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Demodex Testing in Rosacea: Evidence Strength, Clinical Utility, and a Decision-Oriented Approach: A Narrative Review

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Abstract

Demodex mites are found at a higher average density in rosacea than in controls, but this association is often converted too readily into diagnostic and treatment rules. This narrative review uses the hierarchy of diagnostic-test evaluation to appraise five successive claims: association with rosacea, dependence of measured density on the sampling method, validity of a universal threshold, prediction and monitoring of treatment response, and effect on patient outcomes.

PubMed and Google Scholar were searched, supplemented by citation chasing, and 39 clinical studies were appraised narratively. Evidentiary strength declined at each step from biology toward clinical action. Association and method dependence were strongly supported. The threshold of more than 5 mites/cm² is an operational convention rather than a universal disease boundary; baseline density does not identify who should or should not receive ivermectin, and falling counts during therapy are not a validated surrogate for clinical benefit. No comparative study has shown that *Demodex*-test-guided care improves outcomes over phenotype-guided care. Current evidence therefore does not support routine testing in typical rosacea.

Testing is justified when a folliculocentric, scaly, asymmetric, corticosteroid-modified, or treatment-refractory eruption makes demodicosis a genuine differential diagnosis and the result will change management. Dermoscopic *Demodex* signs can raise pretest probability, and every result should be reported with its method, site, sampled area, number of samples, units, and threshold.

Categories: Epidemiology/Public Health, Infectious Disease, Dermatology
Keywords: demodex, demodicosis, dermoscopy, diagnostic testing, ivermectin, rosacea, skin surface biopsy

Introduction And Background

Rosacea is now managed primarily by phenotype rather than by rigid subtype classification. Persistent centrofacial erythema, flushing, telangiectasia, inflammatory papules and pustules, phymatous change, and ocular disease occur in different combinations, and treatment is selected according to the manifestations that dominate the individual presentation [1-4]. *Demodex folliculorum* and *Demodex brevis* complicate this framework because both are common inhabitants of human pilosebaceous units, yet multiple studies show higher average mite burdens in rosacea [5-10].

The clinical question is therefore not whether *Demodex* can participate in rosacea; it can. The question is whether measuring *Demodex* improves care beyond what the clinical phenotype already achieves. Diagnostic tests earn a place in routine practice by clearing successive evidential levels: analytical performance, diagnostic accuracy, influence on diagnostic thinking, influence on therapeutic decisions, and, finally, improvement in patient outcomes [11,12]. Success at a lower level does not transfer upward. An association with disease does not establish a diagnostic boundary, a fall in mite density during treatment does not validate density as a surrogate endpoint, and an analytically sensitive test does not automatically change management or improve outcomes.

Available detection methods include standardized skin surface biopsy (SSSB), direct microscopic examination (DME), polymerase chain reaction (PCR), reflectance confocal microscopy (RCM), and conventional or ultraviolet (UV) dermoscopy; they differ in the compartment they sample and in what they measure.

The aim of this narrative review is to appraise whether measuring *Demodex* improves the care of cutaneous rosacea beyond what the clinical phenotype already achieves. To that end, it applies that hierarchy to *Demodex* testing in cutaneous rosacea, states the strength of support for each claim explicitly (Figure *1*), and converts the resulting evidence gradient into practice recommendations. Ocular *Demodex* blepharitis, for which a targeted acaricide (an agent that kills mites) has shown efficacy in a pivotal randomized trial [13], is a distinct indication and is outside the present scope.

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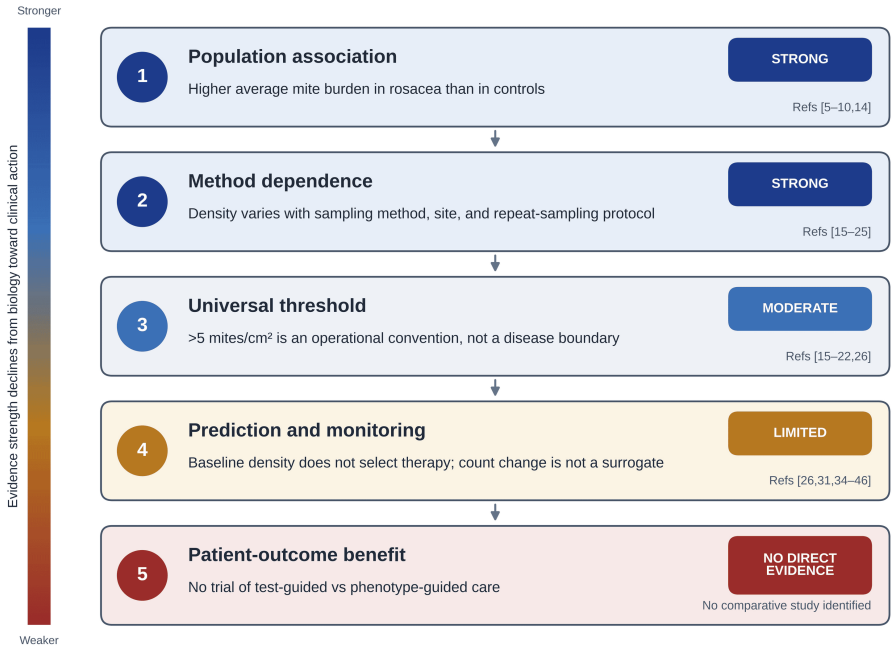


