INPLASY

Smooth Muscle Tumor of Uncertain Malignant Potential (STUMP): a systematic review of the literature in the last 20 years

INPLASY202460100
doi: 10.37766/inplasy2024.6.0100
Received: 25 June 2024
Published: 25 June 2024

Bucuri, CE; Ciortea, R; Malutan, AM; Oprea, V; Toma, M; Roman, MP; Ormindean, CM; Nati, I; Suciu, V; Mihu, D.

Corresponding author:
bucuri carmen elena

cbucurie@yahoo.com

Author Affiliation:
iuliu hatieganu university of medicine and pharmacy cluj napoca.

ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202460100

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 25 June 2024 and was last updated on 25 June 2024.

INTRODUCTION

Review question / Objective The primary objective of this systematic review is to provide a comprehensive analysis of Smooth Muscle Tumor of Uncertain Malignant Potential (STUMP), a rare uterine tumor characterized by ambiguous histological features that challenge its classification as either benign or malignant. The review aims to address several key aspects of STUMP based on literature from the past 20 years:

1. Clinical Characteristics:

o Demographics and Presentation: Identify and describe the demographic characteristics and clinical presentation of patients diagnosed with STUMP. This includes analyzing the age distribution, symptoms such as abnormal uterine bleeding, pelvic pain, and incidental detection of uterine masses. Understanding these characteristics can help in recognizing patterns and improving diagnostic accuracy.

o Diagnostic Challenges: Highlight the diagnostic difficulties posed by STUMP due to its overlapping features with benign leiomyomas and malignant leiomyosarcomas. Discuss the variability in presentation and the importance of considering STUMP in differential diagnoses.

2. Pathological and Histological Features:

o Histological Criteria: Analyze the histological features used to diagnose STUMP, including nuclear atypia, mitotic activity, and focal necrosis. Examine how these features overlap with those of other uterine smooth muscle tumors, complicating definitive classification.

o Diagnostic Criteria: Discuss the current diagnostic criteria and the subjective nature of interpreting features such as cellularity and tumor borders. Emphasize the need for standardized criteria to reduce variability in diagnosis.

3. Immunohistochemical and Molecular Markers:

o Role of Markers: Investigate the use of immunohistochemical markers such as p16, p53, and Ki-67 in differentiating STUMP from other

smooth muscle tumors. Evaluate their prognostic significance in predicting clinical outcomes and recurrence.
o Prognostic Indicators: Analyze studies that explore the association of elevated p16 and p53 expression with aggressive tumor behavior and recurrence. Assess the potential of these markers in guiding treatment decisions and long-term monitoring.
4. Treatment Approaches:
o Surgical Management: Review the surgical strategies employed in treating STUMP, including hysterectomy, myomectomy, and the extent of resection. Discuss the impact of surgical margins and the role of complete resection in reducing recurrence rates.
o Adjuvant Therapies: Evaluate the use of adjuvant therapies such as hormonal treatments and the circumstances under which they are recommended. Discuss the lack of standardization in adjuvant therapy protocols and the need for individualized treatment plans.
o Long-term Surveillance: Highlight the importance of long-term follow-up and surveillance, especially for patients with high-risk features. Discuss the recommended frequency and duration of follow-up visits to monitor for recurrence.
5. Clinical Outcomes and Recurrence:
o Recurrence Rates: Assess the recurrence rates of STUMP and the factors associated with higher risk of recurrence, such as high mitotic counts and coagulative necrosis. Discuss the implications of recurrence on patient management and outcomes.
6. Comparison with Other Uterine Smooth Muscle Tumors:
o : Compare STUMP with benign leiomyomas and malignant leiomyosarcomas in terms of clinical presentation, pathological features, and molecular markers. Discuss the challenges in accurately differentiating these tumors and the potential for misdiagnosis.
By addressing these objectives, this systematic review aims to enhance the understanding of STUMP, improve diagnostic accuracy, and inform effective management strategies.

Rationale Smooth Muscle Tumor of Uncertain Malignant Potential (STUMP) is a rare and diagnostically challenging uterine tumor. Its ambiguous histological characteristics make it difficult to classify definitively as benign or malignant, thus complicating clinical decision-making and management. The clinical presentation, diagnosis, and treatment of STUMP are areas fraught with uncertainty, necessitating a comprehensive review of the literature to better understand and manage this condition.

Clinical and Diagnostic Challenges
STUMP predominantly affects perimenopausal and postmenopausal women, with the average age at diagnosis being around 53 years. These tumors can present with nonspecific symptoms such as abnormal uterine bleeding, pelvic pain, or can be incidentally found during evaluations for other conditions. The clinical presentation often overlaps with other uterine smooth muscle tumors, such as benign leiomyomas and malignant leiomyosarcomas, making accurate diagnosis challenging.

Histologically, STUMPs exhibit features that are intermediate between benign and malignant uterine smooth muscle tumors. These features include mild nuclear atypia, low mitotic indices, and focal necrosis, which can overlap significantly with those seen in leiomyomas and leiomyosarcomas. The interpretation of these histological features is often subjective, leading to variability in diagnosis among pathologists. The absence of standardized diagnostic criteria further complicates this issue, resulting in inconsistent clinical management strategies.

Prognostic Uncertainty
The prognosis of STUMP remains uncertain. While many STUMPs behave in a benign manner, a subset of these tumors can exhibit aggressive behavior, with potential for recurrence and metastasis. Identifying reliable prognostic markers is crucial for risk stratification and guiding treatment decisions. Immunohistochemical markers such as p16 and p53 have shown potential in differentiating aggressive tumors, but their prognostic utility is not yet fully established. Understanding the molecular and genetic underpinnings of STUMP could provide valuable insights into their behavior and inform more precise prognostic assessments.

Management Dilemmas
The management of STUMP typically involves surgical intervention, with hysterectomy or myomectomy being the primary options. However, the extent of surgery required to optimize outcomes remains a subject of debate. More extensive surgery might improve oncological outcomes but is not always warranted given the benign behavior observed in many STUMPs. Adjuvant therapies are not routinely recommended, but the need for long-term surveillance is emphasized due to the risk of recurrence. The rarity of STUMP means there is a paucity of high-quality evidence to guide management, leading clinicians to rely on case reports and small case series.

Need for a Systematic Review

Despite being recognized for over half a century, STUMP remains poorly understood due to the limited number of comprehensive studies. Existing literature primarily consists of isolated case reports and small case series, which do not provide a holistic view of the condition. A systematic review is necessary to aggregate data from multiple studies, offering a more complete understanding of STUMP's epidemiology, pathogenesis, clinical presentation, diagnostic approaches, management strategies, and outcomes.

