RESEARCH PROJECT PROTOCOL

For inclusion in the PhD project in Medicine
Developed at the University of Minho | Institute for Life Sciences Research, in partnership with ciTechCare – Center for Innovation in Healthcare Technologies | Polytechnic of Leiria, funded by the Foundation for Science and Technology (2021.07973.BD)

Title:
Cross-Cultural Adaptation to Portuguese and Psychometric Validation of the DIVA Questionnaire (Day-to-Day Impact of Vaginal Aging)

Short Title:
Validation of the DIVA Questionnaire (Day-to-Day Impact of Vaginal Aging) for Portuguese Women

Protocol ID: 6047/2022 Ethical Commission for Health of Regional Health Administration of Lisbon and Tagus Valley (CES ARS-LVT). 16/09/2022

Responsible Investigator:
Professor Patrício Costa

Principal Investigator:
Andreia Alexandra da Costa Azevedo Ribeiro da Rocha Antunes
Largo Alexandre Herculano, nº6, 2410-083 Leiria
Phone: 933266097

Affiliation of Principal Investigator:
Faculty of Medicine, University of Minho
Institute for Life Sciences Research
ciTechCare – Center for Innovation in Healthcare Technologies
Polytechnic Institute of Leiria

Supervisor:
Professor Cristina Isabel Nogueira da Silva

Co-Supervisor:
Professor Maria Pedro Sucena Guarino

Institutions for Participant Recruitment:

Study Centres:

- Hospital Santo André (CHL, EPE) – Gynaecology Service
- UCSP Sete Rios (ARS-LVT)
- Hospital Dom Manuel de Aguiar, Leiria
- Private Gynaecologic clinic at Braga

Study responsible at UCSP Sete Rios:

Dra. Maria Alexandra Colaço

Key words:
Dyspareunia
Genitourinary syndrome of menopause (GSM)
Female Genital Atrophy
Female Genital Disorder
Female Sexual Dysfunction (FSD)
Vaginal dryness
Vaginal Itching

Start Date:
2/10/ 2022

End Date:
22/01/ 2024

Protocol Index

List of Abbreviations

ARS-LVT – Regional Health Administration of Lisbon and Tagus Valley
ciTechCare – Center for Innovative Care and Health Technology
COSMIN – Consensus-based Standards for the Selection of Health Measurement Instruments
DIVA – Day-to-day Impact of Vaginal Aging
EQ-5D – EuroQol Group 5-Dimension Quality of Life Questionnaire
EQ-VAS – Visual Analog Scale associated with the EQ-5D questionnaire
FMUM – Faculty of Medicine, University of Minho
FDD – Digital Data File
FSFI – Female Sexual Function Index
HDMA – Hospital Dom Manuel de Aguiar
HSA – Hospital Santo André
CHL – Hospital Center of Leiria
ICVC – Institute for Health Sciences Research
IPL – Polytechnic Institute of Leiria
SGUM – Genitourinary Syndrome of Menopause
UCSP – Personalized Health Care Unit
UM – University of Minho

This study protocol is part of a PhD project in Medicine to be developed in partnership between the University of Minho, ciTechCare, and the company DRT Molds. The project has been awarded a PhD scholarship by FCT (ref. 2021.07973.BD). The title of the project is "Regenerative Treatment for Vulvo-Vaginal Atrophy". To assess pre- and post-therapy, it was necessary to include clinical assessment instruments, which, in the case of genital atrophy, include self-assessment questionnaires and the perception of the impact that this clinical problem has on a woman's life. As there are no validated questionnaires in European Portuguese, it is intended to proceed with the cultural adaptation of a questionnaire developed in another sociodemographic context. The DIVA (Day-to-Day Impact of Vaginal Aging) questionnaire was selected because it was designed and constructed according to the guidelines of the COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN), and the construct validity showed adequate values with a comparative fit index of 0.987 and Cronbach's alpha values ranging from 0.82 to 0.93.

We began by informing the authors of the DIVA questionnaire that we would initiate this cultural and linguistic adaptation process, emphasizing that the authors state in the original publication that formal authorization is not required, but they wish to be informed of the results of the translation and cultural adaptation process.

Before the start of this research protocol, a translation process into Portuguese was carried out according to the principles of good practice, which included the following steps: 1) translation by two independent researchers, 2) reconciliation, 3) back translation by two certified translators fluent in English, 4) unification and harmonization of the translated version in Portuguese, 5) evaluation by a group of specialists in gynaecology and sexology, and 6) pre-test in a group of patients with the final cultural adaptation of the DIVA scale translated into European Portuguese.

Project Rationale

Symptoms that cannot be directly quantified but have an impact on quality of life can be assessed through self-perception health questionnaires[1]. These clinical instruments play a key role, not only in identifying the clinical problem but also in assessing the individual impact of the problem on various psychological and physical dimensions, helping to identify the impact of therapeutic strategies on the improvement of these subjective symptoms[2]. For research to be valid, these instruments must be appropriate and accurate to ensure the quality of the results[3,4].

Aging has a significant impact on women's genital health, which results in a set of symptoms and signs known as the Genitourinary Syndrome of Menopause (GSM)[5]. This clinical issue affects approximately 50% of postmenopausal women. While the urinary component of GSM can be quantified through validated diagnostic tests, the vulvovaginal atrophy component is not quantifiable by diagnostic tests. It has an increasing severity with age, impacting self-esteem, well-being, and sexuality, yet remains a stigma for women and is poorly perceived by doctors[6]. It is in this context that the DIVA[7] questionnaire (Day-to-day Impact of Vaginal Aging) was developed, as it brings together characteristics that make it practical for use in population studies, transforms subjective measures into objective, quantifiable, and analysable data, and assesses the relative strength of each domain or

component of female genital atrophy on quality of life. Other advantages of this questionnaire include being a well-studied and validated index with the ability to evaluate therapeutic interventions[8]. It has also been adapted into other languages besides English[9] – including Spanish[10], Italian[5], German[11], and Turkish[12] – and has been validated in these cultural contexts.

