MEDICAL UNIVERSITY – VARNA
FACULTY OF PHARMACY

DEPARTMENT OF ORGANIZATION AND
ECONOMICS OF PHARMACY

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Study on the potential of pharmaceutical care for improving the therapeutic outcomes and preventing complications in patients with ankylosing spondylitis

Thesis summary

of a dissertation submitted for the award of the educational and scientific degree "Doctor (PhD)"

Doctoral programme:

"Pharmacoeconomics and Pharmaceutical Regulation"

Supervisor: Assoc. Prof. Anna Todorova, PhD

Scientific consultant: Prof. Valentina Petkova, D.Sc.

VARNA 2026

The dissertation contains **145** pages, including **38** tables, **4** figures and **2** appendices.

The bibliography contains **254** titles, of which **20** are in Cyrillic and **234** are in Latin script.

The dissertation was discussed at a departmental council meeting of the Department of Organization and Economics of Pharmacy, Faculty of Pharmacy, Medical University "Prof. Dr. P. Stoyanov", Varna, on 15.01.2026.

By Order No. R-109-94 of 12 February 2026, the PhD candidate has been expelled with the right to defend. The dissertation has been scheduled for defense before a scientific jury composed of:

Scientific Jury:

1. Prof. Evgeni Evgeniev Grigorov, Ph.D.
2. Prof. Svetlana Fotkova Georgieva, Ph.D.
3. Prof. Irina Nikolova Nikolova, Ph.D.
4. Assoc. Prof. Daniela Dimitrova Kafalova, Ph.D.
5. Assoc. Prof. Kalina Gocheva Andreevska, Ph.D.

The public defense will be held on **04.05.2026** at…… o'clock at the Medical University "Prof. Dr. P. Stoyanov", Varna.

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Abbreviations used:

AS	Ankylosing spondylitis
bDMARDs	biological disease-modifying antirheumatic medicinal products
NSAIDs	Bulgarian Association of Bechterew's disease patients in Bulgaria
IBD	Inflammatory bowel diseases
GC	Glucocorticosteroids
DRP	Good Pharmaceutical Practice
IPC	Individualized pharmaceutical care
SmPC	Summary of Product Characteristics
CAAD	Commission on Ethics of Scientific Research
MP	Medicinal product
ADR	Adverse drug reaction
NSAIDs	Non-steroidal anti-inflammatory medicinal products
RA	Rheumatoid arthritis
csDMARDs	standard disease-modifying antirheumatic medicinal product
WHO	World Health Organization
ESR	Erythrocyte sedimentation rate
SDO	Postgraduate education
tsDMARDs	targeted synthetic disease-modifying antirheumatic medicinal products
PC	Pharmaceutical care
MRI	Magnetic resonance imaging
ASAS	International Society for the Assessment of SpondyloArthritis
ASDAS	Ankylosing Spondylitis Disease Activity Score (Disease activity score in ankylosing spondylitis)

ASIF	Ankylosing Spondylitis International Federation
BASDAI	Bath Ankylosing Spondylitis Disease Activity Index (Ankylosing spondylitis disease activity index)
COX-2	Cyclooxygenase-2
CRP	C-reactive protein
EULAR	European Alliance of Associations for Rheumatology
EMA	European Medicines Agency
ERAP	Endoplasmic reticulum aminopeptidase
ESSG	European Spondyloarthropathy Study Group
FDA	Food and Drug Administration (USA)
FIP	International Pharmaceutical Federation
HLA	Human leukocyte antigen
JAK	Janus kinase
MCID	Minimal clinically important difference
PCNE	Pharmaceutical Care Network Europe
PCR	Polymerase chain reaction
TNF	Tumor necrosis factor
VAS	Visual analogue scale

I. INTRODUCTION

Ankylosing spondylitis (Bechterew's disease) is a chronic, progressive inflammatory condition affecting primarily the sacroiliac joints and the spine. It is characterized by lumbar pain, morning stiffness, and progressive limitation of axial skeletal function. The disease may present with extra-articular manifestations and involvement of various organs and systems – eyes (uveitis), skin, gastrointestinal tract, limitation of chest movements and respiratory function, and more rarely the cardiovascular system – necessitating an interdisciplinary approach and combined therapeutic strategies.

AS is a prototype of immune-mediated inflammatory rheumatic diseases from the spondyloarthritis group. The importance of early diagnosis is increasing due to the availability of effective therapies, including anti-TNF agents, which achieve better outcomes when used in early stages before irreversible structural changes occur. The disease affects mainly young people (20–30 years), which determines its high social significance, and diagnostic delay remains a common problem.

Key elements in disease control are appropriate physical activity and rational pharmacotherapy. Good adherence to drug treatment leads to better symptom control, slowing of progression, and reduction of the risk of disabling changes, as well as improvement in quality of life. Treatment is long-term and includes analgesic and disease-modifying medicinal products; many patients also have comorbidities requiring additional medicines. This increases the risk of medication-related problems – adverse reactions, interactions, incorrect use, and non-adherence to therapy.

According to the principles of Good Pharmaceutical Practice, the pharmacist is a key link between physician and patient and can contribute to effective prevention and management of chronic diseases. As an

accessible source of health information, the pharmacist in a community pharmacy has the potential to play a more active role in the care of patients with AS – both by referral when inflammatory low back pain is suspected and by providing pharmaceutical care to diagnosed patients. This includes prevention and control of medication-related problems, optimization of therapy, improvement of quality of life, and limitation of direct and indirect costs for the patient and society.

II. AIM, OBJECTIVES AND SCIENTIFIC HYPOTHESES

1. AIM OF THE DISSERTATION

To explore pharmacists' attitudes and competencies in providing pharmaceutical care for patients with ankylosing spondylitis and to analyze the potential for integrating the pharmacist into the multidisciplinary approach to prevent complications and optimize therapeutic outcomes.

2. OBJECTIVES

2.1. To examine and analyze pharmacists' attitudes and barriers, as well as their educational needs, regarding the provision of PC for patients with AS.

2.2. To develop algorithms for screening individuals at risk and for providing PC to patients diagnosed with AS.

2.3. To examine and analyze the demographic and medico-social characteristics, health-behavioral habits, and the applied pharmacological and non-pharmacological therapy among patients with AS in the Ruse region.

2.4. To investigate disease activity in patients with AS and the factors influencing it.

2.5. To assess health-related quality of life, the factors influencing it, and its relationship with disease activity in patients with AS.

2.6. To assess the level of adherence to therapy in patients with AS and the factors influencing it.

3. SCIENTIFIC HYPOTHESES

3.1. Pharmacists' attitudes and competencies for providing pharmaceutical care to patients with AS are associated with their personal and professional characteristics and determine the potential for effective integration of the pharmacist into the multidisciplinary approach to prevention, care, and optimization of disease treatment.

3.2. Unfavorable, potentially modifiable through pharmaceutical care, health-behavioral factors and the low level of adherence to pharmacotherapy are associated with higher disease activity and lower quality of life among patients with AS.

III. MATERIALS AND METHODS

MATERIALS

The study in the dissertation comprises two target groups:
– MSc pharmacists practicing in community pharmacies;
– Patients diagnosed with ankylosing spondylitis (AS).

1. Survey among MSc pharmacists

1.1. Sampling and sample size

Pharmacists from Northeastern Bulgaria were surveyed – members of RFC–Ruse, RFC–Varna, and RFC–Dobrich. According to data from the national register of the BFS, the total population is N = 817 pharmacists. To achieve statistical reliability of the results obtained, the required sample was calculated at approximately n ≈ 260–261. The following criteria were applied in selecting the sample:

– inclusion criteria:
- practicing in community pharmacies;

- membership in RFC – Ruse/Varna/Dobrich;
- voluntary participation and completed documents submitted to KENI at MU–Varna (study information, personal data protection notice, informed consent).

– exclusion criteria:

- assistant pharmacists;
- pharmacists from other regional colleges;
- MSc pharmacists practicing in other professional fields.

1.2. Subject of the study

- Educational needs of MSc pharmacists regarding AS and its pain symptomatology.
- Attitudes, readiness, and barriers to the provision of pharmaceutical care (PC) for patients with AS.

1.3. Units of observation

- awareness of AS;
- ability to distinguish inflammatory from compressive pain in pharmacy practice;
- readiness/barriers to PC for patients diagnosed with AS;
- possibility for early screening at the pharmacy level for patients suspected of having AS.

1.4. Design and period

An online, anonymous questionnaire survey (Google Forms) was conducted during January 2025 – June 2025, with the assistance of RFC – Varna, Ruse, and Dobrich.

2. Survey among patients with ankylosing spondylitis

2.1. Scope and sample size

According to information provided by the NHIF (Decision RD-19-24/18.02.2025), in Ruse Region the registered patients with AS (ICD-10 M45) in 2024 were 207. The aim was to include approximately 1/3 of the patients meeting the listed criteria – about n ≈ 60.

– inclusion criteria:

- AS diagnosis according to the modified New York criteria, ICD-10 M45, within Ruse Region;
- age ≥ 18 years;
- voluntary participation and completed documents submitted to KENI at MU–Varna.

– exclusion criteria:

- lack of a confirmed diagnosis;
- minors;
- refusal to participate;
- individuals with mental disorders;
- individuals with impaired hearing and/or vision.

2.2. Subject of the study

- current health status, disease activity, quality of life, and influencing factors;
- adherence to pharmacotherapy and types of therapy applied;
- patients' awareness and need for IPC.

2.3. Units of observation

- Factor variables: age, sex, education, health-behavioral habits, treatment, comorbidities, physical activity regimen.
- Outcome variables: height/weight, time to diagnosis from the onset of complaints, disease duration.
- Subjective/scales: BASDAI, BAS-G, EQ-5D-5L, Morisky MMAS-8.

2.4. Design and period

A face-to-face survey interview was conducted by the principal investigator and trained MSc pharmacists in selected base pharmacies in the city of Ruse. Data collection period: November 2024 – November 2025.