Objective

This systematic review aims to fill the knowledge gap by synthesizing evidence from the past 20 years of literature on STUMP. By doing so, it seeks to clarify the clinical and pathological characteristics of STUMP, evaluate the effectiveness of current diagnostic and treatment modalities, and identify areas for future research. Specifically, the review will:

Describe the demographic and clinical characteristics of patients diagnosed with STUMP, identifying common symptoms and diagnostic challenges.

Analyze the histological criteria used to diagnose STUMP, including the role of immunohistochemical markers like p16 and p53.

Evaluate the surgical and non-surgical management strategies employed, including the impact of different surgical approaches on recurrence rates.

Assess the long-term outcomes and recurrence rates associated with STUMP, identifying prognostic factors that influence these outcomes.

Compare STUMP with benign leiomyomas and malignant leiomyosarcomas to highlight diagnostic overlaps and differences.

Condition being studied Smooth Muscle Tumor of Uncertain Malignant Potential (STUMP) is a rare uterine tumor that occupies a diagnostic grey zone between benign leiomyomas (fibroids) and malignant leiomyosarcomas. STUMPs are characterized by ambiguous histological features that prevent definitive classification as either benign or malignant. This ambiguity poses significant challenges for diagnosis, prognosis, and treatment, making STUMP a unique and complex condition within gynecologic oncology.

Epidemiology: STUMPs primarily affect women during their perimenopausal and postmenopausal years, with the average age of diagnosis being around 53 years. However, they can also occur in younger women, which adds a layer of complexity regarding fertility preservation and management strategies.

Clinical Presentation: Patients with STUMP often present with nonspecific symptoms, which can include:

• Abnormal Uterine Bleeding: This is the most common symptom, manifesting as heavy or irregular menstrual periods.

• Pelvic Pain: Patients may experience discomfort or pain in the pelvic region.

• Incidental Findings: In some cases, STUMPs are discovered incidentally during imaging or surgical procedures conducted for other reasons.

Given these nonspecific symptoms, STUMPs can be easily confused with other more common uterine conditions, such as leiomyomas or even more sinister pathologies like leiomyosarcomas.

Histological Features: The histopathological examination of STUMPs reveals features that are intermediate between benign and malignant uterine smooth muscle tumors. Key histological characteristics include:

• Mild to Moderate Nuclear Atypia: Unlike the significant atypia seen in leiomyosarcomas, STUMPs exhibit only mild to moderate nuclear abnormalities.

• Low Mitotic Index: STUMPs have a low number of mitotic figures (cell divisions), which is less than what is typically observed in leiomyosarcomas.

• Focal Necrosis: While leiomyosarcomas show extensive areas of necrosis, STUMPs might have only focal (limited) necrotic areas.

These intermediate features make it challenging to categorize STUMPs definitively, leading to their designation as tumors of "uncertain malignant potential."

Immunohistochemical and Molecular Markers: Recent research has explored the use of immunohistochemical markers to aid in the differentiation and prognostication of STUMPs. Notable markers include:

• p16: Overexpression of p16 is often associated with more aggressive tumor behavior and is seen in some STUMPs.

• p53: This tumor suppressor gene, when mutated, can indicate a higher risk of malignant transformation.

• Ki-67 (MIB-1): A marker for cellular proliferation, higher levels of Ki-67 may correlate with increased tumor growth and malignancy potential.

Management: The management of STUMP is primarily surgical, with hysterectomy (removal of the uterus) or myomectomy (removal of the tumor while preserving the uterus) being common approaches. The choice of surgery often depends on factors such as:

• Tumor Size and Location: Larger or more invasive tumors may necessitate more extensive surgery.

• Patient's Age and Desire for Fertility: Younger patients desiring to preserve fertility might opt for myomectomy over hysterectomy.
Prognosis and Recurrence: STUMPs have an uncertain prognosis. While many behave in a benign manner, there is a risk of recurrence and, in rare cases, metastasis. Factors that may influence recurrence include:
• Histopathological Features: Higher mitotic counts and the presence of necrosis can indicate a higher risk.
• Surgical Margins: Complete surgical resection with negative margins reduces the likelihood of recurrence.
Surveillance: Due to the potential for late recurrences, long-term follow-up is recommended. This typically involves regular clinical examinations and imaging studies over several years.
Conclusion: STUMP represents a diagnostic and therapeutic challenge due to its intermediate characteristics between benign and malignant uterine tumors. Understanding its clinical presentation, histological features, and potential for recurrence is crucial for effective management. Continued research is needed to develop standardized diagnostic criteria and optimal treatment strategies to improve patient outcomes. By synthesizing current knowledge, this review aims to provide a comprehensive overview of STUMP.

METHODS

Search strategy This systematic review aims to provide a comprehensive overview of Smooth Muscle Tumor of Uncertain Malignant Potential (STUMP) by examining clinical, pathological, immunohistochemical, and treatment-related characteristics through a rigorous analysis of literature from the past 20 years. To achieve this, a detailed search strategy was employed across multiple electronic databases using specific terms and criteria to ensure the inclusion of relevant studies.
Search Terms: The following search terms and their combinations were used to identify relevant literature on STUMP:
• "Smooth Muscle Tumor of Uncertain Malignant Potential"
• "STUMP"
• "Uterine Smooth Muscle Tumor"
• "Uterine Neoplasm"
• "Leiomyoma"
• "Leiomyosarcoma"
• "Uterine Tumor"
• "Uncertain Malignant Potential"
• "Uterine Cancer"
• "Histopathology"
• "Immunohistochemistry"
• "p16"
• "p53"
• "Ki-67"
• "Treatment"
• "Surgical Management"
• "Hysterectomy"
• "Myomectomy"
• "Recurrence"
• "Prognosis"
Boolean operators (AND, OR) were used to combine these terms to broaden or narrow the search results as needed. Truncation symbols (*) were also employed to capture variations of root words.
Electronic Databases: The following electronic databases were searched to gather a comprehensive collection of studies on STUMP:
1. PubMed:
o PubMed was chosen due to its extensive archive of biomedical literature, including studies from Medline. It provides access to a wide range of medical journals, making it a critical resource for this review.
o Search Query Example: ("Smooth Muscle Tumor of Uncertain Malignant Potential" OR "STUMP") AND ("Uterine Neoplasm" OR "Uterine Tumor" OR "Leiomyoma" OR "Leiomyosarcoma") AND ("Histopathology" OR "Immunohistochemistry" OR "Treatment" OR "Recurrence")
2. Scopus:
o Scopus is a large multidisciplinary database that includes peer-reviewed literature in science, technology, medicine, and social sciences. Its broad coverage and citation tracking capabilities make it an essential tool for comprehensive reviews.
o Search Query Example: TITLE-ABS-KEY ("Smooth Muscle Tumor of Uncertain Malignant Potential" OR "STUMP") AND ("Uterine Tumor" OR "Uterine Cancer" OR "Leiomyoma" OR "Leiomyosarcoma") AND ("Histopathology" OR "Immunohistochemistry" OR "Treatment" OR "Prognosis")
Inclusion and Exclusion Criteria: To ensure the relevance and quality of the studies included in this review, the following inclusion and exclusion criteria were applied:
Inclusion Criteria:
• Studies published in English between January 2003 and December 2023.
• Studies focusing on Smooth Muscle Tumor of Uncertain Malignant Potential (STUMP) of the uterus.
• Studies providing detailed clinical, pathological, immunohistochemical, and treatment-related information.