The DIVA questionnaire analyses and quantifies the impact of female genital aging. It consists of 23 items grouped into 4 constructs, which include the dimensions of daily activities, emotional well-being, sexual function, and self-esteem and body image. There are two versions of the questionnaire: the full version with 23 items, which includes 4 items on sexual function that can only be evaluated in sexually active women, and a shorter version with 19 items that can be applied regardless of sexual activity. Each item is rated on a 5-point Likert scale, with the dimension value obtained by calculating the average of the corresponding items. Higher values indicate a greater adverse impact of atrophy symptoms.

Project Objectives:

General Objective: To determine the reliability, consistency, and validity of the psychometric properties of the Portuguese version of the DIVA questionnaire, adapted for our culture, in peri- and postmenopausal women. This validation will provide the foundation for using this questionnaire both in research and clinical practice with Portuguese women.

Specific Objective: To assess the discomfort of genital atrophy symptoms in the study participants and the impact of this problem on the quality of life of peri- and postmenopausal women in the Portuguese context.

Materials and Methods:

Study Type:

This will be an observational, cross-sectional, and descriptive study, conducted and guided by investigators with the appropriate professional qualifications to carry out the research protocol, in a clinical and human environment suitable for the study. The study will be conducted in accordance with Law No. 21/2014 of April 16 (amended by Law No. 73/2015, July 27) and Decree-Law No. 145/2009 of June 17.

Population and Study Location:

Participants will include woman that had at least one complaint of vaginal atrophy (dryness, itching, burning, irritation, discomfort, or pain when urinating or during intercourse, or bleeding during intercourse, affecting the external genitalia: vulva or vagina).

For the normative convenience sample from the general population, participants will be users of a large urban health centre, the Personalized Health Care Unit (UCSP) of Sete Rios, Lisbon. For the clinical convenience sample, participants will be users of a general gynaecology consultation at a private hospital (Hospital Dom Manuel de Aguiar) and the gynaecology consultation at a public hospital (Hospital Santo André), both located in an urban centre in Leiria, another group of participants came from a private gynaecologic consultation of north of Portugal, at Braga city, aiming to gather 230 valid tests, following COSMIN[13] recommendations, to allow for an assessment of invariance correlation.

Data Collection Instruments:

The methodological approach is a cross-sectional descriptive study of qualitative and quantitative data, including dependent and independent variables organized into a self-administered form completed by the participants. This form includes 5 questionnaires:

1. **Symptom Questionnaire:** This questionnaire will screen participants to be included in the study who must report at least one symptom associated with genital atrophy. The symptoms include dryness, itching, burning, irritation, discomfort or pain when urinating or during intercourse, or bleeding during intercourse, with each symptom rated on a 5-point Likert scale from 0 (no discomfort) to 4 (extreme discomfort) (Annex 2).

2. **Sociodemographic and Clinical Questionnaire:** This questionnaire will characterize the study participants. The sociodemographic section will include variables related to biological profile, such as gender and birth date, as well as socioeconomic variables like marital status, education, and professional activity. Finally, it will cover clinical variables related to gynaecological function, comorbidities, and treatments (Annex 3).

3. **DIVA Questionnaire (Day-to-day Impact of Vaginal Aging):** This questionnaire assesses the impact of vaginal aging on daily life. The original version was developed by Alison J. Huang (Annex 4), Director of the Department of Medicine at the University of California, San Francisco. It included 745 postmenopausal women, from 2008 to 2012, of multiethnic backgrounds with at least one complaint of genital atrophy (dryness, burning, irritation, and itching) or pain during sexual intercourse. The questionnaire is constructed with a multidimensional scale covering 4 domains: (1) daily activities, (2) emotional well-being, (3) sexual function, and (4) self-esteem and body image. The full version consists of 23 items, with a version for women without sexual activity that includes a "not applicable" option for the sexual function domain. The items are scored between 0 and 4, and the overall score is the average of the scores in each domain, with higher scores indicating a greater impact and severity of genital atrophy symptoms. The internal consistency of the original scale in English ranged from 0.47 to 0.72, with Cronbach's alpha between 0.82 and 0.93. Confirmatory factor analysis showed appropriate structural validity with a comparative fit index of 0.987 and a standardized root mean square residual (SRMR) of 0.038. A measurement property assessment of this symptom evaluation questionnaire identified it as one of the best quality and reliable tools for assessing female genital atrophy (Annex 1 and 4).

4. **EQ-5D** is a generic instrument for measuring health-related quality of life, which generates an index representing an individual's health state. Developed by the EuroQoL group since 1987 and made public in 1990, it is based on a classification system that describes health in five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has three associated severity levels: no problems (level 1), some problems (level 2), and extreme problems (level 3) experienced by the individual. Another measure used is the EQ-VAS, a 20 cm vertical visual analog scale (VAS) ranging from 0 to 100, where 0 is the worst and 100 the best imaginable health. This measure of self-perceived health is

evaluated independently for the subject's self-perception. It is available in over 130 languages in various application formats and was validated for European Portuguese in 2013 by Ferreira[14]. It is considered reliable and valid, showing moderate to high correlations with other health status and quality of life measures for various diseases, and the purpose of using this questionnaire is to verify the concurrent validity of DIVA (Annex 5).

5. **FSFI-6 (Female Sexual Function Index)** is an instrument developed by Isidori, based on the longer version of the original questionnaire but designed for easier clinical use, as it is quick to complete but still maintains good internal consistency (Cronbach's alpha of 0.79) and excellent accuracy for differentiating clinical populations, with sensitivity and specificity above 94%. It was validated in the Portuguese population by Pechorro[15], including 6 items that evaluate 6 domains of sexuality: desire, satisfaction, excitement, lubrication, orgasm, and pain. This scale will be used for convergent assessment of the sexual domain of DIVA (Annex 6).

4. Inclusion and Exclusion Criteria:

Inclusion Criteria: Women who agree to participate in the study after giving their informed consent (Annex 7) and who report at least one symptom related to genital atrophy, such as dryness, itching, burning, irritation, discomfort, or pain when urinating or during intercourse, or bleeding during intercourse, affecting the external genitalia (vulva or vagina).