METHODS

1. Documentary method

An analysis of international and national guidelines and standards (for Good Pharmaceutical Practice – FIP/WHO/BFS), as well as summaries of product characteristics of medicinal products used in AS, was performed in order to:

- development of an online questionnaire for pharmacists;
- a structured questionnaire for patients;
- development of a PC scheme for diagnosed patients and a screening algorithm for suspected cases.

2. Sociological method

Instruments:

- online questionnaire for MSc pharmacists;
- structured interview questionnaire for patients with AS.

2.1. Structure of the questionnaire for MSc pharmacists

A total of 20 closed-ended questions, completion time up to 15 minutes, in 4 modules:

1. demographic/educational data (4 questions);
2. educational needs regarding AS (10 questions);
3. attitudes and barriers to PC (5 questions);
4. need for additional training (1 question).

2.2. Structure of the interview questionnaire for patients

Closed- and open-ended questions, organized into 4 modules, including validated instruments:

1. demographic and socio-medical data (incl. time to diagnosis, comorbidity, harmful habits);

2. assessment of disease activity and quality of life: BASDAI, BAS-G, BMI, EQ-5D-5L (incl. VAS);

3. attitudes and awareness regarding pharmaceutical care and counselling (5 questions);

4. therapies, ADRs, and adherence to therapy – MMAS-8.

3. Statistical methods

- The sample size for pharmacists was determined at 95% confidence, allowable error 5%, proportion p = 0.5, with correction for the finite population (N=817), yielding ≈ 260.
- Data were processed using SPSS for Windows.

Analyses used:

- Descriptive statistics: Mean ± SD for quantitative variables; N (%) for categorical variables.
- Normality testing: Kolmogorov–Smirnov or Shapiro–Wilk.
- Comparative tests:
  - Mann–Whitney U (two independent groups with non-normal distribution);
  - Welch t-test (different variances/unequal groups);
  - Pearson's χ^2 test or Fisher's exact test (two categorical variables);
  - One-way ANOVA (more than two groups).
- Correlations: Pearson's r and Spearman's ρ; Bonferroni correction applied for multiple comparisons.
- Regression analysis: linear regression model for the relationship MMAS-8 ↔ BASDAI.
- Effect size and strength of association: Cohen's d, r (for Mann–Whitney), η^2 (ANOVA), Cramer's V (χ^2).
- Significance level: $p < 0.05$ with 95% confidence interval (CI 95%).

- The results were visualized through tables/graphs in MS Word and MS Excel (2025).

Assessment of pharmacists' competence regarding pain in AS

A composite indicator was created from 7 selected questions from the questionnaire assessing knowledge about inflammatory/compressive pain and referral to an appropriate specialist. Each correct answer carried 1 point, total score 0–7. Due to uncertainty regarding normality and different group sizes, the Mann–Whitney U test for independent samples was used to test the hypotheses.

Ethical approval

The study was approved by the Ethics Committee for Research at MU–Varna, Protocol No. 5/17.10.2024. Participation was voluntary, in compliance with the requirements for informed consent and personal data protection.

IV. RESULTS AND DISCUSSION

1. Results from the questionnaire survey among Master Pharmacists in community pharmacies

1.1. Attitudes towards providing pharmaceutical care for patients with AS

In the study, 260 pharmacists meeting the inclusion criteria participated; 77% were women and 23% were men. Approximately every second respondent obtained their higher pharmaceutical education more than 10 years ago, and 89% of respondents graduated from a faculty of pharmacy in Bulgaria. Pharmacists without postgraduate specialization predominated (87%).

The survey includes questions aimed at assessing pharmacists' attitudes (readiness and barriers) for active participation in the comprehensive care of patients with ankylosing spondylitis.

More than half of the surveyed pharmacists (55%) are either unsure or do not feel sufficiently prepared with the knowledge and skills to participate in counseling patients with AS; however, a substantial proportion of respondents (84%) find the participation of a pharmacist in the comprehensive care of patients with AS necessary.

The questionnaire survey showed that 68% of pharmacists are familiar with the concept of individualized pharmaceutical care (IPC), whereas 32% are not. A substantial proportion of respondents stated that the provision of IPC would bring them professional satisfaction; 12% could not judge; no negative answers were provided. The results are shown **in Table 1**.

According to their self-assessment, the surveyed pharmacists indicated that they would be most useful when counseling on correct medicine intake (timing, dose, food), possible drug interactions, and the likelihood of adverse drug reactions, followed by dispensing OTC

products and supporting adherence to prescribed therapy, whereas initial screening was indicated least frequently. The results obtained are presented in **Table 1.**

Table 1. Characteristics and attitudes toward PC of the surveyed pharmacist sample

Demographic characteristics of the surveyed pharmacists (n=260)	**Number**	**%**
Sex		
Male	61	23%
Female	199	77%
Work experience		
Up to 10 years	120	46%
Over 10 years	140	54%
Place of pharmacy education		
Bulgaria	232	89%
Outside Bulgaria	28	11%
Acquired postgraduate specialty		
No	226	87%
Yes	34	13%
Attitude and readiness to participate in the care of patients with AS – questions	**Number respondents**	**%**
1. Do you possess the necessary knowledge and skills for consulting patients with AS?		
Yes	117	45%
No	43	17%
I cannot judge	100	38%
2. Do you consider that pharmacist participation in the treatment of patients with AS is necessary?		
Yes	218	84%

No	31	12%
I cannot judge	11	4%
3. Do you have knowledge of the Individualized Pharmaceutical Care (IPC) concept?		
Yes	177	68%
No	51	20%
I cannot judge	32	12%
4. Do you experience professional satisfaction from providing IPC?		
Yes	229	88%
No	12	5%
I cannot judge	19	7%
Aspects of PC	**Number indicated responses**	**Percentage distribution**
Counseling on possible ADRs	191	20%
When dispensing OTC products	171	18%
Initial screening	87	9%
Counseling on possible drug interactions	200	21%
Counseling on administration method (time, dose, food)	203	21%
Improving adherence rate	112	11%

Graphical analysis of the results of the questionnaire among pharmacists in the present study shows that low back pain is a problem encountered frequently in practice by nearly 80% of the surveyed respondents, as presented in **Figure 1.**

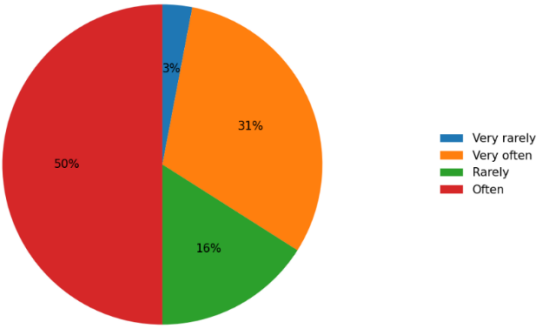

Fig. 1. Frequency of consulting patients with lower back pain

Regarding the most commonly undertaken actions by pharmacists when counseling patients with back and low back pain, dispensing OTC products with the necessary counseling on the mode of administration and referral to a specialist physician is the most frequently applied combination. The least frequently undertaken action, according to the survey, is dispensing dietary supplements – only 2%, an answer included in the "Other" category. The results are presented in **Figure 2**.

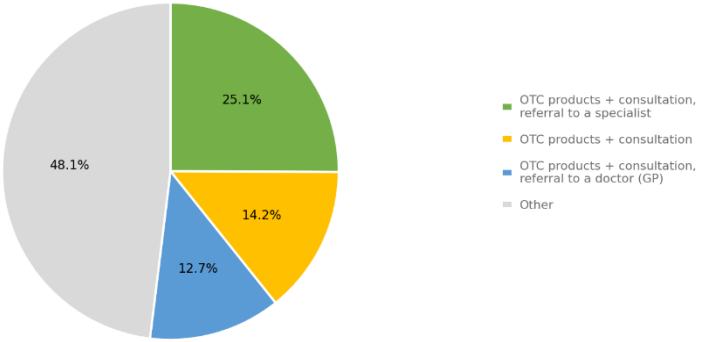

Fig. 2. Distribution of activities of surveyed pharmacists when consulting patients with lower back pain

Most of the surveyed pharmacists would refer a patient with inflammatory low back pain to a neurologist, while a substantial proportion would refer to a rheumatologist. The results are shown in **Figure 3**. Referrals to an orthopedist are less frequent, and to an infectious disease specialist are isolated; a hematologist is not indicated.

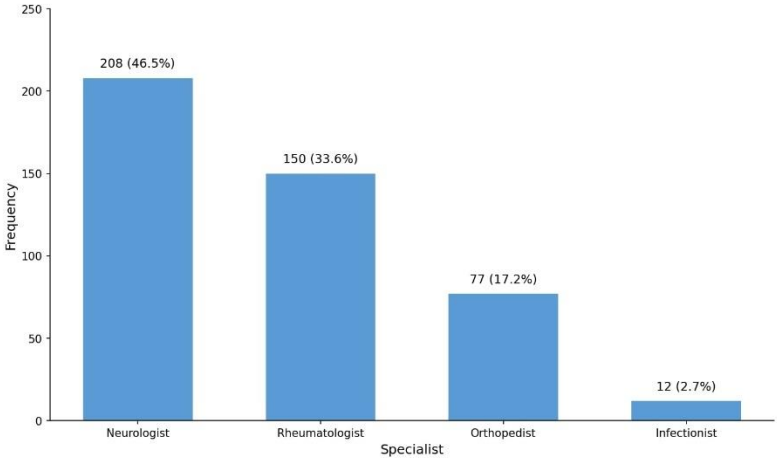

Fig. 3. Frequency of specialists recommended by pharmacists for consultation

As the main barriers to providing PC, the surveyed pharmacists highlight lack of time, lack of a dedicated consultation area, and lack of remuneration for the service, as well as insufficient knowledge about therapy and disease specificity; less frequently, insufficient communication skills and patients' unwillingness are mentioned. The results regarding the main barriers faced by pharmacists in providing IPC are presented in **Table 2.**

Table 2. Perceived barriers in implementing pharmaceutical care

Barrier	Yes, n (%)	No, n (%)	I cannot judge, n (%)
Lack of sufficient time	198 (76)	19 (7)	43 (17)
Lack of dedicated space	163 (63)	54 (21)	43 (17)
Lack of payment for IPC service	139 (53)	82 (32)	39 (15)
Insufficient knowledge of therapy and drug safety profile	138 (53)	80 (31)	42 (16)
Insufficient awareness about the disease	183 (70)	45 (17)	32 (12)
Insufficient communication skills	85 (33)	133 (51)	42 (16)
Patient unwillingness	121 (47)	71 (27)	68 (26)

1.2. Analysis of factors influencing attitudes towards providing pharmaceutical care

Table 3 presents results from a correlation analysis of the influence of gender, work experience (years since graduation), place of education, and postgraduate specialization on readiness for pharmaceutical care (PC). Gender has a weak effect and does not remain significant after correction for multiple comparisons. A statistically significant and robust association was found between shorter professional experience and better knowledge/higher confidence in providing PC, which remains after Bonferroni correction. The place where education was obtained has no influence, while pharmacists with postgraduate specialization are more critical of their own knowledge regarding PC.