FIGURE 1: Evidence-to-decision chain for Demodex testing in rosacea

Each step corresponds to a level of the diagnostic-test evaluation hierarchy. Support is strongest for population-level association and method dependence and becomes progressively weaker for a universal threshold, prediction and monitoring of treatment response, and demonstrated patient-outcome benefit. Numbers in brackets are reference numbers. Evidence-strength labels are qualitative narrative appraisals and are not formal GRADE ratings. This is an original schematic designed by the authors from the evidence summarized in this review. It was drawn in Python (matplotlib) using AI-assisted plotting code and verified by the authors; no image-generation model or previously published material was used.

GRADE: Grading of Recommendations Assessment, Development and Evaluation

Review

Review approach and evidence-strength framework

This is a narrative review; it was not designed or conducted as a systematic review, and no protocol was registered. The literature search and selection are described here so that readers can judge the scope of the evidence base.

Literature Search

PubMed was searched from inception to August 28, 2026, using combinations of the terms "Demodex," "demodicosis," "rosacea," "density," "standardized skin surface biopsy," "dermoscopy," "confocal microscopy," "polymerase chain reaction," "ivermectin," and "treatment response." Google Scholar was searched with the same terms to identify additional records, and the reference lists of retrieved studies and prior reviews were hand-searched. The PubMed search was updated on November 5, 2026, for records added since August 28, 2026, using the title or abstract terms "Demodex," "demodicosis," or "demodicidosis." Only English-language publications were considered.

Study Selection and Data Extraction

Original clinical studies, systematic reviews, and meta-analyses were considered if they reported *Demodex* density or detection in cutaneous rosacea or demodicosis in humans, compared sampling or detection methods, or related *Demodex* to treatment response, prediction, or monitoring. Case reports, animal-only studies, and studies limited to ocular *Demodex* blepharitis were not appraised. Consensus statements, methodological papers, editorials, and mechanistic studies were cited for context only. Selection and data extraction were performed by one author (W.T.H.). Thirty-nine studies were retained for detailed appraisal; their design, population, sample size, sampling or detection method, threshold, and principal finding are summarized in the Appendix. Because phenotype definitions, sampling protocols, thresholds, reference standards, and outcomes were heterogeneous, no pooled estimate was calculated.

Evidence-Strength Framework

Each claim was assigned one of four narrative categories. "Strong" denotes replicated findings from meta-analysis or multiple consistent comparative studies. "Moderate" denotes consistent prospective or comparative observational evidence with important method or population limitations. "Limited" denotes small, single-center, exploratory, or non-randomized evidence. "No direct evidence" indicates that the claim has not been tested in an appropriate comparative study. These categories reflect design, consistency, and directness; they are not a formal Grading of Recommendations Assessment, Development and Evaluation (GRADE) assessment, and no study-level risk-of-bias tool was applied.

What the evidence establishes

Demodex Burden Is Higher on Average in Rosacea (Strong)

A 2017 meta-analysis of 23 case-control studies including 1,513 patients found a substantially greater frequency of *Demodex* infestation in rosacea, although between-study heterogeneity was considerable [5]. Microscopy studies reported higher mean densities or more frequent detection in rosacea than in controls [6-9], histopathological series linked follicular mites with rosacea [14], and quantitative PCR detected a higher *D. folliculorum* burden [10]. These data establish a population-level association. Because controls also carry mites and the distributions overlap, they do not establish a patient-level diagnostic boundary.

