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Oral Candidiasis in the Precision-Diagnostics Era: A Critical Review of Conventional and Molecular Diagnosis, Antifungal Susceptibility, and Therapeutic Decision-Making

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داء المبيضات الفموي في عصر التشخيص الدقيق: مراجعة نقدية للتشخيص التقليدي والجزيئي، وحساسية مضادات الفطريات، واتخاذ القرار العلاجي

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Abstract

Background: Oral candidiasis is usually diagnosed clinically, yet the same Candida species can be recovered from healthy mouths. Precision diagnosis must therefore distinguish carriage from active mucosal disease, select the correct anatomical sample, identify species only when clinically consequential, and interpret antifungal susceptibility in the context of exposure, biofilm, and host factors.

Methods: A structured critical review was conducted through 22 July 2026. PubMed-indexed primary studies, oral diagnostic-accuracy studies, randomized therapeutic trials, and authoritative WHO, NIH, IDSA, CLSI, and EUCAST documents were prioritized. Searches combined oral or oropharyngeal candidiasis with microscopy, culture, fungal burden, MALDI-TOF MS, PCR, sequencing, metabolomics, biosensor, susceptibility, MIC, resistance, recurrence, and therapy. Seminal studies before 2000 were retained when they defined treatment efficacy. Because case definitions, specimens, reference standards, and endpoints were heterogeneous, numerical results are presented as study-specific anchors rather than pooled estimates.

Results: Lesion phenotype and risk context remain the diagnostic gate. Direct microscopy adds evidence of fungal activity; culture enables recovery, mixed-species recognition, identification, and susceptibility testing but is not proof of infection. In 124 suspected cases, fluorescent

staining outperformed 10% KOH for sensitivity (85.48% vs 64.52%), specificity (91.94% vs 72.58%), and AUC (0.887 vs 0.685). Concentrated oral rinse increased Candida recovery relative to swabbing, but high burdens can still occur in asymptomatic carriers. MALDI-TOF accurately identifies cultured isolates when databases and extraction are adequate; qPCR increases analytical sensitivity but may detect non-viable DNA and clinically silent carriage. Oral microbiome, metabolome, microfluidic, and paper-based biosensor studies are promising but remain discovery or prototype evidence. Standardized CLSI or EUCAST broth microdilution is appropriate for selected refractory, recurrent, high-risk, or non-albicans infections. Current EUCAST breakpoints are method- and species-specific; caspofungin lacks direct EUCAST breakpoints, and neither CLSI nor EUCAST provides validated nystatin clinical breakpoints. Oral biofilm tolerance and mucosal drug exposure are not captured by planktonic MIC alone. Randomized trials support fluconazole for moderate-to-severe disease and convenient topical regimens for selected localized disease, but recurrence depends strongly on immune state and unresolved reservoirs.

Conclusions: Precision oral mycology should be organized as a layered decision system: phenotype, lesion-linked fungal evidence, species identification, selective susceptibility testing, and therapy matched to severity, host state, prior exposure, and local reservoirs. The next generation of diagnostics must measure pathogenic activity—not simply fungal presence—and demonstrate incremental clinical utility beyond optimized examination, microscopy, and culture.

Keywords: oral candidiasis; precision diagnostics; Candida albicans; microscopy; MALDI-TOF MS; qPCR; antifungal susceptibility; MIC; resistance; diagnostic stewardship.

الملخص

يُشخَّص داء المبيضات الفموي عادةً بالاعتماد على الفحص السريري، إلا أن النوع نفسه من فطر Candidaيمكن عزله أيضًا من الأفواه السليمة. لذلك، يجب أن يتمكن التشخيص الدقيق من التمييز بين حمل الفطر والاستعمار الفموي وبين المرض المخاطي النشط، واختيار العينة التشريحية المناسبة، وتحديد النوع الفطري فقط عندما يكون لذلك أثر سريري مهم، وتفسير حساسية مضادات الفطريات في سياق التعرض السابق للعلاج، والأغشية الحيوية، وعوامل المضيف.

المنهجية :أُجريت مراجعة نقدية منظمة حتى 22يوليو 2026 .وأُعطيت الأولوية للدراسات الأصلية المفهرسة في PubMed، ودراسات الدقة التشخيصية المتعلقة بالعدوى الفموية، والتجارب العلاجية العشوائية، والوثائق والإرشادات الصادرة عن الجهات المرجعية مثل منظمة الصحة العالمية(WHO) ، والمعاهد الوطنية للصحة(NIH) ، وجمعية الأمراض المعدية الأمريكية(IDSA) ، ومعهد المعايير السريرية والمخبرية(CLSI) ، واللجنة الأوروبية لاختبار الحساسية لمضادات الميكروبات (EUCAST).وجمعت عمليات البحث بين داء المبيضات الفموي أو الفموي البلعومي وبين موضوعات الفحص المجهري، والحمل الفطري، والزراعة، وتقنية MALDI-TOF MS، وتفاعل البوليميراز المتسلسل PCR، وتسلسل الحمض النووي، والأيضيات، وأجهزة الاستشعار الحيوية، واختبارات الحساسية، والتركيز المثبط الأدنى MIC، والمقاومة، والنكس، والعلاج. كما أُبقي على الدراسات الأساسية المنشورة قبل عام 2000 عندما كانت قد أسهمت في تحديد فعالية العلاج. ونظرًا لعدم التجانس في تعريفات الحالات، والعينات المستخدمة، والمعايير المرجعية، ونقاط النهاية، فقد عُرضت النتائج الرقمية باعتبارها مؤشرات خاصة بكل دراسة وليست تقديرات مجمعة.

النتائج :يظل نمط الآفة والسياق السريري وعوامل الخطورة البوابة الأساسية للتشخيص. ويضيف الفحص المجهري المباشر دليلًا على النشاط الفطري، في حين تتيح الزراعة استعادة الفطر، والتعرف على الأنواع المختلطة، وتحديد النوع، وإجراء اختبار الحساسية، لكنها لا تُعد بمفردها دليلًا قاطعًا على وجود العدوى. وفي دراسة شملت 124حالة مشتبهًا بها، تفوق التلوين الفلوري على هيدروكسيد البوتاسيوم KOHبتركيز 10 %من حيث الحساسية (85.48% مقابل 64.52 (%والنوعية (91.94% مقابل 72.58 (%والمساحة تحت المنحنى (0.887 AUCمقابل 0.685).
وأدى غسل الفم المركز إلى زيادة معدل استرداد فطر Candida مقارنةً بأخذ العينات بواسطة المسحة، إلا أن الأحمال الفطرية المرتفعة يمكن أن توجد أيضًا لدى حاملي الفطر الذين لا تظهر عليهم أعراض. وتستطيع تقنية MALDI-TOF MSتحديد العزلات المزروعة بدقة عندما تكون قواعد البيانات وعمليات استخلاص العينات مناسبة. كما يزيد qPCRمن الحساسية التحليلية، إلا أنه قد يكشف عن DNA لفطريات غير حية أو عن استعمار فطري غير مصحوب بأعراض سريرية.
وتُعد دراسات الميكروبيوم الفموي، والأيضيات، والأنظمة الميكروفلويدية، وأجهزة الاستشعار الحيوية القائمة على الورق واعدة، إلا أن الأدلة المتاحة بشأنها لا تزال في مرحلة الاكتشاف أو النماذج الأولية. ويُعد اختبار التخفيف الدقيق في المرق (Broth Microdilution) وفق المعايير الموحدة لـ CLSIأو EUCASTمناسبًا في حالات مختارة، ولا سيما حالات العدوى المقاومة للعلاج، أو المتكررة، أو عالية الخطورة، أو الناجمة عن أنواع غير Candida albicans.
وتُعد نقاط القطع الحالية التي تعتمدها EUCASTخاصة بطريقة الاختبار وبالنوع الفطري؛ كما أن الكاسبوفنجين (Caspofungin) لا يمتلك نقاط قطع مباشرة معتمدة منEUCAST ، ولا يوفر كل من CLSIو EUCASTنقاط قطع سريرية موثقة للـ نيستاتين (Nystatin). كما أن تحمل الأغشية الحيوية الفموية لمضادات الفطريات والتعرض الدوائي داخل الأغشية المخاطية لا يمكن تقييمهما بصورة كافية اعتمادًا على MICللفطريات في الحالة الحرة (planktonic) وحده.
وتدعم التجارب العشوائية استخدام الفلوكونازول (Fluconazole) في الحالات المتوسطة إلى الشديدة، كما تدعم استخدام أنظمة العلاج الموضعية المريحة في بعض الحالات الموضعية المحدودة. إلا أن النكس يعتمد بدرجة كبيرة على الحالة المناعية للمريض واستمرار وجود خزانات فطرية غير معالجة.
الاستنتاجات :ينبغي تنظيم علم الفطريات الفموي الدقيق باعتباره نظامًا لاتخاذ القرار متعدد الطبقات يبدأ بـ النمط السريري، ثم الدليل الفطري المرتبط بالآفة، ثم تحديد النوع الفطري، ثم إجراء اختبار الحساسية بصورة انتقائية، وأخيرًا اختيار العلاج بما يتناسب مع شدة المرض، وحالة المضيف، والتعرض السابق لمضادات الفطريات، والخزانات الفطرية الموضعية.
وينبغي أن تركز الجيل القادم من الاختبارات التشخيصية على قياس النشاط الإمراضي للفطر، وليس مجرد إثبات وجوده، وأن تُثبت قدرتها على تحقيق فائدة سريرية إضافية تتجاوز ما يمكن تحقيقه من خلال الفحص السريري المحسن، والفحص المجهري، والزراعة التقليدية.

