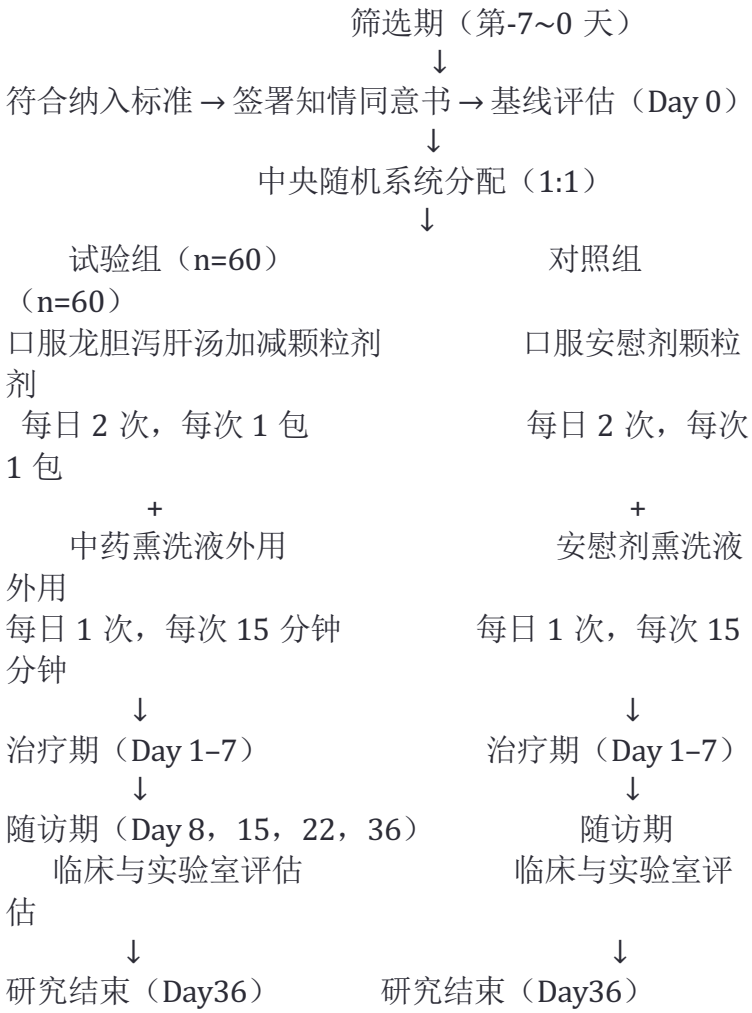
Appendix 1


筛选期（第-7~0 天）
符合纳入标准 → 签署知情同意书 → 基线评估（Day 0）
中央随机系统分配（1:1）
试验组（n=60）
口服龙胆泻肝汤加减颗粒剂
每日 2 次，每次 1 包
+
中药熏洗液外用
每日 1 次，每次 15 分钟
治疗期（Day 1–7）
随访期（Day 8，15，22，36）
临床与实验室评估
研究结束（Day36）
对照组
（n=60）
口服安慰剂颗粒剂
每日 2 次，每次 1 包
+
安慰剂熏洗液外用
每日 1 次，每次 15 分钟
治疗期（Day 1–7）
随访期
临床与实验室评估
研究结束（Day36）

Appendix 2. SPIRIT-TCM Extension 2018 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1a	Specify the patient population in terms of 1) a WM-defined disease, 2) a WM-defined disease with a specific TCM Pattern, or 3) a TCM Pattern.	P1
	1b	Specify the intervention, in terms of 1) CHM formula, 2) acupuncture, 3) moxibustion, or 4) other TCM therapy(ies).	P1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	P2
	2b	All items from the World Health Organization Trial Registration Data Set	Appendix 2
Protocol version	3	Date and version identifier	Version 3; 9 Dec 2021.
Funding	4	Sources and types of financial, material, and other support	P16
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	P1, P16
	5b	Name and contact information for the trial sponsor	NA

	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	P16
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	P14