Measured Density Is Method-Dependent (Strong)

SSSB, DME, scraping, squeezing, PCR, RCM, and UV dermoscopy do not sample the same biological compartment and are not interchangeable (Table *1*) [15-25]. In a 2025 comparison of 61 patients, the median density was 11 mites/cm² by SSSB and 1 mite/cm² by DME, and the proportion above 5 mites/cm² was 64% and 28%, respectively [20]; a retrospective series of 35 patients with demodicosis found the opposite ordering, with higher densities by DME [17]. Repeated sampling can also change classification [15,21]. A *Demodex* result is therefore a protocol-specific measurement, not an invariant property of the patient.

Method	Representative finding	Evidence strength	Clinical interpretation
Two consecutive SSSBs	Sensitivity 98.7% and specificity 95.5% in one combined rosacea/demodicosis framework [15]	Moderate	High performance is protocol-specific, not a universal constant
SSSB vs DME	Median 11 vs 1 mites/cm²; >5 mites/cm² in 64% vs 28% of 61 patients[20]	Moderate	Counts from different methods are not interchangeable
Repeated SSSB	Additional samples can convert an initially low count to a positive classification [15,21]	Strong	The number of samples must be prespecified and reported
PCR vs microscopy	Sensitivity at the face approximately 93.8% vs 50% in a small comparison [22]	Moderate	Greater analytical sensitivity does not establish actionable disease
Conventional dermoscopy vs SSSB	Tails in 88% of positive samples in 30 patients[26]; sensitivity 50%, specificity 77.5% for *Demodex folliculorum* in 60 patients with papulopustular rosacea [27]; positive LR 12.1 for tails in suspected demodicosis [28]	Limited to moderate	Accuracy depends on pretest probability; useful for triage, does not replace standardized sampling in rosacea
UV dermoscopy vs SSSB	Sensitivity 82.1%, specificity 71.4%, AUC 0.793 against SSSB[25]	Moderate	Describes agreement with SSSB, not treatment benefit
RCM	Non-invasive in vivo visualization and quantification[23,24]	Moderate	No validated outcome-linked treatment threshold exists

TABLE 1: Method-dependent performance of Demodex testing

Evidence-strength categories are qualitative narrative appraisals, not formal GRADE ratings.

AUC: area under the receiver operating characteristic curve; DME: direct microscopic examination; GRADE: Grading of Recommendations Assessment, Development and Evaluation; LR: likelihood ratio; PCR: polymerase chain reaction; RCM: reflectance confocal microscopy; SSSB: standardized skin surface biopsy; UV: ultraviolet

The Threshold of More Than 5 mites/cm² Is an Operational Convention, Not a Universal Disease Boundary (Moderate)

The cut-off has been valuable for research standardization, but its meaning varies with sampling method, site, repeat-sampling rule, and disease spectrum [15-22]. Studies using the squeezing technique have applied different cut-offs [19,29], which acknowledges that no single number transfers across methods. A value of 4 mites/cm² versus 6 mites/cm² should not create two different diseases or dictate two different treatments. Detection of mites alone is not an indication for treatment. Treatment decisions should rest on the clinical phenotype and the patient's signs and symptoms; a standardized count, when one has been obtained, is interpreted within that context and should not by itself start or withhold therapy.

Higher Analytical Sensitivity Does Not Equal Higher Clinical Utility (Strong for the Analytical Claim; No Direct Evidence for Outcomes)

PCR detects *Demodex* spp. more frequently than microscopy, and confocal or UV imaging can visualize follicular mites non-invasively [22-25]. These methods show that a target can be detected. They do not show that the detected burden is causally important or that acting on it improves care.

Dermoscopy as a triage step

Dermoscopic Demodex Signs Raise Pretest Probability but Do Not Replace Sampling in Rosacea (Limited to Moderate)

Demodex tails and *Demodex* follicular openings were associated with SSSB positivity in a study of 30 patients, with tails present in 88% of *Demodex*-positive samples [26]. In 60 patients with papulopustular rosacea, however, conventional dermoscopy showed a sensitivity of 50% and a specificity of 77.5% against SSSB for *D. folliculorum* [27]. Performance appears higher when the pretest probability is higher: in 64 adults with suspected demodicosis, *Demodex* tails at 11-20 per field had a positive likelihood ratio of 12.1 against skin scraping, and a combination of signs had a negative likelihood ratio of 0.11, leading the authors to propose that dermoscopy alone may suffice [28]; in a case-control study of 121 patients with facial dermatoses, predominantly pityriasis folliculorum and only 5.8% rosacea, dermoscopy and SSSB had similar yields [30]. These spectrum differences matter, because estimates obtained in suspected demodicosis may not transfer to a general rosacea clinic. UV dermoscopy improves agreement with SSSB but has been validated against a sampling reference rather than a clinical outcome [25], and dermoscopic predictors of response to ivermectin remain exploratory [31]. Dermoscopy is therefore best used at the bedside to select patients for confirmatory sampling: prominent tails or follicular openings in an atypical eruption strengthen the case for a standardized test, whereas their absence does not exclude demodicosis [26,27,32].