الكلمات المفتاحية: داء المبيضات الفموي؛ التشخيص الدقيق؛ Candida albicans؛ الفحص المجهري؛ MALDI-TOF MS؛ qPCR؛ الحساسية لمضادات الفطريات؛ MIC؛ المقاومة؛ ترشيد التشخيص.

Highlights

- A positive culture or qPCR result is evidence of presence, not proof of mucosal infection.
- Sampling must represent the lesion: whole-mouth rinse, saliva, denture biofilm, and biopsy answer different questions.
- Species identification becomes decision-relevant in refractory, recurrent, high-risk, mixed-species, and epidemiologically unusual disease.

MIC interpretation is species-, method-, and drug-specific; no validated oral nystatin breakpoint exists.

Clinical response, recurrence, adherence, exposure, and reservoir control must be reconciled with laboratory results.

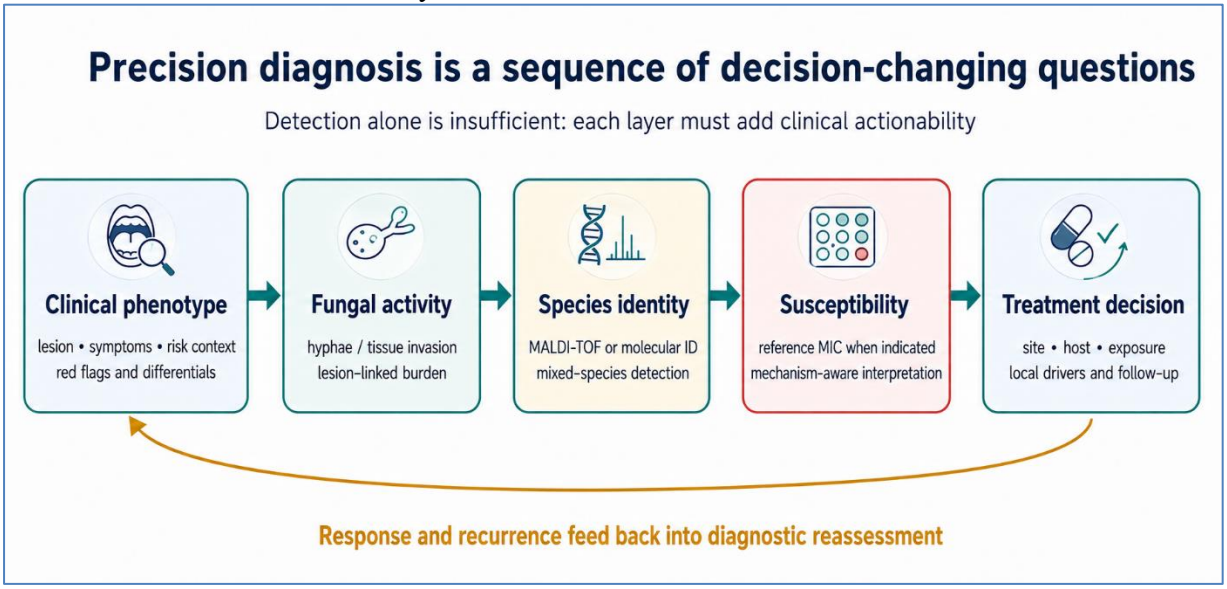

Figure 1. *Precision-diagnostic architecture for oral candidiasis. The sequence moves from phenotype to activity, identity, susceptibility, and a patient-level treatment decision. The loop emphasizes reassessment after non-response or recurrence. This is a conceptual synthesis, not a validated prediction model.*

1. Introduction

Oral candidiasis sits at an unusual diagnostic boundary. Candida albicans is a frequent oral commensal, yet it can produce painful pseudomembranous, erythematous, hyperplastic, angular, prosthesis-associated, and oropharyngeal disease when mucosal ecology or host containment is disrupted. WHO classifies C. albicans as a critical-priority fungal pathogen in the broader global context, while its 2025 candidiasis update highlights infants, immunocompromised people, denture wearers, inhaled-steroid users, and people with uncontrolled diabetes as important oral-risk groups [1–3]. The diagnostic problem is not merely whether Candida is present. It is whether fungal activity explains the lesion, whether the process is confined to the mouth, and whether additional laboratory resolution will change treatment.

Traditional workflows—smear, culture, germ-tube testing, chromogenic agar, assimilation—remain relevant because they are inexpensive, interpretable, and often sufficient. Precision technologies add different forms of resolution: MALDI-TOF MS improves isolate identification, targeted PCR detects low-abundance DNA, sequencing characterizes community structure, metabolomics measures a composite host–microbe state, and biosensors promise chairside speed. Yet analytical sensitivity can worsen clinical specificity when the organism is a commensal. A test that detects one genome equivalent in saliva may be technologically impressive but diagnostically harmful if it converts asymptomatic carriage into antifungal exposure.

This review evaluates the entire decision chain rather than ranking platforms by novelty. Four questions structure the analysis: Which specimen represents the clinical lesion? What does the signal prove—presence, viability, invasion, species, or resistance? Does the result have a

validated interpretive threshold? Will it change therapy or follow-up? These questions place antifungal susceptibility and therapeutic decision-making inside the diagnostic pathway rather than treating them as separate laboratory and prescribing exercises.

2. Review methodology

2.1 Design and search strategy

The article is a structured critical review with targeted evidence updating, not a registered systematic review or meta-analysis. Searches were completed through 22 July 2026 using PubMed-indexed records, primary-journal platforms, and official WHO, NIH, IDSA, CLSI, and EUCAST resources. Core search strings combined (oral candidiasis OR oropharyngeal candidiasis OR oral Candida) with (diagnosis OR microscopy OR KOH OR fluorescent stain OR culture OR oral rinse OR CHROMagar OR MALDI-TOF OR PCR OR qPCR OR sequencing OR metagenomics OR metabolomics OR biosensor OR susceptibility OR MIC OR breakpoint OR resistance OR randomized trial). Citation chaining was used for foundational diagnostic and treatment studies.

2.2 Eligibility and synthesis

Human oral or oropharyngeal studies were prioritized. Diagnostic-accuracy studies required a stated reference standard or comparator. Oral-isolate susceptibility studies were retained when the species, method, and interpretive rule were reported. Foundational platform studies using saliva matrices were included as translational evidence but were not treated as clinical validation. Invasive-candidiasis tests were excluded from clinical recommendations for localized oral disease unless they informed general method principles or official susceptibility standards. Vulvovaginal studies were not used to infer oral diagnostic accuracy.

Heterogeneity precluded quantitative pooling. Clinical case definitions ranged from signs alone to combined clinical and culture criteria; specimens included swabs, scrapes, rinses, saliva, prosthetic surfaces, and biopsy; and reference standards ranged from culture to composite clinical–microbiological adjudication. Accordingly, sensitivity, specificity, AUC, MIC, and cure values are reported with their original population and limitations. The review distinguishes five evidence states: established clinical practice, validated laboratory support, context-dependent specialist use, translational prototype, and discovery-only signal.

Table 1. Review questions, evidence priorities, and interpretive safeguards

Domain	Primary question	Preferred evidence	Critical safeguard
Pre-analytics	Does the specimen represent the lesion?	Comparative sampling studies; anatomical logic	Do not equate saliva or whole-mouth burden with lesion invasion
Detection	Is there viable or morphologically active fungus?	Direct microscopy; culture linked to phenotype	Hyphae support activity but are not universally present
Identification	Which species or mixture is present?	MALDI-TOF or validated molecular identification	Database and target coverage determine accuracy
Susceptibility	Is reduced susceptibility plausible and actionable?	CLSI/EUCAST reference testing with valid interpretive criteria	Do not invent breakpoints or transfer them across methods

Therapy	Will the result change drug, route, duration, or reservoir control?	Guidelines plus randomized trials	Clinical and mycological endpoints are not interchangeable
Innovation	Does a new platform improve outcomes beyond standard care?	Prospective oral-specific impact studies	Analytical performance alone is insufficient

The framework was used to prevent analytical sensitivity from being mistaken for clinical utility.

3. Defining the diagnostic target

3.1 Colonization, infection, and pathogenic activity

Colonization is recovery or detection of Candida without sufficient evidence that it causes symptoms or tissue change. Infection requires a compatible clinical phenotype plus evidence that fungal activity is anatomically linked to the lesion. This distinction is especially important in denture wearers, older adults, children, diabetes, HIV, cancer therapy, and xerostomia, where carriage may be common. A positive result has higher post-test value when the pre-test probability is increased by a wipeable plaque, erythematous painful mucosa under a prosthesis, angular fissuring, or odynophagia, and lower value in an asymptomatic mouth [11,12,47].