Table 3. Influence of demographic and educational factors on attitudes toward PC

Factor	Dependent variable	ρ (Spearman)	p	Significant Bonferroni (p<0.002)
Sex	Self-assessment of knowledge	0.075	0.2256	No
	Need for pharmacist participation	0.001	0.9919	No
	Knowledge of IPC	-0.147	**0.01806**	**No**
	Satisfaction from IPC	-0.132	0.03285	No
Work experience (≤10/>10)	Self-assessment of knowledge	0.196	**0.001501**	**Yes**
	Pharmacist participation	0.174	**0.004832**	**No**
	Knowledge of IPC	0.353	**4.99×10^{-9}**	**Yes**
	Satisfaction from IPC	0.103	0.09893	No
Place of education	Self-assessment of knowledge	0.003	0.9667	No
	Pharmacist participation	0.062	0.3154	No
	Knowledge of IPC	0.025	0.6885	No
	Satisfaction from IPC	0.128	**0.03944**	**No**
Presence of postgraduate special-ization	Self-assessment of knowledge	0.224	0.0002723	Yes
	Pharmacist participation	0.034	0.5855	No
	Knowledge of IPC	0.126	0.04247	No
	Satisfaction from IPC	0.104	0.09516	No

Table 4 presents results from a correlation analysis of the influence of demographic and educational factors on perceived barriers to the provision of pharmaceutical care. After Bonferroni correction, only one association remains statistically significant: pharmacists with shorter work experience more often perceive patients' unwillingness as a barrier to providing IPC. At $p<0.05$, weaker dependences are also observed, mainly related to years since graduation: more experienced pharmacists more often cite lack of space and insufficient awareness, whereas more recently graduated pharmacists emphasize communication skills and patients' unwillingness. Weak effects of gender, place of education, and the presence of a specialization are also reported.

Table 4. Factors influencing barriers to providing PC.

Predictor	Barrier	ρ (Spearman)	p	Significant Bonferroni (p<0.0014)
Sex	Lack of sufficient time	-0.094	0.129	No
	Lack of dedicated space	-0.145	**0.019**	No
	Lack of payment	0.095	0.125	No
	Insuff. knowledge of therapy	0.031	0.624	No
	Insuff. awareness	-0.093	0.135	No
	Insufficient communication skills	-0.095	0.124	No
	Patient unwillingness	-0.075	0.225	No
Work experience (≤10/>10)	Lack of sufficient time	-0.066	0.286	No
	Lack of dedicated space	0.091	0.141	No
	Lack of payment	0.055	0.376	No

	Insuff. knowledge of therapy	-0.082	0.201	No
	Insuff. awareness	0.19	**0.00215**	No
	Insufficient communication skills	-0.129	**0.0379**	No
	Patient unwillingness	-0.19	**0.00211**	**Yes**
Place of pharmaceutical edication	Lack of sufficient time	-0.003	0.967	No
	Lack of dedicated space	-0.07	0.266	No
	Lack of payment	-0.133	**0.0317**	No
	Insuff. knowledge of therapy	0.013	0.838	No
	Insuff. awareness	-0.07	0.271	No
	Insufficient communication skills	-0.014	0.671	No
	Patient unwillingness	-0.083	0.141	No
postgraduate specialization	Lack of sufficient time	0.034	0.599	No
	Lack of dedicated space	0.146	**0.0187**	No
	Lack of payment	0.062	0.315	No
	Insuff. knowledge of therapy	-0.023	0.768	No
	Insuff. awareness	-0.073	0.294	No
	Insufficient communication skills	-0.091	0.212	No
	Patient unwillingness	-0.085	0.259	No

1.3. Pharmacists' competence regarding AS and influencing factors

Arithmetic mean values (X) of the sum of competency points of pharmacists regarding knowledge of pain in AS were calculated by indicators such as gender, work experience, acquired postgraduate qualification, place of obtaining pharmaceutical education, and other indicators. Differences were analyzed to establish statistical significance and reliability. The results obtained are presented in **Table 5**.

Several statistically significant differences are observed. Pharmacists with work experience under 10 years have a higher mean score (3.90) compared with those with over 10 years (3.47), p=0.031. Individuals without postgraduate specialization achieve a higher mean score (3.54) than those with postgraduate specialization (2.68), p=0.00046. Respondents who report a need for additional training to provide IPC have a higher mean score (3.49) compared with those who do not see such a need (2.54), p=0.00045. Participants who consider pharmacists' participation in comprehensive AS care necessary have a higher mean score (3.47) compared with those who do not support it (3.02), p=0.0024.

Alongside this, non-significant differences are also found. Men have a higher mean score (3.76) than women (3.27), but without statistical significance (p=0.407). Graduates outside Bulgaria show a higher mean score (4.18) compared with graduates in Bulgaria (3.36), but the difference does not reach statistical significance (p=0.078).

Table 5. Comparative analysis of competency scores distributed by different indicators

Indicator	Group 1	X_1	S_1	V_1%	Group 2	X_2	S_2	V_2%	p
Sex	**Women**	3.27	1.74	53.30	**Men**	3.76	1.45	38.52	0.40700
Experience	**Under 10 y.**	3.90	2.27	58.13	**Over 10 y.**	3.47	2.02	58.22	**0.03100**
Postgraduate specialization	**Acquired**	2.68	1.84	68.66	**Without postgraduate specialization**	3.54	1.74	49.07	**0.00046**
Acquired education	**In Bulgaria**	3.36	1.68	50.10	**Outside Bulgaria**	4.18	1.72	41.22	0.0780
Need for additional. training on AS	**Needs**	3.49	1.71	49.03	**Does not need**	2.54	1.84	72.39	**0.00045**
Pharmacist participation in AS care	**Consider necessary**	3.47	1.77	51.00	**Do not consider necessary**	3.02	1.54	50.94	**0.0024**

The results of the correlation analysis presented in **Table 6** show that pharmacists' confidence and readiness to provide PC for patients with ankylosing spondylitis depend not only on general theoretical knowledge but also on specific practical and clinical skills, such as the ability to differentiate inflammatory from compressive pain. The frequency of consultations with patients with low back pain has limited influence, and knowledge of referring to the appropriate specialist physician alone does not change readiness, suggesting that motivation to participate in PC is

rather a function of overall clinical competence than of isolated knowledge.

Table 6. Correlation analysis of skills and knowledge for PC in patients with AS relative to individual factors

№	Investigated relationship	Para-meter for relationship	χ^2	p	OR
1.	Knowledge of AS/frequency of consultations for lower back pain	$\rho \approx 0.12$	—	≈0.058	—
2.	Knowledge of AS/ability to differentiate inflammatory/ compression pain	$\Phi = 0.17$	7.56	**0.006**	2.19
3.	Knowledge of AS/referral to rheumatologist	$\Phi \approx 0.04$	0.34	0.56	0.83

Legend: Φ – Cramer's coefficient (for 2×2 – φ of Pearson); ρ – coefficient of Spearman; χ^2 – criterion of Pearson; OR – odds ratio; "–": not applicable/not calculated.

The online survey among practicing pharmacists in community pharmacies in the territory of RFC–Ruse, RFC–Dobrich, and RFC–Varna aims to examine their knowledge regarding ankylosing spondylitis (AS), differentiation of mechanical and inflammatory pain, and the need for additional training. The results show that pharmacists frequently counsel patients with low back pain but experience difficulties in recognizing the characteristic features of AS. Almost 70% of respondents cannot or are not sure whether they can differentiate inflammatory from compressive/mechanical pain. The proportion of pharmacists who cannot judge whether they have sufficient knowledge to counsel on pain syndrome in AS, or believe they do not have such knowledge, is 55%. Although AS is a noninfectious inflammatory rheumatologic disease,

47% of pharmacists refer patients to a neurologist, probably due to associating low back pain with disc disease and compressive syndromes. This carries a risk of delayed diagnosis and incorrect referral, which may prolong the time to initiation of adequate therapy. In the survey, only 43% correctly indicate that in inflammatory pain symptoms decrease with movement, while 57% believe the opposite or are unsure.

The obtained data highlight the need to develop targeted training and informational materials for pharmacists aimed at improving counselling in low back pain and recognising AS. Based on international recommendations (ACR, ASAS–EULAR), FIP materials, and the guidance of the Bulgarian Society of Rheumatology, the following core educational needs can be formulated:

1. knowledge of the pathophysiology and clinical manifestations of AS;
2. rational and safe pharmacotherapy (NSAIDs, biological/targeted therapy) and the pharmacist's role;
3. monitoring of adverse drug reactions and drug–drug interactions;
4. improving adherence to therapy through structured support, a therapeutic plan, and effective communication (including motivational interviewing and digital reminders);
5. counselling on health-behaviour change and possible non-pharmacological measures (physical activity, posture and ergonomics, smoking cessation, maintaining optimal weight, and sleep hygiene);
6. documentation, follow-up, and collaboration with rheumatologists and other specialists.