What the evidence does not support

Routine Demodex Testing in Typical Rosacea (No Direct Evidence of Benefit)

No study identified for this review compared a *Demodex*-test-guided pathway with phenotype-guided care while measuring clinical response, time to control, adverse effects, quality of life, or cost. The absence of such a trial does not prove that testing cannot help, but decision analysis also argues against routine use. A test changes management only when the pretest probability lies between the threshold at which a clinician would treat without testing and the threshold at which the clinician would not treat at all [33]. In typical papulopustular rosacea, topical ivermectin is already among the best-supported first-line therapies [4]. A positive result therefore rarely changes the choice, and a negative result should not remove it, because ivermectin also has anti-inflammatory activity [34] and, in erythematotelangiectatic rosacea with low or absent mite counts, persistent erythema improved with either ivermectin or metronidazole [29], although this evidence is indirect for papulopustular disease. In the most common clinical scenario, the decision value of the test is likely to be low, whereas a false-negative result from a low-recovery sample can lead to appropriate therapy being withheld.

Baseline Density as a Gatekeeper for Ivermectin (Limited)

A rater-blinded, randomized split-face trial in 27 patients with erythematotelangiectatic rosacea and mean baseline densities below one mite/cm² showed equivalent improvement in erythema with ivermectin and metronidazole [29]. This evidence is indirect for the present question: the trial enrolled erythematotelangiectatic rather than papulopustular disease and assessed erythema rather than inflammatory lesions, whereas topical ivermectin is supported primarily for papules and pustules [4]. It shows that improvement can occur despite low baseline counts, but it cannot be extrapolated with confidence to papulopustular rosacea. Conversely, high baseline density does not prove that inflammation is exclusively mite-driven or that non-acaricidal treatment will fail. No study has demonstrated a replicated, prespecified treatment-by-biomarker interaction [26,27,29,31,32,34-46]. Baseline density is therefore not a validated treatment-selection biomarker.

Serial Counts as a Treatment Target (Moderate That Counts Fall; Limited That Change Tracks Success)

Mite density frequently decreases during effective therapy [29,36-40], but density change has not consistently correlated with lesion clearance. After 577-nm pro-yellow laser treatment in 34 patients, mean SSSB density fell from 18.1 to 10.2 mites/cm^2, yet the decrease was not correlated with regression of erythema [39]. Mite reduction is a biological-response marker, not a validated surrogate endpoint.

Detection as Proof of Demodicosis (Strong That Carriage Is Common; Diagnostic Meaning Is Context-Dependent)

Because mites are normal pilosebaceous inhabitants, diagnostic meaning depends on morphology, distribution, sampling protocol, and competing diagnoses. The terms "increased density," "demodicosis," and "*Demodex*-associated rosacea" should not be used interchangeably: the first is a measurement, the second a clinicopathological diagnosis, and the third an etiological interpretation.

Addressing the case for broader testing

The strongest argument for broader testing is that rosacea and demodicosis overlap clinically, that high-density disease may be under-recognized, and that some treatment failures reflect an unaddressed mite burden [15,43,47]. This scenario is real. It is, however, an argument for testing when disease is atypical or refractory, which is precisely the selective strategy recommended here, rather than for testing every patient before first-line therapy. A second argument is that standardized sampling is inexpensive and low-risk. Low cost lowers the bar for a test but does not remove the requirement that its result alter a decision. A result that changes nothing still consumes clinical time, can generate misleading negatives, and may prompt unnecessary escalation when a high count is found in a patient who is already improving.

When testing changes practice

Selective Testing Is Useful When It Resolves a Genuine Diagnostic Problem (Moderate, Indirect)

Testing is reasonable when lesions are unusually folliculocentric, scaly, rough, asymmetric, corticosteroid-modified, or refractory to an adequate first-line course; when demodicosis is a meaningful alternative diagnosis; and when confirmation will change whether a *Demodex*-directed regimen is used [26,27,32]. In these settings, the value of testing lies not in proving causation but in reducing clinically relevant uncertainty. A high density obtained with a standardized protocol strengthens a *Demodex*-predominant interpretation; a low density weakens it only to the extent that the method and sampling were sufficiently sensitive.