Pathogenic activity can be approached through several imperfect proxies. Hyphae or pseudohyphae on a lesion smear suggest active morphogenesis; tissue-associated fungi on PAS or GMS staining demonstrate anatomical invasion; increasing lesion-linked burden may support the diagnosis; candidalysin or host-response signatures are biologically attractive but not validated clinical assays. The candidalysin literature illustrates why activity markers matter: Ece1-derived peptide toxin links hyphal growth to epithelial damage, but measuring its pathway in routine oral samples remains experimental [43,44].

3.2 Phenotype first and red flags

Pseudomembranous candidiasis classically produces removable white plaques with an erythematous or bleeding base. Erythematous candidiasis may appear as burning red mucosa and is less specific. Denture stomatitis is anatomically related to the prosthetic-bearing mucosa and should trigger evaluation of the appliance as a reservoir. Chronic hyperplastic or non-wipeable plaques require biopsy because epithelial dysplasia, leukoplakia, lichen planus, frictional keratosis, and carcinoma may coexist or mimic Candida-associated change. Dysphagia or odynophagia raises concern for oesophageal involvement, for which systemic therapy and a different diagnostic pathway may be required [4,5,11].

Table 2. Clinical phenotype, priority specimen, and decision-changing differential diagnosis

Presentation	Priority specimen/test	What supports candidiasis	Must not miss
Wipeable white plaque	Lesion scrape for microscopy ± culture	Yeast with hyphae/pseudohyphae linked to lesion	Chemical burn; debris; leukoplakia if non-wipeable
Erythematous/burning mucosa	Targeted swab or scrape; assess saliva and exposures	Compatible risk context plus fungal elements or treatment response	Erythroplakia; nutritional deficiency; contact reaction
Denture stomatitis	Palatal lesion plus fitting surface of denture	Anatomical concordance and biofilm reservoir	Trauma; allergy; poor fit; bacterial inflammation

Angular cheilitis	Fissure swab; assess S. aureus and denture support	Candida recovery with compatible fissuring	Bacterial co-infection; iron/B-vitamin deficiency
Non-wipeable plaque / induration	Biopsy with PAS/GMS and histopathology	Tissue-associated fungi with clinicopathological concordance	Epithelial dysplasia or squamous carcinoma
Dysphagia / odynophagia	Oesophageal assessment according to host risk	Compatible syndrome and response; endoscopy when needed	Viral, pill, reflux, malignant, or immune-mediated oesophagitis

Clinical appearance narrows the question; laboratory evidence should be lesion-linked whenever possible [4,5,11,12].

4. Pre-analytical precision: the specimen is part of the test

Pre-analytical variation may exceed the difference between two analytical platforms. Sampling before antifungal exposure, selecting an active lesion edge, standardizing oral-rinse volume and duration, recording denture wear and cleaning, and minimizing transport delay all affect yield. A dry swab from keratinized mucosa is not equivalent to a scrape from a plaque, and a pooled saliva sample is not equivalent to tissue histology. Reports should therefore state specimen type, anatomical site, collection timing, transport medium, culture volume, and whether a quantitative or semiquantitative result is intended.

In 200 consecutive outpatients, concentrated oral rinse detected Candida in 52.0% compared with 33.5% by swab; in the pilot comparison, median recovery was 23 CFU/swab, 56 CFU/100 µL for rinse, and 485 CFU/100 µL for concentrated rinse [14]. The increased yield supports surveillance and burden estimation, but it also broadens detection of commensal carriage. White et al. detected Candida loads up to 9×10^3 CFU/mL in healthy controls and noted that some patients with clinical disease had lower surface burdens [13]. No universal CFU threshold can therefore diagnose all phenotypes.

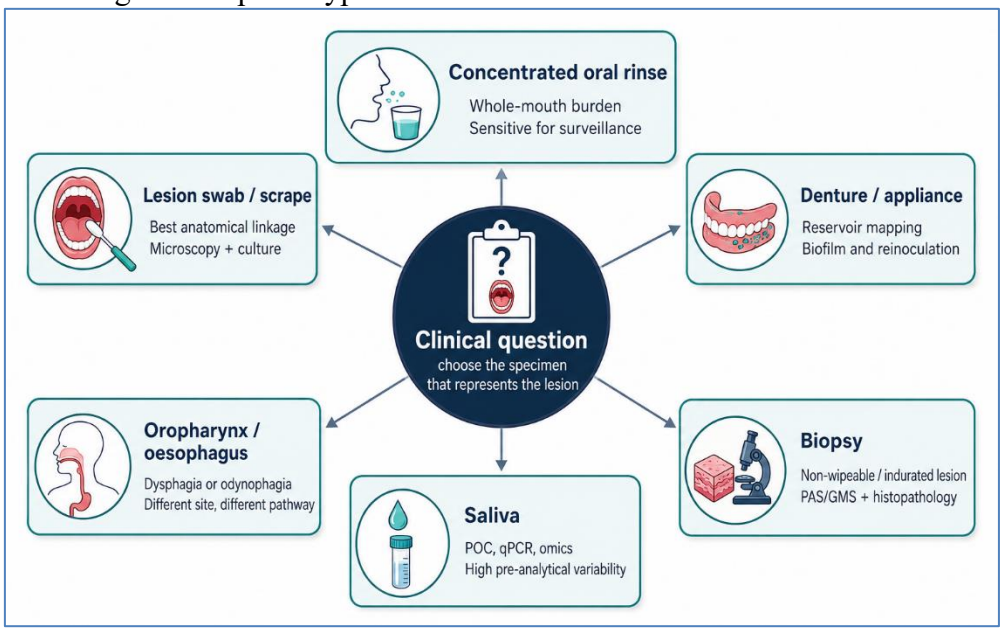

Figure 2. *Specimen topology for oral candidiasis. Each sample represents a different anatomical and clinical question; more sensitive whole-mouth sampling does not automatically improve lesion-specific diagnosis.*

Table 3. Oral specimen options and pre-analytical controls

Specimen	Best use	Strength	Primary limitation
Lesion scrape	Direct microscopy; plaque-associated disease	High anatomical specificity; visualizes morphology	Operator dependent; small sampled area
Lesion swab	Culture and isolate recovery	Simple; compatible with chromogenic media	Variable biomass and pressure; poor quantitation
Concentrated oral rinse	Whole-mouth carriage and quantitative surveillance	High recovery; samples multiple sites	Dilutes anatomical linkage; may detect carriage
Unstimulated saliva	qPCR, POC prototypes, multi-omics	Non-invasive and repeatable	Flow, time, food, drugs, and storage strongly affect signal
Denture/appliance swab	Reservoir and recurrence investigation	Directly addresses reinoculation source	Surface result does not prove mucosal invasion
Biopsy	Non-wipeable or indurated lesion	Shows tissue relationship and alternative pathology	Invasive; focal sampling; histology expertise needed

Sample choice should be documented before the platform is selected.

5. Conventional detection: still the diagnostic backbone

5.1 Direct microscopy

KOH wet mount clears host material and can rapidly reveal budding yeast, pseudohyphae, and hyphae. Gram stain adds cellular context, while fluorescent chitin- or cellulose-binding stains increase contrast. Direct microscopy is inexpensive and strongly linked to active lesion morphology, but performance depends on sampling, fungal density, reader training, and the reference standard. A negative smear does not exclude erythematous or previously treated disease.

In 124 patients with suspected oral candidiasis, fluorescein-labelled chitinase staining achieved 85.48% sensitivity, 91.94% specificity, and AUC 0.887, compared with 64.52%, 72.58%, and 0.685 for 10% KOH; the difference in AUC was significant (p=0.0005) [16]. In a separate study of 106 swabs and 122 biopsy specimens, fluorescent staining yielded sensitivity/specificity of 82.7%/93.5% for swabs and 90.0%/92.9% for biopsy tissue [15]. These studies support rapid fluorescence as a useful enhancement, not as an autonomous definition of infection.