• Case reports, case series, retrospective studies, prospective studies, and systematic reviews.
Exclusion Criteria:
• Studies not available in full text.
• Non-English language publications.
• Studies not focusing on STUMP or lacking detailed information.
• Abstracts, conference presentations, letters, and editorials without substantial data.
Search Strategy: A comprehensive search strategy was developed and implemented across the selected databases. The initial search yielded a total of 178 records from all databases combined. After removing duplicate articles, 102 unique titles and abstracts were screened for relevance to the review's objectives. Articles not focusing on STUMP or lacking detailed case information were excluded, resulting in 43 potentially eligible articles. The full texts of these 43 articles were then assessed for inclusion, and reference lists of included studies were manually searched to identify additional relevant publications. This thorough process led to the final inclusion of 32 studies that met all criteria and provided comprehensive descriptions of STUMP cases.
Data Extraction and Management: Data were extracted from the included studies using a standardized form to ensure consistency and accuracy. Key information extracted included study design, sample size, patient demographics, clinical presentation, histological features, immunohistochemical markers, treatment approaches, and outcomes. The data were then analyzed to identify common themes, variations, and gaps in the current understanding of STUMP.
Conclusion: This systematic review aims to synthesize existing knowledge on Smooth Muscle Tumor of Uncertain Malignant Potential (STUMP) by leveraging a comprehensive search strategy across multiple electronic databases. By meticulously selecting and analyzing relevant studies, the review seeks to enhance the understanding of STUMP, inform clinical practice, and guide future research efforts. The findings will provide valuable insights into the diagnosis, management, and prognosis of this rare and diagnostically challenging uterine tumor.

Participant or population This systematic review focuses on individuals diagnosed with Smooth Muscle Tumor of Uncertain Malignant Potential (STUMP) of the uterus. The types of participants that will be addressed in the review include the following:
1. Women Diagnosed with STUMP:
o Age Range: The primary participants will be women diagnosed with STUMP, typically in the perimenopausal and postmenopausal age range, around 40 to 60 years old. However, younger women, including those of reproductive age, will also be included if they have been diagnosed with STUMP.
o Clinical Presentation: Participants will include those presenting with various symptoms commonly associated with STUMP, such as abnormal uterine bleeding, pelvic pain, or those who had incidental findings of STUMP during evaluations for other conditions.
o Diagnosis Confirmation: Only women with a confirmed histopathological diagnosis of STUMP, based on established diagnostic criteria, will be included. This ensures that the review focuses on accurately identified cases of STUMP.
2. Subgroups Based on Clinical Characteristics:
o Symptomatic vs. Asymptomatic: The review will address participants who are symptomatic (experiencing abnormal bleeding, pain, etc.) and those who are asymptomatic but had incidental findings of STUMP during routine examinations or procedures.
o Tumor Size and Location: Participants will be categorized based on the size and location of their tumors (e.g., intramural, subserosal, or cervical STUMPs) to analyze if these factors influence clinical outcomes and treatment strategies.
3. Subgroups Based on Histological Features:
o Mitotic Index: Participants will be classified according to the mitotic index of their tumors (low vs. high mitotic activity) to evaluate its impact on prognosis and recurrence rates.
o Cytological Atypia: The degree of cytological atypia (mild, moderate, or severe) present in the tumors will be used to subgroup participants and investigate correlations with clinical outcomes.
o Necrosis: Participants with and without focal or extensive necrosis in their tumors will be separately analyzed to understand the significance of this feature in predicting malignant potential and recurrence.
4. Subgroups Based on Immunohistochemical Markers:
o p16 and p53 Expression: Participants will be categorized based on the expression levels of immunohistochemical markers such as p16 and p53. This will help determine if these markers can reliably predict the behavior and prognosis of STUMP.
o Ki-67 (MIB-1) Proliferation Index: Participants will be grouped according to their Ki-67 proliferation index to assess the correlation between cellular proliferation rates and clinical outcomes.
5. Treatment-Based Subgroups:
o Surgical Management: Participants will be grouped based on the type of surgical intervention received (e.g., hysterectomy vs. myomectomy) to

compare the effectiveness of different surgical strategies.
o Adjuvant Therapy: Those who received additional treatments, such as hormonal therapy, will be analyzed to evaluate the impact of these adjuvant therapies on long-term outcomes and recurrence rates.
6. Follow-Up and Recurrence:
o Follow-Up Duration: Participants will be categorized based on the length of their follow-up periods to examine how long-term monitoring influences the detection of recurrences and overall outcomes.
o Recurrence Status: The review will address participants who experienced recurrence of STUMP and those who remained recurrence-free, aiming to identify factors associated with recurrence.
Inclusion Criteria:
• Women of any age diagnosed with STUMP based on histopathological examination.
• Participants with detailed clinical, pathological, and treatment-related information available in the study reports.
• Studies published in English between January 2003 and December 2023.
Exclusion Criteria:
• Participants from studies that do not provide a clear histopathological confirmation of STUMP.
• Participants from studies lacking comprehensive clinical and pathological data.
• Non-human studies, reviews, editorials, and commentaries without original patient data.
By focusing on these specific participant types and subgroups, the review aims to provide a thorough and nuanced understanding of STUMP, addressing the variability in clinical presentation, histological features, treatment approaches, and outcomes. This approach will help identify patterns and inform better management strategies for this complex and rare uterine tumor.