Exclusion Criteria: Pregnancy, neoplasms under treatment, inability to speak Portuguese, or any mental or physical disability that prevents coherent responses to the questionnaire.

---

5. Recruitment Model:

The recruitment for the project will be conducted by the researchers involved, and the selection of participants will be voluntary and carried out on a convenience basis, in a non-random manner.

In all cases, the referred participant must give prior informed consent for referral, by signing the informed consent form and verifying that they meet the inclusion criteria and none of the exclusion criteria.

---

6. Informed Consent:

In accordance with the provisions of the Clinical Research Law (Law No. 21/2014 of April 16, amended by Law No. 73/2015, July 27), the researcher will provide the informed consent document to the volunteer. The information will be provided verbally and in writing, in accessible language, and the volunteer will be given time to read the document and ask any questions.
It will be ensured that the participant receives the appropriate information to consent to the research procedures, preserving their autonomy and decision-making power regarding participation. All information about the project, including its objectives, procedures, participant duties and rights, risks and benefits, data handling, civil liability insurance, as well as the contact person's details, will be included.

The informed consent will be signed by the volunteer if they agree to participate, and by the researcher, in duplicate, with one copy for the participant and another for the researcher. The participant can withdraw their informed consent for participation in the project at any time, by notifying a member of the research team, preferably in writing, without the need for justification, without incurring any form of liability, and without suffering any harm. If the participant withdraws their consent, all data collected about that participant will be excluded, respecting the right to be forgotten.

---

7. Participant Confidentiality:

The participant will not be identified by any of their personal data. To ensure the anonymization of the data collected during the study, each participant will be assigned an identification number, consisting of an alphanumeric code with 3 digits: the first digit corresponds to one of three letters identifying the interview location: A (HDM), B (HSA), C (CS7R), while the last two digits correspond to a sequential number for the participant, starting from 01. In the case of participants being "re-tested," the code will include an apostrophe after the letter.

In all documents, databases, or others, the participant's information will only be identified by this alphanumeric code.

Only the Principal Investigator will have access to the list that links the identification number to the participant's personal data. This list will be in electronic format with restricted access permissions, preventing unauthorized individuals from accessing, printing, forwarding, or copying confidential information.

---

8. Process Implementation:

- Provision of "Link" at the selected data collection units the materials (questionnaires, informed consents, and envelopes).
- Distribution of data collection materials to data collection units by colleagues interested in collaborating.
- Identification of participants in the clinic, either because they express complaints or through regular medical history taken during consultation.
- Invitation to identified participants to complete the questionnaire in the nearest waiting room, in a more private space designated for the process.
- Sealing of the envelope in person in the consultation room and placing it in a closed box with a slot for insertion.
- Return of completed questionnaires to the Principal Investigator.

---

9. Data Collection Method:

After voluntary recruitment and confirmation of inclusion criteria and the absence of exclusion criteria, the possibility of inclusion in the study and the volunteer's willingness to participate will be certified. The Informed Consent Form will be provided for the participant to read carefully, while being verbally informed about the details of the study. Once consent is obtained, the participant will complete the form, which will include the participant ID according to a sequential number assigned to each participant. A researcher will be available for any clarification needed during the self-completion of the form.

---

10. Participant Benefits:

The participant will not receive any individual benefits apart from the opportunity to participate in the study and the chance to raise and clarify any concerns regarding this specific and sensitive health issue (female genital atrophy). However, their participation in this research project may help other patients receive better healthcare in the future. The participant will have the right to request, in writing, the final publication results from the Principal Investigator.

---

11. Data Review and Database Management:

This project complies with the legal provisions and regulations applicable, namely, the Clinical Research Law No. 21/2014 of April 16 in its current version, Law No. 12/2005 of January 26 ("Genetic and personal health information"), the General Data Protection Regulation, as well as international Good Clinical Practice (GCP) guidelines (International Conference on Harmonization).

Signed informed consents will be stored in a secure physical location with restricted access specifically for that purpose. The student/Principal Investigator will be responsible for entering data into the digital data files (DDF), which will be stored in a specific physical location with restricted access. The data from the DDF will be transferred by the student/Principal Investigator into a global electronic database, which is secure and has restricted access, ensuring that the data is entered completely and accurately. Personal data collected within the framework of this research project and shared between FMUM/ICVC, IPL/ciTechCare, and the Sete Rios Health Center will be kept in secure files, with restricted access, whether electronic or physical, for 15 years after the completion of the study, in compliance with current legislation. The personal data identifying the participants (list linking the participant's name to the alphanumeric identification code) will only be kept by the Principal Investigator in a secure location, and only the investigator will have access to their identity.

The personal data of participants and researchers and the electronic databases will only be accessible to authorized members of the research team. Additionally, study data may be communicated to the competent Ethics Committees and other entities under the relevant clinical trial legislation, who may have access to this data. It will be ensured that all individuals or entities with access to personal data are bound by confidentiality agreements.

The electronic data will have restricted access permissions to prevent unauthorized persons from accessing, printing, forwarding, or copying confidential information.

12. Statistical Analysis:

An anonymized data sheet will be constructed for statistical treatment to validate the questionnaire by determining its reliability and validity using appropriate statistical methods.

---

13. Ethical Considerations:

This study will be approved by the Administration Council and the Ethics Committee of CHL-HSA, the clinical directors of HDMA and UCSP Sete Rios, as well as the Ethics Committee of the Lisbon and Tagus Valley Regional Health Administration.
This clinical study has been designed, and will be implemented, executed, and reported in accordance with the current and future amendments of the International Conference on Harmonization – Good Clinical Practice (ICH-GCP) guidelines, laws, regulations, and ethical codes applicable to the locations where the clinical study is conducted, including but not limited to Law No. 21/2014, of April 16, and all decisions and instructions from relevant authorities, boards of directors, and/or ethics committees.
All participants will be informed and clarified about the procedures, study objectives, and data confidentiality. It will be ensured, prior to data collection, that participation in the study is voluntary and informed, and that all participants will be guaranteed the right to withdraw from the study at any time, without any penalties. All participants will sign the Informed Consent Form, which will be provided in duplicate, one for the participant and the other for inclusion in the project. To ensure ethics in data collection, the questionnaires used in the study will be given to participants in envelopes, which will be sealed in the participant's presence.
It is emphasized that there are no direct risks from participating in the study that need to be disclosed.