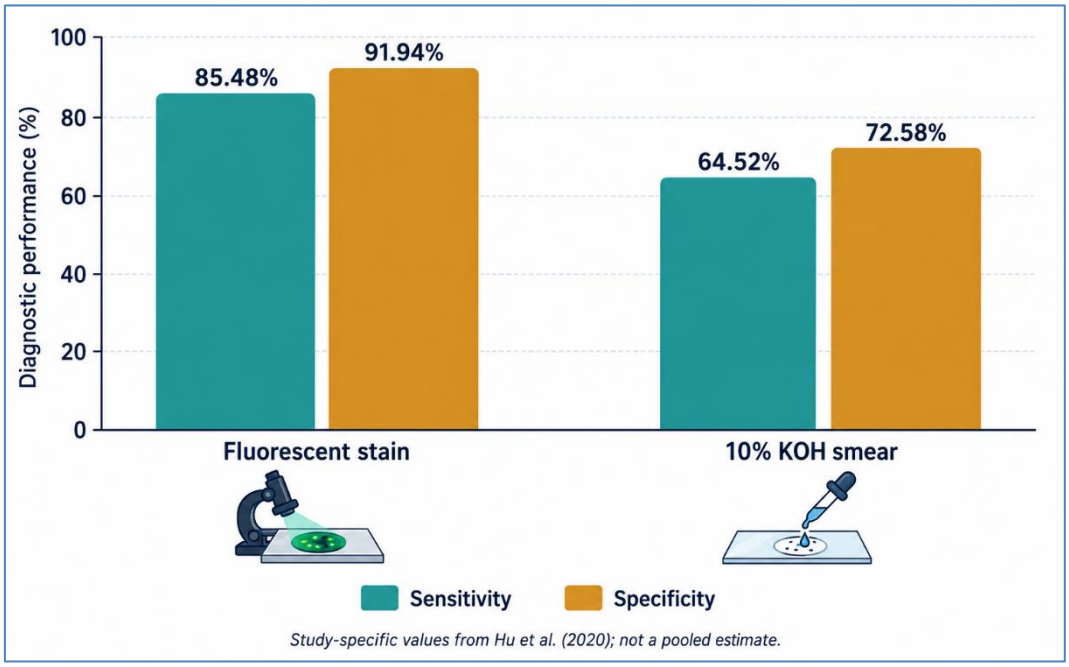

Figure 3. *Study-specific comparison of fluorescent staining and 10% KOH in 124 suspected oral-candidiasis cases [16]. Values are not pooled and depend on the original composite reference process.*

5.2 Culture and chromogenic media

Culture establishes viability, recovers an isolate for identification and AFST, and can reveal mixed populations. Sabouraud dextrose agar remains a robust recovery medium; chromogenic media add presumptive differentiation through colony colour and morphology. In a large multi-specimen evaluation, CHROMagar showed high sensitivity and specificity for C. albicans but lower sensitivity for C. tropicalis, illustrating that colour is species- and condition-dependent [18]. CHROM-Pal improved differentiation of C. dubliniensis from C. albicans in oral cultures [19]. Presumptive colour identification should be confirmed when species changes therapy or epidemiological interpretation.

Culture has two opposing biases. It may be falsely negative after antifungal exposure, with sparse focal disease, or when viable cells are below the inoculated volume. Conversely, it may be clinically false positive because Candida carriage is common. Quantitative culture can support longitudinal monitoring if the sampling method is standardized, but a burden threshold should never override phenotype or histology.

Table 4. Conventional methods: analytical output and clinical role

Method	Typical output	Decision value	Failure mode
KOH wet mount	Yeast and filamentous forms within minutes	Rapid support for active lesion	Lower contrast; reader and burden dependent
Gram stain	Morphology plus bacteria and inflammatory cells	Useful mixed-microbial context	No definitive species identification

Fluorescent fungal stain	High-contrast fungal elements	Improved rapid detection in primary studies	Requires fluorescence optics and validated reagent
PAS/GMS histology	Tissue-associated fungal elements	Essential in non-wipeable or suspicious lesions	Invasive; focal; does not provide isolate
Sabouraud culture	Viable colony recovery	Isolation, quantitation, downstream ID/AFST	Slower; colonization remains possible
Chromogenic agar	Presumptive species and mixed-colony recognition	Low-cost triage of common species	Colour overlap, database limits, incubation effects
Germ-tube test	Rapid presumptive C. albicans complex result	Useful low-resource screen	C. dubliniensis can also be positive

No conventional method should be interpreted without the anatomical sample and clinical phenotype [12–19].

6. Species identification in the precision era

6.1 MALDI-TOF mass spectrometry

MALDI-TOF MS identifies a cultured isolate from its protein-spectrum fingerprint. Once a pure colony is available, preparation and acquisition are rapid, and per-isolate cost can be low in a high-throughput laboratory. Accuracy depends on extraction, spectral quality, database coverage, score thresholds, and current taxonomy. Rare yeasts and recently renamed species require database governance and dual-name clinical reporting [20–22,46].

In 350 cancer patients, Aslani et al. recovered 162 yeasts; MALDI-TOF securely identified all isolates with scores above 2.0 and resolved uncommon species missed by conventional/PCR-RFLP workflows. The same cohort included 11.7% fluconazole resistance overall, demonstrating why accurate identification and susceptibility data may become linked in high-risk populations [20]. Importantly, the study did not show that MALDI-TOF can diagnose candidiasis directly from the mouth; it identified cultured isolates after clinical sampling.

6.2 PCR and quantitative nucleic-acid detection

Targeted PCR can identify species directly or from cultured colonies, and multiplex designs can recognize mixed infections. In 95 subjects with suspected oral candidiasis, multiplex PCR detected the same species in colony and oral-rinse material in 60 samples (74%) and revealed discrepancies with several phenotypic systems [17]. Real-time PCR in 193 concentrated oral-rinse specimens showed 94% agreement among culture-positive samples and detected Candida DNA in 20 of 91 culture-negative samples. Its analytical detection was reported at approximately 1–10 yeasts/mL compared with a concentrated-rinse culture threshold above 20 CFU/mL [13].

The additional PCR-positive/culture-negative fraction may represent improved sensitivity, non-viable cells, low-level carriage, or contamination. It is therefore unsafe to call every molecular-positive sample disease. Quantitative thresholds require calibration against lesion type, morphology, immune status, and outcome, not simply against culture. Viability PCR, RNA targets, or activity-linked transcripts may improve biological specificity, but robust oral clinical validation is limited.

Table 5. Advanced identification and activity platforms

Platform	Signal	Key advantage	Current oral limitation
MALDI-TOF MS	Protein fingerprint of cultured isolate	Fast, broad species identification after isolation	Requires viable pure culture and current database
Species-specific qPCR	DNA target and cycle threshold	High analytical sensitivity; quantitation potential	DNA may reflect carriage or non-viable cells
Multiplex PCR	Several species/resistance targets	Mixed-species and targeted panels	Coverage limited to chosen targets
Amplicon sequencing	Community ITS/18S profile	Detects uncultured and mixed mycobiota	Relative abundance; contamination; slow actionability
Metatranscriptomics	Expressed RNA pathways	Closer to fungal activity than DNA	RNA instability; analytical and interpretive complexity
Metabolomics	Composite host–fungus–microbiome metabolites	Potential activity and response signatures	Small discovery cohorts; non-specific pathways
Microfluidic electrochemical sensor	Captured cells plus immunoelectrochemical signal	Saliva-compatible; one-hour prototype	Analytical prototype; disease threshold unvalidated
Paper protease biosensor	Enzyme cleavage and colour change	Very rapid and potentially low cost	Specificity and oral clinical validation insufficient

Advanced platforms should be described by what they measure, not by technology name alone [13,17,20–27].

7. From molecular detection to multi-omics and point-of-care testing

Oral microbiome profiling has shifted the unit of analysis from a single pathogen to an ecological state. A 2026 cohort included 16 patients with primary oral candidiasis, seven post-treatment follow-ups, and seven controls; its small size is valuable for hypothesis generation but cannot establish a diagnostic classifier [26]. In a related metabolomic study, oral rinses from 26 active cases, 12 post-treatment samples, and 12 controls showed extensive lipid, amino-acid, oxidative-stress, and host-response differences. Of 295 significantly altered metabolites, most signals occurred in the supernatant fraction, and 95 metabolites were shared across clinical variants [27]. These data support biological stratification but also illustrate dimensionality, multiplicity, and overfitting risks.

Point-of-care development is moving faster than oral clinical validation. A 2024 microfluidic electrochemical device captured more than 95% of C. albicans across 30 to 3,000,000 CFU in a saliva matrix and generated a signal within one hour [24]. A paper-based protease sensor reported a lower detection limit of 3.5×10^3 CFU/mL, approximately five-minute readout, and projected material cost below US$2 [25]. Both are promising engineering demonstrations. Neither yet proves that the device distinguishes oral candidiasis from colonization across representative dental populations, medications, diets, mixed biofilms, and non-albicans species.