Intervention In this systematic review, we aim to evaluate the various interventions used in the management of Smooth Muscle Tumor of Uncertain Malignant Potential (STUMP). Given the rarity and diagnostic complexity of STUMP, it is essential to assess the effectiveness and outcomes of different treatment strategies to provide evidence-based guidance for clinicians. The interventions to be evaluated include:

1. Surgical Interventions:
Hysterectomy:
Description: This procedure involves the complete removal of the uterus and is often considered the definitive treatment for STUMP, especially in postmenopausal women or those who do not wish to preserve fertility.
Evaluation Focus: We will assess the recurrence rates, overall survival, and disease-free survival associated with hysterectomy. The review will also compare outcomes based on whether the procedure included bilateral salpingo-oophorectomy (removal of ovaries and fallopian tubes) and its impact on recurrence and prognosis.
Myomectomy:
Description: Myomectomy involves the surgical removal of the tumor while preserving the uterus. This is commonly considered for younger women who wish to retain fertility.
Evaluation Focus: The review will examine the effectiveness of myomectomy in terms of recurrence rates, fertility outcomes, and complications. We will also analyze the impact of tumor size, location, and the extent of resection on these outcomes.
Extent of Surgical Resection:
Description: This involves varying degrees of surgical excision, ranging from complete removal with clear margins to more conservative approaches.
Evaluation Focus: We will compare outcomes between extensive resections with clear margins versus less radical surgeries. The impact of surgical margins on recurrence and long-term prognosis will be a key focus.
2. Adjuvant Therapies:
Hormonal Therapy:
Description: Hormonal treatments such as GnRH agonists or selective estrogen receptor modulators (SERMs) are sometimes used to manage STUMP, particularly in premenopausal women.
Evaluation Focus: The review will evaluate the effectiveness of hormonal therapy in reducing tumor size, delaying recurrence, and managing symptoms. We will also assess the side effects and long-term outcomes associated with these treatments.
Chemotherapy and Radiation Therapy:
Description: Although not routinely recommended, some cases of STUMP with high-risk features may receive adjuvant chemotherapy or radiation therapy.
Evaluation Focus: We will assess the indications, effectiveness, and outcomes of these adjuvant therapies in managing STUMP. This includes analyzing recurrence rates, overall survival, and treatment-related morbidity.
3. Surveillance Strategies:
Regular Monitoring:
Description: Post-surgical surveillance typically involves regular clinical examinations and imaging studies to monitor for recurrence.

Evaluation Focus: The review will evaluate the effectiveness of different surveillance strategies, including the frequency and types of imaging used (e.g., MRI, CT scans, ultrasound). We will assess how these strategies impact early detection of recurrence and overall patient outcomes.
Follow-Up Duration:
Description: The recommended duration for follow-up varies, with some guidelines suggesting long-term monitoring for several years.
Evaluation Focus: We will examine the optimal duration of follow-up and its correlation with recurrence rates and patient outcomes. The impact of extended follow-up on early detection and management of recurrent disease will be a key area of analysis.
4. Comparative Effectiveness of Interventions:
Comparison of Surgical Techniques:
Description: Comparing outcomes between different surgical approaches (e.g., hysterectomy vs. myomectomy).
Evaluation Focus: We will compare recurrence rates, complications, and overall survival between various surgical techniques to determine the most effective approach.
Combination of Interventions:
Description: Evaluating the combined effect of surgical and adjuvant therapies.
Evaluation Focus: The review will assess whether combining surgical interventions with adjuvant therapies (e.g., hormonal therapy) provides better outcomes compared to surgery alone.
Inclusion Criteria for Interventions:

Studies that provide detailed descriptions of the interventions used to manage STUMP.
Studies reporting outcomes related to recurrence rates, overall survival, disease-free survival, and complications.
Studies published in English between January 2003 and December 2023.
Exclusion Criteria for Interventions:

Studies lacking detailed intervention descriptions.
Studies not reporting relevant clinical outcomes.
Non-human studies, reviews, editorials, and commentaries without original data.
By evaluating these interventions, the review aims to provide comprehensive insights into the most effective management strategies for STUMP, ultimately guiding clinical practice and improving patient outcomes.f applicable, describe the intervention or group of interventions that you want to evaluate in your review.

Comparator In this systematic review, we aim to compare different interventions applied to women diagnosed with Smooth Muscle Tumor of Uncertain Malignant Potential (STUMP). The comparative analysis will focus on evaluating the effectiveness, safety, and outcomes of various treatment strategies. The primary comparative interventions include:
1. Hysterectomy vs. Myomectomy:
Hysterectomy:
• Description: Complete removal of the uterus, often considered the definitive treatment for STUMP, especially in postmenopausal women or those who do not wish to preserve fertility.
• Target Population: Women with STUMP, particularly those who are postmenopausal, do not desire future fertility, or have larger or more invasive tumors.
Myomectomy:
• Description: Surgical removal of the tumor while preserving the uterus. This option is typically considered for younger women who wish to retain fertility.
• Target Population: Premenopausal women with STUMP who desire to maintain fertility or have smaller, less invasive tumors.
Comparative Evaluation:
• Recurrence Rates: Comparing the recurrence rates between hysterectomy and myomectomy.
• Fertility Outcomes: Assessing the impact of myomectomy on fertility and pregnancy outcomes.
• Complications: Evaluating surgical complications and recovery times associated with each procedure.
• Survival Outcomes: Comparing overall survival and disease-free survival between the two surgical options.
2. Extent of Surgical Resection:
Extensive Resection (Clear Margins):
• Description: Complete surgical removal of the tumor with clear margins, potentially involving more radical procedures.
• Target Population: Women with larger or more invasive STUMP where a more extensive resection is deemed necessary to ensure complete removal.
Less Radical Surgery:
• Description: Conservative surgical approaches with less emphasis on obtaining clear margins.
• Target Population: Women with smaller, well-defined tumors where less invasive surgery is sufficient.
Comparative Evaluation:
• Recurrence Rates: Comparing the effectiveness of extensive resection versus less radical surgery in preventing recurrence.
• Morbidity: Evaluating the morbidity and recovery associated with different extents of surgical intervention.
• Long-term Outcomes: Assessing the long-term outcomes, including recurrence and survival rates, associated with the extent of surgical resection.