We did not identify published Bulgarian studies that systematically assess pharmacists' preparedness for early recognition of inflammatory back pain and participation in PC for AS. International evidence in other rheumatological conditions shows that short, low-cost training programmes developed jointly with rheumatologists improve knowledge

and practical readiness. The present study supports the need for jointly developed continuing education programmes between rheumatologists and pharmacists, which would increase the applicability of knowledge and the quality of everyday practice.

1.4. Educational materials for pharmacy practice

1.4.1. Algorithm for the provision of pharmaceutical care for patients with AS

The developed concise PC algorithm for patients with AS, based on global practical guidelines but adapted for Bulgaria, is necessary and applicable for community pharmacists, with the aim of enabling the pharmacist's active participation in comprehensive care for patients with AS.

PHARMACEUTICAL CARE IN ANKYLOSING SPONDILITIS

Pharmacy for population service — brief practice algorithm practice

SCREENING UNDIAGNOSED PATIENTS

- Differentiation of pain: inflammatory pain, neurogenicala pain; key symptoms of AS.
- Rapid onset of inflammatory back pain (morning stiffness, nighttime pain, improvement with movement, age <45 y.. chronicity > 3 m., gradual onset, "red flags": neurological deficit, fever, trauma, tumor/infection) – urgent referral to GP or reumatnologist.

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DIAGNOSED PATIENTS WITH AS

INFORMATION ABOUT THE DISEASE

- What is AS and why early diagnosis is important.
- Long-term consequences: fractures, uveitis, psoriasis, IBD, cardiovascular nd and metab— complications, depression.

THERAPIES AND MONITORING

- Pharmacotherapy: NSAIDs, biologic/targeted therapy, EULAR recommondations
- Medication adherence - important for the effect and monitoring.
- Assessment and maintenance of efficacy, safety, adverse events management, therapeutic plan.

BEHAVIOR DURING FLARE-UPS

- Following prescribed medication; exercise and physical therapy.
- When to consult a GP/rheumatologist.

LIFESTYLE

- Movement, posture/ergonomics, smoking cessation, dietary adjustments, stress reduc-
- Referral to appropriate expert, dietician, psychologist if needed.

DOCUMENTATION AND EDUCATION

- Patient records: medication, effect, ADRs.
- Useful education and collaboration with rhemautologists/GPs.

Source: ASAS–EULAR, ACR, PIP; adapted for pharmaceatical practice

1.4.2. Rapid screening questionnaire for AS

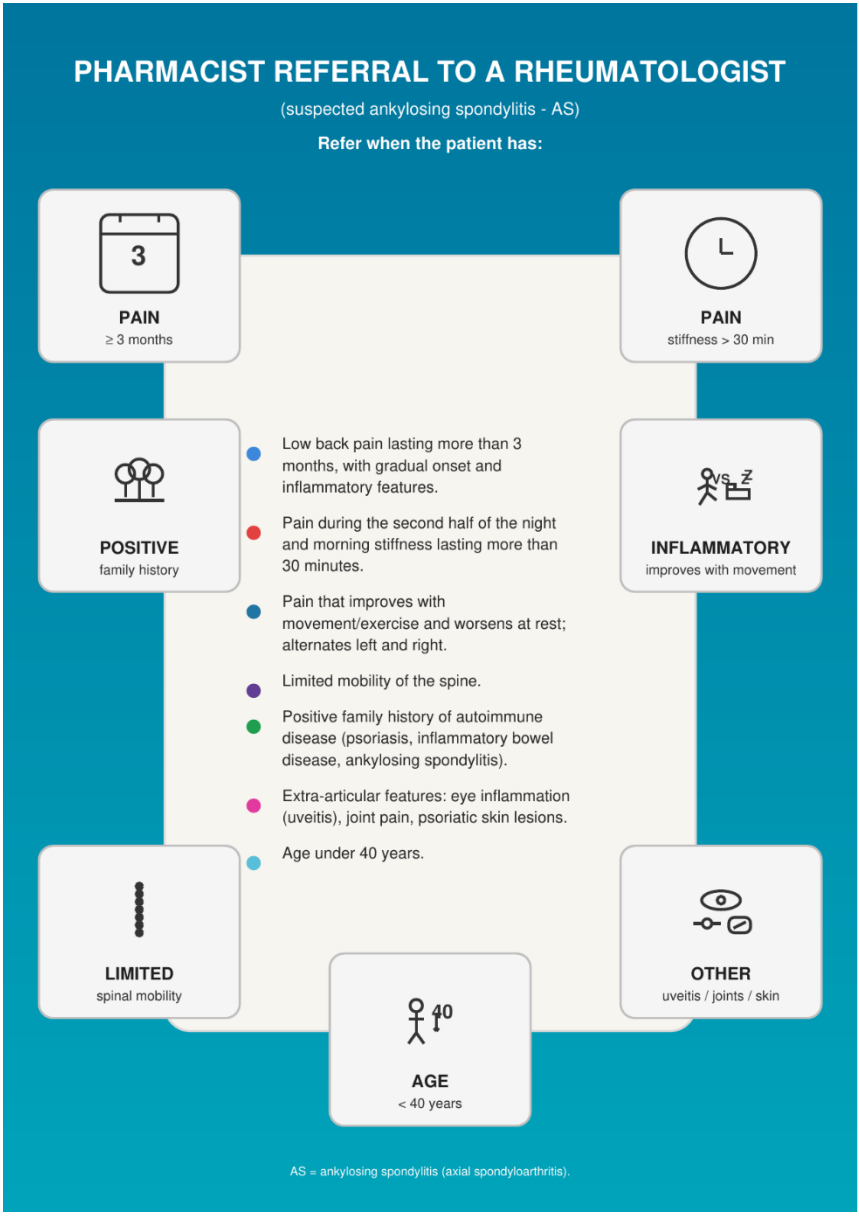
One of the main reasons for delayed diagnosis of AS is insufficient knowledge about the condition among healthcare professionals. This includes lack of awareness of the different subtypes of spondyloarthropathies, lack of knowledge about associated clinical features (e.g., differences between inflammatory and mechanical back pain), or characteristics of patient populations (e.g., that spondyloarthritis affects a similar number of men and women, or that a substantial proportion of people with spondyloarthritis are HLA-B27 negative).

In order to provide appropriate counselling to patients with low back pain and to improve recognition of ankylosing spondylitis, the community pharmacist should be able to distinguish inflammatory from mechanical pain; the differences are shown in **Table 7**.

Table 7. Differentiation of inflammatory from mechanical pain

Characteristic	Inflammatory pain, characteristic of AS	Mechanical pain (discopathy, sciatica)
Onset	Gradual	Sudden, after physical exertion
Duration	> 3 months	Often < 6 weeks
Worsens at rest?	✅ Yes (strongest at night, early morning)	❌ No
Relieved with movement?	✅ Yes	❌ No
Morning stiffness	✅ Yes, > 30 minutes	❌ No or brief

The pharmacist should know when and to whom to refer patients with low back pain:



Based on the ASAS–EULAR recommendations and those of the American College of Rheumatology, a checklist (rapid questionnaire) can be developed and adapted for the community pharmacist's practice, presented in **Table 8**, in order to perform rapid pharmacy-level screening of suspected but undiagnosed AS patients and to refer them in a timely manner to a rheumatologist for an accurate diagnosis and appropriate treatment.

Table 8. Rapid questionnaire for patients with low back pain

Question	YES	NO
1. Has the lower back pain persisted for more than 3 months?		
2. Did the pain start before age 40?		
3. Does the pain worsen at rest (at night and early morning)?		
4. Morning stiffness persists for more than 30 minutes?		
5. Does the pain decrease after movement or exercise?		
6. Do you feel limitations when performing certain movements?		
7. Do you visit a pharmacy more than once a week to purchase pain-relieving medicinal products to alleviate your lower back pain?		

If the patient answers "YES" to 5 or more questions, there is suspicion of inflammatory pain characteristic of ankylosing spondylitis and referral for rheumatology consultation and imaging is required.

Pharmacists can use this checklist with any patient with chronic low back pain. Improving knowledge and attention to this type of patient will reduce diagnostic delay and ensure timely treatment.

Discussion

The results show a sex profile consistent with national and international data for the pharmacy profession (FIP, BPhU). There is a high self-reported readiness to provide individualised PC, mainly in direct counselling (mode and timing of administration, drug interactions, adverse drug reactions), while the lowest confidence is reported for initial assessment and screening. This supports the need for structured screening questions and practical algorithms in chronic diseases, including AS. The community pharmacy emerges as a key point for early referral and for differentiating inflammatory from mechanical pain in complaints of low back and back pain, given the frequent initial use of OTC analgesics and NSAIDs.

The main barriers to providing PC are structural (insufficient time, lack of a dedicated area, lack of a financial framework for the service) and educational (insufficient therapeutic knowledge and disease awareness), showing similarity with international data and the need for a combined approach (training, organisational changes, and remuneration models). The most robust association is between years since graduation and knowledge of PC – more recently graduated pharmacists are better informed – whereas sex is not a significant factor.

Competence does not differ by sex, but there is a trend towards higher scores among pharmacists with shorter professional experience. Pharmacists without postgraduate specialisation rate themselves higher (possibly due to more critical self-assessment among those with a specialty, or a thematic mismatch between the specialty and AS). Higher scores among those who report a need for additional training indicate good self-awareness and motivation for development, and support for an active pharmacist role in comprehensive care is associated with higher competence.

An effective training programme should include criteria for inflammatory pain and its differentiation from compressive pain, "red flags" for periods of disease flare, algorithms for early screening and referral to a rheumatologist, as well as communication training. The results indicate that theoretical knowledge is necessary but insufficient without practical skills, organisational support, and adequate time.