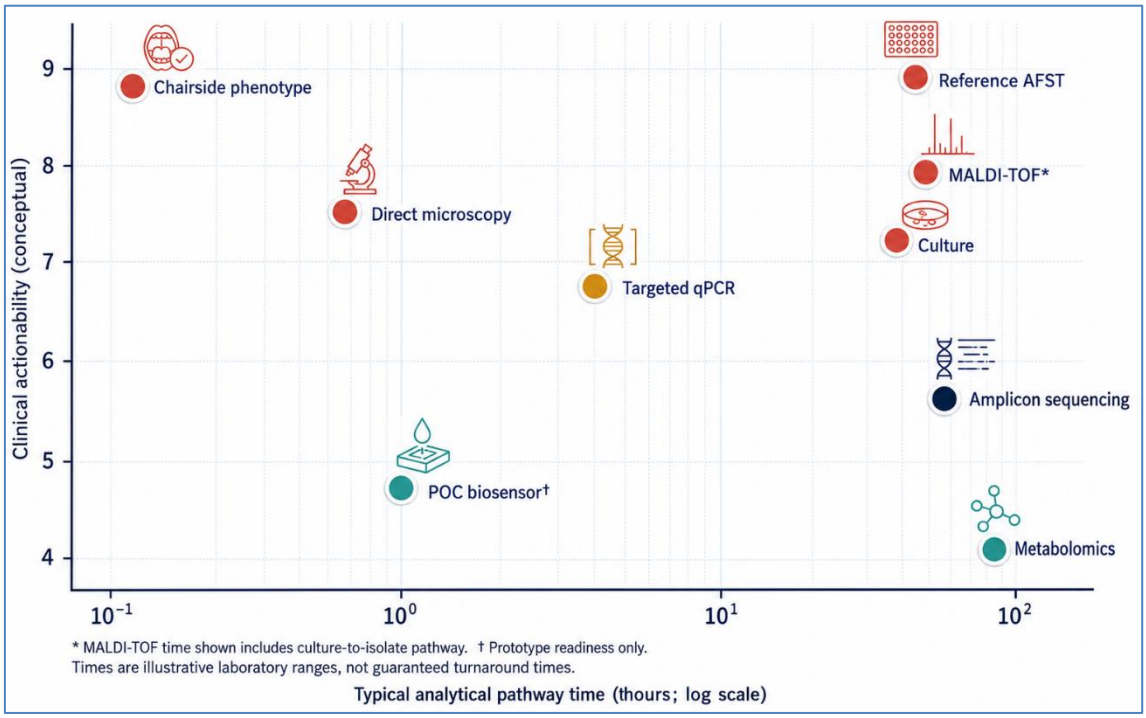

Figure 4. *Typical speed versus clinical actionability across the oral-candidiasis diagnostic pathway. Times are illustrative ranges and vary by laboratory; the positions of omics and biosensors reflect current oral-specific maturity rather than analytical novelty.*

Table 6. Selected numerical anchors from oral diagnostic and translational studies

Study / population	Method	Numerical result	Interpretive limit
Hu 2020; n=124 suspected cases	Fluorescence vs 10% KOH	Sensitivity 85.48% vs 64.52%; specificity 91.94% vs 72.58%; AUC 0.887 vs 0.685	Single diagnostic study and local reference process
Zhang 2019; 106 swabs, 122 biopsies	Fungal fluorescent stain	Swab sensitivity/specificity 82.7%/93.5%; biopsy 90.0%/92.9%	Highly selected suspected cases
White 2004; 193 rinse specimens	Real-time PCR	96/102 culture-positive samples PCR positive; 20/91 culture-negative PCR positive	Culture is an imperfect comparator; DNA ≠ disease

Ueta 2015; n=200 outpatients	Concentrated oral rinse	Candida detected in 52.0% vs 33.5% by swab	Higher recovery increases carriage detection
Aslani 2018; n=350 cancer patients	MALDI-TOF on 162 isolates	100% secure identification among isolates with score >2.0	Post-culture isolate identification
Liang 2024; saliva matrix	Microfluidic sensor	30–3,000,000 CFU range; >95% capture; 1-hour detection	Prototype; no validated disease cutoff
Suaifan 2024; culture/clinical isolates	Paper protease sensor	LOD 3.5×10^3 CFU/mL; ~5 min; projected cost <US$2	Limited oral clinical validation

Values are transcribed as study-specific results and must not be combined as if the designs shared a common gold standard [13–16,20,24,25].

8. Antifungal susceptibility testing: when an MIC helps

8.1 Indications

Routine AFST is unnecessary for a typical first mild episode that responds to standard therapy and correction of local drivers. It becomes useful when disease is refractory or rapidly recurrent, the patient is severely immunocompromised, prior azole exposure is substantial, a non-albicans species is recovered, the isolate has an unusual identification, or a treatment-limiting interaction makes the choice narrow. Sampling should occur before changing therapy when feasible, because post-exposure cultures may select a minority population or become negative.

8.2 Standard methods and non-equivalence

CLSI M27 and EUCAST E.Def 7.4 are reference broth-microdilution frameworks, but inoculum, medium glucose, reading, endpoint, and breakpoint systems differ. A numerical MIC is not portable across unqualified commercial devices or methods. EUCAST issued specific 2026 guidance for qualifying commercial AFST systems before applying EUCAST breakpoints [6–9]. Reports should name the method, incubation, endpoint, species, drug, MIC, interpretive document/version, category, and any technical uncertainty.

Clinical breakpoints predict probability of therapeutic success at defined exposures. ECOFFs/ECVs separate wild-type from non-wild-type populations and do not themselves predict cure. This distinction is critical for agents or species without breakpoints. EUCAST version 12.1 directly states that caspofungin breakpoints are not established because of significant inter-laboratory MIC variation; susceptibility can be inferred from anidulafungin and micafungin when both are susceptible [6]. Nystatin has no validated CLSI or EUCAST clinical breakpoint or standard ECV for oral Candida. Labelling an oral isolate “nystatin-resistant” through an amphotericin-B proxy is exploratory, not standardized [28].

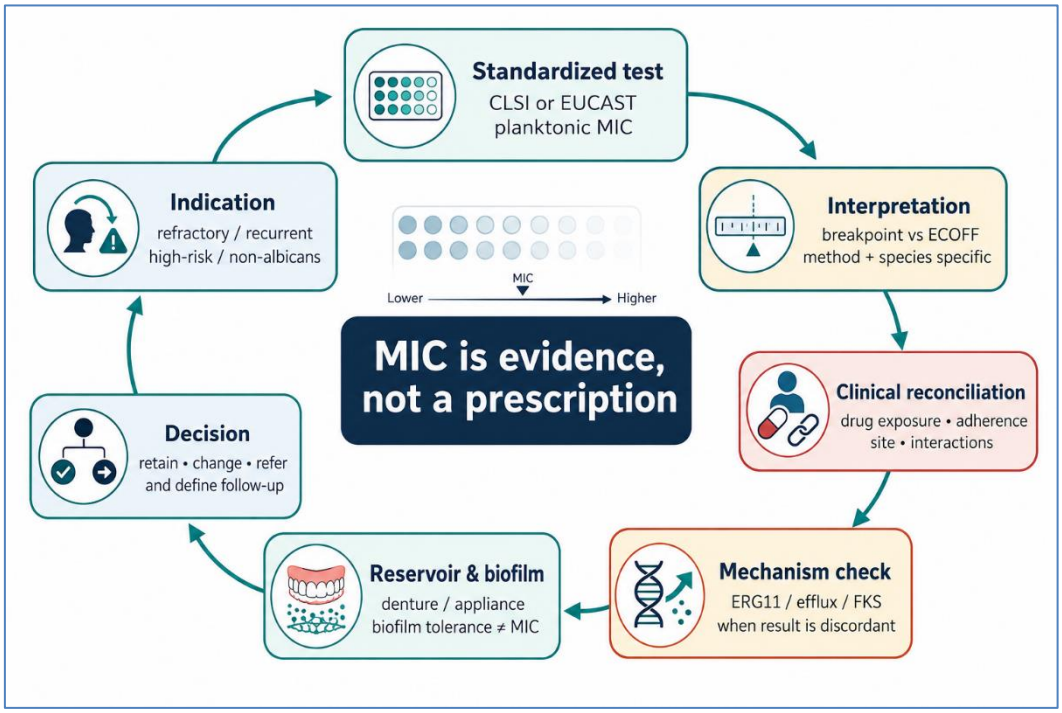

Figure 5. *AFST interpretation loop. A planktonic MIC becomes clinically useful only after indication, standardized measurement, valid species–drug interpretation, reconciliation with exposure and biofilm, and a defined management consequence*

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Table 7. Reference AFST concepts and reporting consequences

Concept	Meaning	Appropriate use	Common error
MIC	Lowest concentration meeting the method-specific growth endpoint	Quantitative input to species/drug interpretation	Treating one dilution as exact; ignoring method variability
Clinical breakpoint	MIC threshold linked to exposure, outcomes, and species	S/I/R categorization when a valid breakpoint exists	Applying invasive or other-method thresholds without qualification
ECOFF / ECV	Upper boundary of the phenotypic wild-type distribution	Flagging possible acquired/non-wild-type resistance	Calling all non-wild-type isolates clinically resistant
ATU	Area of technical uncertainty in EUCAST	Repeat, alternative test, mechanism test, or expert communication	Passing unresolved technical uncertainty directly to the patient
Biofilm tolerance	Phenotypic survival within structured biofilm	Explaining failure despite planktonic susceptibility	Replacing standard MIC with unvalidated biofilm cutoff
Genotypic resistance marker	Defined mutation or expression mechanism	Resolving selected discordant or epidemiologically important isolates	Assuming absence of known mutation proves susceptibility

Definitions follow CLSI/EUCAST logic; categories are not interchangeable across methods [6–9].