Introduction

Background and rationale	6a. 1	Provide the background and rationale of the research question with TCM theory.	P3-4
	6a. 2	Describe the rationale of the utilized TCM interventions with references.	P3-4
	6a. 3	Provide the rationale of adding experimental TCM interventions if WM intervention is used as basic or combined remedy. If possible, the potential interaction between WM intervention and TCM intervention (especially for CHM) should also be explained with related reference(s).	P3-4
	6b	Describe the rationale and principle(s) for selecting comparators corresponding to certain interventions (i.e. CHM formula, acupuncture, moxibustion or other TCM interventions), considering 1) comparable with tested intervention; 2) success of blinding.	P4
Objectives	7	State the objectives or hypotheses regarding the specific TCM intervention for 1) a WM-defined disease, 2) a WM-defined disease with a specific TCM Pattern or 3) a TCM Pattern.	P4
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	P4-5

Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	P5
Eligibility criteria	10a	State whether participants with a specific TCM Pattern will be recruited, in terms of 1) diagnostic criteria, and 2) inclusion and exclusion criteria. All criteria utilized should be universally recognized, or reference(s) where detailed explanation can be found should be given.	P5-6

	10b	Descriptions of the roles, qualifications and other relevant experience of the researchers (e.g. participant screeners, care providers, outcome assessors, data analysts) in TCM research are recommended.	P6

Methods: Participants, interventions, and outcomes

	10c	Descriptions of the qualification and relevant experience of study center(s) involved in a TCM trial are recommended.	P5
Interventions	11a. 1	Interventions for the experimental group(s) with sufficient detail to allow replication.	P7-8
	11a.1A	CHM formulae	P7-8; Appendix 5

For fixed CHM formulae

1. Name, source and dosage form (e.g. decoction, granules, powder, pills).
2. Name, source, processing method and dosage of each medical substance. Name of all substances should be presented in at least two types of languages: Chinese (Pinyin), Latin or English. Names of the parts of the substances used should be specified.
3. Authentication method of each ingredient, and how, when, where, by whom it will be conducted.
4. Production method of the formula.
5. Quality control of each ingredient and the whole formula.
6. Safety assessment of the formula, containing heavy metals and toxic elements test, pesticide residue test, microbial limit test, acute/chronic toxicity test.
7. Dosage of the formula, and how the dosage was determined.
8. Administration route (e.g. oral, external).

	11a.2	Interventions for the control group(s) with sufficient detail to allow replication.	P8

	11a.2A	CHM formulae Placebo control 1. Name and dosage of each ingredient. 2. Description of the similarity of placebo with intervention (e.g. color, smell, taste, appearance, packing). 3. Quality control and safety surveillance, if any. 4. Administration route, dosage and regimen. 5. Production information: when, where, how and by whom the placebo was produced.	P8
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	P8; P15
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	P11-12; P15
	11d	Descriptions of other interventions that will be administrated to experimental and/or control groups are recommended (e.g. rescue interventions), with enough details to allow replication.	P8
Outcomes	12a	Provide the rationale of TCM-related indexes as outcomes (e.g. the change of degree and scope of symptoms and signs related to Pattern differentiation).	P9-11
	12b	Provide the details of the TCM-related outcomes assessment, including i) the measuring methods and standard (e.g. frequency, severity rating scale of symptoms and signs, verified Pattern questionnaire, time points for assessment and corresponding rationale), ii) assessor qualification (e.g. relevant assessment experience, years in clinical practice), iii) methods used to enhance the quality of assessment (e.g.multiple repeated observation, training of assessors), and iv) related reference(s).	P9-11
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	P6-7, Table 1

Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	P13
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	P6

Methods: Assignment of interventions (for controlled trials)

Allocation:

Sequence numbers), generation sequence, details of any unavailable to those who	16a	Method of generating the allocation sequence (eg, computer-generated random and list of any factors for stratification. To reduce predictability of a random planned restriction (eg, blocking) should be provided in a separate document that is enrol participants or assign interventions	P8-9
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	P8-9
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	P8-9
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	P9
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	P9

Methods: Data collection, management, and analysis

Data collection methods	18a	When trial targeting on TCM Pattern, or a WM-defined disease with a specific TCM Pattern, baseline data about TCM Pattern should be provided.	P12-13
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	P12
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	P12
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	P13-14 Appendix 7
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	P14 Appendix 7
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	Appendix 7

Methods: Monitoring

Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed.	P15
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	P14-15

Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	P14
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	P11
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	P4
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	P15
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	P5 Appendix 4
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	P13 Appendix 4
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	P12; P15
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	P17
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	P12; P15

