svar pr række)

	Aldrig	Sjældent	Ofte	Altid
Q13a1. Jeg informerer dem om vigtigheden af effektiv prævention	○	○	○	○
Q13a2. Jeg fortæller dem at de skal stoppe med at tage lægemidlet hvis de tror de er gravide	○	○	○	○
Q13a3. Jeg informerer dem om de skal kontakte deres læge hvis de tror de er gravide	○	○	○	○
Q13a4. Jeg understreger vigtigheden af at teste for graviditet før, under og efter behandling	○	○	○	○

Q13b. Er der forskel på den rådgivning du giver kvinder ved den første udlevering/ekspedition af valproat eller anden medicin indeholdende valproat til kvinder i den fødedygtige alder, sammenlignet med de næste udleveringer?

(1) Ja

(2) Nej

Q13b ad. Forklar venligst forskellen:

_____

Q14. Mener du at mængden af den information, du giver om valproat eller anden medicin indeholdende valproat, når du ekspederer til kvinder i den fødedygtige alder, har ændret sig siden 2018 pga. de nye graviditets forebyggende tiltag (fx sundhedspersonalets vejledning patientkort, advarsel på lægemiddelpakning, brev fra sundhedsmyndighed eller lægemiddelproducent med sikkerhedsinformation (DHPC))?

(1) Helt sikkert ikke

(2) Sandsynligvis ikke

(3) Ikke sikker
(4) Sandsynligvis ja
(5) Helt sikkert ja

Q17. Efter din mening, hvilke barrierer hindrer implementering og/eller anvendelsen af de nye graviditetsforebyggende tiltag fra 2018 (fx Sundhedspersonalets vejledning*, patientkort*, advarsel på indlægsseddel, brev fra sundhedsmyndighed eller lægemiddelinstitution med sikkerhedsinformation (DHPC))? Nævn venligst mindst et eksempel.

_____

Q18. Er der nogle pointer/forslag/bekymringer du gerne vil tilføje i forhold til udlevering/rådgivning/implementering af graviditetsforebyggende tiltag i forhold til valproat eller anden medicin indeholdende valproat?

_____

Mange tak for din deltagelse!

8.2 Oral Retinoids survey

Kære farmakonom,

Som du ved, bliver viden omkring lægemidler ikke kun indsamlet under udviklingen af lægemidlet men også efter lægemidlet er markedsført og bliver brugt af en større gruppe af patienter.
Vores undersøgelse vedrører brugen af orale retinoider. Nedenfor er en liste med lægemidler som er orale retinoider og godkendt i Danmark.
Accutin® Sandoz, Isotretinoin "Orion", Isotretinoin "Teva", Acitretin "Orifarm", Neotigason® eller Toctino.
Du er inviteret til at udfylde dette spørgeskema, da vi antager at du regelmæssigt er i kontakt med patienter der bruger orale retinoider.
Vi er især interesserede i at vide mere omkring den information du har modtaget omkring disse lægemidler og hvordan det har påvirket den rådgivning du har givet patienter tidligere og vil give i fremtiden.

Det vil tage ca. 10 min at udfylde spørgsmålene nedenfor. Den information du videregiver bidrage til øget viden omkring forbedret rådgivning af patienter omkring brugen af valproat. Din deltagelse er frivillig. Svarene registreres anonymt og håndteres i overensstemmelse med den generelle forordning for databeskyttelse (GDPR) (EU) 2016/679 af 27. april 2016.

Jeg giver samtykke til at jeg har læst ovenstående information, at jeg deltager frivilligt og giver tilladelse til at i må bruge mine svar i forskningsøjemed.

- Ja

A. Er du på nuværende tidspunkt ansat på et apotek?
(1) Ja, jeg er ansat på et privatapotek
(2) Ja, jeg er ansat på et sygehusapotek
(3) Ja, jeg er både ansat på et privat- og sygehusapotek
(4) Nej, jeg er ikke ansat på et apotek på nuværende tidspunkt

B. Du er ansat i apoteksregi som:
(1) Farmakonom
(2) Farmaceut
(3) Farmakonom elev
(4) Farmaceutstuderende
(5) Andet

C. I hvilken region ligger det apotek/de apoteker du er ansat på?
(1) Region Nordjylland
(2) Region Midtjylland
(3) Region Syddanmark
(4) Region Sjælland
(5) Region Hovedstaden

(6) Flere af ovenstående (hvis du arbejder på flere apoteker)
(7) Andet (fx Grønland)
(8) Ved ikke

Q2. Hvad er dit køn?
(1) Mand
(2) Kvinde
(3) Ønsker ikke at oplyse

Q4. Hvor længe har du praktiseret i nuværende stilling?
(1) 0-5 år
(2) 6-10 år
(3) 11-20 år
(4) 21-30 år
(5) 31 år eller længere

Q5a. I gennemsnit hvor ofte ekspederer du orale reinoider til kvinder i den fødedygtige alder?
(1) En gang om ugen eller oftere
(2) Et par gange om måneden
(3) En gang om måneden eller sjældnere
(4) Aldrig

Q5b. I gennemsnit hvor ofte rådgiver du kvinder i den fødedygtige alder om orale retinoider når du ekspedere medicinen til de kvinder?
(1) En gang om ugen eller oftere
(2) Et par gange om måneden
(3) En gang om måneden eller sjældnere
(4) Aldrig

Q6. I din praksis har du da mistænkt eller været vidne til misdannelser eller udviklingsdefekter ved nyfødte der kan være forårsaget af brug af lægemidler under graviditet?
(1) Ja
(2) Nej
(3) Jeg er ikke sikker

Q7. Var de mistænkte misdannelser eller udviklingsdefekter relateret til brugen af orale retinoider?

(1) Ja

(2) Nej

(3) Jeg er ikke sikker

Q8. Hvornår har du haft hørt om den teratogene risiko af orale retinoider når de indtages under graviditet?

(1) Lige nu, gennem dette spørgeskema

(2) Indenfor de sidste 2 år

(3) Indenfor de sidste 5 år

(4) Længere end 5 år siden

Q10.Sidste gang du ekspederede orale retinoider til en kvinde i den fødedygtige alder, benyttede du da nogen af de nedenfor listede graviditets forebyggende tiltag fra 2018-2019? (vælg én mulighed pr. række)

	Ja, jeg benyttede den	Jeg har set den, men benyttede den ikke	Nej, jeg har aldrig set/ benyttet den	Jeg er usikker
Q10a. Læste i "Sundhedspersonalets vejledning"	○	○	○	○
Q10c. Viste en kvinde advarslen om ikke at anvende medicinen under graviditet, udenpå medicinpakningen	○	○	○	○
Q10d. Gav en kvinde et "Patientkort" med aftaleskema	○	○	○	○
Q10e. Læste brev med sikkerhedsinformation fra sundhedsmyndigheder eller lægemiddelproducent(DHPC)	○	○	○	○
Q10b. Brugte "Tjekliste til apotekspersonale"	○	○	○	○

Q11c. Hvor sandsynligt er det, at du gør kvinden opmærksom på **advarslen om ikke at anvende medicinen under graviditet, udenpå medicinpakningen**, næste gang du ekspederer orale retinoider til kvinder i den fødedygtige alder?

(1) Meget usandsynligt

(2) Usandsynligt

(3) Hverken usandsynligt eller sandsynligt

(4) Sandsynligt

(5) Meget sandsynligt

Q11d. Hvor sandsynligt er det, at du udleverer et "**Patientkort**" med aftaleskema næste gang du ekspederer orale retinoider til kvinder i den fødedygtige alder?
(1) Meget usandsynligt
(2) Usandsynligt
(3) Hverken usandsynligt eller sandsynligt
(4) Sandsynligt
(5) Meget sandsynligt

Q11d_ad Forklar gerne, hvorfor ikke

_____

Q11e. Hvor sandsynligt er det at du læser **brev fra sundhedsmyndigheder eller lægemiddelinstitution med sikkerhedsinformation** (DHPC) om orale rerinoider næste gang du ekspederer medicinen?
(1) Meget usandsynligt
(2) Usandsynligt
(3) Hverken usandsynligt eller sandsynligt
(4) Sandsynligt
(5) Meget sandsynligt

Q12. Hvilken alder har kvinder i den fødedygtige alder ifølge dig (vælg alle relevante):
(1) 15-17 år
(2) 18-44 år
(3) 45-50 år
(4) 51-55 år
(5) Andet
Hvis andet, forklar gerne:

Q13a. Vi er interesserede i at vide mere omkring din nuværende praksis, med at rådgive kvinder i den fødedygtige alder omkring orale retinoider. (Et svar pr række)