---

14. Publication of Results:

The dissemination of the study results is part of the research project process, with the confidentiality and privacy of the participants' personal data ensured, guaranteeing that their identification will not be possible, regardless of the form of result dissemination. This is an academic study of a non-commercial nature.

---

15. Funding:

The research project budget will be funded by financial instruments in the health sector, which are being identified for application, with funding already guaranteed for materials, data transportation logistics, and postage. No additional costs are expected for the involved entities, including UCSP Sete Rios, HSA, or HDMA, particularly no extra costs for the working hours of the staff involved in the study.

---

16. Timeline:

The proposed work plan for this research project, to be carried out in the year 2022, involves the following work plan and schedule:

Tasks

- **Literature Review**

2022	2023	2024	2025

- **Translation and Cultural Adaptation:** January to April 2022
- **Presentation of the Study to Participating Health Units:** April to June 2022
- **Protocol Instruction to the Ethics Committees:** June to September 2022
- **Conducting the Study with Participants:** October 2022 to January 2024
- **Development of the Digital Database and Statistical Data Analysis:**

2023	2024	2025

- **Scientific Dissemination of the Data:** From 2025

Bibliography

1. Mattos S, Moreira T, Pereira D, et al. INSTRUMENTS FOR MEASURING SELF-PERCEPTED HEALTH AMONG ADULTS: A SCOPING REVIEW. *Psicol Saúde Doença*. 2020;21(03):878-895. doi:10.15309/20PSD210328

2. Calvert M, King M, Mercieca-Bebber R, et al. SPIRIT-PRO Extension explanation and elaboration: guidelines for inclusion of patient-reported outcomes in protocols of clinical trials. *BMJ Open*. 2021;11(6). doi:10.1136/BMJOPEN-2020-045105

3. Eremenco S, Pease S, Mann S, Berry P. Patient-reported outcome (PRO) consortium translation process: Consensus development of updated best practices. *J Patient-Reported Outcomes*. 2018;2. doi:10.1186/S41687-018-0037-6

4. Mckown S, Acquadro C, Anfray C, et al. Good practices for the translation, cultural adaptation, and linguistic validation of clinician-reported outcome, observer-reported outcome, and performance outcome measures. doi:10.1186/s41687-020-00248-z

5. Nappi RE, Palacios S, Bruyniks N, Particco M, Panay N. The burden of vulvovaginal atrophy on women's daily living: implications on quality of life from a face-to-face real-life survey. *Menopause*. 2019;26(5):485-491. doi:10.1097/GME.0000000000001260

6. Nappi RE, Palacios S, Panay N, Particco M, Krychman ML. Vulvar and vaginal atrophy in four European countries: Evidence from the European REVIVE Survey. *Climacteric*. 2016;19(2):188-197. doi:10.3109/13697137.2015.1107039

7. Huang AJ, Gregorich SE, Kuppermann M, et al. Day-to-Day Impact of Vaginal Aging questionnaire: a multidimensional measure of the impact of vaginal symptoms on functioning and well-being in postmenopausal women. *Menopause J North Am Menopause Soc*. 2015;22(2):144-154. doi:10.1097/gme.0000000000000281

8. Gabes M, Knüttel H, Stute P, Apfelbacher CJ. Measurement properties of patient-reported outcome measures (PROMs) for women with genitourinary syndrome of menopause: a systematic review. *Menopause*. 2019;26(11):1342-1353. doi:10.1097/GME.0000000000001390

9. Hunter MM, Guthrie KA, Larson JC, et al. Convergent-Divergent Validity and Correlates of the Day-to-Day Impact of Vaginal Aging Domain Scales in the MsFLASH Vaginal Health Trial. *J Sex Med*. 2020;17(1):117-125. doi:10.1016/J.JSXM.2019.10.010

10. Moral E, Delgado JL, Carmona F, et al. The impact of genitourinary syndrome of menopause on well-being, functioning, and quality of life in postmenopausal women. *Menopause*. 2018;25(12):1418-1423. doi:10.1097/GME.0000000000001148

11. Gabes M, Stute P, Apfelbacher C. Validation of the German Day-to-Day Impact of Vaginal Aging (DIVA) Questionnaire in Peri- and Postmenopausal Women. *Sex Med*. 2021;9(4):100382. doi:10.1016/j.esxm.2021.100382

12. Sert B, Özgül S. Turkish day-to-day impact of vaginal aging questionnaire: reliability, validity and relationship with pelvic floor distress. *Int Urogynecology J 2022*. Published online January 27, 2022:1-10. doi:10.1007/S00192-022-05085-W

13. Mokkink Cecilia AC Prinsen Donald L Patrick Jordi Alonso Lex M Bouter LB, Mokkink CL. COSMIN Study Design checklist for Patient-reported outcome measurement instruments. Accessed May 15, 2022. www.cosmin.nl

14. Ferreira PL, Ferreira LN, Pereira LN. Contribution for the Validation of the Portuguese Version of EQ-5D. *Acta Med Port*. 2013;26(6):664-675. doi:10.20344/AMP.1317

15. Santos Pechorro P, Monteiro Pascoal P, Monteiro Pereira N, Poiares C, Neves Jesus S, Xavier Vieira R. Validação da versão portuguesa do Índice de Funcionamento Sexual Feminino – 6. Published online 2016. doi:10.1016/j.androl.2016.06.001

Annex 1: Portuguese Version of DIVA Questionnaire

QUESTIONÁRIO DE IMPACTO DO ENVELHECIMENTO VAGINAL NO DIA-A DIA
COD:.....

Estamos interessados em entender o impacto dos sintomas vaginais como: secura vaginal, dor, irritação e comichão no seu dia-a-dia. Para cada pergunta abaixo, marque a resposta que melhor descreve como as suas atividades, relacionamentos e sentimentos foram afetados por qualquer um destes sintomas durante as últimas 4 semanas.