Ancillary and posttrial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	P16	*It is
Dissemination policy	31a	Plan for raw data sharing, if any. The contents should contain: i) when the data will become available; ii) how the data will be shared iii) what data in particular will be shared; iv) who could acquire the data; v) through what access data will be shared.	P17	
	31b	Authorship eligibility guidelines and any intended use of professional writers	P17	
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	P17	
Appendices				
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Appendix 4	
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	P13	

strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

Appendix 3. WHO TRDS- TCM extension 2020 checklist

Number	Original Item	Extension for TCM Item	Information
1	Primary Registry and Trial Identifying Number		Chinese Clinical Trial Registry, ChiCTR2100043200
2	Date of Registration in Primary Registry		Registered on 8 February 2021.
3	Secondary Identifying Numbers		NA
4	Source(s) of Monetary or Material Support	*Statement of whether any conflicts of interest exist.*	Health@InnoHK Initiative Fund of the Hong Kong Special Administrative Region Government (ITC RC/IHK/4/7). The funder had no role in the design of the study, in the collection, analysis, and interpretation of data, nor in the writing of the manuscript.
5	Primary Sponsor		Centre for Chinese Herbal Medicine Drug Development Limited, Hong Kong Baptist University, HKSAR, China.
6	Secondary Sponsor(s)		NA
7	Contact for Public Queries		ZXB, MD, PHD [bzxiang@hkbu.edu.hk]
8	Contact for Scientific Queries		ZXB, MD, PHD [bzxiang@hkbu.edu.hk]
9	Public Title		Efficacy and Safety of Chinese Herbal Formula CDD-2103 for Remission Maintenance of Ulcerative Colitis: Study Protocol for a Randomized, Double-blinded, Placebo-controlled Trial

10	Scientific Title	*10a. Statement of whether the trial targets a TCM Pattern, or a Western medicine–defined disease, or a Western medicine–defined disease with a specific TCM Pattern.* *10b. Illustration of the name of the TCM intervention, in terms of 1) Chinese herbal medicine (CHM) or CHM formula, 2) acupuncture, 3) moxibustion, or 4) other TCM therapies (i.e. cupping, Taichi, etc.).*	Efficacy and Safety of Chinese Herbal Formula CDD-2103 for Remission Maintenance of Ulcerative Colitis: Study Protocol for a Randomized, Double-blinded, Placebo-controlled Trial
11	Countries of Recruitment	*The research setting(s) or centre(s) from which participants will be, are being, or have been recruited at the time of registration.*	Hong Kong SAR, China
12	Health Condition(s) or Problem(s) Studied	*If the study is conducted on participants with a TCM Pattern, or a Western medicine–defined disease with a specific TCM Pattern, enter the specific name(s) of TCM Pattern(s) studied (e.g., qi deficiency pattern, deficiency of stomach yin pattern, qi stagnation pattern).*	Remission stage of Ulcerative colitis (UC) with traditional Chinese medicine (TCM) pattern of Spleen Deficiency with Dampness Obstruction (SDDO).

13	Intervention(s)	*13a. Descriptions of TCM interventions.* *Details for the three most common interventions (Chinese herbal medicine formulas, acupuncture and moxibustion) are given below:* ● *Chinese herbal medicine formulas* *1) For fixed CHM formulas: name (e.g., Chinese Pinyin, Latin, or English), source (if any), dosage form, dosage and administration route of the CHM formula; name and dosage of each medical substance.* *13b. Descriptions of control group(s).* *For interventions with the control group(s), descriptions of the control groups should include the following:* ● *For CHM formulas*	Experimental group: CDD-2103 soft extract (*Gao Fang*). Control group: Placebo soft extract (*Gao Fang*). Patients will take one sachet orally, twice daily half an hour after a meal for 24 weeks. Details are provided in Page 7-8; Appendix 5.

	1) Placebo control: name and amount of each ingredient (if applicable); description whether the placebo is the physical identical to the tested drug and pharmacological inert (if any); quality control and safety assessment (if any); administration route, regimen, and dosage; production information (e.g., planned manufacturer).	
	13c. Statement of the qualifications or experiences criteria of possible treatment providers, if applicable.	Hong Kong Registered Chinese medicine practitioners (CMPs)