	Aldrig	Sjældent	Ofte	Altid
Q13a1. Jeg informerer dem om vigtigheden af effektiv prævention	○	○	○	○
Q13a2. Jeg fortæller dem at de skal stoppe med at tage lægemidlet hvis de tror de er gravide	○	○	○	○
Q13a3. Jeg informerer dem om de skal kontakte deres læge hvis de tror de er gravide	○	○	○	○
Q13a4. Jeg understreger vigtigheden af at teste for graviditet før, under og efter behandling	○	○	○	○

Q13b. Er der forskel på den rådgivning du giver kvinder ved den første udlevering/ekspedition af orale retinoider til kvinder i den fødedygtige alder, sammenlignet med de næste udleveringer?
(1) Ja
(2) Nej

Q13b ad. Forklar venligst forskellen:

_____

Q14. Mener du at mængden af den information, du giver om orale retinoider, når du ekspederer til kvinder i den fødedygtige alder, har ændret sig siden 2018 pga. de nye graviditets forebyggende tiltag (fx sundhedspersonalets vejledning, patientkort, advarsel på lægemiddelpakning, brev fra sundhedsmyndighed eller lægemiddelproducent med sikkerhedsinformation (DHPC), tjekliste til apotekspersonale)?
(1) Meget usandsynligt
(2) Usandsynligt
(3) Hverken usandsynligt eller sandsynligt
(4) Sandsynligt
(5) Meget sandsynligt

Q17. Efter din mening, hvilke barrierer hindrer implementering og/eller anvendelsen af de nye graviditetsforebyggende tiltag fra 2018 (fx Sundhedspersonalets vejledning, patientkort med aftaleskema, advarsel på indlægsseddel, brev fra sundhedsmyndighed eller

lægemiddelinstitution med sikkerhedsinformation(DHPC), tjekliste til apoteksperonale)? Nævn venligst mindst et eksempel.

_____

Q18. Er der nogle pointer/forslag/bekymringer du gerne vil tilføje i forhold til udlevering/rådgivning/implementering af graviditetsforebyggende tiltag i forhold til orale retinoider?

_____

Mange tak for din deltagelse!

Part II

Aim

The aim of this report is to critically evaluate the teratogenic risks associated with valproate, isotretinoin, and acitretin, and to assess the effectiveness of current regulatory strategies – specifically the Pregnancy Prevention Programmes (PPP) – in minimizing fetal exposure across Europe. The report seeks to:

- Summarize the current scientific understanding of the fetal risks linked to these medications, based on observational studies, case reports, and pharmacovigilance data.
- Examine the implementation, compliance, and practical challenges of PPPs in various European healthcare settings.
- Investigate factors influencing adherence to PPPs, including prescriber behavior, patient awareness, age, socioeconomic status, and healthcare infrastructure.
- Identify gaps in clinical practice and propose areas for improvements in patient education, healthcare provider training, and policy enforcement.

1. Valproate

1.1 Valproate and its indications

Valproate and its derivatives – including valproic acid, sodium valproate, magnesium valproate, valproate semisodium, and valpromide – have been widely used in clinical practice across Europe since their initial regulatory approval several decades ago (1), (2). First authorized in 1967 for the treatment of epilepsy, valproate's indications were expanded in 1995 to include bipolar disorder. In some European Union (EU) member states, it is also approved for migraine prophylaxis.

As each EU country authorizes medicines independently, prescribing patterns and approved uses for valproate vary across member states (3). While the exact mechanism of action is not fully understood, valproate is believed to function as a γ-aminobutyric acid (GABA) agonist, increasing GABA levels in the brain. It may also reduce excessive neuronal activity by inhibiting voltage-sensitive sodium channels (4).

1.2 Fetal risks linked to Valproate-based exposure

Valproic acid is primarily metabolized in the liver and readily crosses the placenta, often resulting in fetal concentrations that exceed maternal levels. The first report of its teratogenic effects in

humans was published in 1980 (5). Since then, accumulating evidence has highlighted valproate's potential to cause significant developmental harm when used during pregnancy.

Early research into its teratogenicity was complicated by the fact that valproate was often co-administered with other antiepileptic drugs. Nevertheless, human observational studies have consistently identified a distinct pattern of facial dysmorphism, systematic malformations, and central nervous system impartments associated with prenatal exposure to valproate and its derivatives (6).

Due to ethical constraints that limit clinical trials involving pregnant women and women of childbearing age, most of the available data on valproate's risks comes from observational studies. To better understand its teratogenic profile, researchers have investigated both monotherapy and polytherapy regimens involving valproate. A wide range of major and minor congenital anomalies have been associated with in utero exposure (7).

These effects are collectively referred to as fetal valproate syndrome, first described by DiLiberti et al. in 1984 (8). The syndrome is characterized by distinctive craniofacial features, organ malformations, neurological dysfunction, and impaired physical development.

1.3 Awareness and compliance with teratogenic risks communication for valproate

Valproate has been widely prescribed in Europe since the 1960s and became the most commonly used antiepileptic drug worldwide by 2002 (9). Over time, growing evidence has linked prenatal exposure to valproate with a range of congenital malformations and neurodevelopmental disorders in children. These findings have prompted significant concern among researchers and regulatory authorities, including the European Medicines Agency (EMA).

A 2007 study by James et al. examined whether women of childbearing age had been informed by psychiatrists about the teratogenic risks of valproate. The study found that only a minority of women recalled discussing these risks or the importance of contraception with their healthcare providers (10).

Similarly, Atturu et al. investigated women aged 18-45 who were prescribed valproate for psychiatric conditions at the Rochdale General Adult Psychiatric Service between 2005 and 2012. Their study assessed the extent and quality of counseling provided. Findings showed a decline in risk communication over time. Additionally, clinicians reported only low to moderate confidence

in their knowledge of valproate's teratogenic risks and in their ability to provide effective contraceptive counseling and pregnancy planning – highlighting the need for further training (11).

In a 2018 study, Friedrich et al. evaluated awareness of valproate-associated risks among female users in Croatia. Most participants reported that their neurologists had not provided counseling on the drug's teratogenic effects or its implications future pregnancy. Interestingly, the highest rate of valproate use was among the youngest group (aged 15-19), who also had the lowest fertility rates. This limited the study's ability to assess awareness and counseling effectiveness among women in their peak reproductive years (12).

In 2014, the European Medicines Agency's Pharmacovigilance Risk Assessment Committee (PRAC) conducted a comprehensive review of clinical trial data, non-clinical studies, pharmacoepidemiological research, published literature, case reports, and expert opinions. Based on this assessment, PRAC confirmed that valproate poses a significant teratogenic risk when used during pregnancy (18). The committee later advised the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), which includes representatives from all EU member states, introduce stricter restrictions on the use of valproate-containing medications in women who are pregnant or of childbearing age. These measures aimed to raise awareness and reduce the risk of fetal exposure (13).

Following PRAC's recommendations, the UK's Medicines and Healthcare products Regulatory Agency (MHRA) implemented several risk minimisation measures in 2015. These included a professional guidebook, a consultation checklist, a patient information booklet, and a patient card (14). However, despite these initiatives, surveys revealed that a substantial proportion of women remained unaware of valproate's teratogenic risks (14).

In France, the national regulatory agency – Agence Nationale de Sécurité du Médicament et des Produits de Santé (ANSM) – conducted multiple evaluations in 2016. The assessments indicated that the post-2014 measures had limited impact, with continued prescribing of valproate to pregnant women and women of childbearing age (15).

In contrast, a Finnish outpatient registry study covering the period from 2008 to 2016 showed a consistent decline in valproate use among women of reproductive age. This downward trend

became more pronounced following the 2014 regulatory changes and was observed across all three major indications for valproate use (16).

In response to these mixed outcomes, France formally requested that PRAC re-evaluate the benefit-risk profile of valproate-containing products in 2017 and provide updated guidance to marketing authorisation holders (MAHs) (17). As a result, the CMDh approved new regulatory measures in 2018. Under these updated guidelines, valproate-containing medicines are contraindicated for girls and women of childbearing potential for the treatment of epilepsy, bipolar disorder, or migraine prevention – unless they are enrolled in a formal Pregnancy Prevention Programme (PPP).

Although completely avoiding the use of valproate in women of childbearing age may seem like the most straightforward strategy, evidence indicates that valproate remains the most effective treatment for certain types of epilepsy. The Standard and New Antiepileptic Drug (SANAD) study – an open-label, real-world clinical trial conducted in UK hospital clinics – demonstrated that many clinicians and patients consider valproate superior to alternative treatments particularly for generalized epilepsy. These findings reflect the practical realities and clinical preferences observed in day-to-day practice (18).

Additionally, a national survey of UK clinicians reported that patients who transitioned from valproate to alternative medications such as lamotrigine or levetiracetam often experienced worse clinical outcomes, including reduced seizure control (19). In such cases, current guidelines recommend prescribing the lowest effective dose of valproate and avoiding polytherapy – particularly combinations involving topiramate – due to the heightened risk of adverse effects (19).