Table 8. EUCAST v12.1 MIC breakpoints for Candida albicans (mg/L)

Important interpretive note	R >	S ≤	Agent
Complete-inhibition endpoint	1	1	**Amphotericin B**
Species- and method-specific	0.016	0.016	**Anidulafungin**
Infer from anidulafungin and micafungin when both susceptible	Not set	Not set	**Caspofungin**
I category is 4 mg/L	4	2	**Fluconazole**
Breakpoints do not replace exposure assessment	0.06	0.06	**Itraconazole**
Species- and method-specific	0.03	0.03	**Micafungin**
Clinical use must match indication and exposure	0.06	0.06	**Posaconazole**
Tween-20 supplemented EUCAST medium required	0.008	0.008	**Rezafungin**
Values between S and R are I	0.25	0.06	**Voriconazole**
Insufficient evidence for a breakpoint	IE	IE	**Isavuconazole**
No validated EUCAST clinical breakpoint	None	None	**Nystatin**

Source: EUCAST antifungal clinical breakpoint table v12.1, valid from 10 April 2026 [6]. These planktonic reference thresholds are not oral fungal-load thresholds and do not capture biofilm response.

9. What oral-isolate susceptibility studies show—and cannot show

Oral susceptibility studies are heterogeneous in host group, carriage versus disease definition, species distribution, method, and breakpoint choice. In 126 isolates from 41 mother–child dyads, Alkhars et al. found 5.6% classified as nystatin resistant using an amphotericin-B proxy because no nystatin breakpoint existed. Among 21 children with longitudinal C. albicans isolates, approximately 70% had unchanged MICs; increases occurred in 19% for nystatin, 10% for fluconazole, and 29% for caspofungin [28]. The findings are useful for within-host evolution but are not prevalence estimates and do not validate the proxy breakpoint.

A 2026 β-thalassemia study reported 6.29% candidiasis and 8.14% colonization among 270 patients, with C. albicans, Pichia kudriavzevii, and Nakaseomyces glabratus prominent. The candidiasis-isolate MIC90 values were 0.032 µg/mL for voriconazole, 8 µg/mL for fluconazole, and 16 µg/mL for nystatin [29]. Interpretation requires caution because the paper reports a CLSI M38 procedure for Candida—where M27 is the yeast reference—and because nystatin categories lack standardized breakpoints. The numerical MIC distribution remains informative; categorical “resistance” claims are less secure.

In 25 C. albicans isolates from HIV-positive patients with oral candidiasis, fluconazole susceptibility was 96%, itraconazole susceptibility 72%, and one itraconazole-resistant isolate was found; two isolates were intermediate to caspofungin [30]. A Ugandan HIV cohort found 7.6% oropharyngeal candidiasis and fluconazole resistance in 7/35 isolates (20%), including 4/20 C. albicans isolates [31]. Such regional differences reinforce targeted identification and surveillance, but small isolate denominators produce wide uncertainty and should not drive universal empirical policy.

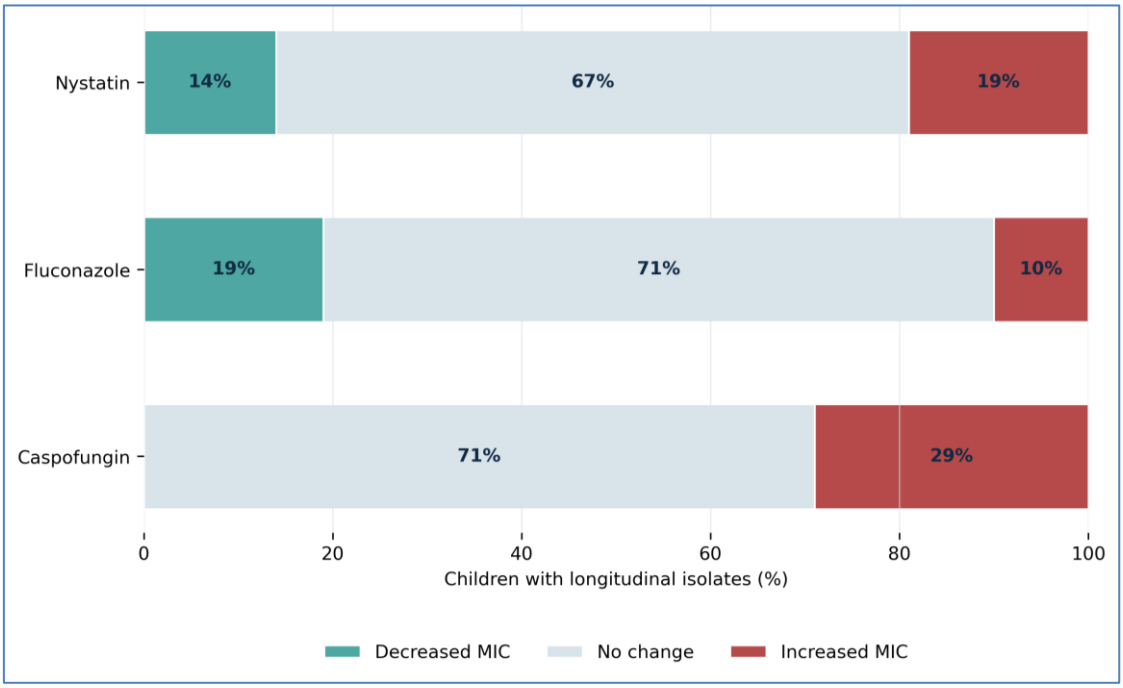

Figure 6. Direction of MIC change in 21 children with longitudinal oral C. albicans isolates [28]. 'No change' is the reported remainder. The figure describes within-cohort change and is not antifungal-resistance prevalence.

Table 9. Selected oral AFST cohorts and critical interpretation

Cohort	Methods / isolates	Selected result	Critical appraisal
Mother–child dyads, 2023	Broth microdilution; 126 Candida isolates	5.6% proxy-defined nystatin resistance; 29% longitudinal caspofungin MIC increase in 21 children	No validated nystatin breakpoint; small longitudinal subset
β-thalassemia major, 2026	270 patients; culture, molecular ID, reported CLSI M38 AFST	Candidiasis MIC90: voriconazole 0.032, fluconazole 8, nystatin 16 µg/mL	Yeast-method reporting and nystatin categorization limit inference
HIV oral C. albicans, 2024	25 isolates; CLSI M27	Fluconazole susceptible 96%; itraconazole susceptible 72%	Single region and small isolate count
Ugandan HIV cohort, 2024	35 isolates; VITEK 2 AFST	Fluconazole resistant 7/35 overall; 4/20 C. albicans	Automated method and small species strata
Cancer cohort, 2018	162 oral yeasts; CLSI M27-A3; MALDI-TOF	Overall fluconazole resistance 11.7%	Colonization and infection mixed; high-risk referral population

MIC distributions are more transportable than categorical claims when methods or breakpoints are uncertain [20,28–31].

10. Mechanisms of reduced response

Azole resistance may involve ERG11 alteration or overexpression, increased efflux through CDR1/CDR2 or MDR1, and broader genomic adaptation. Echinocandin resistance is most strongly linked to FKS hot-spot mutations, while polyene response can change through sterol-pathway remodeling. These mechanisms occur within a dynamic genome and may accumulate under repeated exposure [33,34]. Genotypic testing is most useful when the phenotype is reproducible, the mechanism–drug relationship is validated, and the result will resolve a consequential uncertainty.

Clinical failure is broader than resistance. Inadequate mucosal contact, poor adherence to frequent topical dosing, drug–drug interactions, reduced azole absorption, continued inhaled-steroid deposition, hyperglycaemia, xerostomia, immunodeficiency, an untreated denture reservoir, or a wrong diagnosis may all produce non-response. Biofilm extracellular matrix, persister subpopulations, metabolic heterogeneity, and high local cell density can reduce drug effect while the planktonic MIC remains susceptible. The correct response to failure is diagnostic reassessment before automatic escalation.

Table 10. Laboratory and clinical explanations for apparent treatment failure

Pattern	Likely explanations	Recommended verification	Decision consequence
Symptoms persist; culture negative	Wrong diagnosis, prior therapy, focal/tissue disease	Re-examine lesion; biopsy if indicated; review exposure	Avoid blind antifungal escalation
Culture positive; MIC susceptible	Adherence, contact time, reservoir, biofilm, immune deficit	Observe administration; inspect denture; assess host factors	Optimize delivery and source control
Reproducibly elevated azole MIC	ERG11/efflux adaptation; non-albicans species	Confirm ID and reference AFST; mechanism test selectively	Choose guideline-supported alternative
Caspofungin result discordant	Method variability	Repeat/reference testing; use anidulafungin/micafungin inference per EUCAST	Do not act on isolated unqualified MIC
Rapid recurrence after cure	Persistent reservoir or host driver	Denture/appliance culture, saliva, diabetes/immune review	Prevention and maintenance strategy
Positive PCR after clinical cure	Residual/non-viable DNA or carriage	Clinical follow-up; avoid treating molecular positivity alone	No therapy if asymptomatic and lesion resolved

The table frames discordance as a diagnostic problem rather than proof of resistance.