14	Key Inclusion and Exclusion Criteria	*Statement of whether participants with a specific TCM Pattern will be recruited, in terms of 1) diagnostic criteria and 2) inclusion and exclusion criteria, if applicable. All criteria used should be universally recognized, or reference given to where detailed explanation can be found.*	The participants eligible for this study must comply with all of the following at randomization: (1) Aged 18-65 years; (2) UC in remission for less than 18 months, of which the corticosteroid -induced remission should be maintained for more than 3 months prior to study entry; (3) The diagnostic criteria for spleen deficiency with dampness obstruction, which can be diagnosed on the basis of any two main symptoms and at least one or two secondary symptoms, with reference to the tongue and pulse, as follows: main symptoms include diarrhea or loose stools (with mucus or not); abdominal dull pain; and poor appetite or anorexia. Secondary symptoms include abdominal bloating with borborygmus; bodily indolence and weakness of limbs; lassitude and disinclination to talk; and shallowness of complexion. pale, puffy and tooth-printed tongue with white and greasy fur; as well as thready and weak pulse or soggy and moderate pulse; (4) Normal liver and renal function in blood test prior to study entry; and (5) Individuals should fully understand what is involved in this study and give documented consent (Appendix

4) to participate in the study.

Patients will be excluded if they have one or more of the following: (1) presence of active UC within 3 months prior to study entry; (2) abnormal colonoscopy and histopathology report (e.g., crypt epithelial dysplasia or cancerous), or the number of polyps is more than 3 with the individual size larger than 0.5cm; (3) intestinal stenosis; (4) infectious enteritis or any suspicion of the presence of infectious enteritis; (5) have used biological drugs or antibiotics within the last three months before eligibility determination, or patients with biological drugs-induced UC remission; (6) laparotomy or laparoscopic surgery, surgery for hemorrhoids or perianal abscess, endoscopic mucosal resection or endoscopic intestinal dilation or endoscopic intestinal dilatation of the colon within 60 days before eligibility determination; (7) history of resection of the small intestine, cecum, colon or rectum; (8) moderate or severe hepatic or renal disease abnormalities; (9) serious comorbid disease, such as hematological, respiratory, cardiovascular, or neuropsychiatric disease, or metabolic/electrolyte abnormality; (10) undergoing treatment or follow-up under 5 years for a malignant tumor; (11) history of allergy to Chinese herbal medicine (e.g., G6PD deficiency); (12) alcohol or drug abuse; (13) pregnant and nursing women and women suspected of being pregnant; (14) individuals who are participating in any other clinical researches at study entry; and (15) others whom the investigator or co-investigator considered to be inappropriate for enrollment.

15	Study Type		Interventional allocation: randomized Intervention model: parallel assignment Masking: double blind Primary purpose: Treatment
			Pilot study
16	Date of First Enrollment		6 Jan 2022
17	Sample Size		82
18	Recruitment Status		Started
19	Primary Outcome(s)	*If TCM-related outcome (e.g., Pattern outcome) involved, illustration of method of measurement in detail, if applicable.*[†]	nonrecurrence rate at weeks 24. It is calculated as “nonrecurrence rate = (nonrecurrence cases/total case) ×100%”. Nonrecurrence is based on the modified Mayo score of less than or equal to 2 with no individual subscore greater than 1. According to the Ulcerative Colitis: Clinical Trial Endpoints Guidance for Industry, issued by US FDA in 2016 [38], a modified Mayo score omitting the physician’s global assessment is recommended as a primary endpoint of clinical remission. Compared with full Mayo score, the modified Mayo score = sum of the scores of three parameters: Stool frequency, Rectal bleeding, and Endoscopic evaluation. Each parameter of the score ranges from zero (normal or inactive disease) to 3 (severe activity), and total score ranges from zero to 9.
20	Key Secondary Outcomes		Partial Mayo Score, Inflammatory bowel disease questionnaire (IBDQ), Simple clinical colitis activity index (SCAAI), TCM syndrome scale and safety assessment. Details are provided in Page 9-11.