Parte A. Durante as últimas 4 semanas, quanto é que os sintomas vaginais como: secura, ardor, irritação ou comichão, foram desconfortáveis ou interferiram na sua capacidade de:

1. Andar á velocidade habitual?

☐0 Nada ☐1 Um pouco ☐2 Moderadamente ☐3 Bastante ☐4 Extremamente

2. Usar a roupa e lingerie que quer?

☐0 Nada ☐1 Um pouco ☐2 Moderadamente ☐3 Bastante ☐4 Extremamente

3. Usar a casa de banho ou limpar-se após o uso desta?

☐0 Nada ☐1 Um pouco ☐2 Moderadamente ☐3 Bastante ☐4 Extremamente

4. Ficar sentada mais de 1 hora?

☐0 Nada ☐1 Um pouco ☐2 Moderadamente ☐3 Bastante ☐4 Extremamente

5. Ter uma boa noite de sono?

☐0 Nada ☐1 Um pouco ☐2 Moderadamente ☐3 Bastante ☐4 Extremamente

Parte B. Durante as últimas 4 semanas, com que frequência os sintomas vaginais como: secura, ardor, irritação ou comichão, fizeram com que se sentisse:

6. Deprimida ou em baixo?

☐0 Nunca ☐1 Raramente ☐2 Às vezes ☐3 Frequentemente ☐4 Quase sempre

7. Embaraçada?

☐0 Nunca ☐1 Raramente ☐2 Às vezes ☐3 Frequentemente ☐4 Quase sempre

8. Frustrada ou ressentida?

☐0 Nunca ☐1 Raramente ☐2 Às vezes ☐3 Frequentemente ☐4 Quase sempre

9. Mal consigo própria?

☐0 Nunca ☐1 Raramente ☐2 Às vezes ☐3 Frequentemente ☐4 Quase sempre

Parte C. As perguntas que se seguem são sobre o impacto dos seus sintomas, nas relações sexuais e outros tipos de atividade sexual, como autoestimulação ou masturbação. Durante as últimas 4 semanas, sintomas vaginais como: secura, ardor, irritação ou comichão, <u>afetaram</u>:

10. O seu desejo ou interesse em ter relações sexuais ou outros tipos de atividade sexual (autoestimulação ou masturbação)?

☐0 Nada ☐1 Um pouco ☐2 Moderadamente ☐3 Bastante ☐4 Extremamente

☐ Não aplicável- não tive atividade sexual de nenhum tipo recentemente.

11. A frequência com que teve relações sexuais, ou outros tipos de atividade sexual (incluindo autoestimulação ou masturbação)?

☐0 Nada ☐1 Um pouco ☐2 Moderadamente ☐3 Bastante ☐4 Extremamente

☐ Não aplicável- não tive atividade sexual de nenhum tipo recentemente.

12. A sua capacidade de ficar excitada durante a atividade sexual (incluindo autoestimulação ou masturbação)?

☐0 Nada ☐1 Um pouco ☐2 Moderadamente ☐3 Bastante ☐4 Extremamente

☐ Não aplicável- não tive atividade sexual de nenhum tipo recentemente.

13. A sua capacidade de espontaneamente se dedicar á atividade sexual (incluindo autoestimulação e masturbação)?

☐0 Nada ☐1 Um pouco ☐2 Moderadamente ☐3 Bastante ☐4 Extremamente

☐ Não aplicável- não tive atividade sexual de nenhum tipo recentemente.

14. A sua capacidade de relaxar e desfrutar da atividade sexual (incluindo autoestimulação ou masturbação)?

☐0 Nada ☐1 Um pouco ☐2 Moderadamente ☐3 Bastante ☐4 Extremamente

☐ Não aplicável- não tive atividade sexual de nenhum tipo recentemente.

15. O nível de prazer que experienciou durante a atividade sexual (incluindo autoestimulação ou masturbação)?

☐0 Nada ☐1 Um pouco ☐2 Moderadamente ☐3 Bastante ☐4 Extremamente

☐ Não aplicável- não tive atividade sexual de nenhum tipo recentemente.

16. O seu desejo ou interesse em ter um relacionamento sexual?

☐0 Nada ☐1 Um pouco ☐2 Moderadamente ☐3 Bastante ☐4 Extremamente

☐ Não aplicável- não tive atividade sexual de nenhum tipo recentemente.

17. A sua confiança em ser capaz de satisfazer sexualmente um parceiro(a)?

☐0 Nada ☐1 Um pouco ☐2 Moderadamente ☐3 Bastante ☐4 Extremamente

☐ Não aplicável- não tive atividade sexual de nenhum tipo recentemente.

18. A sua satisfação geral com a sua vida sexual?

☐0 Nada ☐1 Um pouco ☐2 Moderadamente ☐3 Bastante ☐4 Extremamente

☐ Não aplicável- não tive atividade sexual de nenhum tipo recentemente.

Parte D. As afirmações que se seguem descrevem a forma pela qual os seus sintomas vaginais podem ter afetado o que sente por si e pelo seu corpo. Por favor, indique o <u>quão verdadeira</u> cada uma das seguintes afirmações foi para si durante as últimas 4 semanas.

19. Os meus sintomas vaginais fazem sentir-me como se estivesse a envelhecer.

☐0 Nada ☐1 Um pouco ☐2 Às vezes ☐3 Muitas vezes ☐4 Sempre

20. Sinto-me indesejável devido aos meus sintomas vaginais.

☐0 Nada ☐1 Um pouco ☐2 Às vezes ☐3 Muitas vezes ☐4 Sempre

21. Quando penso nos meus sintomas vaginais, sinto como se tivesse perdido algo.

☐0 Nada ☐1 Um pouco ☐2 Às vezes ☐3 Muitas vezes ☐4 Sempre

22. Os meus sintomas vaginais fazem-me sentir como se o meu corpo se estivesse a deteriorar

☐0 Nada ☐1 Um pouco ☐2 Às vezes ☐3 Muitas vezes ☐4 Sempre

23. Sinto-me menos sexualmente atraente (sexy) devido aos meus sintomas vaginais.

☐0 Nada ☐1 Um pouco ☐2 Às vezes ☐3 Muitas vezes ☐4 Sempre

Agradecemos as suas respostas.