11. Therapeutic decision-making

11.1 Match treatment intensity to phenotype

Current guideline logic remains phenotype-based. Mild localized oropharyngeal disease can be treated with topical agents when adherence and contact are feasible. Moderate-to-severe disease, oesophageal concern, substantial immunosuppression, or failure of topical therapy

favors systemic fluconazole when appropriate. Refractory disease requires confirmation of diagnosis, species and susceptibility resolution, exposure review, and consideration of itraconazole solution, posaconazole, voriconazole, or parenteral options according to authoritative guidance and patient-specific constraints [4,5].

Local correction is not an adjunct of minor importance; it is part of causal therapy. Denture hygiene and nocturnal removal, correction of poor fit, rinsing after inhaled corticosteroids, improved salivary support, glycaemic control, and reduction of unnecessary antimicrobial exposure can determine recurrence. Drug selection must also account for pregnancy, age, hepatic and renal function, QT risk, drug interactions, and regional formulation availability. The doses summarized below reproduce adult guideline pathways for scholarly comparison and are not individualized prescribing instructions.

Table 11. Guideline-based therapeutic pathway for adult oropharyngeal candidiasis

Scenario	Guideline option	Typical duration	Precision-diagnostic trigger
Mild localized disease	Miconazole 50-mg mucoadhesive buccal tablet once daily or clotrimazole 10-mg troche five times daily; nystatin suspension is an alternative	7–14 days	Clinical phenotype; test if atypical or non-responsive
Moderate–severe disease	Fluconazole; NIH lists 200-mg loading dose then 100–200 mg orally once daily	7–14 days	Review interactions, prior azole exposure, host risk
Possible oesophageal disease	Systemic therapy required; fluconazole preferred when appropriate	14–21 days	Dysphagia/odynophagia; consider endoscopic evaluation if non-response
Fluconazole-refractory OPC	Itraconazole oral solution or posaconazole; alternatives depend on guideline and host	Up to 28 days in selected regimens	Obtain lesion culture, species ID, AFST; reassess diagnosis/exposure
Severe refractory/high-risk disease	Specialist-guided systemic alternatives, including echinocandin or amphotericin formulations	Individualized	Reference testing, mechanism/exposure assessment, evaluate deeper disease

Verify the current local product label, pregnancy/age restrictions, interactions, and regional guidance before prescribing. Sources: IDSA and NIH [4,5].

11.2 What randomized trials contribute

Randomized trials establish that formulations and dosing burden matter. In 167 adults with HIV, day-14 clinical cure was 87% with fluconazole suspension and 52% with nystatin; mycological eradication was 60% versus 6%, and day-28 relapse was 18% versus 44% [35]. In 159 evaluable immunocompromised children, clinical cure was 91% with fluconazole and 51% with nystatin, while eradication was 76% versus 11% [36]. These trials demonstrate efficacy in specific immunocompromised populations and should not be generalized without considering current antiretroviral therapy, resistance ecology, or host differences.

Once-daily miconazole buccal tablet was non-inferior to clotrimazole troches five times daily in 578 HIV-positive participants (ITT clinical cure 61% vs 65%) [37]. In a 2022 phase III trial of 431 adults, miconazole buccal tablet achieved 68% clinical cure compared with 59% for itraconazole, with mycological cure 68.2% versus 42.0% [38]. Posaconazole and fluconazole had similar day-14 clinical success (91.7% vs 92.5%) in a 350-participant HIV trial, though sustained mycological success at day 42 favored posaconazole (40.6% vs 26.4%) [40]. Trial endpoints confirm that clinical cure, mycological clearance, and recurrence are distinct outcomes.

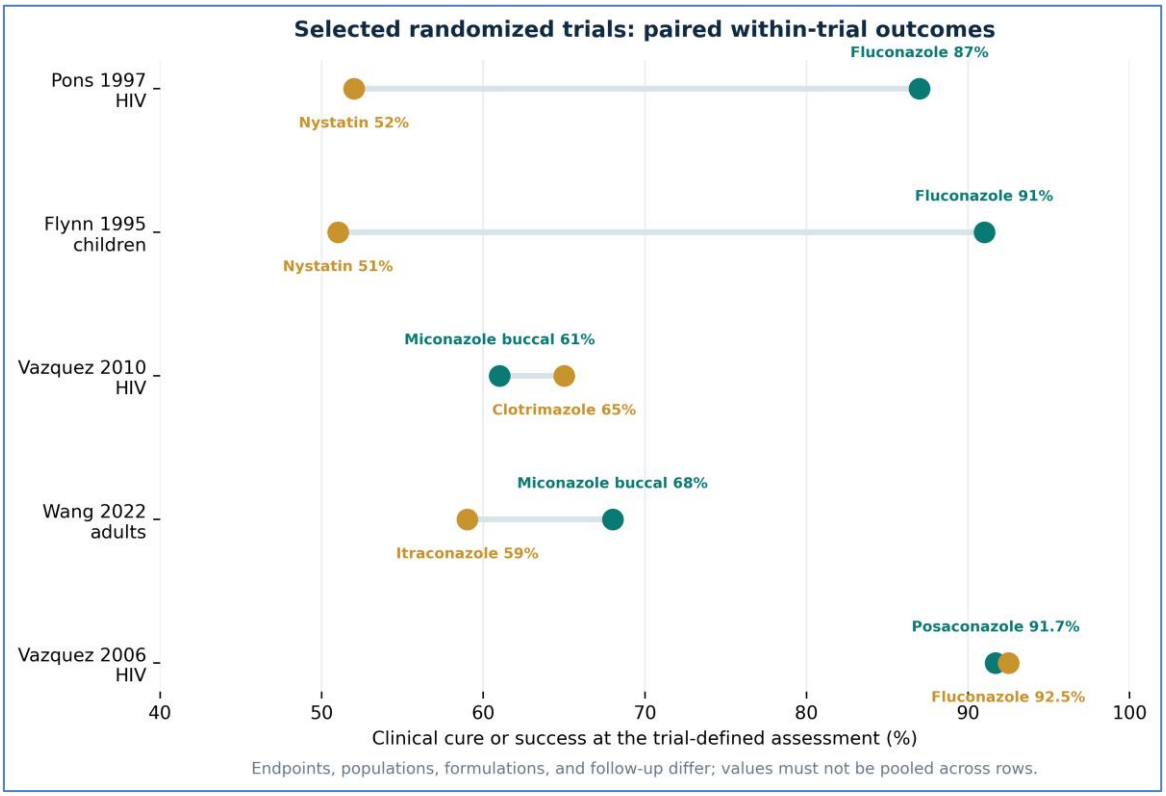

Figure 7. *Selected randomized oral/oropharyngeal-candidiasis trials [35–40]. Each row is a within-trial comparison; populations, formulations, endpoints, and follow-up differ, so the values are not a meta-analysis.*

Table 12. Selected randomized treatment trials with numerical outcomes

Trial / population	Comparison	Primary numerical result	Decision insight
Pons 1997; HIV; n=167	Fluconazole vs nystatin, 14 days	Clinical cure 87% vs 52%; day-28 relapse 18% vs 44%	Systemic exposure outperformed frequent topical suspension in this population
Flynn 1995; immunocompromised children; n=182	Fluconazole vs nystatin	Clinical cure 91% vs 51%; eradication 76% vs 11%	Clinical and microbiological advantages, but relapse later converged
Vazquez 2010; HIV; n=578	Miconazole buccal daily vs clotrimazole 5×/day	ITT clinical cure 61% vs 65%; non-inferior	Convenience can preserve efficacy
Wang 2022; adults; n=431	Miconazole buccal vs itraconazole	Clinical cure 68% vs 59%; mycological cure 68.2% vs 42.0%	Local delivery achieved non-inferior clinical outcome
Hamza 2008; HIV; n=220	Fluconazole 750-mg single dose vs 150 mg/day ×14	Clinical cure 94.5% vs 95.5%	Trial-specific equivalence; not current universal dosing guidance
Vazquez 2006; HIV; n=350	Posaconazole vs fluconazole	Day-14 success 91.7% vs 92.5%; day-42 mycological success 40.6% vs 26.4%	Short-term clinical equivalence with durability difference

Historical trials remain informative but many predate contemporary HIV treatment and current resistance surveillance [35–40].