21	Ethics Review	The study had been approved by the Research Ethics Committees of Hong Kong Baptist University (HKBU) [REC/21-22/0011] on 27 Oct 2021. Twice updated approval letter for amendment is issued on 22 Dec 2021 and 11 March 2022, respectively.
22	Completion date	The recruitment period will be scheduled for approximately 20 months. As each participant will be taken 52 weeks to complete the study (including 4 weeks for screening, 24 weeks for treatment, and 24 weeks for follow-up).
23	Summary Results	This trial was registered on ChiCTR website and relevant results will be uploaded to the Registry after the study completed. The results of this study may be published in a peer-reviewed journal according to the CONSORT Statement for Chinese Herbal Medicine Formulas 2017, and/or presented at conferences, both nationally and internationally. All of the individual participant data collected during the trial, after deidentification, will be shared accordingly. The results will be reported to the Research Ethics Committee and DSMB, respectively. All participants will be also informed of the results by phone or email.
24	IPD sharing statement	Yes
A1	URL	NA

B1	Lay Summary	*Provide a brief statement regarding the specific TCM intervention for a TCM Pattern, a Western medicine–defined disease, or a Western medicine–defined disease with a specific TCM Pattern, as well as a short description of relevant rationale and selection principle of the utilized TCM intervention(s) with references.*	Ulcerative colitis (UC) is a chronic inflammatory bowel disease at the colonic mucosa and submucosa. Chinese herbal medicines (CHM) have been reported to be beneficial for UC patients. CDD-2103 is a new formulation for the treatment of UC remission, with clinical and preclinical data support. However, its effects and safety remain uncertain. This protocol is described for a randomized, double-blinded, placebo-controlled trial to investigate whether CDD-2103 can effectively and safely induce remission maintenance in UC patients with the TCM pattern of Spleen Deficiency with Dampness Obstruction.
B2	Approvals		As attached in the Appendices

Appendix 4

Study No.: 龙胆泻肝汤加减联合中药熏洗

Enrolment No.: _____

香港浸會大學同意聲明書

龙胆泻肝汤加减联合中药熏洗治疗外阴阴道念珠菌病有效性与安全性的随机、双盲、安慰剂对照、单中心临床研究

閣下被邀請參與這項研究，旨在評估龙胆泻肝汤加减联合中药熏洗对外阴阴道念珠菌病湿热下注证患者中的有效性和安全性。該研究由浸会大学支持开展。研究人員將逐頁為您閱讀並詳細說明本知情同意書的所有內容。

背景

外阴阴道念珠菌病(Vulvovaginal Candidiasis, VVC) VVC 是全球引起外阴阴道瘙痒和分泌物最常见的病因之一，其特征是酵母菌（最常见的是白色念珠菌）定植。在美国，VVC 是第二大常见的阴道感染病因，影响 70%至 75%的女性，每年估计导致 140 万人次门诊就诊。VVC 的年度治疗费用至少为 3.68 亿美元，仅复发性 VVC 就造成超过 48 亿美元的生产力损失。70%-75%的女性至少得过一次 VVC，40%-45%会复发（每年四次或更多），5%-8%发展为复发性 VVC(RVVC)。根据中国流行病学调查，已婚育龄妇女中 VVC 患病率可达 20%-30%。VVC 反复发作，加重医疗负担、严重影响患者生活质量（QOL）。现有 VVC 的治疗主要是局部使用唑类抗真菌药(如克霉唑、咪康唑)或口服氟康唑[6]。尽管短期疗效良好，但停药后复发率极高，患者还很容易出现耐药情况，而且长期使用抗真菌药会破坏阴道微生态平衡。因此，越来越多的患者寻求补充和替代疗法，尤其是中医药治疗。

研究目的

我们希望可以通过与安慰剂作比较，证明龙胆泻肝汤加减+中药熏洗对于外阴阴道念珠菌“湿热下注证”患者的疗效。本研究将为龙胆泻肝汤加减+中药熏洗治疗降低 VVC 患者临床复发风险的有效性和安全性提供证据，并为中医药在 VVC 中的应用提供启示。

計劃名稱

龙胆泻肝汤加减+中药熏洗治療外阴阴道念珠菌的隨機、雙盲、安慰劑對照臨床研究

參與者簡簽:

研究計劃

本研究為期 6 個星期，當中包括 1 周的篩選期、1 周的治療期及 4 周的隨訪期。本研究为单中心、随机、双盲、安慰剂对照试验，历时 6 周：筛选 1 周、治疗 1 周，随访 4 周。符合条件的受试者按 1:1 分配至药物治疗组或安慰剂组。在第 0、1、2、3、4 周于指定门诊面对面随访（附录 A）。整個研究將招募 120 位參加者。為確定閣下適合參與研究，您需要完成一套問卷調查，並前往指定的病理檢驗中心提交尿液、糞便和血液樣本用於診斷是否納入研究。血常規、尿常規、大便常規、肝腎功能檢驗將由指定的病理檢驗中心檢測。若受試者需要西醫診斷或阴道鏡（活檢）檢查以評估納入/排除標準，將會由研究者醫生負責協助。 所有樣本將交由香港浸會大學中藥創新研發中心。