Annex 2: Symptom Questionnaire

Objective: To correctly identify your genital discomfort (vagina and vulva). Please describe the discomfort caused by each of the following symptoms. If you do not have this complaint, please mark as "no discomfort".

Symptom Classification:
☐ 1 - No Discomfort
☐ 2 - Mild Discomfort
☐ 3 - Moderate Discomfort
☐ 4 - Intense Discomfort

---

1. Vaginal or Vulvar Dryness
☐ 1 No Discomfort
☐ 2 Mild Discomfort
☐ 3 Moderate Discomfort
☐ 4 Intense Discomfort

2. Vaginal or Vulvar Irritation
☐ 1 No Discomfort
☐ 2 Mild Discomfort
☐ 3 Moderate Discomfort
☐ 4 Intense Discomfort

3. Vaginal or Vulvar Itching
☐ 1 No Discomfort
☐ 2 Mild Discomfort
☐ 3 Moderate Discomfort
☐ 4 Intense Discomfort

4. Vaginal or Vulvar Burning or After Sexual Intercourse
☐ 1 No Discomfort
☐ 2 Mild Discomfort
☐ 3 Moderate Discomfort
☐ 4 Intense Discomfort

5. Vulvar or Vaginal Discomfort or After Sexual Intercourse
☐ 1 No Discomfort
☐ 2 Mild Discomfort
☐ 3 Moderate Discomfort
☐ 4 Intense Discomfort

6. Pain During Sexual Intercourse
☐ 1 No Discomfort
☐ 2 Mild Discomfort
☐ 3 Moderate Discomfort
☐ 4 Intense Discomfort

7. Bleeding or Unpleasant Odor During or After Sexual Intercourse
☐ 1 No Discomfort

☐ 2 Mild Discomfort
☐ 3 Moderate Discomfort
☐ 4 Intense Discomfort

Of these 7 symptoms, the one that bothers you the most or disturbs your life the most is:

Annex 3: Sociodemographic and Clinical Questionnaire

Questionnaire: _____

Age: _____ years **Height:** _____ cm **Weight:** _____ kg

1. **Ethnicity:**
    - White (European, Hispanic, North African, Middle Eastern)
    - Black (African, Caribbean, African American)
    - South Asian (Indian, Pakistani, Bangladeshi)
    - East Asian (Chinese, Japanese, Korean)
    - Other
2. **Marital Status:**
    - Single
    - Cohabiting
    - Married
    - Divorced
    - Widowed
3. **Education Level:**
    - Up to 4th grade
    - 5th to 9th grade
    - 10th to 12th grade
    - Bachelor's degree
    - Master's/Doctorate
4. **Employment Status:**
    - Employed
    - Retired
    - Unemployed
5. **Current Occupation (or previous occupation if retired):**
    - Executive/Manager
    - Specialist in intellectual and scientific professions
    - Technicians and intermediate-level professionals
    - Administrative and similar staff
    - Service personnel and salespeople

- Industrial workers, agriculture, cleaning

6. **Profession:** _____
7. **Do you smoke?**
   - Yes
   - No
8. **Do you drink wine weekly (more than 3 glasses)?**
   - Yes
   - No
9. **Type of residence:**
   - Owned
   - Rented
   - Shared
   - Apartment
   - House
   - Nursing home
10. **Menopausal status:**
    - Perimenopausal
    - Don't know
    - Postmenopausal
      Age of menopause: _____ years
11. **N^{er} of pregnancies:** _____**N^{er} of vaginal births:** _____ **N^{er} of caesarean sections:** _____
12. **Gynecological surgeries:**
    - No
    - Yes
      If yes, which ones: _____
13. **Hormonal treatments (creams or vaginal suppositories):**
    - No
    - Yes
      If yes, which one: _____
14. **Do you use vaginal lubricants?**
    - No
    - Yes

Do you use vaginal moisturizers?

- No
- Yes

14. **Contraceptive treatments (pills, patches, implants, devices):**
    - No
    - Yes
15. **Hormonal treatment for menopause:**
    - No
    - Yes
      If yes, which one: _____
16. **Current sexual activity:**
    - Yes
    - No
      Number of years without intercourse: _____
17. **Do you leak urine when coughing?**
    - No
    - Yes
18. **Do you feel that the walls of your vagina are prolapsed or loose?**
    - No
    - Yes
19. **Do you have diabetes?**
    - No
    - Yes

    Do you take medication for diabetes?
    - Yes
    - No
20. **Do you have high blood pressure?**
    - No
    - Yes
      Do you take medication for high blood pressure?
    - Yes

- No

21. **Do you have difficulty sleeping?**
    - No
    - Yes
      Do you have anxiety?
    - No
    - Yes

22. **Have you had cancer?**
    - No
    - Yes
      If yes, where: _____

23. **Have you undergone chemotherapy/radiotherapy?**
    - No
    - Yes

Annex 4 – DIVA English Version

The Day-to-Day Impact of Vaginal Aging Questionnaire

We are interested in understanding the impact of vaginal symptoms such as vaginal dryness, soreness, irritation, and itching on your day-to-day life. For each question below, please check the answer that best describes how your activities, relationships, and feelings have been affected by any of these symptoms during the past four weeks.