12. Diagnostic stewardship by clinical scenario

Table 13. Decision matrix linking phenotype, testing, and therapy

Scenario	Minimum sufficient evidence	Escalate diagnostics when…	Therapeutic implication
First typical mild episode	Compatible lesion + risk factor; microscopy if uncertain	Atypical, non-wipeable, severe, or no response	Topical or standard therapy plus driver correction
Denture-associated recurrence	Palatal phenotype + appliance assessment	Repeated relapse or mixed species suspected	Treat mucosa and reservoir; improve fit/hygiene
HIV / profound immune risk	Phenotype; low threshold for microscopy/culture	Moderate–severe, recurrent, prior azole, oesophageal symptoms	Systemic therapy often preferred; species/AFST if refractory
Cancer therapy / xerostomia	Lesion-targeted culture and direct exam	Persistent symptoms, unusual isolate, prophylaxis exposure	Balance local therapy, interactions, mucosal injury, and reference ID
Non-wipeable plaque	Biopsy with histology and fungal stain	Always if induration, ulceration, persistence, or dysplasia risk	Do not substitute empiric antifungal response for pathology

PCR positive, clinically normal	No further fungal therapy	Only if a new lesion or high-risk syndrome develops	Document carriage; avoid antifungal treatment
Treatment failure	Repeat phenotype, adherence, reservoir, culture/ID; AFST if indicated	Discordant MIC, unusual species, systemic signs	Change therapy only after reconciling patient and organism

The matrix defines the least burdensome decision-changing pathway rather than a universal testing panel.

13. Implementation in resource-variable laboratories

Precision does not require maximum technology. A resource-efficient tier can begin with standardized clinical photography, lesion scraping, KOH or Gram stain, Sabouraud and chromogenic culture, and referral access for MALDI-TOF or sequencing. The laboratory should invest first in specimen instructions, internal quality control, isolate purity, current nomenclature, and reliable turnaround communication. A poorly sampled qPCR is not more precise than a well-sampled smear.

Hub-and-spoke systems can separate detection from high-complexity resolution. Local laboratories recover and preserve isolates; reference centers perform species confirmation, reference AFST, and selected resistance sequencing. Telepathology or digital microscopy can support training, while electronic reports should explicitly state when a result indicates colonization, when a breakpoint is absent, and when expert consultation is recommended. New POC devices must be compared with this optimized conventional pathway, including total cost, operator steps, invalid rate, storage, contamination, and effect on inappropriate antifungal use.

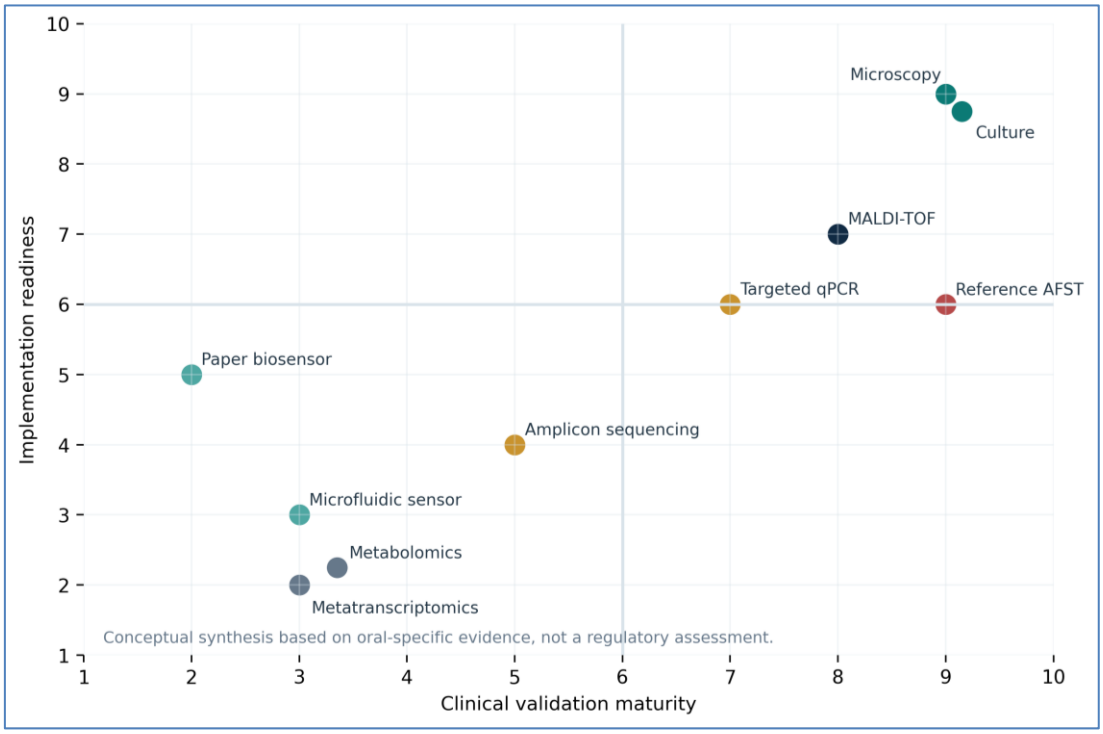

Figure 8. *Diagnostic technology maturity map for oral candidiasis. Positions are a qualitative synthesis of oral-specific clinical validation and operational readiness; they are not regulatory classifications.*

14. Research agenda

The most important unmet need is an activity-sensitive definition of oral candidiasis. Future cohorts should enroll symptomatic cases, asymptomatic carriers, and matched lesion mimics; sample the lesion and whole mouth; record recent antifungals; quantify viable fungi; document morphology; and collect patient-reported pain, taste, eating, and recurrence outcomes. A diagnostic signature should be trained and externally validated against a blinded clinical–pathological reference, then tested for incremental benefit over examination plus microscopy. AFST studies should report CLSI/EUCAST version, quality-control strains, full MIC distributions, species-stratified denominators, and whether isolates represent carriage or infection. Nystatin work urgently needs harmonized testing and outcome-linked interpretive criteria rather than borrowed amphotericin thresholds. Oral biofilm susceptibility assays should not enter routine reporting until reproducibility and clinical predictive value are demonstrated.

Table 14. Prioritized research roadmap

Priority	Minimum design	Primary endpoint	Decision threshold for translation
Activity-sensitive diagnostic	Prospective, lesion-resolved, carrier and mimic controls, external validation	Incremental AUC and net benefit beyond phenotype + microscopy	Improves patient outcome or reduces unnecessary therapy
Quantitative fungal burden	Standardized swab/rinse volumes and viable counts across phenotypes	Lesion-specific likelihood ratios and repeatability	Robust across sites, devices, and host strata
Nystatin susceptibility	Harmonized method plus pharmacodynamic and clinical-outcome linkage	Reproducible MIC distribution and outcome-predictive threshold	Independent multicenter validation
Biofilm response	Paired planktonic/biofilm testing with denture and mucosal outcomes	Added prediction of persistence/recurrence	Reproducible and management-changing
POC biosensor	Prospective chairside comparison with lesion adjudication	Sensitivity, specificity, invalid rate, time, cost, antibiotic/antifungal use	Superiority or non-inferiority to optimized low-cost pathway
Multi-omics classifier	Locked model, pre-specified features, external cohort	Calibration, discrimination, clinical utility	Stable across diet, age, xerostomia, drugs, and geography
Treatment-response monitoring	Serial lesion, burden, symptom, and recurrence measures	Time to durable clinical resolution	Predicts relapse before symptoms without overtreating carriage

Research should prioritize decision-changing validation rather than additional cross-sectional detection studies.

15. Limitations

This is a structured critical review rather than an exhaustive systematic review. No dual-reviewer screening, formal risk-of-bias instrument, or meta-analysis was performed. The

evidence base is limited by small oral cohorts, inconsistent case definitions, mixed specimens, older HIV-era treatment trials, and incomplete oral validation of modern platforms. Numerical comparisons are therefore study-specific. Some official AFST standards are copyrighted documents; the manuscript summarizes current interpretive principles and EUCAST v12.1 public values but cannot substitute for the full current CLSI or EUCAST document.

Therapeutic recommendations evolve and differ by country, formulation availability, pregnancy, age, immune status, and drug interactions. The treatment tables synthesize guidelines and trials for scholarly purposes and require verification against current local prescribing information. Finally, taxonomic names change; clinical reports should retain recognizable synonyms when needed to prevent communication error [46].

16. Conclusions

Oral candidiasis should be diagnosed as a clinicopathological and ecological state, not as a positive fungal test. Conventional examination, lesion-linked microscopy, and culture remain the backbone because they preserve anatomical and biological meaning. MALDI-TOF and targeted molecular assays add valuable resolution when species, mixed populations, or low-level detection matter, but they cannot independently distinguish carriage from disease. Multi-omics and biosensors are moving toward activity-sensitive and chairside detection, yet their next milestone is prospective clinical utility rather than lower analytical detection limits.

AFST is a selective stewardship tool. A reproducible MIC interpreted with the correct method, species, breakpoint or ECOFF, and drug exposure can guide refractory or high-risk disease. It does not measure denture biofilm tolerance, adherence, or host failure. The safest precision pathway therefore integrates the organism with the phenotype: confirm the lesion, sample the relevant site, identify only to the level needed, test susceptibility when it can change management, correct reservoirs and host drivers, and define a clinical follow-up endpoint. This sequence converts technology into better decisions while protecting patients from both missed disease and treatment of harmless carriage.

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Compliance with ethical standards

Disclosure of conflict of interest

The authors declare that they have no conflict of interest.