這是一份需要收集的生物樣本清單：

- 血液 （每次採血量約為 10-15 毫升）
- 尿液
- 糞便
- 阴道組織活檢樣本

合理可預見風險或不適

- 抽血的針刺部位可能會出現局部疼痛、瘀青及出血，但感染的機會很低。
- 在阴道镜（活檢）檢查後的首次排便時可能會出現少量出血等不良反應，進行檢查時使用的鎮靜劑或會導致不適。然而，出現上述情況的機會很低。

參與者簡簽:

- 部分參與者可能會在研究過程中出現潰瘍性結腸炎的臨床復發，必要時，患者可根據自身具體情況服用藥物或直接求診。
- 在家中收集尿液及糞便樣本時可能會對你及你的家人帶來不便。

Appendix 4

緊急醫療

如閣下因參與本研究而造成人身傷害時，緊急醫療治療將會被提供，您無需承擔任何成本。如在研究過程中受傷，請緊記立即通知研究人員。如果你需要額外的醫療處理，所需成本將自行負責。如果你在這項研究中受傷，將不會有任何其他補償。

緊急聯絡人資料：李熙 地址：九龍塘浸會大學道 7 號賽馬會中醫藥學院大樓 電話：84960543

益處

科學研究有助於探索外阴阴道念珠菌的新療法，參與是次研究除了可能幫助閣下改善外阴阴道念珠菌的相關症狀，避免復發，同時會給您提供免費的健康檢查和阴道鏡檢查（如適用）。不過由於這是一項試驗性研究，我們亦無法保證或承諾您會從參與此研究而直接得益。但本研究的結果必將對研發中藥新藥治療外阴阴道念珠菌有貢獻性作用。

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每位參與者將擁有一個獨特的編號，研究所收集的所有數據會根據編號記錄。參與者的編號文件為唯一能夠識別參與者身份的文件，將被嚴格保存。僅有主要研究者及安排及進行訪視的研究人員能夠獲取此檔資訊。載有參與者資料的實體文件會被存放於有鎖的檔櫃中，並由負責安全的機構保管。電子資料將受密碼保護並儲存於大學的安全伺服器。參與者編碼檔以及研究數據檔將存放於不同的地點。你的個人資料及所有實體檔將於項目完成後 7 年內銷毀。只有與編號相連而不載有任何可以識別參與者的電腦資料會繼續由研究團隊保存。所有資料只作研究用途，任何個人資訊均不會被揭露。倫理委員會或有關的監督管理部門在工作需要時，可按規定查閱參加試驗的受試者資料。

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聯絡資料

閣下對是次的研究有任何查詢，請隨時向研究人員提出，我們非常樂意為你作進一步解釋。

在參與研究的過程中,您可以在任何時間及階段就研究的流程及個人權益等問題向研究人員提問，如您遇到不良反應，請立即聯絡研究人員。

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參與條款

閣下是自願參與是次臨床研究，有責任瞭解相關檔資料及依從臨床研究的流程，並擁有隨時退出本研究的權利。閣下拒絕或提前退出參與本研究，是不會對你的醫療護理構成任何損失或懲罰的。如閣下在完成收集所需資料前決定退出本研究，我們會保留已收集的數據及樣本，您亦有權撤回其使用權，但需以書面形式通知研究總負責人：卞教授（地址：九龍塘浸會大學道 7 號賽馬會中醫藥學院大樓）。在研究過程中若有顯著新發現，而新發現可能影響受試者考慮是否繼續參與，研究人員會及時通知閣下，並由您自行選擇是否願意繼續參

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在移除所有可能識別到參與者的個人資料後，數據及生物樣本（血液、尿液、糞便及黏膜）或會被用於其他試驗但只限於研究用途，我們將不會再次獲取您的知情同意。