The 2018 Pregnancy Prevention Programme emphasizes individualized risk assessment for pregnancy and encourages shared decision-making between patients and healthcare providers (20). A central component of the PPP is the Risk Acknowledgement Form, which supports structured discussions about treatment options. This form ensures that patients fully understand and acknowledge the potential teratogenic risks of valproate, empowering them to make an informed decision about whether to proceed with treatment after carefully weighing the benefits against the risks (21).

Despite the intended goals of the Pregnancy Prevention Programme (PPP), Watkins et al. have raised concerns that its implementation may not be suitable for all women of childbearing age using valproate. They highlighted the need to adapt the Risk Acknowledgement Form for women with intellectual disabilities (ID), who may lack the capacity to consent to sexual activity or to make informed decisions about treatment. The form also presents challenges for women who decline contraception for religious, cultural, or medical reasons (22).

In 2018, Harris et al. compared the information given to women prescribed valproate with those prescribed lamotrigine or levetiracetam. While women using valproate were generally more aware of the drug's teratogenic risks, most participants in both groups reported feeling excluded from the decision-making process regarding their antiepileptic therapy (23).

Similarly, a 2020 survey by Angus-Leppan et al. revealed dissatisfaction among UK clinicians with the PPP process and the Risk Acknowledgment Form. Many patients found the form confusing, offensive, or discriminatory, particularly those in unique situations such as severe intellectual disability, same-sex relationships, hysterectomy, or sterilization 24). Furthermore, only a small proportion of clinicians reported completing the form for all their female patients of reproductive age. (24)

These findings underscore the need to improve the decision-making process surrounding valproate treatment. This includes providing clear, accessible, and regularly updated information, as well as allowing sufficient time and support for patients to ask questions, explore their options, and make informed choices based on their individual circumstances.

1.4 Risk Awareness and prescribing behavior: Valproate use in women of reproduction age

A retrospective study published in 2018 analyzed prescribing pattern for valproate in the treatment of bipolar disorder among women of childbearing age using data from UK Mental Health Trusts. The study concluded that prescribers often fell short in informing patients about the potential risks valproate poses to a developing fetus when used during pregnancy (25).

Similarly, a retrospective study conducted in France examined adherence to risk minimization measures related to valproate prescribing, both in psychiatric institutions and community pharmacies (26). Although the number of women of childbearing age being treated with valproate

declined modestly during the study period, overall awareness of risk reduction strategies remained limited among both healthcare professionals and patients (26). These findings suggest that, despite increased regulatory efforts, clinical practice related to valproate in prescribing in bipolar disorder has shown only minimal improvement – highlighting the continued need for stronger risk communication and consistent implementation of safety measures.

2. Oral Retinoids

2.1 Therapeutic indications for oral retinoids: Isotretinoin

Isotretinoin (13-cis-retinoic acid) has been approved for use in Europe since 1984 for the treatment of severe, treatment-resistant cystic acne and other dermatological conditions. It is widely regarded as the most effective medication for reducing sebum production (27), (28), (29), (30). Isotretinoin targets all major pathogenic mechanisms involved in acne, including reducing the size of sebaceous glands, lowering sebum output, and providing both comedolytic and mild anti-inflammatory effects (31).

Although, the product information clearly contraindicated its use during pregnancy at the time of approval, cases of congenital malformations due to in utero exposure have still been reported (32).

Oral retinoids provide therapeutic benefits for several dermatological conditions, but their use is limited by a wide range of adverse effects, particularly among certain patients populations (32). Isotretinoin was identified as a teratogen in animal studies even before it received market authorization in the treatment of various dermatological conditions (33), (34). Later, numerous cases involving women of reproductive age confirmed that these teratogenic effects also occur in humans (34).

Because ethical constraints prohibit controlled clinical trials involving pregnant women, most evidence of isotretinoin's teratogenicity in humans has been drawn from observational studies and case reports (35). Oral retinoids are known to increase the risk of miscarriage and to cause variety of congenital malformations – most notably those affecting the central nervous system (CNS) – which can result in psychomotor and intellectual impairments (36). Consequently, the use of oral retinoids is strictly contraindicated during pregnancy and in women who are planning to conceive (36).

2.2 The teratogenic effects of Isotretinoin

Like other retinoids, isotretinoin is a synthetic derivative of vitamin A and is recognized as a potent human teratogen (37). It has been strongly associated with a high incidence of spontaneous abortions and major congenital malformations – a condition referred to in the literature as isotretinoin embryopathy (38), (39). Notably, within a year of isotretinoin's approval in the U.S. market in 1982, the manufacturer began receiving reports of adverse fetal outcomes following in utero exposure (39).

The first human evidence of isotretinoin's teratogenicity was published by Lammer et al. in 1988 who examined 154 pregnancies exposed to isotretinoin. Among them, 21 infants (13.6%) were born with major congenital malformations. In a prospective cohort of 36 pregnancies, 5 infants (13.8%) had major malformations. The relative risk of major malformations was calculated as 25.6 (95% CI: 11.4-57.5) compared to the general population (38). These findings were later supported by Adams et al. (1996) who reported a 25% malformations rate (30) and a 40% rate of spontaneous miscarriages among exposed pregnancies (30), (35).

Interestingly, a 1984 study by Chen et al. found no significant difference in dosage or duration of exposure between malformed and unaffected infants (34). This suggest that even short-term or low-dose exposure may result in serious outcomes. In fact, congenital abnormalities have been reported after as little as one day treatment (40). Furthermore, isotretinoin may persist in maternal tissues, especially with low-dose regimens, potentially extending the window of teratogenic risks even after the drug has been discontinued (41).

After initial reports confirmed isotretinoin's teratogenic effects in humans, a consistent pattern of congenital malformations emerged among exposed pregnancies. These most commonly involved the craniofacial region, central nervous system, heart and thymus. (30), (38)

In a 1990 literature review by Salevits et al. identified bilateral microtia or anotia, along with facial bone abnormalities, as the most frequently observed craniofacial defects (42). Later, Soprano et al. (1995) added cleft palate to the list of frequently reported abnormalities (43). Other documented anomalies included abnormal development of the ear canals, mild facial asymmetry, facial nerve paresis, and mandibular hypoplasia (30).

Central Nervous System (CNS) abnormalities are among the most commonly reported malformation following in utero exposure to isotretinoin. Documented defects include cerebellar hypoplasia, agenesis of the vermis, enlargement of the fourth ventricle, hydrocephalus, cortical malformations, encephalocele, and, in some microcephaly (30), (35), (44). Moreover, evidence suggests that even in the absence of visible structural brain anomalies, children exposed to isotretinoin during pregnancy may exhibit reduced intellectual performance (45).

However, current data on long-term neuropsychological and developmental outcomes among children exposed during early embryonic stages remain limited. There is a need for further research to explore potential neuropsychological impairments and genetic abnormalities related to hindbrain and craniofacial development in this population (30).

A variety of cardiovascular malformations have also been linked to prenatal isotretinoin exposure, including transposition of the great arteries, tetralogy of Fallot, truncus arteriosus communis, ventricular septal defects, and aortic arch hypoplasia (35), (46). A 1990 retrospective observational study conducted in the United States identified ear anomalies as the most sensitive indicator of in utero isotretinoin exposure. However, the most indicative pattern of teratogenicity involved a combination of ear, CNS, and cardiovascular defects (38).

Thymic abnormalities – such as ectopia, hypoplasia, or aplasia – have also been reported, though less frequently (46). Additionally, ocular malformations have been associated with prenatal isotretinoin exposure, including telecanthus, microphthalmia, and underdevelopment of the visual pathways, which may result in cortical blindness and optic nerve hypoplasia (47).

Recent observational studies have aimed to assess fetal outcomes in pregnancies exposed to isotretinoin, either during or prior to conception. A large cohort study using data from Teratology Information Services showed that women exposed during pregnancy gave birth to infants with significantly higher rates of congenital anomalies compared to those exposed before conception or to unexposed controls (40). Specifically, over one-quarter of live births in the pregnancy-exposed group exhibited congenital anomalies – emphasizing the serious teratogenic risk isotretinoin during gestation. While some women chose elective termination following detection or suspicion of fetal abnormalities, the incidence of congenital anomalies among live births in the exposed group remained notably high (40).

There was a statistically significant difference in pregnancy termination rates between groups, with the highest rate (32.5%) observed among those exposed to isotretinoin during pregnancy, compared to 9.3% in the group exposed before pregnancy and 2.7% in the control group. This reflects both the high teratogenic risk and the impact of teratological counseling on pregnancy management decisions.