2. Results from the questionnaire survey among Patients with AS

2.1. Health status, behavioural habits and patients' attitudes towards pharmaceutical care

The study included 66 patients with ankylosing spondylitis (38 men and 28 women), with more than half having higher education. The majority of participants (74.3%) are aged 31–50 years, consistent with the predominance of the disease in younger people. **Table 9** presents the socio-demographic characteristics and data related to the time to diagnosis. In almost two-thirds of patients, the diagnosis was made after more than 5 years, which increases the risk of structural damage and functional loss and underlines the need for earlier recognition. In more than half of the patients, the diagnosis was made at the age of 21–30 years, and no cases of diagnosis before the age of 20 years were recorded in the sample.

Table 9. Distribution of patients by demographic indicators, education, age, and time to diagnosis of AS

Indicator	Category	n (%)
Sex	Male	38 (58.0)
	Female	28 (42.0)
Age (years)	31–40	17 (25.8)
	41–50	32 (48.5)
	51–60	13 (19.7)
	>60	4 (6.1)
Time to establish AS diagnosis	<5 y.	23 (34.8)
	5–10 y.	31 (47.0)
	>10 y.	12 (18.2)
Age at diagnosis	21–30	35 (53.0)
	31–40	13 (19.7)
	≥41	9 (13.6)
	Missing data	9 (13.6)
Education	Primary	2 (3.0)
	Secondary	21 (32.0)
	Higher	43 (65.0)

In the studied sample, 92.4% of patients are HLA-B27 positive. Over 70% (71%, n = 47) report at least one comorbid condition, most commonly conditions within the metabolic syndrome spectrum (diabetes mellitus, dyslipidaemia, gout – over 60%), as well as osteoporosis, cardiovascular disease, peripheral arthritis, and fibromyalgia. About 42% of patients follow a diet related to the disease, and in the majority BMI is ≥25 (overweight). In 70% sleep is under 6 hours; more than half are physically active, and non-smokers represent a higher proportion. The

assessment of overall health status by BAS-G shows a mean value of 5.81 (median 6; range 2–10), reflecting a moderate to strong impact of the disease on quality of life. **Table 10** summarises the results.

Table 10. Clinical and health-behaviour characteristics of the studied group of AS patients

Characteristic	Number	%
Comorbidities		
Yes	47	71
No	19	29
HLA- B27		
Positive	61	92.4
Negative	5	7.6
Following a specific diet		
Yes	28	42
No	38	58
Body Mass Index (BMI)		
< 25	31	47
≥ 25	35	53
Actively exercising		
Yes	35	53
No	31	47
Smokers		
Yes	29	44
No	37	56
Hours of night sleep		
< 6 hours	46	70
≥ 6 hours	20	30

The study also examined the frequency of types of therapies used by the surveyed patients. The results are summarised in **Table 11.**

Table 11. Therapy used in relation to the underlying disease

Characteristic	Number	%
Biological therapy		
Yes	43	65
No	23	35
Application of non-pharmacological		
Yes	40	60
No	26	40

A substantial proportion of surveyed patients are on biological therapy (65%); more than half additionally use non-pharmacological therapy in controlling their disease.

When asked whether they would use individualised PC, 88% of participants responded positively, and no negative responses were recorded. The results are presented in **Table 12.**

Table 12. AS patients' attitude towards individualised PC

Response	Number of patients (n)	Proportion (%)
Yes	58	88.0%
I cannot judge	8	12.0%
No	0	0.0%
Total	66	100%

Table 13 presents the results of assessing the need for individualised PC on a scale from 0 (not needed) to 10 (extremely needed). A high proportion (89.4%) of respondents give a score above 8 for the need for PC in their disease.

Table 13. Assessment of the need for PC

Mean value	SD	95% CI	Lowest score	Proportion (high score 8–10)
8.73	1.38	8.39 – 9.07	5	89.4 %

Regarding readiness to react during disease flare (from 1 to 10), the mean value is 7.67 (median = 8), indicating that patients feel relatively prepared to cope with these episodes.

Use of dietary supplements on one's own initiative or on a recommendation other than that of the rheumatologist was reported by 47% of participants, and more than 60% of them would not consult a pharmacist regarding their use. More than 90% report at least one adverse effect from the prescribed therapy, most commonly gastrointestinal complaints, skin reactions, fatigue, dizziness, and local pain at the injection site.

2.2. Analysis of disease activity, quality of life and influencing factors

2.2.1. Assessment of disease activity in patients with AS

Investigating and understanding which factors influence BASDAI and in what direction is key – it guides personalisation of comprehensive care for AS patients, with the aim of slowing the progressive course of the disease and reducing adverse effects from the applied therapy, both pharmacological and non-pharmacological.

Table 14 shows the distribution of BASDAI values in the studied population, as well as descriptive indicators that outline a cohort with a moderately high to high average disease activity – an outcome that requires targeted intervention to achieve control targets according to international standards.

Table 14. Distribution of patients by BASDAI and descriptive characteristics

Category/ Indicator	Patients (n)	Patients (%)	Value
BASDAI Groups			
0–2	0	0.0%	—
2–4	20	30.3%	—
≥4	46	69.7%	—
8–10	8	12.1%	—
Descriptive statistics			
Minimum value	—	—	2.17
Maximum value	—	—	9.30
Mean value (Mean)	—	—	5.53
Standard deviation (SD)	—	—	2.15
Coefficient of variation	—	—	38.9%
Median	—	—	5.855

BASDAI values range from 2.17 to 9.30; most patients have BASDAI values in the 5–7 interval (29 patients, 43.94%), indicating moderate to high disease activity. The mean and median suggest a relatively symmetric distribution and that most patients have moderate to high disease activity. Approximately 70% of patients are at the clinical threshold for initiating biological therapy according to BASDAI (BASDAI ≥ 4, in combination with other factors). Eight patients have BASDAI > 8, indicating extremely high disease activity and poor control. The "8–10" category is a subset of "≥4", therefore the percentages do not sum to 100%.

2.2.2. Investigation of factors influencing disease activity

Table 15 presents the investigated factors and their impact on disease activity in the studied patients with ankylosing spondylitis, measured by the BASDAI index.

Table 15. Investigated factors influencing disease activity

Factor	N	mean BASDAI	SD	CV (%)	P value
Sex					
Men	38	5.02	2.17	43.2 %	**p = 0.031**
Women	28	6.22	1.97	31.7 %	
Comorbidities					
Without comorbidities	19	3.42	1.66	48.4 %	**p = 0.000001**
With comorbidities	47	6.40	1.72	26.8 %	
Diet					
Without diet	28	5.11	2.14	41.9 %	p = 0.101
With diet	38	6.02	1.83	30.4 %	
Presence of biological treatment					**p = 0.000006**
Without biological treatment	23	6.73	1.30	19.3 %	
With biological treatment	43	4.57	1.51	33.1 %	

Non-pharmacological methods					
Without non-pharmacological treatment	26	5.21	2.03	39.0 %	p = 0.102
With non-pharmacological treatment	40	6.00	1.78	29.7 %	
Sports activity					**p = 0.019**
Non-exercising	31	6.07	2.14	35.2	
Exercising	35	5.05	2.08	41.3	
Smoking					**p ≈ 3.5 × 10^{-5}**
Non-smokers	37	4.61	1.90	41.2	
Smokers	29	6.70	1.90	28.3	
Sleep duration					**p = 0.029**
Sleep less than 6 h.	46	5.90	1.64	27.8	
Sleep more than 6 h.	20	4.68	2.91	62.1	
BMI					p=0.39
normal weight. BMI <25	31	5.18	2.05	39.6 %	
overweight, BMI ≥ 25	35	5.84	2.22	38.1 %	

In the studied group of 66 patients with ankylosing spondylitis, women report higher disease activity than men, with sex exerting a statistically significant and moderate effect on BASDAI. Patients with comorbidities have a statistically and clinically significantly higher BASDAI compared with those without comorbidity. Treatment with biological drugs is associated with significantly lower disease activity: patients without biological therapy are concentrated mainly in the severe

zone (BASDAI > 6), whereas in those treated with biological therapy mean values are lower and the distribution is wider.

Non-pharmacological methods do not show a statistically significant effect, although patients with higher activity use them more often. Regular physical activity is associated with lower BASDAI, whereas smoking and sleep under 6 hours are associated with higher disease activity, with the difference among smokers being highly significant ($p \approx 3.5 \times 10^{-5}$). Overweight shows a tendency towards higher BASDAI, but with a weaker effect than the other factors.

2.2.3. Assessment of quality of life in patients with AS

The results of the survey among 66 AS patients regarding quality of life measured by the EQ-5D-5L index are presented in **Table 16**. The data are grouped into three categories according to EQ-5D-5L (EuroQol 5 Dimensions 5 Levels) values. Most participants fall into the good health group, while a much smaller percentage show severely impaired quality of life.

Tabl. 16. Distribution of EQ-5D-5L index values

Category	Number	Percent
Good health (0.8 – 1)	40	60.61 %
Moderate problems (0.6 – 0.799)	23	34.85 %
Severely impaired quality of life (<0.6)	3	4.55 %

Descriptive statistics show a mean value of about 0.80, corresponding to good overall health status. The median of 0.83 confirms that most participants are in the good health group.

When compared with healthy adults from the general Polish population (EQ-5D-5L mean 0.900; Polish EQ-VT tariff 2019 – the most methodologically comparable and regulatorily recognised 5L tariff, used

temporarily in the absence of a Bulgarian tariff), the studied cohort shows a lower index by 0.097 points (mean ≈ 0.803). The difference is highly statistically significant ($t = -7.98$; $df = 65$; $p < 0.0001$) and with a large effect (Cohen $d \approx -0.98$). It is also clinically significant, as it exceeds the threshold for minimal clinically important difference (MCID ≈ 0.05–0.08 for EQ-5D-5L; for EQ-VAS ≈ 10 mm). This means that patients' quality of life is on average about one standard deviation lower than that of the reference population, underlining the burden of the disease and the need for targeted interventions. The results are consistent with international literature, according to which physical activity, pain control, sleep quality, and smoking cessation are key modifiable predictors of better health-related quality of life in ankylosing spondylitis.