PART A. During the past four weeks, how much have vaginal symptoms such as dryness, soreness, irritation, or itching made it uncomfortable or interfered with your ability to:

1. Walk at your usual speed?

☐0	☐1	☐2	☐3	☐4
Not at all	A little bit	Moderately	Quite a bit	Extremely

2. Wear the clothing or underwear you want?

☐0	☐1	☐2	☐3	☐4
Not at all	A little bit	Moderately	Quite a bit	Extremely

3. Use the toilet or wipe yourself after using the toilet?

☐0	☐1	☐2	☐3	☐4
Not at all	A little bit	Moderately	Quite a bit	Extremely

4. Sit for more than an hour?

☐0	☐1	☐2	☐3	☐4
Not at all	A little bit	Moderately	Quite a bit	Extremely

5. Get a good night's sleep?

☐0	☐1	☐2	☐3	☐4
Not at all	A little bit	Moderately	Quite a bit	Extremely

PART B. During the past four weeks, how often have vaginal symptoms such as dryness, soreness, irritation, or itching caused you to feel:

6. Depressed or down?

☐0	☐1	☐2	☐3	☐4
Never	Rarely	Sometimes	Fairly often	Very often

7. Embarrassed?

☐0	☐1	☐2	☐3	☐4
Never	Rarely	Sometimes	Fairly often	Very often

8. Frustrated or resentful?

☐0	☐1	☐2	☐3	☐4
Never	Rarely	Sometimes	Fairly often	Very often

9. Bad about yourself?

☐0	☐1	☐2	☐3	☐4
Never	Rarely	Sometimes	Fairly often	Very often

PART C. The following questions ask about the impact of your symptoms on vaginal sexual intercourse as well as other types of sexual activity such as self-stimulation or masturbation. During the past four weeks, have vaginal symptoms such as dryness, soreness, irritation, or itching affected:

10. Your desire or interest in having sexual intercourse or other types of sexual activity (including self-stimulation or masturbation)?

☐0	☐1	☐2	☐3	☐4
Not at all	A little bit	Moderately	Quite a bit	Extremely

11. How frequently you had sexual intercourse or other types of sexual activity (including self-stimulation or masturbation)?

☐0	☐1	☐2	☐3	☐4
Not at all	A little bit	Moderately	Quite a bit	Extremely

12. Your ability to become aroused during sexual activity (including self-stimulation or masturbation)?

☐0	☐1	☐2	☐3	☐4
Not at all	A little bit	Moderately	Quite a bit	Extremely

☐Not applicable – I have not had sexual activity of any kind recently

13. Your ability to be spontaneous about sexual activity (including self-stimulation and masturbation)?

☐0	☐1	☐2	☐3	☐4
Not at all	A little bit	Moderately	Quite a bit	Extremely

☐Not applicable – I have not had sexual activity of any kind recently

15. The amount of pleasure you experienced during sexual activity (including self-stimulation or masturbation)?

☐0	☐1	☐2	☐3	☐4
Not at all	A little bit	Moderately	Quite a bit	Extremely

☐Not applicable – I have not had sexual activity of any kind recently

16. Your desire or interest in being in a sexual relationship?

☐0	☐1	☐2	☐3	☐4
Not at all	A little bit	Moderately	Quite a bit	Extremely

17. Your confidence that you could sexually satisfy a partner?

☐0	☐1	☐2	☐3	☐4
Not at all	A little bit	Moderately	Quite a bit	Extremely

18. Your overall satisfaction with your sex life?

☐0	☐1	☐2	☐3	☐4
Not at all	A little bit	Moderately	Quite a bit	Extremely

PART D. The following statements describe ways in which your vaginal symptoms may have affected your feelings about yourself and your body. Please indicate how true each of the following statements has been for you during the past four weeks.

19. My vaginal symptoms make me feel like I'm getting old.

☐0	☐1	☐2	☐3	☐4
Not at all true	A little true	Somewhat true	Mostly true	Definitely true

20. I feel undesirable because of my vaginal symptoms.

☐0	☐1	☐2	☐3	☐4
Not at all true	A little true	Somewhat true	Mostly true	Definitely true

21. When I think about my vaginal symptoms, I feel like I have lost something.

☐0	☐1	☐2	☐3	☐4
Not at all true	A little true	Somewhat true	Mostly true	Definitely true

22. My vaginal symptoms make me feel like my body is deteriorating.

☐0	☐1	☐2	☐3	☐4
Not at all true	A little true	Somewhat true	Mostly true	Definitely true

22. I feel less sexy because of my vaginal symptoms.

☐0	☐1	☐2	☐3	☐4
Not at all true	A little true	Somewhat true	Mostly true	Definitely true

Thank you!

Recommended scoring

Total scores for each domain scale are computed by calculating the average of scores for the corresponding individual items. The possible score range for all domain scales is 0 to 4, with higher scores denoting greater impact of vaginal symptoms.

Two versions of the sexual functioning scale are available: 1) a short, 5-item version that can be administered to all postmenopausal women, regardless of sexual activity status; and 2) a longer, 9-item version that includes 4 additional items (12, 13, 14, and 15) that are only appropriate for women with a history of recent sexual activity.

Activities of daily living domain: items 1, 2, 3, 4, 5
Emotional well-being domain: items 6, 7, 8, 9
Sexual functioning domain (short version): items 10, 11, 12, 16, 17, 18
Sexual functioning domain (longer version): items 10, 11, 12, 13, 14, 15, 16, 17, 18, Self-concept and body image domain: items 19, 20, 21, 22, 23

Permissions

Although the DIVA questionnaire is copyrighted, it is available without charge from the authors, and no written permission is required for its use, provided that the following conditions are followed:

- Please refer to the questionnaire using its complete name – the Day-to-Day Impact of Vaginal Aging questionnaire - and provide the appropriate citation.
- Modifications may be made without written permission. However, please clearly identify any modifications in any publications as having been made by the users. Please let the corresponding author know of any changes for our records.

Huang AJ, Gregorich SE, Kuppermann M, et al. Day-to-Day Impact of Vaginal Aging questionnaire: a multidimensional measure of the impact of vaginal symptoms on functioning and well-being in postmenopausal women. Menopause. 2015;22(2):144–154. doi:10.1097/GME.0000000000000281

Annex 5: EuroQol 5D

EQ-5D (UK English version)

By placing a tick in one box in each group below, please indicate which statements best describe your own health state today.