In a separate cohort study, MacDonald et al. analyzed data from the Truven Health MarketScan database, covering the period from 2011 to 2015, to examine the risk of adverse pregnancy outcomes associated with isotretinoin use (48). Their analysis revealed a five-fold increase in elective abortions among pregnancies exposed to isotretinoin compared to unexposed ones. However, due to low pregnancy rates in the exposed group and insufficient outcome data, the study was unable to directly assess teratogenic effects (48). The authors emphasized that much of the current knowledge about isotretinoin-related fetal risks is based on voluntary case reports, and highlighted the need to utilize large healthcare databases to better understand the full scope of risks associated with isotretinoin exposure during pregnancy (48).

The precise mechanisms underlying isotretinoin's teratogenicity remain incompletely understood. Early research suggests that craniofacial abnormalities may stem from isotretinoin's disruption of neural crest cell migration (34). This hypothesis was supported supported by Melnik et al. (2017), who identified increased apoptosis of neural crest cells as a central mechanism behind isotretinoin-induced craniofacial malformations (31). They also linked impaired migration of these cells to cardiac malformations, reinforcing the idea that neural crest cell apoptosis plays a critical role in isotretinoin's teratogenic profile (31).

Although synthetic retinoids exert therapeutic effects in dermatology by regulating cell proliferation and differentiation, these same mechanisms may interfere with normal embryonic development and contribute to structural birth defects (34). Retinol, a natural form of vitamin A, is essential for maintaining normal tissue function. Its derivatives – retinoic acids – play a crucial role in embryogenesis, particularly in the development of the nervous system, craniofacial structures, and limbs (27), (30).

2.3 The teratogenic effects of Acitretin

Unlike isotretinoin, there is limited conclusive evidence confirming the teratogenicity of acitretin in humans. Still, as a synthetic retinoid, acitretin is known to have teratogenic potential because it interferes with cellular differentiation and proliferation (49). The most informative, though minimal, data come from pregnancy case reports submitted to the drug manufacturer. These suggest an increased risk of spontaneous abortion and congenital malformations, especially when acitretin is taken during the first trimester of pregnancy (50). The risk appears to decrease around three years after stopping treatment, aligning with a recued chance of fetal abnormalities (51).

In 1999, Maradit and Geiger conducted a global review of pregnancy cases reported to the most manufacturer since acitretin became available internationally. Most pregnancies occurred within two years of stopping treatment, and among 44 infants identified, only three were born with malformations. As a result, the study could not definitively confirm a link between acitretin and birth defects in humans (49).
The study also looked at the pharmacokinetics of acitretin, building on earlier suggestions that its metabolism and elimination might affect how long the teratogenic risk lasts after treatment.However, the findings were inconclusive, and no clear threshold blood level could be identified to determine fetal risk (49).

Interestingly, studies on isotretinoin's pharmacokinetics in women of childbearing age have shown that its half-life can vary widely, making it challenging to say exactly how long women should wait after stopping treatment before trying to conceive (52). As a precaution, all countries where acitretin is marketed currently recommend that women use effective contraception for two to three years after ending treatment (53).

2.4 Implementation and Effectiveness pf Pregnancy Prevention Programs for Oral Retinoids in Europe

Oral retinoids are lipid-soluble compounds, allowing them to persist in the body long after administration. (35) Because of this, pregnancies must be carefully planned, and strict adherence to safety guidelines is essential when prescribing these medicines to women of childbearing age. It is equally important that both healthcare professionals and patients have access to clear, accurate information about the teratogenic risks linked to these drugs.

To address these concerns, Pregnancy Preventions Programmes (PPPs) were introduced to reduce the risk of fetal exposure. These initiatives aim to either prevent pregnancy during treatment or ensure patients are well-informed and able to make safe decisions.
The first PPP for isotretinoin was launched in 2003, and similar measures were gradually extended to other oral retinoids. However, despite the EU-wide introduction of PPPs that same year, cases of fetal exposure to isotretinoin continued to be reported (28), raising concerns about how effective these programs were in clinical practice.
In response, on 22 March 2018, the Committee for Medicinal Products for Human Use (CHMP) at the European Medicines Agency (EMA), following recommendations from the Pharmacovigilance Risk Assessment Committee (PRAC), updated the PPP guidelines aimed at improving their impact and consistency across all EU countries.

2.5 Isotretinoin

In 1988, the Marketing Authorization Holder (MAH), Roche, introduced a Pregnancy Prevention Programme (PPP) for oral isotretinoin to help reduce the risk of teratogenic effects following in utero exposure. This program was included in the product information worldwide (54).

In 1997, French health authorities introduced stricter prescribing and dispensing guidelines for isotretinoin (55). Following the introduction of generic isotretinoin products in Europe in 2001, variations in the PPPs linked to different formulations began to appear (55). That same year, France adopted additional regulatory measures to modify the marketing authorization conditions, aiming to further control how isotretinoin was prescribed and dispensed (55).

In 2005, Bensouda-Grimaldi et al. conducted a study to evaluate the effectiveness of these updates. The findings revealed poor compliance with the revised prescribing guidelines, including low use use of effective contraception and pregnancy testing. The study also emphasized that patients often failed to understand the information they received from healthcare professionals, highlighting a communication and awareness gap (49).

To address these issues, the European Commission updated the PPP in 2003 and introduced a standardized EU-wide program for all oral isotretinoin products, regardless of the manufacturer (54). The updated program included two major additions: specific guidance for pharmacists and educational materials aimed at patients (54). At that time, the approved indication for isotretinoin

across the EU was limited to treating severe acne that had not responded to systemic antibacterial therapy and topical treatments (43).

There are multiple Marketing Authorization Holders (MAHs) for oral isotretinoin. While the core elements of PPPs are harmonized across EU member states, there are minor differences in the educational materials provided (29). In 2012, Crijns et al. evaluated PPP compliance across the EU and found that, although the programs were implemented and most countries had incorporated the required components from the EU review, half of the respondents felt the effectiveness of the programs was inadequate (28).

To improve implementation, some countries introduced additional national measures. These included reminders to prescribers about PPP requirements, guidance for pharmacists on proper dispensing, or restrictions limiting isotretinoin prescribing to dermatologists only (28). However, the variation in how these elements were adopted, and the possibility of socially desirable responses from participants, made it difficult to fully assess how effective the PPPs had been (28). Additional shortcomings were highlighted in a systematic literature review. This review included case reports, observational studies on women exposed to isotretinoin before or during pregnancy, and surveys of dermatologists and pharmacists across Europe (55).

Several studies have investigated the compliance with isotretinoin PPPs, and the results have been consistent: overall adherence remains too low and needs to be strengthened (37). A 1998 study in Scotland recommended that dermatologists take lead in ensuring contraceptive use and pregnancy prevention when prescribing isotretinoin to women of childbearing age (37).

In the Netherlands, a 2011 study showed mixed views among healthcare professionals. Pharmacists and dermatologists generally agreed that PPP compliance should be the prescriber's responsibility, or at least shared between prescriber and patient. Pharmacists often felt the main responsibility belonged to the treating physician (54).

A case-control study using data Dutch database records (1999-2006) found that women were more likely to use contraception when isotretinoin was prescribed by general practitioners (GPs) rather than dermatologists (55). This may be due to dermatologists having less expertise or confidence in contraceptive counseling (55), leading women to turn to their GPs for this advice.

However, a later retrospective cohort study using data from the Dutch Foundation of Pharmaceutical Statistics (2005-2008) reported the opposite trend. In that study, women who received isotretinoin from specialists were more likely to use contraception compared to those treated by GPs (49). Still, overall contraceptive use – including oral and intrauterine methods – remained low among women aged 15 to 45 receiving isotretinoin (49).

Both studies were based on pharmacy dispensing data and could not account for non-documented contraceptive methods such as condoms, sterilization, or vasectomy, making it difficult to fully assess contraceptive coverage (32).

A separate cross-sectional study in the Netherlands examined PPP compliance over time among dermatologists and pharmacists (33). The study found that pharmacists poorly monitored both contraceptive use and pregnancy testing, and that overall compliance had not improved between 2007 and 2011. While dermatologists showed some progress – mainly in patient counseling and risk communication – compliance remained low, particularly regarding monthly prescriptions and consistent contraceptive use (33).

Recent studies in Estonia and Belgium also reported low rates of effective contraception among women of reproductive age prescribed isotretinoin (20), (51). In Estonia, a retrospective cohort study used national health insurance databases to assess contraceptive use and counseling during treatment (29). Most women had no documented contraceptive use, and effective contraception was more common in women over 30. In contrast, younger women in their 20s and early 30s had only partial coverage (29).

In Belgium, a survey study conducted between 2014 and 2015 gathered response from dermatologists, GPs, pharmacists, and female patients (55). While healthcare professionals were generally aware of isotretinoin's teratogenic risks and reported counseling patients, both patients and providers demonstrated limited awareness of the PPP. Key program elements – such as using a second contraceptive method and conducting monthly pregnancy testing – were not routinely followed. Although overall PPP awareness was lower in Belgium than in France or the Netherlands, actual healthcare practices were found to be similar across all three countries.