3. Surgical Management with and without Adjuvant Therapy:
Surgery Alone:
• Description: Management of STUMP through surgical intervention (hysterectomy or myomectomy) without additional treatments.
• Target Population: Women diagnosed with STUMP, particularly those with low-risk features where surgery alone is considered sufficient.
Surgery with Adjuvant Therapy:
• Description: Surgical management combined with additional treatments such as hormonal therapy, chemotherapy, or radiation therapy.
• Target Population: Women with high-risk STUMP features or those who have recurrent or residual disease post-surgery.
Comparative Evaluation:
• Effectiveness: Comparing the effectiveness of surgery alone versus surgery with adjuvant therapy in preventing recurrence and improving survival.
• Side Effects: Assessing the side effects and overall impact on quality of life associated with adjuvant therapies.
• Long-term Outcomes: Evaluating the long-term outcomes, including disease-free survival and overall survival, for each treatment approach.
4. Regular Monitoring vs. Intensive Surveillance:
Regular Monitoring:
• Description: Standard post-surgical follow-up with routine clinical examinations and periodic imaging.
• Target Population: Women with STUMP who have undergone surgical treatment, particularly those with low to moderate risk of recurrence.
Intensive Surveillance:
• Description: More frequent follow-up visits and imaging studies aimed at early detection of recurrence.
• Target Population: Women with high-risk STUMP features or those who have a history of recurrence.
Comparative Evaluation:
• Detection of Recurrence: Comparing the effectiveness of regular monitoring versus intensive surveillance in early detection of recurrent STUMP.
• Patient Outcomes: Assessing the impact of different surveillance strategies on patient outcomes, including recurrence rates and survival.
• Quality of Life: Evaluating the impact of follow-up intensity on patients' quality of life and psychological well-being.
Inclusion Criteria for Comparative Interventions:
• Studies comparing the specified interventions (e.g., hysterectomy vs. myomectomy, surgery with and without adjuvant therapy).
• Studies reporting relevant clinical outcomes such as recurrence rates, overall survival, disease-free survival, complications, and quality of life.
• Studies published in English between January 2003 and December 2023.
Exclusion Criteria for Comparative Interventions:
• Studies lacking a clear comparative framework.
• Studies not reporting on relevant clinical outcomes.
• Non-human studies, reviews, editorials, and commentaries without original data.
By defining and evaluating these comparative interventions, the review aims to provide comprehensive insights into the most effective management strategies for STUMP, ultimately guiding clinical practice and improving patient outcomes.

Study designs to be included The review will include the following study designs to address the objective:

- Randomized Controlled Trials (RCTs): To provide high-quality evidence on the effectiveness of various interventions.
- Cohort Studies: Both prospective and retrospective cohort studies to evaluate long-term outcomes and recurrence rates.
- Case-Control Studies: To compare characteristics and outcomes of STUMP cases versus controls.
- Case Series and Case Reports: To gather detailed clinical, pathological, and treatment-related information on STUMP.
- Systematic Reviews and Meta-Analyses: To synthesize existing evidence and provide comprehensive insights.

These study designs will ensure a thorough examination of clinical characteristics, diagnostic methods, treatment strategies, and outcomes related to STUMP.

Eligibility criteria

Inclusion Criteria:
1. Publication Type:
o Peer-reviewed articles.
o Full-text articles available.
o Studies published between January 2003 and December 2023.
2. Language:
o Articles published in English to ensure consistency in data extraction and analysis.
3. Study Population:
o Studies involving human participants only.
o Studies specifically addressing STUMP of the uterus.
4. Data Completeness:
o Studies that provide comprehensive clinical, pathological, and treatment-related data.
o Studies with clear definitions and criteria for diagnosing STUMP.
5. Outcome Reporting:

o Studies reporting relevant clinical outcomes such as recurrence rates, overall survival, disease-free survival, complications, and quality of life.
Exclusion Criteria:
1. Publication Type:
o Abstracts, conference presentations, letters, editorials, and commentaries without substantial original data.
o Non-peer-reviewed articles.
2. Language:
o Articles published in languages other than English due to potential issues with accurate translation and data extraction.
3. Study Population:
o Studies involving animal models or in vitro experiments.
o Studies not focusing specifically on STUMP or including mixed populations without separate analysis for STUMP.
4. Data Completeness:
o Studies lacking detailed clinical, pathological, or treatment-related information.
o Studies with incomplete or unclear definitions and diagnostic criteria for STUMP.
5. Outcome Reporting:
o Studies not reporting on relevant clinical outcomes related to the diagnosis, treatment, or prognosis of STUMP.
o Studies with insufficient follow-up data to assess long-term outcomes.
These additional inclusion and exclusion criteria ensure that the review focuses on high-quality, relevant studies that provide comprehensive insights into the clinical characteristics, diagnostic methods, treatment strategies, and outcomes related to STUMP.

Information sources To conduct a comprehensive systematic review on Smooth Muscle Tumor of Uncertain Malignant Potential (STUMP), a wide range of information sources will be utilized to ensure the inclusion of all relevant studies and data. The following information sources will be employed:
1. Electronic Databases:
• PubMed: PubMed provides access to a vast archive of biomedical literature, including studies from Medline. It is an essential source for peer-reviewed articles in the fields of medicine and health sciences.
• Scopus: Scopus is a large multidisciplinary database that covers peer-reviewed literature across various fields including science, technology, medicine, and social sciences. Its broad coverage and citation tracking capabilities make it a crucial tool for comprehensive reviews.
2. Trial Registers:
• ClinicalTrials.gov: A registry and results database of publicly and privately supported clinical studies conducted around the world, providing access to ongoing and completed trials relevant to STUMP.
• International Clinical Trials Registry Platform (ICTRP): Managed by the World Health Organization, ICTRP ensures that a complete view of research is accessible to all those involved in health care decision making.
3. Grey Literature:
• OpenGrey: OpenGrey provides access to grey literature produced in Europe, including technical reports, theses, dissertations, and conference papers, which may contain relevant studies not published in peer-reviewed journals.
• ProQuest Dissertations and Theses: This database includes a comprehensive collection of dissertations and theses from around the world, offering insights into original research that might not be available elsewhere.
4. Reference Lists:
• Manual Search: Reference lists of all included studies will be manually searched to identify additional relevant publications. This ensures that no significant studies are missed, and it often uncovers important research cited in other works.
5. Professional Societies and Organizations:
• Gynecological Oncology Societies: Organizations such as the International Gynecologic Cancer Society (IGCS) and the Society of Gynecologic Oncology (SGO) may provide access to conference proceedings, guidelines, and other resources relevant to STUMP.
Search Strategy: A comprehensive search strategy will be developed and applied across all selected databases. The search will include a combination of keywords and MeSH terms related to STUMP, such as "Smooth Muscle Tumor of Uncertain Malignant Potential," "STUMP," "Uterine Tumor," "Leiomyoma," "Leiomyosarcoma," "Histopathology," "Immunohistochemistry," "Treatment," "Recurrence," and "Prognosis." Boolean operators (AND, OR) and truncation symbols (*) will be used to refine the search results.
Screening and Selection: The initial search results will be screened by title and abstract to identify potentially relevant studies. Full-text screening will be conducted for all articles that meet the initial criteria. Studies will be selected based on predefined inclusion and exclusion criteria to ensure the relevance and quality of the included literature.
Conclusion: By utilizing a diverse range of information sources, including electronic databases, trial registers, grey literature, and direct contact with authors, this review aims to capture a comprehensive set of data on STUMP. This approach will enhance the robustness of the

review, ensuring that it provides a thorough and accurate synthesis of the current knowledge on this rare and diagnostically challenging condition.