In **Figure** 4 (distribution of the EQ-5D-5L index) the reference Polish value of 0.90 is marked, and the histogram is shifted to the left: most values are in the 0.75–0.90 range, while the left tail reflects a subgroup with markedly impaired quality of life.

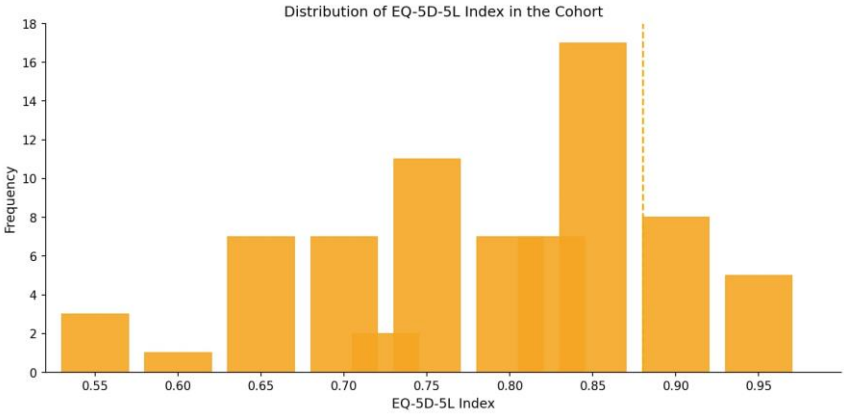


Fig. 4 Distribution of EQ-5D-5L values

Participants were asked to rate their health on the day of completing the questionnaire using a visual analogue scale (VAS) from 0 (very poor) to 100 (excellent health). The mean score of 68.6/100 indicates moderately good subjective health; participants perceive themselves as having a controlled but not perfect condition. The median of 70 confirms that half of participants rate their health at 70 or higher. The results are presented in **Table 17**.

Table 17. Descriptive VAS values

Indicator	N (number of participants	Minimum value	Maximum value	Mean value (Mean ± SD)	Median
VAS	66	50.0	90.0	68.46 ± 10.07	70.0

Most study participants experience mild to moderate difficulties across different health domains, particularly in pain and usual activities. Mental health (anxiety/depression) is affected in a substantial proportion of participants, which warrants attention. The standard deviations indicate considerable variability between respondents, especially regarding anxiety/depression. Interventions should focus both on adequate pain management and on significant mental health support for these patients. Domain values are presented in **Table 18**.

Tabl.18. Distribution of EQ-5D-5L domains

Parameter (Domain)	Level 1 (n, %)	Level 2 (n, %)	Level 3 (n, %)	Level 4 (n, %)	Level 5 (n, %)	Mean	SD
Mobi-ization	20 (31.2%)	27 (39.1%)	14 (21.9%)	4 (6.2%)	1 (1.6%)	2.08	0.95
Self--care	16 (25.0%)	22 (31.2%)	20 (31.2%)	8 (12.5%)	—	2.30	0.98

Usual-activities	9 (14.1%)	24 (37.5%)	27 (39.1%)	5 (7.8%)	1 (1.6%)	2.47	0.88
Pain/-discom-fort	10 (15.6%)	18 (28.1%)	20 (31.6%)	17 (23.0%)	1 (1.7%)	2.71	1.06
Anxi-ization/ depression	21 (32.8%)	16 (25.0%)	12 (18.0%)	13 (18.0%)	4 (6.2%)	2.44	1.29

2.2.4. Investigation of factors influencing quality of life

Table 19 presents the results of the analysis of the influence of certain factors on quality of life in patients with ankylosing spondylitis, measured by the EQ-5D-5L index, and the calculated statistical significance.

Tabl. 19. Investigated factors influencing quality of life

Factor	N	Mean EQ-5D-5L	SD	CV (%)	p-value
Sex					
Men	38	0.803	0.093	11.6 %	p = 0.785
Women	28	0.806	0.088	10.9 %	
Comorbidities					p = 0.403
Without comorbidities	19	0.808	0.117	14.5 %	
With comorbidities	47	0.800	0.092	11.5 %	
Diet					p = 0.728
Without diet	28	0.802	0.101	12.6 %	
With diet	38	0.808	0.089	11.0 %	

Presence of biological treatment					p = 0.289
Without biological treatment	23	0.781	0.086	11.0 %	
With biological treatment	43	0.800	0.072	9.0 %	
Non-pharmacological methods					p = 0.442
Without non-pharmacological treatment	26	0.804	0.093	11.6 %	
With non-pharmacological treatment	40	0.811	0.083	10.2 %	
Sports activity					p = 0.063
Non-exercising	31	0.777	0.102	13.2 %	
Exercising	35	0.827	0.090	10.9 %	
Smoking					p = 0.821
Non-smokers	37	0.804	0.087	10.8	
Smokers	29	0.808	0.086	10.7	
Sleep duration					p = 0.091
Sleep less than 6 h	46	0.819	0.086	10.5 %	
Sleep more than 6 h	20	0.767	0.117	15.3 %	
BMI					p = 0.46
normal weight. BMI ≤ 24.9	31	0.811	0.089	10.9 %	
overweight. BMI ≥ 25	35	0.784	0.093	11.9 %	

The study did not establish a substantial effect of sex on the EQ-5D-5L index in patients with ankylosing spondylitis ($p \approx 0.79$). The presence of comorbidities is associated with a minimal and clinically insignificant difference (+0.008), with mean values remaining around 0.80. Dietary regimen, biological therapy (0.78 vs. 0.80; $p > 0.05$**)** and non-pharmacological methods ($\Delta = 0.007$; $p \approx 0.44$) also show no significant differences in quality of life, likely due to a low "dose" and lack of controlled application of these approaches.

A trend towards a higher EQ-5D-5L index is observed in patients exercising more than once per week ($\Delta \approx 0.05$; $p \approx 0.063$), but without statistical certainty. No difference is found between smokers and non-smokers ($\Delta = 0.004$). Shorter sleep duration (< 6 h) is associated with a slightly higher index (+0.052), but without statistical significance ($p = 0.091$), which necessitates additional analyses including assessment of sleep quality**.** Overweight shows a small decrease in EQ-5D-5L (−0.027), below the clinical threshold and statistically non-significant.

2.2.5. Analysis of the relationship between disease activity and quality of life

In the overall sample (n = 66), no statistically significant association was found between the BASDAI disease activity index and the EQ-5D-5L quality-of-life index ($r = −0.06$; $p = 0.63$; 95% CI: −0.30 to 0.18). When analysed by sex, in men the correlation is weak, positive, and statistically non-significant ($r = +0.07$; $p = 0.69$), suggesting that increased disease activity does not substantially affect their self-rated health. In women, however, a moderate and statistically significant negative association was found ($r = −0.47$; $p = 0.012$), meaning that each one-point increase in BASDAI is associated with an average decrease of the EQ-5D-5L index by about 0.05–0.06. This difference reaches the MCID threshold. The results are presented in **Table 20.**

Tabl. 20. Correlation between disease activity (BASDAI) and quality of life (EQ-5D-5L) – overall population and sex subgroups

Group	n	r (Pearson)	p-value
Total sample	66	–0.06	0.63
Men	38	+0.07	0.69
Women	28	–0.47	**0.012**

2.3. Analysis of adherence to drug therapy among patients with AS and influencing factors

2.3.1. Assessment of the degree of adherence to drug therapy

Patients' adherence to prescribed drug therapy is a critical indicator of therapeutic success, and the pharmacist plays a leading role in supporting it. In the present study, the validated Morisky 8-Item Medication Adherence Scale (MMAS-8) was used to assess adherence to therapy in patients with ankylosing spondylitis. The results shown in **Table 21** indicate a predominantly low to moderate level of adherence in the studied group.

Table 21. Distribution and descriptive statistics of medication adherence according to MMAS-8

Indicator	n (%)	Value
MMAS-8 categories		
< 6 (low adherence)	36 (54.5 %)	—
6.0–7.9 (moderate adherence)	22 (33.3 %)	—
= 8 (high adherence)	8 (12.1 %)	—
Descriptive statistics		
Minimum value	—	2.50

Maximum value	—	8.00
Mean value (Mean ± SD)	—	5.696 ± 1.515
Median	—	5.500
Coefficient of variation (CV, %)	—	26.593

These results indicate that more than half of the studied patients do not adequately follow the prescribed therapy, which is particularly concerning given the chronic and progressive nature of the disease. Low adherence can lead to insufficient control of inflammation, faster structural damage, increased pain, and limited functionality, thereby worsening the quality of life of affected individuals.

The reasons for impaired adherence are multifactorial and may include adverse effects of the prescribed drug therapy, lack of a subjective sense of improvement, forgetfulness, low motivation, or limited access to medicines. Identifying this trend highlights the need for targeted interventions – educational programmes, regular follow-up, and psychosocial support – aimed at increasing therapeutic engagement in this population of AS patients.