Mobility

I have no problems in walking about	❑
I have some problems in walking about	❑
I am confined to bed	❑

Self-Care

I have no problems with self-care	❑
I have some problems washing or dressing myself	❑
I am unable to wash or dress myself	❑

Usual Activities (*e.g. work, study, housework, family or leisure activities)*

I have no problems with performing my usual activities	❑
I have some problems with performing my usual activities	❑
I am unable to perform my usual activities	❑

Pain/Discomfort

I have no pain or discomfort	❑
I have moderate pain or discomfort	❑
I have extreme pain or discomfort	❑

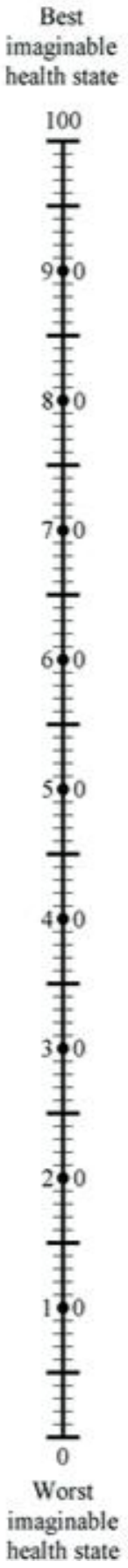
Anxiety/Depression

I am not anxious or depressed	❑
I am moderately anxious or depressed	❑
I am extremely anxious or depressed	❑

To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate on this scale how good or bad your own health is today, in your opinion. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your health state is today.

Your own health state today



Annex 6; Female Sexual Function Index (short version 6)

1. Over the past 4 weeks, how often did you feel sexual desire or interest?

Please circle your response and enter the score below

5 = Almost always or always

4 = Most times (more than half the time)

3 = Sometimes (about half the time)

2 = A few times (less than half the time)

1 = Almost never or never

Score:_____

2. Over the past 4 weeks, how often did you feel sexually aroused "turned on" during sexual activity or intercourse?

Please circle your response and enter the score below

0 = No sexual activity

5 = Almost always or always

4 = Most times (more than half the time)

3 = Sometimes (about half the time)

2 = A few times (less than half the time)

1 = Almost never or never

Score:_____

3. Over the past 4 weeks, how often did maintain your lubrication ("wetness") until completion of sexual activity/ intercourse?

Please circle your response and enter the score below

0 = No sexual activity

5 = Almost always or always

4 = Most times (more than half the time)

3 = Sometimes (about half the time)

2 = A few times (less than half the time)

1 = Almost never or never

Score:_____

4. Over the past 4 weeks, when you had intercourse, how difficult was it for you to reach orgasm (climax)?

Please circle your response and enter the score below

0 = No sexual activity

1 = Extremely difficult or impossible

2 = Very difficult

3 = Difficult

4 = Slightly difficult

5 = Not difficult

Score:_____

5. Over the past 4 weeks, how satisfied have you been overall with your sex life?

Please circle your response and enter the score below

5 = Very satisfied

4 = Moderately satisfied

3 = About equally satisfied and dissatisfied

2 = Moderately dissatisfied

1 = Very dissatisfied

Score:_____

6. Over the past 4 weeks how often did you experience pain or discomfort during vaginal penetration?

Please circle your response and enter the score below

0 = Did not attempt intercourse

1 = Almost always or always

2 = Most times (more than half the time)

3 = Sometimes (about half the time)

4 = A few times (less than half the time)

5 = Almost never or never

Score:_____

Annex 7 – Informed Consent

INFORMED, FREE, AND VOLUNTARY CONSENT FOR PARTICIPATION IN RESEARCH

You are being invited to participate in the study: **"Cross-cultural adaptation to Portuguese and psychometric validation of the DIVA questionnaire (Day-to-day Impact of Vaginal Aging) - Impact of vaginal aging on daily life."** This study is being conducted by Dr. Andreia Antunes as part of her PhD project at the University of Minho, involving several healthcare professionals, such as doctors and researchers. The aim of this research is to validate a clinical questionnaire for the Portuguese population to identify complaints related to genital atrophy and how it impacts the quality of life of women. Self-administered questionnaires will be used, but you may clarify any doubts with the person handing you the questionnaire. You are expected to respond to the following questionnaires:

1. **Genital Symptoms Questionnaire**
2. **Sociodemographic and Clinical Data Questionnaire**, which will evaluate possible factors associated with genital atrophy.
3. **DIVA Questionnaire** (Day-to-day Impact of Vaginal Aging), which evaluates the impact of genital atrophy symptoms on:
    - (1) Daily activities,
    - (2) Emotional well-being,
    - (3) Sexual functioning,
    - (4) Self-esteem and body image.
4. **EQ-5D**, which evaluates your general quality of life.
5. **Female Sexual Function Index (FSFI-6)**, which evaluates female sexual function.

The total time for completing the questionnaires will be approximately 20 minutes. You may feel discomfort in responding to the questionnaires, and certain questions may evoke unpleasant memories due to potential references to anatomical or functional changes. To minimize discomfort, the questionnaire will be completed individually. Participation in the study is voluntary and can be withdrawn at any time without any penalty. There is no cost or risk involved in participating.

The data collected will be used exclusively for this study, ensuring anonymity and confidentiality. The identification of participants will not be disclosed. The researcher is available for any clarifications.

After reading and understanding this document, I declare that I agree to participate in this study and allow the use of the data I voluntarily provide. The informed consent will be completed in duplicate, one for inclusion in the project and the other for the participant.

PARTICIPANT IDENTIFICATION AND CONSENT

Full Name: _____

ID Number: _____

POST-INFORMED CONSENT:

I declare that, on **/**/____, I agreed to participate as a subject in the research project entitled **"Cross-cultural adaptation to Portuguese and psychometric validation of the DIVA questionnaire (Day-to-day Impact of Vaginal Aging) - Impact of Vaginal Aging on Daily Life"** after being fully informed about the study's objectives, purpose, and terms of my participation. The information provided to the researchers will be used solely for the objectives and purposes of the research project, ensuring my identification remains confidential under the responsibility of the project proponents (Andreia Antunes, email: id10188@alunos.uminho.pt).

I will not receive any compensation, nor will I incur any financial costs as a result of my voluntary consent to participate in this research project.