2.6 Acitretin and PPP

Acitretin, a synthetic aromatic analogue of retinoic acid, has been used in Europe since 1988 for the treatment of severe psoriasis (42). Like other retinoids, it carries significant teratogenic risks, which means strict pregnancy prevention measures are essential. However, there is limited data on how well women taking acitretin follow Pregnancy Prevention Programme (PPP) guidelines.

In France, two prospective cohort studies (53), (55) using national reimbursement and hospitalization databases to assess compliance with PPP recommendations, focusing on pregnancy testing and pregnancy occurrence (53). Both studies found poor adherence, although there was a modest improvement in pregnancy test uptake between 2007 and 2013.

Pregnancy test use varied depending on age, socioeconomic background, and the type of prescriber. Dermatologists were more likely to request pregnancy tests than general practitioners. Raguideau et al. found that fewer pregnancy tests were conducted before starting acitretin compared to isotretinoin, and more pregnancies occurred in women using acitretin. These differences may be partly explained by the age groups involved – since isotretinoin is typically prescribed to younger women for acne, while acitretin is often used in older women with psoriasis (53). Younger patients may also receive closer monitoring.

Unlike isotretinoin, which generally clears from the body about a month after stopping treatment, acitretin's teratogenic risk persists for much longer. This extended risk window makes ongoing monitoring and long-term PPP compliance more challenging (51).

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Part III

Abstract

Objectives: This study aimed to conduct a systematic literature review to identify, examine, and evaluate existing research on pharmacy technicians' knowledge and attitudes toward prescription medications in community pharmacy settings across the world.

Methods: A systematic literature search was carried out using PubMed for studies published between 2017 and 2025. Eligible studies included English-language quantitative cross-sectional studies and qualitative studies focused on pharmacy technicians' knowledge and attitudes toward prescription medicines in community pharmacy settings, globally.

Results: The search identified 10 articles from 9 countries across four global regions: Europe, Africa, Asia, and South America. Together, these studies offer a broad perspective on pharmacy technicians' knowledge, attitudes, and practices related to prescription medications. Key themes included the impact of education, training, regulatory frameworks, and workplace culture. Regional differences were evident, with studies from Western countries generally reporting higher knowledge levels than those from Africa and Asia.

Conclusion: The review highlights important factors that influence pharmacy technicians' knowledge and attitude toward prescription medicines in community pharmacies worldwide. Understanding these factors can help healthcare organizations design strategies to improve pharmacy technicians' knowledge, attitudes and practices (KAP). More research is needed to develop evidence-based interventions that strengthen KAP, support workforce retention, and improve healthcare outcomes globally.

Investigating Pharmacy Technicians' Knowledge, Attitudes and Practices towards Prescription medication in Community Pharmacies: A Systematic Review

1. Aim

The main objective of this review was to conduct a systematic literature review and a thematic narrative analysis to examine and evaluate existing research on pharmacy technicians' knowledge, attitudes, and practices regarding prescription medications and dispensation in community pharmacies worldwide.

2. Methods

This review followed selected components of the PRISMA Scoping Review guidelines, including the PRISMA flowchart to tract the study selection process. A scoping overview was conducted to summarize key characteristics of the included studies – such as article title, authors, year of publication, research objectives, target population, countries, methodological approaches (e.g. type of survey), sample sizes, and key findings.

To synthesize the findings, a narrative approach was used. This allowed for a broad analysis of the included studies across different professional roles and workplace settings. It also supported comparisons across geographic regions, helping to highlight similarities and differences between continents.

2.1 Data collection

The research question guiding the review was: *"What is the most recent published literature on pharmacy technicians' knowledge, attitudes and practice towards prescription drugs in community pharmacies worldwide?"*.

A systematic search was conducted in PubMed on Marts 20th 2025, covering studies published between 2017 and 2025. Articles that were not accessible through PubMed were retrieved manually via the Danish Royal Library's website. The total number of studies identified during the search process is shown in Figure 3.

2.2 Search terms

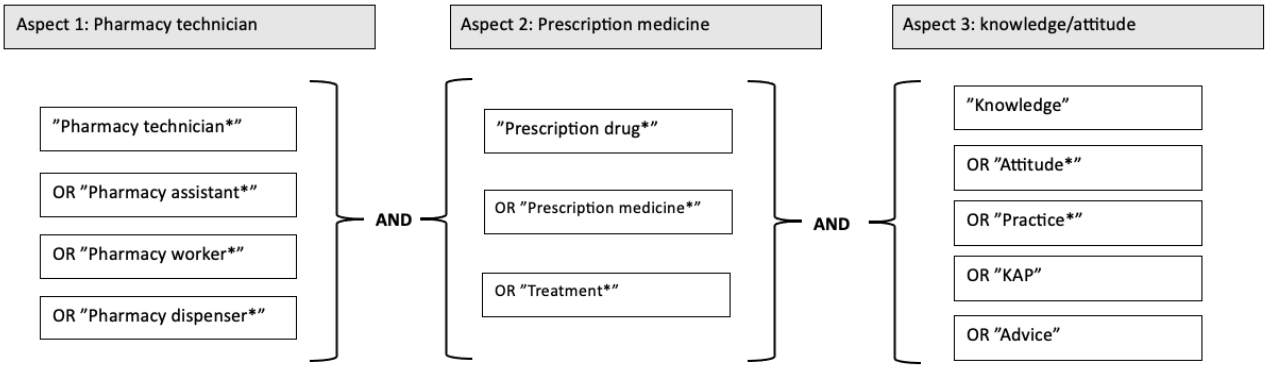

Figure 1: Overview of search terms used in database queries.

The final search strategy, shown in Figure 1, was developed to identify the most relevant literature for this review. Three main aspects were identified: Pharmacy Technicians, Prescription medicine and Knowledge, Attitude and Behavior. These concepts were combined using the Boolean operator 'AND'. Within each category, a combination of Medical Subject Headings (MeSH terms) and free-text keywords was applied, connected by the operator 'OR' to broaden the scope.

2.3 Eligibility Criteria

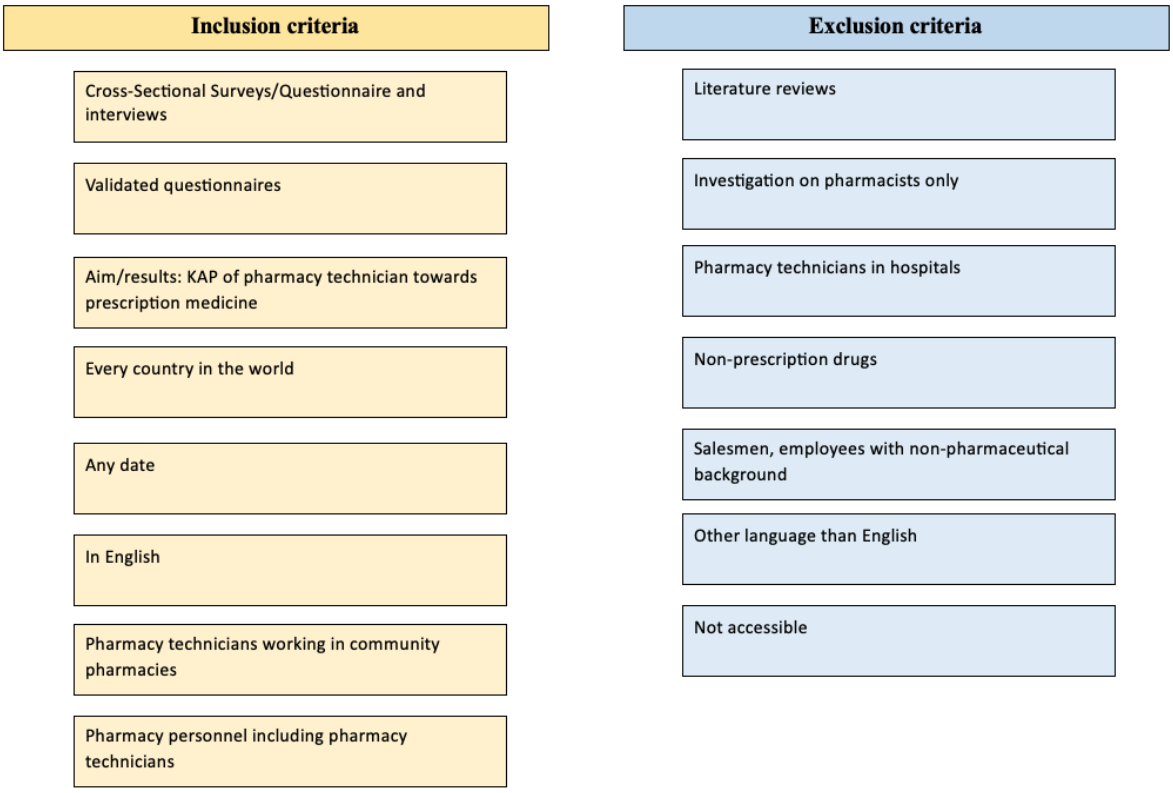

Figure 2: The eligibility criteria for the literature search

The eligibility criteria are illustrated in Figure 2. These were developed to match the purpose of the study. The review included literature in English or Scandinavian language, focusing on quantitative surveys and qualitative studies. Studies were eligible if they used validated questionnaires or aimed to validate them, while investigating pharmacy technicians' knowledge and attitude towards prescription medicine. Qualitative studies using structured patient-simulation interviews were also included.