Main outcome(s) The systematic review on Smooth Muscle Tumor of Uncertain Malignant Potential (STUMP) will evaluate multiple outcomes to provide a comprehensive understanding of the condition. The primary and secondary outcomes will include:
Primary Outcomes:
1. Recurrence Rates:
o Timing: The incidence of tumor recurrence at various follow-up intervals (e.g., 6 months, 1 year, 5 years post-treatment).
o Effect Measures: Proportion of patients experiencing recurrence, recurrence-free survival (RFS), and time to recurrence (TTR).
2. Overall Survival (OS):
o Timing: Survival rates at specified intervals (e.g., 1 year, 3 years, 5 years post-diagnosis).
o Effect Measures: Overall survival rate, median survival time, and hazard ratios for survival.
3. Disease-Free Survival (DFS):
o Timing: Duration of survival without evidence of disease post-treatment.
o Effect Measures: Disease-free survival rate and median DFS.
Secondary Outcomes:
1. Surgical Outcomes:
o Timing: Short-term (within 30 days post-surgery) and long-term surgical outcomes.
o Effect Measures: Complication rates, need for reoperation, and completeness of tumor resection (clear surgical margins).
2. Treatment-Related Morbidity:
o Timing: Immediate and delayed complications associated with different treatment modalities (e.g., surgery, adjuvant therapy).
o Effect Measures: Incidence of adverse events, severity of complications, and impact on quality of life.
3. Prognostic Factors:
o Timing: Evaluation at diagnosis and throughout follow-up.
o Effect Measures: Impact of histological features (e.g., mitotic index, necrosis), immunohistochemical markers (e.g., p16, p53), and clinical characteristics on prognosis.
4. Quality of Life:
o Timing: Assessment at multiple time points during and after treatment.
o Effect Measures: Patient-reported outcomes using validated quality of life questionnaires.
5. Follow-Up Strategies:
o Timing: Effectiveness of different follow-up intervals and methods.
o Effect Measures: Early detection rates of recurrence and patient adherence to follow-up protocols.
By evaluating these outcomes, the review aims to provide detailed insights into the clinical course, management, and prognosis of STUMP.

Additional outcome(s) In addition to the primary and secondary outcomes, the review will consider the following additional outcomes to provide a more holistic understanding of the management and prognosis of Smooth Muscle Tumor of Uncertain Malignant Potential (STUMP):

Histopathological Consistency:

Timing: Assessed at initial diagnosis and through subsequent pathology reviews.
Effect Measures: Consistency of initial histopathological diagnosis with follow-up biopsies or surgical specimens, inter-observer agreement rates among pathologists, and the frequency of reclassification of STUMP to either benign or malignant categories over time.
Impact of Diagnostic Techniques:

Timing: Evaluation at diagnosis and during follow-up.
Effect Measures: Diagnostic accuracy of imaging techniques (e.g., MRI, CT, ultrasound) and histopathological assessments, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of different diagnostic tools.
Molecular and Genetic Markers:

Timing: Assessed at initial diagnosis and during any subsequent tumor analysis.
Effect Measures: Prevalence and prognostic significance of genetic mutations and molecular markers (e.g., genomic alterations, expression of specific genes or proteins), correlation between these markers and clinical outcomes such as recurrence and survival.
Cost-Effectiveness of Treatment Strategies:

Timing: Evaluated over the course of treatment and follow-up.
Effect Measures: Cost-effectiveness analysis comparing different treatment approaches (e.g., hysterectomy vs. myomectomy, use of adjuvant therapies), healthcare resource utilization, overall treatment costs, and economic impact on patients and healthcare systems.

Role of Multidisciplinary Care:

Timing: Throughout the treatment and follow-up phases.
Effect Measures: Impact of multidisciplinary team involvement on treatment decisions, patient outcomes, and adherence to follow-up protocols, comparison of outcomes in centers with and without multidisciplinary teams.
These additional outcomes will enrich the review by addressing various aspects of STUMP management and patient care, providing a comprehensive evaluation that extends beyond basic clinical metrics to include diagnostic, economic, and psychosocial dimensions.

Data management The systematic review on Smooth Muscle Tumor of Uncertain Malignant Potential (STUMP) will employ a rigorous and structured approach to manage records and data, ensuring accuracy, transparency, and reproducibility. The following mechanisms will be used to manage records and data throughout the review process:
1. Database Search and Record Management:
• Search Strategy Development: A comprehensive search strategy will be developed using predefined keywords and Boolean operators across multiple electronic databases (PubMed, Scopus).
• Record Identification: All identified records from the database searches will be imported into a reference management software (e.g., EndNote, Mendeley) to organize and manage citations.
• Deduplication: The software will be used to identify and remove duplicate records, ensuring each study is uniquely represented.
2. Screening and Selection:
• Title and Abstract Screening: Two independent reviewers will screen the titles and abstracts of all identified records using predefined inclusion and exclusion criteria. A third reviewer will resolve any discrepancies.
• Full-Text Screening: Full texts of potentially eligible studies will be retrieved and assessed independently by two reviewers. Discrepancies will be resolved through discussion or consultation with a third reviewer.
• PRISMA Flow Diagram: A Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram will be used to document the selection process, including the number of records identified, screened, excluded, and included in the final review.
3. Data Extraction:
• Data Extraction Form: A standardized data extraction form will be developed to ensure consistency. The form will capture key information such as study design, population characteristics, interventions, outcomes, and findings.
• Independent Extraction: Two reviewers will independently extract data from each included study. Extracted data will be cross-checked for accuracy, and discrepancies will be resolved through discussion or consultation with a third reviewer.
4. Data Management:
• Database Creation: Extracted data will be entered into a secure electronic database (e.g., Excel, REDCap) designed for systematic reviews.
• Data Storage: All records and data will be stored in a secure, cloud-based platform with regular backups to prevent data loss. Access will be restricted to the review team members to ensure confidentiality.
• Data Cleaning: The database will be regularly reviewed and cleaned to correct any inconsistencies or errors in the data.
By implementing these mechanisms, the review will maintain a high standard of methodological rigor, ensuring the reliability and validity of the findings.