病人同意書

本人已瞭解以上所有內容，並持有同意聲明書副本。

☐ 我同意參加這項研究並同意為這項研究提供本人的生物學樣本。

☐ 我不同意參加這項研究。

參加者簽名：_____ 日期 _____ 研究者簽名：_____日期 _____

Appendix 5. 不良事件报告表

患者姓名：	性别：男□女□	出生日期： 年 月 日 或年龄：	民族：	体重（kg）：	联系方式：			
原患疾病：	医院名称：	既往药品不良反应/事件：有□_无□ 不详□						
	病历号/门诊号：	家族药品不良反应/事件：有□_无□ 不详□						
相关重要信息： 吸烟史□ 饮酒史□ 妊娠期□ 肝病史□ 肾病史□ 过敏史□_其他□								
药品	批准文号	商品名称	通用名称（含剂型）	生产厂家	生产批号	用法用量（次剂量、途径、日次数）	用药起止时间	用药原因
怀疑药品								
并用药品								
不良反应/事件名称：	不良反应/事件发生时间：年 月 日							
不良反应/事件过程描述（包括症状、体征、临床检验等）及处理情况（可附页）：								
不良反应/事件的结果：痊愈□ 好转□ 未好转□ 不详□ 有后遗症□ 表现： 死亡□ 直接死因：_死亡时间： 年 月 日								
停药或减量后，反应/事件是否消失或减轻？ 是□ 否□ 不明□ 未停药或未减量□ 再次使用可疑药品后是否再次出现同样反应/事件？ 是□ 否□ 不明□ 未再使用□								
对原患疾病的影响： 不明显□ 病程延长□ 病情加重□ 导致后遗症□ 导致死亡□								
关联性评价	报告人评价：肯定□ 很可能□ 可能□ 可能无关□ 待评价□ 无法评价□ 签名： 报告单位评价： 肯定□ 很可能□ 可能□ 可能无关□ 待评价□ 无法评价□ 签名：							
报告人信息	联系电话：	职业：医生□ 药师□ 护士□ 其他□						
	电子邮箱：	签名：						
报告单位信息	单位名称：	联系人：	电话：	报告日期： 年月日				
生产企业请填写信息来源	医疗机构□ 经营企业□ 个人□ 文献报道□ 上市后研究□ 其他□							
备 注								

Appendix 6. 统计分析计划（Statistical Analysis Plan, SAP）

1. 研究概述

本统计分析计划适用于"一项龙胆泻肝汤加减联合中药熏洗治疗外阴阴道念珠菌病有效性与安全性的随机、双盲、安慰剂对照、单中心临床试验方案"。本计划详细描述了用于分析该临床试验数据的统计方法，包括主要和次要结局指标的分析策略。

2. 统计原则

2.1 分析人群

- 意向性治疗分析集（Intent-to-Treat, ITT）：包含所有随机化并接受至少一次治疗的受试者。ITT 分析将作为主要分析，遵循"随随机化分析"（as randomized）原则，即使受试者未能完成治疗或有重大方案违背。
- 符合方案集（Per-Protocol, PP）：包含所有完成治疗且无重大方案违背的受试者。PP 分析将作为敏感性分析，用于评估结果的稳健性。
- 安全性分析集（Safety Set, SS）：包含所有接受至少一次治疗并完成至少一次安全性评估的受试者。

2.2 缺失数据处理

- 主要结局（临床总有效率）：缺失数据视为"无效"，进行保守性分析；同时采用多重插补法进行敏感性分析。
- 次要结局：
  - 连续变量（如 pH 值、症状评分、生活质量评分）：采用末次观测值结转法（LOCF）处理缺失值。
  - 二分类变量（如镜检转阴率）：缺失数据视为"未转阴"。
  - 若缺失率>15%，将进行多重插补敏感性分析。

2.3 显著性水平

- 主要分析采用双侧检验，显著性水平 $\alpha=0.05$。
- 亚组分析不进行多重比较校正，结果仅作探索性解释。
- 计量资料以均数±标准差（$\bar{x} \pm s$）表示，偏态分布资料以中位数（四分位距）[M (P25, P75)]表示。
- 计数资料以例数（百分比）表示。

3. 基线分析

3.1 人口学和基线特征

- 比较两组受试者在人口学特征（年龄、BMI、生育史等）和基线临床特征（病程、症状评分、pH 值等）的均衡性。
- 计量资料采用独立样本 t 检验或 Mann-Whitney U 检验；计数资料采用卡方检验或 Fisher 确切概率法。
- 基线不均衡变量将作为协变量纳入后续分析模型。