However, studies focusing only on pharmacists, OTC medications, or hospital pharmacy technicians were excluded. Non-English language studies were also excluded to maintain clarity and relevance. To broaden the scope, global studies without a publication time limit were considered. Although the primary focus was on pharmacy technicians, studies involving broader pharmacy staff (e.g. pharmacists or mixed groups) were included if the number of pharmacy technician respondents was clearly stated.

Only studies involving pharmacy technicians working in community pharmacies were included. Those employed in hospitals, self-employed individuals, or those in non-pharmacy settings were excluded. Lastly, any studies that were inaccessible were also excluded from the review.

2.4 Literature Selection

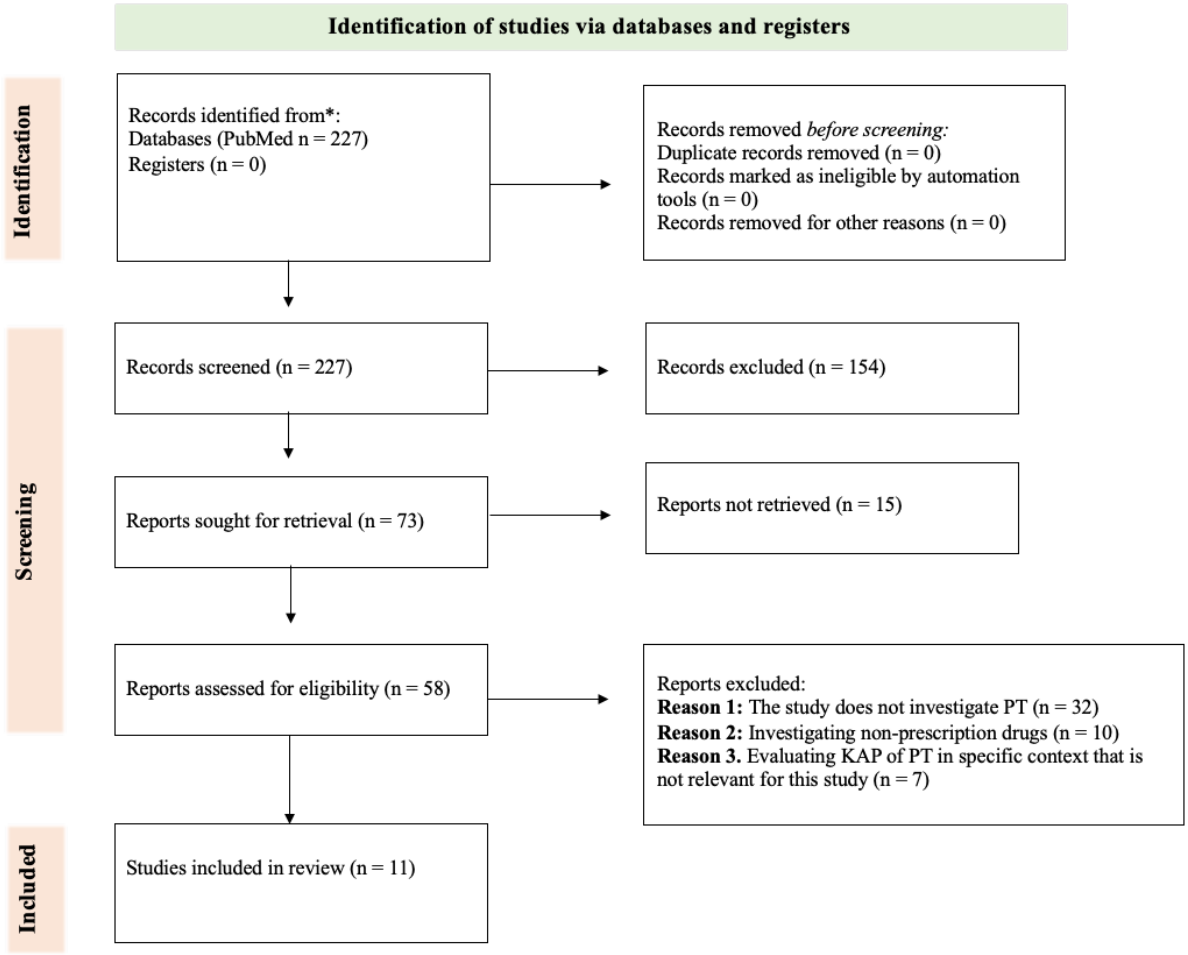

Figure 3: Results of the literature search presented according to the PRISMA flow diagram (KAP = knowledge, attitude, practice, PT = pharmacy technicians)

The systematic literature search yielded a total of 227 studies. Figure 3 presents a PRISMA flow chart outlining the steps taken during the search and selection process. Articles titles and abstracts were manually screened using the defined search terms and eligibility criteria (see Figures 1 and 2).

As shown in Figure 3, 73 articles were initially selected, while 154 were excluded. After a full-text review, 49 articles were excluded for not meeting the inclusion criteria. This left 10 relevant articles, which were then thematically analyzed and categorized. For clarity in the scoping overview, each article was assigned a number. The article titles, authors, publication years, research aims, target groups, countries, methods (questionnaire structure), sample sizes and key findings were documented and organized in a table. A summary version of this table is available in Appendix 7.1.

3. Results

Research Trends in Knowledge, Attitude and Practice on Prescription Medicine

The literature search identified 10 articles that met the eligibility criteria. These studies were conducted in 9 countries across four global regions, as illustrated in Figures 4 and 5.

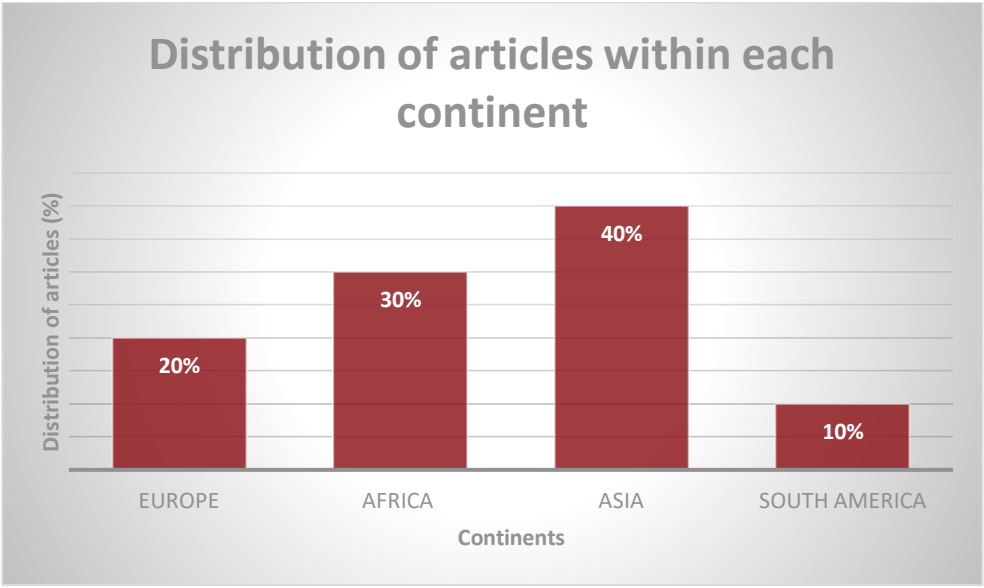

***Figure 4**: The percentage distribution of the 10 included articles across world regions.*

The included studies span a period of eight years, from 2017 to 2025, as shown in Figure 5.