Quality assessment / Risk of bias analysis The quality assessment of primary studies included in this systematic review on Smooth Muscle Tumor of Uncertain Malignant Potential (STUMP) will be conducted using standardized tools and criteria to ensure methodological rigor and reliability. The following steps outline the process:
1. Selection of Quality Assessment Tools:
• Randomized Controlled Trials (RCTs): The Cochrane Risk of Bias (RoB) tool will be used to assess the quality of RCTs. This tool evaluates potential biases in the domains of random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other biases.
• Observational Studies (Cohort and Case-Control Studies): The Newcastle-Ottawa Scale (NOS) will be employed to assess the quality of observational studies. The NOS evaluates studies based on three broad criteria: selection of study groups, comparability of groups, and ascertainment of the outcome of interest.
• Case Series and Case Reports: The Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Case Reports and Case Series will be used.
2. Independent Assessment:
• Dual Review: Two reviewers will independently assess the quality of each included study using the appropriate assessment tool. This dual review process helps to minimize subjective bias and ensures a comprehensive evaluation.
3. Quality Criteria:
• Cochrane Risk of Bias Tool: Each domain will be rated as 'low risk,' 'high risk,' or 'unclear risk' of

bias. Studies with a majority of domains rated as 'low risk' will be considered high quality, while those with multiple 'high risk' domains will be considered low quality.
4. Data Synthesis and Reporting:
• Stratified Analysis: The results of the quality assessment will be used to perform stratified analyses, comparing outcomes between high-quality and lower-quality studies to examine the potential impact of study quality on the review's findings.
• Sensitivity Analysis: Sensitivity analyses will be conducted to determine if excluding lower-quality studies significantly alters the overall conclusions of the review.
5. Documentation and Transparency:
• Detailed Reporting: The results of the quality assessments will be documented in detail, including individual study ratings and justifications for each rating.
• PRISMA Compliance: The review will adhere to PRISMA guidelines, ensuring that the quality assessment process is thoroughly documented and reported.
By employing these standardized and rigorous quality assessment methods, the review aims to ensure the validity and reliability of its findings, ultimately providing high-quality evidence on the management and outcomes of STUMP.

Strategy of data synthesis The analysis of data in this systematic review on Smooth Muscle Tumor of Uncertain Malignant Potential (STUMP) will involve a structured approach to synthesize qualitative and quantitative findings from the included studies. The following steps outline the data analysis plan:
1. Data Extraction:
• Standardized Forms: Data will be extracted using standardized forms that capture study characteristics, participant demographics, intervention details, and outcomes. This ensures consistency and comprehensiveness in data collection.
• Double Extraction: Two reviewers will independently extract data to minimize errors and discrepancies. Disagreements will be resolved through discussion or consultation with a third reviewer.
2. Data Synthesis:
• Qualitative Synthesis: For studies that do not provide quantitative data suitable for meta-analysis, a qualitative synthesis will be conducted. This involves summarizing findings narratively, identifying common themes, patterns, and discrepancies across studies.
• Quantitative Synthesis (Meta-Analysis): Where appropriate, data from comparable studies will be pooled using meta-analytic techniques. The meta-analysis will be conducted using statistical software such as Review Manager (RevMan) or Stata.
3. Statistical Analysis:
• Effect Measures: For dichotomous outcomes (e.g., recurrence rates, survival rates), effect measures such as risk ratios (RRs) or odds ratios (ORs) with 95% confidence intervals (CIs) will be calculated. For continuous outcomes (e.g., time to recurrence, quality of life scores), mean differences (MDs) or standardized mean differences (SMDs) with 95% CIs will be computed.
• Heterogeneity Assessment: Heterogeneity among studies will be assessed using the I^2 statistic and Chi-squared test. An I^2 value greater than 50% indicates substantial heterogeneity. The sources of heterogeneity will be explored through subgroup analyses and sensitivity analyses.
4. Publication Bias Assessment:
• Funnel Plots: Publication bias will be assessed using funnel plots if a sufficient number of studies (usually more than 10) are included in the meta-analysis. Asymmetry in the funnel plot may indicate potential publication bias.
• Egger's Test: Additionally, Egger's test for small-study effects will be used to statistically assess the presence of publication bias.
5. Data Presentation:
• Tables and Figures: Detailed tables and figures will be used to present the characteristics of included studies, quality assessment results, and findings from the qualitative and quantitative syntheses.
6. Interpretation and Contextualization:
• Contextual Interpretation: The findings will be interpreted in the context of existing literature, considering the clinical significance and applicability of the results. Potential implications for clinical practice and future research will be discussed.
• Limitations: The limitations of the included studies and the review process will be acknowledged to provide a balanced interpretation of the findings.
7 Compliance with Reporting Standards:
• PRISMA Guidelines: The review will adhere to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure comprehensive and transparent reporting of the methodology and findings.
By following this structured data analysis plan, the review aims to provide robust, reliable, and comprehensive insights into the management and outcomes of STUMP, ultimately contributing to improved patient care and guiding future research.

Subgroup analysis Subgroup analyses will be conducted to explore potential sources of

heterogeneity and to provide more detailed insights into the management and outcomes of Smooth Muscle Tumor of Uncertain Malignant Potential (STUMP). These analyses will help identify specific factors that may influence the effectiveness of interventions and the prognosis of patients with STUMP. The following subgroups will be analyzed:

1. Age:
• Premenopausal vs. Postmenopausal Women:
o Rationale: Hormonal status can influence tumor behavior and treatment outcomes. Premenopausal women may have different responses to hormonal therapies and fertility preservation strategies compared to postmenopausal women.
o Outcomes Analyzed: Recurrence rates, overall survival, disease-free survival, and treatment-related complications.
2. Tumor Characteristics:
• Tumor Size (Small vs. Large Tumors):
o Rationale: Larger tumors may have different biological behaviors and surgical challenges compared to smaller tumors.
o Outcomes Analyzed: Surgical outcomes, recurrence rates, and need for adjuvant therapies.
• Mitotic Index (Low vs. High Mitotic Activity):
o Rationale: The mitotic index is a key histological feature that may correlate with tumor aggressiveness and recurrence risk.
o Outcomes Analyzed: Recurrence rates, overall survival, and impact of surgical margins.
• Presence of Necrosis (With vs. Without Necrosis):
o Rationale: Necrosis within the tumor can indicate a higher risk of malignancy and recurrence.
o Outcomes Analyzed: Recurrence rates, disease-free survival, and overall survival.
3. Surgical Approach:
• Hysterectomy vs. Myomectomy:
o Rationale: The extent of surgical intervention can influence recurrence rates and long-term outcomes. Hysterectomy is often considered more definitive, while myomectomy is preferred for fertility preservation.
o Outcomes Analyzed: Recurrence rates, fertility outcomes, and overall survival.
• Extent of Surgical Resection (Clear Margins vs. Conservative Surgery):
o Rationale: Achieving clear surgical margins may reduce recurrence risk but can involve more extensive surgery.
o Outcomes Analyzed: Recurrence rates, surgical complications, and long-term prognosis.
4. Adjuvant Therapies:
• With vs. Without Hormonal Therapy:
o Rationale: Hormonal therapy may be used in conjunction with surgery to manage STUMP, particularly in premenopausal women.
o Outcomes Analyzed: Recurrence rates, overall survival, and hormonal side effects.
5. Follow-Up Duration:
• Short-term vs. Long-term Follow-Up:
o Rationale: The length of follow-up can impact the detection of late recurrences and overall survival analysis.
o Outcomes Analyzed: Recurrence rates, overall survival, and disease-free survival.