2.3.2. Investigation of factors influencing the level of adherence

The influence of sex, education level, presence of comorbidities, type of therapy – biological and non-pharmacological – on adherence to rheumatologist-prescribed therapy, measured by the Morisky MMAS-8 test, was examined. The results are presented in **Table 22.**

Tabl. 22. Influence of investigated factors on the degree of adherence to drug therapy

Factor	Group	N	Mean value Morisky	SD	CV (%)	p-value
Sex	Men	38	5.62	1.26	22	0.640
	Women	28	5.80	1.82	31.40	
Education	Primary	2	7.69	0.12	1.60	**<0.001**
	Secondary	21	7.43	1.34	18	
	Higher	43	4.50	1.80	39.90	
Comor-bidities	Without comorbiditi es	19	5.86	1.62	27.70	0.546
	With comorbiditi es	47	5.60	1.48	26.50	
Biological therapy	Without biological therapy	35	5.63	1.66	29.50	0.697
	With biological therapy	31	5.78	1.36	23.50	
Non-pharma-cological intervention	Without non-pharmacolo gical	20	5.19	1.74	33.60	0.072
	With non-pharmacolo gical	46	5.92	1.37	23.10	

Substantial differences are observed by education: patients with secondary education have the highest mean scores, whereas patients with higher education – a group often considered well informed – show the lowest adherence and the greatest variability. One-way ANOVA shows a significant effect ($p < 0.001$), with a large effect size, $\eta^2 \approx 0.43$. Descriptive analysis shows that women have a slightly higher mean Morisky score (5.80 versus 5.62 in men), but variability is greater in their

group. Welch's t-test does not show a statistically significant difference between sexes ($t = -0.47$; $p = 0.64$), with a negligible effect (Cohen's $d = 0.12$). Therefore, in this sample, sex does not have a substantial influence on adherence. No significant difference ($p > 0.05$) is found regarding the presence of comorbidities: patients without comorbidities tend to have better adherence, but the effect is not significant. There is no significant difference ($p > 0.05$) regarding biological therapy; a minimal trend towards better adherence is observed in patients on biological therapy. For non-pharmacological methods, the difference does not reach statistical significance ($p \approx 0.07$), but there is a trend towards better adherence among patients using some type of non-pharmacological method.

The study also examined the influence of sex, education, presence of comorbidities, and type of therapy on the categorical distribution of adherence levels. The results are shown in **Table 23**.

Tabl. 23. Categorical distribution of adherence levels by factors – number of patients

Factor	Group	< 6 pts (low)	6 – 7.99 pts (medi-um)	8 pts (hi-gh)	p-value
Sex	Men (n = 38)	25	10	3	p = 0.051
	Women (n = 28)	10	13	5	
Education	Primary (n = 2)	0	2	0	**p < 0.001**
	Secondary (n = 21)	3	10	8	
	Higher (n = 43)	32	11	0	
Non-pharma-cological methods	Without non-pharma-cological treatment	12	5	1	p = 0.605

	With non-pharma-cological treatment	24	17	7	
Comor-bidities	Without comorbidities	12	10	2	**$p \approx 0.0176$**
	With comorbidities	24	15	3	
Biological therapy	Without biological therapy	19	9	3	$p = 0.872$
	With biological therapy	17	13	5	

Regarding education, a strong and statistically significant difference between groups was found. To assess the influence of education on adherence categories, Pearson's χ^2 test showed a strong and statistically significant association: $\chi^2 = 32.34$; $df = 4$; $p < 0.001$; Cramer's V = 0.49 (strong effect). This indicates that the higher the level of education, the more often patients fall into the low-adherence group (< 6 points). The primary-education group is too small (n = 2) for categorical conclusions. To assess the influence of sex on adherence categories, a χ^2 test of independence was applied, showing a borderline value: $\chi^2 = 5.94$; df = 2; p = 0.051. *There* is a *trend* for men to be more often in the low-adherence group and women to be more often in the moderate and high adherence groups, with the proportion with high adherence approximately double among women. For comorbidities, the categorical distribution also differs significantly: patients without comorbidities more often fall into the high-adherence category, whereas those with comorbidities show a shift towards lower adherence. No significant difference is found between groups in the categorical distribution regarding non-pharmacological intervention. No significant difference is found in the distribution of adherence categories between patients with and without biological therapy.

2.3.3. Analysis of the relationship between adherence to therapy and disease activity in patients with AS

A correlation analysis was performed between the main variables – sex, disease activity, and adherence to drug therapy – for the entire studied population, and the results are presented in **Table 24.**

Tabl.24. Correlation Analysis between Medication Adherence, Disease Activity, and Sex

Variable 1	Variable 2	Correlation coefficient	p-value
MMAS-8 score	BASDAI score	r = 0.45 (Pearson)	**< 0.001**
MMAS-8 score	BASDAI score	ρ = 0.37 (Spearman)	**< 0.001**
Sex	BASDAI score	r = 0.28 (Pearson)	**0.025**
Sex	BASDAI score	ρ = 0.27 (Spearman)	**0.030**
Sex	MMAS-8 score	r = 0.06 (Pearson; n.s.)	> 0.05
Sex	MMAS-8 score	ρ = 0.06 (Spearman; n.s.)	> 0.05

The analysis shows that patients with more complaints and higher disease activity are more disciplined in adhering to their prescribed therapy. The moderate positive Morisky–BASDAI correlation ($r \approx 0.45$) suggests that high disease activity is likely a reason for stricter adherence, rather than the reverse. It was also established that in the studied population, sex influences adherence to prescribed therapy through disease activity.

The effect of adherence to therapy on disease activity depending on sex and education level was also evaluated. The results are shown in **Table 25.**

Tabl. 25. Effect of adherence to therapy on disease activity, depending on sex and education level

Factor	Group	n	Morisky (mean ± SD)	BASDAI (mean ± SD)	ρ Spearman	p (ρ)	Slope β (OLS)	p (β)
Sex	Men	38	5.62 ± 1.26	5.02 ± 2.17	+0.18	0.28	+0.49	0.085
	Women	28	5.80 ± 1.82	6.22 ± 1.97	+0.39	**0.038**	+0.71	**0.00015**
Education	Primary	2	5.17 ± 0.25	6.32 ± 1.24	n/a	n/a	n/a	n/a
	Secondary	21	5.40 ± 1.77	6.17 ± 2.13	+0.69048	**0.00053**	0.84767	**0.00036**
	Higher	43	5.84 ± 1.41	5.22 ± 2.16	+0.28788	0.06450	0.64367	**0.00564**

"*n/a*" = *not applicable/no value due to a limited sample*

Women show higher disease activity (mean BASDAI 6.22) at a similar level of adherence compared with men. In women, a moderate positive and statistically significant correlation between Morisky and BASDAI was also found ($\rho = +0.39$, $p = 0.038$). Linear regression analysis confirms the association ($\beta = +0.71$, $p = 0.00015$). In men, the correlation between Morisky and BASDAI is weak, positive, and statistically non-significant ($\rho = +0.18$, $p = 0.28$). Regarding education, the strongest positive association is observed in the secondary-education group, a more moderate one in the higher-education group, and it is not evaluable in the primary-education group ($n = 2$). This suggests that education also modifies the association between adherence and disease activity.

2.4. Development of educational materials for patients with AS

After a meeting with AS patients and the leaders **of the Bulgarian Association of People with Bechterew's Disease,** held in November 2025 in the city of Ruse**,** presentation of specific results from the practice-oriented dissertation and based on the conducted literature review, training materials were prepared regarding the possibilities for the pharmacist's participation in comprehensive care for their disease.

1. Early recognition and referral when AS is suspected A pharmacist can recognise characteristic symptoms such as: • inflammatory-type low back pain, • morning stiffness, • pain that improves with movement, • heel pain, peripheral joint pain, • recurrent eye inflammation. In patients with such complaints, the pharmacist can recommend a timely consultation with a rheumatologist, which is important because globally the diagnosis is often delayed for years.	**2. Information about the disease and support for everyday control** Many patients remain uncertain about what the diagnosis means. The pharmacist can clarify: • what inflammatory pain is, • why exercise and activity are important, • why smoking worsens the disease, • what the patient can expect with therapy with NSAIDs, biological medicines, JAK inhibitors, etc. Education increases confidence, motivation, and active participation in treatment
3. Supporting correct medicine use Treatment in AS is often long-term and includes different therapeutic groups. The pharmacist can help by: • Clarifying the dosage, timing, and method of administration. • Advice on how to use the biological medicine or JAK inhibitor safely. • Support when transitioning through therapeutic changes. • Suggestion of alternative dosage forms (e.g., when there is difficulty swallowing).	**4. Support and advice for common problems accompanying treatment** Patients with AS often have: • gastrointestinal complaints from NSAIDs, • fatigue, • insomnia, • anxiety or depressive episodes. The pharmacist can suggest appropriate OTC products and advice or recommend consultation with a physician in the case of more serious symptoms.

5. Improving adherence to treatment Insufficient adherence to drug therapy is common in chronic diseases. The pharmacist can help by: • reminder schedules, • a clearly prepared personal therapeutic plan, • monitoring regular intake, • support when there are fears or hesitations about biological therapies. This significantly improves disease control.	**6. Advice on non-pharmacological approaches** The pharmacist can guide you to: • useful exercises and physiotherapy, • proper posture and daily activity, • techniques to reduce pain, • recommendations for smoking cessation, sleep hygiene, weight control • appropriate dietary supplements (calcium, vitamin D, omega-3, magnesium, probiotics, etc.) when needed – without allowing a risk of interactions.
7. Monitoring adverse drug reactions and interactions In AS, medicines for pain, biological therapy, and treatment of concomitant intestinal, skin, cardiovascular, or gastrointestinal diseases are often combined, which increases the risk of interactions and adverse reactions. The pharmacist can: • recognise potential drug interactions; • warn about specific risks (e.g., gastric irritation with NSAIDs, infections with TNF or JAK inhibitors); • advise when to seek medical attention. With biological and targeted therapies, it is crucial: • to report unusual symptoms; • to monitor the risk of infections; • to assess the effect of treatment	The pharmacist does not replace the physician, but is a constant partner in treatment – accessible, informed, and ready to help!!! *This material was created jointly by pharmacists from the Medical University – Varna, the University of Ruse, "Astra" pharmacies, and the Association of People with Bechterew's Disease in Bulgaria in order to support patients with ankylosing spondylitis and encourage them to include the pharmacist as a source of health information.* . *Contact: landreeva@uni-ruse.bg*

Discussion

The studied group of AS patients confirms the more frequent occurrence of AS in men, but the results underline that in women the diagnosis is more often delayed due to a more atypical clinical presentation, which necessitates earlier recognition and referral to a rheumatologist; the low rate of diagnosis after the age of 50 likely reflects under-recognition and difficult differentiation from degenerative diseases. HLA-B27 positivity is high and comparable to European data, and frequent comorbidity supports the need for a multidisciplinary approach due to polypharmacy and the risk of interactions and adverse drug reactions, where the pharmacist can contribute through therapeutic counselling and safety monitoring.