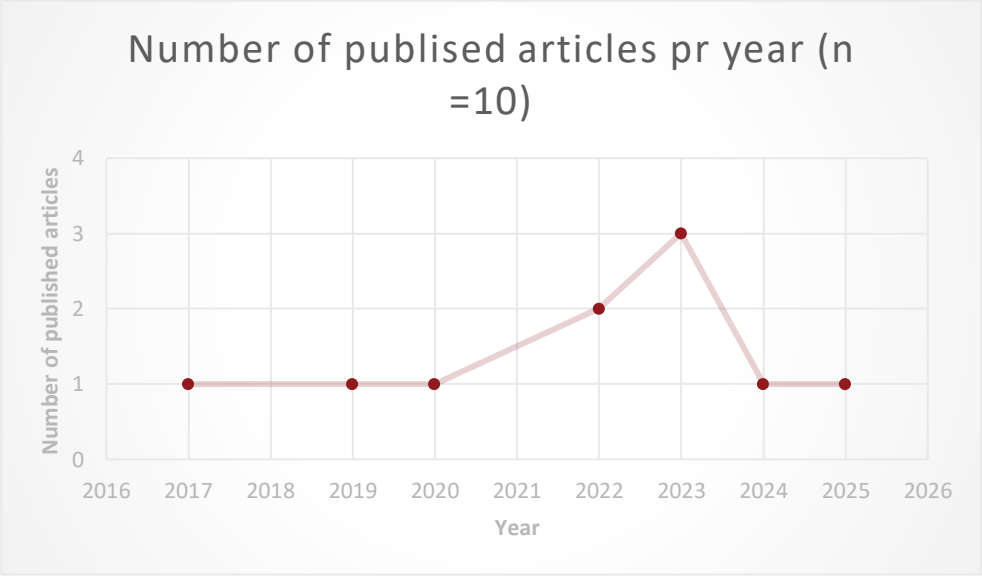

***Figure 5**: The number of publications per year from 2017 to 2025, based on the 10 articles include in this study.*

The systematic review analyzed the selected articles to examine pharmacy technicians' knowledge, attitudes, and practices (KAP) regarding prescription medicine in various regions around the world. The review applied a broad approach to explore key themes across continents, offering insight into factors that influence pharmacy technician behavior and awareness globally. The review applied a broad approach to explore key themes across continents, offering insight into the factors that influence pharmacy technician behavior and awareness globally.

Europe (2 articles)

In Portugal, a study found that 91.4% of pharmacy technicians were able to identify the main cause of Vulvovaginal Candidiasis (VVC) – a figure that was lower than both pharmacists (97.2%) and what would generally be considered adequate. The difference between pharmacy technicians and pharmacists was statistically significant (P = 0.005) (1).

Pharmacy technicians showed knowledge gaps in distinguishing between uncomplicated and complicated/recurrent VVC. Their ability to apply these classifications was more limited compared to pharmacists and female respondents. Awareness of evidence-based pharmacologic treatments for both uncomplicated and complicated VVC was also low.

While many technicians recognized classic symptoms such as itching and thick vaginal discharge, fewer were able to identify fewer common symptoms or accurately differentiate VCC from other vaginal conditions. This limited ability to differentiate conditions and recommend appropriate treatments is concerning – especially given their frontline role in advising on over the counter (OTC) medications.

These gaps may contribute to inappropriate use of antifungals and delays in patients seeking the right medical care. The study underlined the importance of improving both undergraduate and postgraduate training, as well as supporting ongoing professional development, particularly in VVC management. Continuing education is recommended to close these knowledge and practice gaps.

In the UK, pharmacy technicians showed a high level of general knowledge about antimicrobial resistance (AMR) and antibiotic stewardship (2). Their mean knowledge score was 7 out of 8, which was higher than that of dispensers (6.5) and healthcare assistants, but slightly lower than pharmacists (7.4)

Pharmacy technicians reported a strong awareness of antibiotic resistance and recognized their responsibility in supporting appropriate antibiotic use. However, a notable 64.6% said they had

not received any additional training on AMR since becoming Antibiotic Guardians, pointing to a need for more structured ongoing education.
When asked about their workplace antimicrobial stewardship action plans, many technicians were unsure of the specific content. This uncertainty suggests room for improvement in internal communication and training at the workplace level.
Despite these gaps, the Antibiotic Guardian (AG) campaign and mandatory training requirements within UK community pharmacies appear to have had a positive effect on pharmacy staff's knowledge, awareness, and behaviors related to antimicrobial stewardship (2).

Both the UK and Portugal studies underline a consistent theme: initial education is working, but there is a challenge in keeping pharmacy technicians up to date with new guidelines and protocols (1), 2). Ongoing training is essential to bridge the gap between foundational knowledge and current practice.

Africa (3 articles)

In Somalia, a study explored the knowledge, attitudes and practices (KAP) of community pharmacy technicians regarding erectile dysfunction (ED) and its treatment (3). The findings showed that
60% had limited knowledge of ED and its pharmacological management, especially around risk factors, possible complications, and clinical decision-making. A notable proportion of technicians did not follow good standard practices. 64.5% of the pharmacy technicians repeatedly dispensed the same ED medication – mostly sildenafil 100 mg – and 64% did so without a prescription.

In Ethiopia, a similar pattern emerged (4). The average ED knowledge score among pharmacy technicians was moderate, with female technicians and those with 5-10 years of experience scoring slightly better. However, less than half could identify key risk factors such as diabetes, hypertension, or smoking, and only about a third correctly recognized oral medications as the primary treatment. Knowledge of contraindications and adverse effects was also limited. Almost half of Ethiopian technicians admitted to dispensing ED medications without a prescription.

In both countries, there was a common practice of recommending unverified herbal remedies, such as honey-based preparations – reported by over 45% of Somali and nearly 40% of Ethiopian

technicians. These practices are not supported by clinical guidelines and highlight the ongoing challenge of aligning pharmacy practice with evidence-based care.

In Benin, most pharmacy technicians – referred to in the study as "auxiliaries" – showed limited knowledge of national malaria guidelines (5). Only 3.4% could correctly name the recommended artemisinin-based combination therapies (ACTs) outlined in the National Malaria Control Programme (NMCP).

Many technicians struggle to recognize severe clinical signs of malaria, and many mistakenly linked general, non-specific symptoms to serious cases, pointing to confusion and a lack of accurate clinical understanding.

Almost 90% (89.8%) pharmacy technicians dispensed anti-malarial medications based solely on patient request, without requiring any diagnostic confirmation – a practice that clearly contradicts NMCP guidelines.

The findings underline a bigger issue seen across multiple countries: many pharmacy technicians lack the clinical knowledge needed for safe and rational dispensing, especially for high-risk or disease-specific treatments. This gap not only raises patient safety concerns but also risks undermining national disease control efforts. Stronger regulatory oversight and focused training are needed to improve standards and ensure the safe use of essential medicines.

Asia (4 articles)

In Indonesia, a study explored community pharmacy personnel's knowledge, attitudes, and practices (KAP) in relation Tuberculosis Patient Detection (TBPD) (6). While pharmacy technicians generally had a basic understanding of tuberculosis (TB), many lacked deeper knowledge about key symptoms, at-risk populations, and TB medications. Pharmacists tended to score higher on knowledge, pointing to a need for more focused training for pharmacy technicians, especially given their hands-on role in medicine dispensing and counseling.

Interestingly, most pharmacy technicians showed a positive attitude toward their responsibilities in TB detection. However, this attitude did not always lead to action – actual involvement in TBPD, such as identifying or referring suspected cases, was low. Common barriers included lack of training and heavy workloads. This study suggest that structured TB training and better support systems are needed to help technicians engage more effectively in TBPD in community pharmacy settings (6).

In a related study conducted in Eastern Indonesia, the focus shifted to self-medication services in community pharmacies (7). Pharmacy technicians appeared willing to offer advice, but this did not consistently lead to effective patient interactions. Often the main form of advice was a simple product recommendation, with little to no probing into the patient's conditions. Key challenges included limited training, low motivation, and weak consultation skills. Although technicians may have the theoretical knowledge, the lack of practical guidance and continuing education held them back. The study calls for targeted interventions to boost patient assessment skills and improve training, aiming to raise the overall quality of self-medication services in Indonesian pharmacies (7).

In Pakistan, a study investigated how private pharmacy staff manage tuberculosis (TB) (8). The results showed a general lack of awareness and involvement in TB care. Many pharmacy technicians could not properly identify TB symptoms and rarely provided counseling or referred suspected cases, reflecting a limited understanding of their potential public health role. Poor practices were also reported, including frequent dispensing of TB medications without prescriptions and inadequate storage conditions, both pf which pose risks to treatment outcomes and drug resistance. Notably, 30% of sampled rifampicin drugs had quality issues due to improper storage – a responsibility typically handled by technicians. The study emphasized the pharmacy technicians in Pakistan's private sector are undertrained and poorly equipped to participate meaningfully in TB control programs. Toimprove this, the study calls for mandatory training, stricter regulation, and better integration with national TB initiatives (8).

In Bangladesh, private pharmacies are often staffed by informally trained or unlicensed pharmacy technicians, rather than certified pharmacists. One study explored their knowledge of antihypertensive and anticonvulsant drugs used to treat pre-eclampsia (PE/E) (9). Pharmacy technicians had limited knowledge of these critical medicines, despite often being the first point of contact for pregnant women.
Their ability to provide safe advice or make appropriate referrals was hindered by a lack of training and supervision. In many cases, technicians dispensed drugs without prescriptions and had little understanding of the urgency surrounding proper PE/E management. The study highlights unsafe practices such as irrational dispensing and low awareness, which can directly threaten maternal health. Strengthening training and oversight is urgently needed to address these gaps (9).