By conducting these subgroup analyses, the review aims to identify factors that significantly influence the management and prognosis of STUMP, thereby providing more tailored and effective clinical recommendations.

Sensitivity analysis Sensitivity analysis is a critical component of the systematic review on Smooth Muscle Tumor of Uncertain Malignant Potential (STUMP) to assess the robustness and reliability of the findings. This process involves systematically varying the inclusion criteria, methodological approaches, and analytical techniques to determine the impact on the overall results. The following outlines the sensitivity analysis plan:

1. Inclusion Criteria Variability:
• Study Quality:
o Approach: Sensitivity analyses will exclude studies identified as having a high risk of bias based on quality assessment tools (e.g., Cochrane Risk of Bias tool for RCTs, Newcastle-Ottawa Scale for observational studies). This will help determine if lower-quality studies disproportionately influence the overall findings.
o Outcomes: Effect estimates and conclusions drawn from high-quality studies will be compared to those including all studies.
• Publication Date:
o Approach: The analysis will be repeated by including only studies published in the last 10 years to assess the impact of recent advancements and changes in clinical practice.
o Outcomes: Changes in effect sizes and overall conclusions will be evaluated to understand the temporal influence on the findings.
2. Methodological Approaches:
• Statistical Models:
o Fixed-Effects vs. Random-Effects Models:
? Approach: Sensitivity analysis will compare results obtained using fixed-effects models with those from random-effects models to account for heterogeneity among studies.
? Outcomes: Differences in pooled effect estimates and confidence intervals will be assessed to understand the impact of between-study variability.
• Handling of Missing Data:
o Approach: Different methods for handling missing data (e.g., complete case analysis,

imputation methods) will be applied to evaluate their effect on the results.
o Outcomes: The consistency of effect estimates and robustness of conclusions across different handling methods will be examined.
3. Analytical Techniques:
• Subgroup and Stratified Analyses:
o Approach: Sensitivity analyses will be conducted within key subgroups (e.g., by age, tumor size, surgical approach) to assess the consistency of findings across different patient populations and treatment modalities.
o Outcomes: The robustness of subgroup-specific findings will be examined to ensure reliability.
4. Outcome Definitions and Measures:
• Consistency in Outcome Measures:
o Approach: Sensitivity analyses will be performed using different definitions and measures of key outcomes (e.g., recurrence rates, overall survival) to assess their impact on the results.
o Outcomes: The influence of varying outcome definitions on effect estimates and conclusions will be evaluated.
By conducting these sensitivity analyses, the review aims to ensure that the findings are robust, reliable, and not unduly influenced by specific studies, methodological choices, or assumptions. This comprehensive approach enhances the credibility and applicability of the review's conclusions.

Language restriction Only studies published in English will be included in the review. This restriction is implemented to ensure that all included articles are accessible and can be accurately interpreted.

Country(ies) involved Romania.

Keywords Uterine Smooth Muscle Tumor, Recurrence, Tumor Markers, Mitotic Index.

Dissemination plans The findings of this systematic review on Smooth Muscle Tumor of Uncertain Malignant Potential (STUMP) will be disseminated through multiple channels to ensure broad reach and impact:
1. Peer-Reviewed Publication:
o The results will be submitted to a high-impact peer-reviewed journal, such as Biomedicines, to ensure the research reaches a wide audience of clinicians, researchers, and healthcare professionals.
2. Conference Presentations:
o The findings will be presented at relevant national and international conferences, such as the International Gynecologic Cancer Society (IGCS) and the Society of Gynecologic Oncology (SGO) annual meetings. These presentations will facilitate the sharing of results with experts in the field and promote discussion on best practices and future research directions.
3. Academic and Clinical Networks:
o Results will be shared through academic and clinical networks, including university departments, hospital oncology units, and professional societies. This will include email newsletters and internal seminars to disseminate findings to practicing clinicians and researchers.
4. Online Platforms:
o The research will be promoted on social media platforms (e.g., Twitter, LinkedIn) and academic research sharing sites (e.g., ResearchGate) to reach a broader audience and encourage engagement with the study's findings.
5. Open Access Repository:
o The full-text article will be deposited in an open access repository to ensure free and easy access to the research findings.
By utilizing these dissemination strategies, we aim to maximize the visibility and impact of the research, promoting better understanding and management of STUMP.

Contributions of each author
Author 1 - bucuri carmen elena - The main author developed the research concept and design, conducted literature searches, supervised data collection and screening, performed data extraction and quality assessment, analyzed and interpreted results, and drafted and revised the manuscript, ensuring accuracy and coherence throughout the study.
Email: cbucurie@yahoo.com
Author 2 - ciortea razvan - The correspondent author coordinated communication among co-authors. He also facilitated data collection, contributed to data analysis, and provided critical revisions to the manuscript, ensuring clarity and coherence in the final document.
Email: r_ciortea@yahoo.com
Author 3 - malutan andrei mihai - Contributed to the development of the search strategy, conducted literature searches, and participated in data extraction. They also assisted in the screening process and provided critical feedback on the manuscript draft.
Email: andreimalutan1@gmail.com
Author 4 - oprea valentin - Performed data extraction and quality assessment of included studies. Contributed to the statistical analysis and interpretation of results. Reviewed and edited the manuscript for technical accuracy and clarity.
Email: valioprea@yahoo.com
Author 5 - toma mihai - Engaged in the literature screening and selection process. Assisted with

data extraction and quality appraisal. Contributed to the writing of the results section and provided significant revisions to the manuscript.
Email: mihaitoma1@yahoo.com
Author 6 - roman maria patricia - Supported the conceptualization of the study and helped develop the data extraction forms. Conducted quality assessments and provided insights into clinical implications of findings. Contributed to manuscript editing and review.
Email: mpr138@gmail.com
Author 7 - ormindean cristina mihaela - Led the statistical analysis, including meta-analysis where applicable. Interpreted data and results, and helped draft the discussion section. Provided expert advice on methodological approaches and manuscript revisions.
Email: cristinaormindean@yahoo.com
Author 8 - nati ionel - Participated in data collection and analysis, focusing on subgroup and sensitivity analyses. Contributed to the interpretation of results and helped draft relevant sections of the manuscript. Reviewed the final draft for coherence.
Email: ionelnati1@yahoo.com
Author 9 - suciu viorela - Assisted in the initial literature search and data extraction. Contributed to the quality assessment of studies and helped in synthesizing findings. Provided substantial input into the writing and revision of the manuscript.
Email: viosuciu1@yahoo.com
Author 10 - mihu dan - Involved in the development and refinement of the research methodology. Participated in data analysis and interpretation. Provided critical revisions and final approval of the manuscript, ensuring it met publication standards.
Email: danmihu1@yahoo.com