Disease activity measured by BASDAI is higher than in European observations, suggesting suboptimal control and a need for therapy optimisation and probably more intensive non-pharmacological measures. Women have higher BASDAI and more impaired quality of life at similar activity, supporting the need for a personalised, sex-specific approach and assessment for concomitant conditions (depression, fibromyalgia). The most unfavourable associations with BASDAI are observed for smoking and insufficient sleep; physical activity is associated with lower BASDAI, whereas the influence of diet and BMI is more moderate and, in the present sample, without statistical certainty. Biological therapy demonstrates effectiveness in reducing activity, but with a smaller effect under real-world conditions; concordance with recommendations (ASAS–EULAR) supports a trend towards earlier initiation.

Quality of life measured by EQ-5D-5L shows no significant differences according to sex, comorbidities, diet, smoking, and therapy, likely due to the generic nature of the instrument and unstructured/self-

initiated use of non-pharmacological measures; only trends in the expected direction are observed for physical activity and sleep.

Adherence to therapy (MMAS-8) does not differ by sex, but education is a key factor: the lowest adherence is observed among patients with higher education, indicating the need for targeted pharmaceutical support. The Morisky–BASDAI correlation is positive in women (likely due to reverse causality – higher activity motivates stricter adherence), and in remission reminder mechanisms are needed to prevent missed doses. The limited sample size is acknowledged, but the results support the pharmacist's role in long-term care through education, monitoring of adverse drug reactions and drug interactions (including with dietary supplements), assessment of adherence, and provision of written or digital materials, complementing the rheumatologist within a multidisciplinary care model.

V. CONCLUSIONS

1. Attitudes and knowledge regarding PC among surveyed pharmacists are statistically significantly associated with length of professional experience, likely as a result of the development of pharmaceutical education and the introduction of PC training in Bulgaria. The results justify the need to adapt continuing education and include specialised PC modules in order to achieve a higher level of awareness and confidence within the professional community.

2. A high motivation of pharmacists to participate in comprehensive care for AS patients was established, but combined with a perception of insufficient professional preparation. The main reported barriers – lack of time, insufficient information about the disease, lack of a financial mechanism to reimburse the service, and an inadequate organisational environment – are statistically associated with years of professional experience and with the presence of a postgraduate specialisation, and they limit the implementation of individualised PC in practice.

3. The analysis demonstrates a clear need for structured training and standardised tools to support early screening and the provision of pharmaceutical support for AS patients.

4. AS patients in the Ruse region are predominantly men of working age and experience substantial delay in establishing an accurate diagnosis.

5. Significant comorbidity and unfavourable health-behaviour factors (short sleep, overweight, smoking) were reported, which further worsen the course of the disease. A substantial proportion of patients are on biological therapy and use non-pharmacological methods, indicating good therapeutic engagement.

6. Most studied patients have a moderate to high level of disease activity (BASDAI ≥ 4). Female sex, presence of comorbidities, smoking, lack of physical activity, and insufficient sleep are statistically associated

with higher disease activity. Biological therapy is the only factor that clearly and statistically significantly reduces disease activity;

7. Quality of life assessed by EQ-5D-5L in the studied patient group is moderately impaired and shows no significant association with most investigated health-behaviour factors. Physical activity demonstrates a trend towards improved quality of life. A statistically significant association between disease activity (BASDAI) and quality of life is established only in women.

8. A low level of adherence to prescribed therapy was established in the majority of studied patients, placing long-term disease control at risk. Higher education level in the studied AS sample is associated with a lower degree of adherence to treatment. The results justify the need for targeted PC and systematic monitoring of drug therapy.

VI. RECOMMENDATIONS

Based on the obtained results, the following recommendations can be formulated for legislators, faculties of pharmacy, and the professional organisation of pharmacists:

1. Strengthen the multidisciplinary approach in the care of patients with ankylosing spondylitis, with an emphasis on controlling comorbidities, optimising therapy, and the pharmacist's role in follow-up and primary screening for AS;

2. Prepare measures targeting modifiable health-behaviour risk factors such as smoking, insufficient physical activity, and impaired sleep hygiene, with the aim of reducing disease activity;

3. Introduce appropriate measures to improve adherence to therapy, including patient education, pharmaceutical consultations, and regular assessment of patient behaviour regarding treatment;

4. Develop targeted continuing education for pharmacists who completed their higher education before the introduction of the PC concept;

5. Postgraduate specialisations should include more in-depth and extensive modules related to PC in order to increase the confidence of specialists who provide PC in their everyday community-pharmacy practice.

VII. GENERAL CONCLUSION

The development of the pharmaceutical profession and updated educational models directly influence awareness, confidence, and overcoming barriers to the provision of individualised PC by community pharmacists.

The study found that pharmacists frequently encounter patients with low back pain but experience a significant lack of knowledge and skills for recognising and counselling patients with ankylosing spondylitis. Despite high motivation to participate in comprehensive care, lack of training and organisational barriers limit the real implementation of individualised PC. The developed training materials, algorithms, and screening checklist have educational and practical applicability and have the potential to improve early referral to a physician and the quality of pharmaceutical care for AS patients. The study also outlines a characteristic profile of AS patients in the Ruse region, characterised by high disease activity, significant comorbidity, and substantial delay in the diagnostic process. Modifiable health-behaviour factors such as smoking, physical inactivity, and insufficient sleep have a clear influence on disease activity, which underscores the need for targeted lifestyle-change interventions. Quality of life is moderately impaired, with a stronger dependence on disease activity among women. The low level of adherence to therapy found in a large proportion of patients emphasises the importance of individualised PC and targeted patient support. The results confirm the need for an integrated, multidisciplinary approach to optimise treatment and improve long-term outcomes in AS patients, in which the Master of Pharmacy in the community pharmacy has an important place and role.

VIII. CONTRIBUTIONS

As a result of the conducted studies and analyses within the dissertation, the following contributions were outlined:

1. Scientific-theoretical

1.1. The study enriches theoretical knowledge about the pharmacist's role in early recognition and comprehensive care for patients with ankylosing spondylitis by identifying specific knowledge gaps and factors influencing professional preparedness;

1.2. For the first time on a regional scale, a comprehensive characterisation of patients with ankylosing spondylitis has been performed, including socio-demographic profile, comorbidities, health-behaviour habits, types of therapies used, disease activity, quality of life, and degree of adherence to drug therapy;

1.3. Key associations between modifiable health-behaviour factors (smoking, physical activity, sleep) and disease activity have been demonstrated, contributing to deeper understanding and control of the clinical course of the disease.

2. Scientific-practical

2.1. Practical algorithms, a screening checklist, and training materials were developed, addressing the identified educational and practical needs of the surveyed pharmacists, supporting pharmacists in real community-pharmacy practice in early referral to a rheumatology specialist and in providing PC for AS patients;

2.2. Factors of practical importance for controlling disease activity were identified, enabling targeted and individualised care;

2.3. A high risk of low adherence to prescribed therapy was established and the role of educational programmes for improving patient compliance was highlighted;

2.4. Arguments were formulated in support of the pharmacist's active participation in comprehensive care for AS patients;

IX. PUBLICATIONS AND PARTICIPATIONS IN SCIENTIFIC FORA RELATED TO THE DISSERTATION

PUBLICATIONS

1. Andreeva, L., A. Todorova. Evolution in the pharmacotherapy of ankylosing spondyloarthritis. In: Management & Education/Upravlenie i Obrazovanie, University "Prof. A. Zlatarov" – Burgas, 2024, pp. 35–40, ISSN 1312-6121

2. Andreeva, L., A. Todorova. Application of chronopharmacology in patients with ankylosing spondyloarthritis. In: Management & Education/Upravlenie i Obrazovanie, Academic Journal – University of Burgas, 2024, pp. 30–34, ISSN 1312-6121

3. Andreeva, L., Todorova, A. (2024). Role and place of the pharmacist in the comprehensive care of patients with ankylosing spondylitis (Bechterew's disease). Varna *Medical Forum, 13 (Supplement* 2). MU–Varna. pp. 39–45;

4. Andreeva, L., Todorova, A. (2024). Pharmacists' attitudes towards providing pharmaceutical care to patients with ankylosing spondylitis – a pilot *study. Varna Medical Forum,* 13 (Supplement 2). MU–Varna, pp. 25–29;

8. Andreeva, L., Todorova, A., & Petkova, V. (2026). *Medication adherence and disease activity in patients with ankylosing spondylitis: A pilot study* [Manuscript submitted for publication]. *Pharmacia*.

PARTICIPATIONS

1. Tenth anniversary Pharmaceutical Business Forum and scientific-practical conference "New horizons in cooperation between science and business"*, 7–9 November 2024, Varna; Andreeva, L., Todorova, A. (2024). Analysis of the educational needs of pharmacists in Northeastern Bulgaria for improving therapeutic outcomes in patients with ankylosing spondylitis: A pilot study, Scripta Scientifica Pharmaceutica, vol. 11, 2024, p. 55;*

2. Participation with a report at the International Scientific Conference "Education, Science, Economics and Technology", University "Prof. Dr. Asen Zlatarov", Burgas, June 20–21, 2024;

3. Participation with two reports in the Eleventh Scientific Session with International Participation of the Medical College at MU - Varna, November 22, 2024, Varna;

X. ACKNOWLEGMENTS

I would like to express my sincere gratitude to my supervisor, Assoc. Prof. Todorova, and to my scientific consultant, Prof. Petkova, for their support and guidance throughout the development of this dissertation. I also thank the members of the Department of Organization and Economics of Pharmacy at the Faculty of Pharmacy, Medical University of Varna, for their specific recommendations and valuable feedback. I am grateful for the support of the members of the Regional Pharmaceutical Colleges in Ruse, Varna, and Dobrich, as well as the patient organization of people living with ankylosing spondylitis. The completion of this dissertation would not have been possible without the unconditional support of my family.