Across the three Asian countries analyzed, pharmacy technicians typically had limited formal education and little to no post-graduation or disease-specific training. Although they often serve as the first point of contact for patients, their knowledge, attitudes, and practices were frequently inadequate for safe and effective care. A lack of regulatory oversight and support has contributed to high rates of irrational dispensing, a poor patient assessment, and limited public health engagement.

South America (1 article)

In Colombia, a study looked at pharmacy technicians‘ knowledge, attitudes and practices related to antibiotics sales (10). Pharmacy technicians demonstrated higher knowledge (79.2%) about antibiotics compared to other pharmacy staff, likely reflecting the positive influence of education and experience. However, misconceptions persisted – 35% believed that antibiotics were effective against the common flu or COVID-19, and 33% thought antibiotics could be taken without a prescription.

Although they held stronger knowledge scores overall, their attitudes reflected uncertainty about compliance and concerns that stricter regulations could reduce their income. In practice, many continued to sell antibiotics without prescriptions, often justifying it by citing patients’ limited access to care or belief that patients would obtain the medication elsewhere anyway. The findings show that even among relatively well-informed pharmacy technicians, misconceptions and unsafe practices remain common.

4. Reflections

4.1 Geographic and time-based trends

This analysis highlights notable geographic differences in pharmacy technicians’ knowledge and attitudes towards prescription medicines. The data presented in the figures reveal emerging trends and areas of focus across global regions and professional settings.

As shown in Figure 4, most studies on pharmacy technicians’ knowledge and attitudes were conducted in Asia (40%), followed by Africa (30%). In contrast, Europe (20%) and South America (10%) were less represented, indicating an uneven distribution of research across regions. The findings show that pharmacy technicians’ knowledge and attitudes are shaped by local training

standards, healthcare infrastructure, regulatory frameworks, and cultural practices. This underscores the need for region-specific interventions to improve the safe use of prescription medicines globally.

Figure 5 shows that most research activity peaked between 2020 and 2023, with 2023 marking the highest number of published studies on pharmacy technicians' knowledge, attitudes, and practices regarding prescription medicines.

There are several likely reasons why publications on this topic increased after 2020. The COVID-19 pandemic, which began in 2019, disrupted healthcare systems worldwide. As hospitals and clinics became overwhelmed or harder to access, pharmacies and their staff stepped into a more visible, frontline role, supporting everyday healthcare needs (11). The pandemic also drew attention to the importance of public health education, especially around medication dispensing and patient counseling during COVID-19 and beyond (12).

4.1.1 Global differences in Pharmacy Technician training

In economically developed and well-regulated healthcare systems – such as the UK and Portugal – pharmacy technicians tend to show higher baseline knowledge and more positive attitudes toward prescription medicine use and stewardship (2).

In contrast, studies from Bangladesh, Ethiopia, Indonesia, Somalia, Pakistan, Benin and Colombia, consistently highlight major challenges, including limited formal training, lack of ongoing education, and minimal regulatory oversight. In the UK and Portugal, standardized qualifications, mandatory continuing education, and national initiatives like the Antibiotic Guardian campaign help support consistent knowledge and safe practices. However, in many developing countries, especially in the private sector, pharmacy technicians are often inconsistent, informal, or absent altogether. This leads to knowledge gaps, misinterpretation of prescription rules, and weak implementation of national treatment guidelines.

When reflecting on these findings, it is important to recognize that pharmacy technicians' knowledge and attitudes toward prescription medicines and treatment are not only shaped by education alone. They are also influenced by broader systemic factors like healthcare infrastructure, regulatory frameworks, socioeconomic conditions, and geographic context.

Urban areas with strong healthcare systems, solid professional oversight, and access to employer-supported training tend to create environments that support better knowledge and attitudes. In contrast, rural or under-sourced areas, especially within loosely regulated private sectors, arem ore likely to see gaps in pharmacy technicians' competence and commitment to safe medication practices.

These patterns show that simply improving education is helpful, but not enough. Meaningful change also required ongoing training, stronger accountability, and a culture of shared responsibility. It depends on consistent policy enforcement and broader health system reforms that improve access to medical care. (13)

5. Conclusion

This study highlights global differences in pharmacy technicians' knowledge, attitudes, and practices toward prescription medications in community pharmacy setting. The biggest gaps were seen in low- and middle-income countries – especially across parts of Asia and Africa – where formal training and regulatory oversight are often lacking. In contrast, pharmacy technicians in high-income countries generally benefit from more structured education and stronger professional regulation, leading to more consistent and informed practices.

The COVID-19 pandemic brought renewed attention to the role of pharmacy technicians as accessible healthcare providers. As healthcare systems came under pressure, the pharmacy workforce became increasingly vital – especially in communities where access to other care was limited.

Overall, the findings point to the need for coordinated, long-term strategies to strengthen the pharmacy technicians workforce globally. This includes investing in continuous training, creating standardized education programs, and making sure technicians, creating standardized education programs, and making sure technicians are fully integrated into broader healthcare systems. These steps are essential for ensuring the safe, effective, and responsible use of prescription medications.

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7. Appendixes

7.1 Further processing of the final included articles

Table: A table was developed to present the article titles, authors, publication years, target groups, countries, method (structure), and sample sizes in an organized and structured format.

Article name, author, year	**Target group**	**Country**	**Methods (type)**	**Methods (sample size)**
Knowledge of Vulvovaginal Candidiasis Characteristics, Signs, Symptoms, and Appropriate Treatment Among Portuguese Pharmacy Professionals Oliveira Tiago, Jesus Angelo et. Al., 2025	Pharmacy professionals	Portugal	A cross-sectional study using an online questionnaire	A total of 128 respondents were pharmacy technicians
Evaluation of community pharmacy technicians' knowledge, attitudes, and practices about erectile dysfunction and its predictors in Gondar Town: A cross-sectional descriptive study Mengesha Kebad Assefa, Limenh	Community pharmacy technicians	Ethiopia	A cross-sectional descriptive study	165 respondents were included in the study

Workie Liknaw et. Al., 2024				
Knowledge, attitude, and practice (KAP) regarding erectile dysfunction disease and its medication among community pharmacy technicians in Mogadishu Somalia Mohamud Ali Hussein, Warsame Farah Feysal et. Al., 2023	Community pharmacy technicians	Somalia	A cross-sectional descriptive study	200 respondents participated in the study
Potential and weak links in the management of tuberculosis by Pakistani private pharmacy staff Balquis Fatima, Hamid Huma et. Al., 2023	Private pharmacy staff	Pakistan	A two-phase study. Phase I: A cross-sectional study using two quantitative research design, exploratory and descriptive	A total of 400 eligible respondents, comprising of 25% pharmacy assistants
Knowledge, Attitudes, and Practices Regarding Antibiotic Sales in Pharmacies in Medellín, Colombia 2023	Pharmacy personnel	Colombia	A cross-sectional descriptive study	A total of 277 pharmacies, 48.8% were attended by pharmacy assistants

Colonia M. R. Daniel, Daniela R. Patino et. Al., 2023				
Knowledge, attitude and practice of community pharmacy personnel in tuberculosis patient detection: a multicentre cross-sectional study in a high-burden tuberculosis setting Pradipta Surya Ivan, Khairunnisa Khairunnisa et. Al., 2022	Community pharmacy personnel	Indonesia	A multicentre cross-sectional study	A total of 1129 participants from 979 pharmacies where 43.4% of them were pharmacy technicians
Evaluating UK Pharmacy Workers' Knowledge, Attitudes and Behaviour Regarding Antimicrobial Stewardship Seaton Donna, Ashiro-Oredope Diane et. Al., 2022	Pharmacy workers	UK	A cross-sectional study using a self-completion questionnaire	A total of 767 eligible participants, 17.2% were pharmacy technicians, 17.7% were dispensers
Knowledge of pharmacy workers on antihypertensive and anticonvulsant drugs for managing	Pharmacy workers	Bangladesh	A cross-sectional survey	Out of 382 pharmacy workers 41 pharmacy technicians responded the survey

pre-eclampsia and eclampsia in Bangladesh Roy Shongkour, Sultana Kanij et. Al., 2020				
The provision of advice by pharmacy staff in eastern Indonesian community pharmacies Brata, Cecilia, Schneider R. Carl et. Al., 2019	Pharmacy staff	Indonesia	A patient simulation study followed by a structured interview	19% of 173 pharmacy staff interviewed were pharmacy technicians
Evaluation of the knowledge and attitude of pharmacists about the national malaria control policy in southern Benin Ganfon Habib, Ekanmian Giraud, 2017	Pharmacy staff	Benin	A quantitative survey	A total of 101 dispensator/pharmacy assistants responded the survey