4. 主要结局分析

4.1 临床总有效率（第 8 天）

- 分析方法：
  - 两组间临床总有效率比较采用卡方检验（Chi-square test）。
  - 若任一单元格期望频数<5，则使用 Fisher 确切概率法。
  - 计算相对风险（RR）及其 95%置信区间（CI）。
- 统计模型：
  - 主要分析采用未调整的卡方检验。
  - 敏感性分析将采用 Logistic 回归模型，调整潜在混杂因素（如基线症状

严重程度、年龄、病程等）。

- 亚组分析：按年龄（≤35 岁 vs >35 岁）、病程（≤6 个月 vs >6 个月）、基线症状严重程度（轻度 vs 中重度）进行亚组分析，并通过添加组别×亚组交互项检验异质性（P<0.10 视为存在异质性）。

5. 次要结局分析

5.1 阴道 pH 值

- 分析方法：
  - 两组间 pH 值比较（第 8、16、24 天）采用协方差分析（ANCOVA），基线 pH 值作为协变量。
  - 重复测量数据采用线性混合效应模型（Linear Mixed-effects Model），固定效应包括组别、时间点、组别×时间点交互作用，随机效应为受试者个体差异。
- 效应量：计算组间差异的均值（95% CI）。

5.2 阴道分泌物镜检转阴率

- 分析方法：
  - 两组间转阴率比较（第 8、16、24 天）采用卡方检验或 Fisher 确切概率法。
  - 计算相对风险（RR）及其 95%置信区间（CI）。
- 时间-事件分析：对达到转阴的时间进行 Kaplan-Meier 生存分析，组间比较采用 log-rank 检验。

5.3 症状评分（VAS 视觉模拟量表）

- 分析方法：
  - 总分及各单项（瘙痒、灼痛、白带量、白带气味）分析方法同 pH 值。
  - 临床有意义的改善定义为总分降低≥50%或单项评分降低≥3 分。
- 最小临床重要差异（MCID）：瘙痒和灼痛评分降低≥2 分视为有临床意义的改善。

5.4 生活质量评分（VVS-QoL）

- 分析方法：
  - 与症状评分分析方法相同。
  - 此外，计算达到最小临床重要差异（MCID）的比例。VVS-QoL 量表的 MCID 定义为总分降低≥10 分。
- 维度分析：对生理症状、心理影响、社会功能、治疗满意度四个维度分别进行分析。

6. 安全性分析

6.1 不良事件

- 描述：按治疗组汇总所有不良事件（AE）和严重不良事件（SAE），包括类型、发生率、严重程度（CTCAE v5.0 标准）、与研究药物相关性。
- 比较：两组间 AE/SAE 发生率比较采用卡方检验或 Fisher 确切概率法。
- 时间模式：分析 AE 发生时间与治疗的关系。

6.2 实验室安全性指标

- 异常值分析：定义临床显著异常（较基线恶化≥2 级或超出正常范围 3 倍以上）。
- 重复测量：采用线性混合效应模型分析组间差异及随时间变化趋势。

7. 探索性分析

7.1 中医证候积分分析

- 构建中医证候评分标准（参照《中医妇科学》），分析两组中医证候积分变化。
- 证候积分与西医症状评分、生活质量评分的相关性分析（Pearson 或 Spearman 相关）。

7.2 依从性分析

- 依从性定义为实际用药次数/计划用药次数×100%。
- 按依从性高低（>80% vs ≤80%）进行亚组分析，评估依从性对疗效的影响。

8. 敏感性分析

1. 不同缺失数据处理方法：比较 LOCF 与多重插补法结果的一致性。
2. 不同人群分析：比较 ITT、PP、SS 分析结果的一致性。
3. 调整基线协变量：在主要分析中加入潜在混杂因素作为协变量。
4. 符合治疗分析：仅纳入实际接受分配治疗的受试者进行分析。

9. 临时分析与数据监查

- 本研究不计划进行正式的中期分析，但数据与安全监查委员会（DSMB）将定期审查安全性数据。
- 如发生严重安全性问题，DSMB 有权建议调整样本量或提前终止研究。

10. 统计软件与质控

10.1 统计软件

- 主要分析采用 SPSS 28.0 与 R 4.3.1 软件。
- 多重插补采用 R 的 mice 包。
- 混合效应模型采用 SPSS 的 MIXED 过程。

10.2 质量控制

- 统计分析程序将由两名独立统计师验证。
- 所有分析代码将存档并可在审计时提供。
- 任何与本计划的偏离将在最终报告中详细说明。