If testing is performed, the report should state the method, facial site, sampled area, number of sequential samples, units, threshold applied, and species when feasible. Results should not be reported simply as positive or negative. For SSSB, local standardization is essential because repeat sampling and operator technique influence recovery [15,21]. Molecular, confocal, and UV methods are useful adjuncts, but their results must be interpreted against the reference standard used for their validation [22-25].

Phenotype, species, and biological context

Rosacea is biologically heterogeneous. Persistent erythema reflects neurovascular mechanisms, papules and pustules arise through several immune pathways, and follicular scale or roughness increases the plausibility of a *Demodex*-predominant process without being specific for it [1-5]. *D. folliculorum* and *D. brevis* differ in distribution and follicular ecology [48], so their relative recovery may depend on the sampling method. Small studies link UV dermoscopic features with *D. folliculorum* density and greater scale or pustulation with detection of both species [25,26] (limited evidence). *Demodex* has also been associated with activation of the transient receptor potential vanilloid 1-nerve growth factor-tropomyosin receptor kinase A (TRPV1-NGF-TrkA) neurogenic inflammatory pathway [49]. These findings explain why mites can matter biologically in some patients; they justify species-aware reporting when feasible, but they do not define a treatment threshold.

Practice recommendations

Table *2* summarizes the strength of support for each clinical claim, Table *3* translates that gradient into seven practice recommendations, and Figure *2* places them in a clinical pathway. The clinical endpoint throughout remains improvement in signs, symptoms, and patient goals.

Clinical claim	Conclusion	Evidence strength	Practice implication
Rosacea is associated with increased *Demodex* burden	Supported	Strong	*Demodex* is biologically relevant, but association is not a stand-alone diagnosis
Measured density is method-dependent	Supported	Strong	Report the protocol with every number
>5 mites/cm² is a universal disease threshold	Not supported	Moderate	Treat it as an operational, method-specific cut-off rather than a natural boundary
Dermoscopic *Demodex* signs identify demodicosis	Partly supported	Limited to moderate	Use to select patients for confirmatory sampling, not as a stand-alone test
Baseline density predicts who should receive ivermectin	Not validated	Limited	Do not use a low count to deny ivermectin or a high count to mandate it
Serial density is a surrogate for treatment success	Not validated	Limited	Use clinical response as the endpoint; repeat testing only for a defined question
Routine testing improves outcomes in typical rosacea	Not demonstrated	No direct evidence	Do not require testing before phenotype-directed treatment
Selective testing helps in atypical or refractory follicular eruptions	Supported as a decision aid	Moderate, indirect	Test when demodicosis is a meaningful differential diagnosis and the result will change management

TABLE 2: Clinical claims and strength of evidence

Evidence-strength categories are qualitative narrative appraisals based on study design, consistency, directness, and clinical applicability; they are not formal GRADE ratings. "No direct evidence" means that the claim has not been tested in an appropriate comparative pathway study.

GRADE: Grading of Recommendations Assessment, Development and Evaluation

No.	Recommendation	Principal basis	Evidence strength
1	Routine testing is not supported in a typical rosacea phenotype; select treatment by phenotype	No test-guided outcome trial; the result rarely changes the first-line choice [4,29,33,34]	No direct evidence of benefit
2	Consider testing when the eruption is folliculocentric, scaly or rough, asymmetric, corticosteroid-modified, or refractory to an adequate first-line course, and only if the result will change management	Clinical overlap with demodicosis; decision-changing value [15,26,27,32]	Moderate, indirect
3	Use dermoscopy to select patients for sampling; do not diagnose or exclude demodicosis on dermoscopy alone	Tails and follicular openings associated with SSSB positivity; accuracy modest in rosacea and higher in suspected demodicosis [25-28,30]	Limited to moderate
4	Do not use baseline density to withhold or mandate ivermectin	Low-count erythematotelangiectatic rosacea improved with either agent; no replicated biomarker interaction [29,34]	Limited; indirect for papulopustular rosacea
5	Judge response clinically; do not repeat counts as a routine target. Repeat only for a prespecified question (sampling failure, adherence, changed phenotype, competing diagnosis)	Count change dissociates from clinical success [29,36-40]	Limited
6	Report every result with method, site, sampled area, number of samples, units, threshold, and species when feasible; avoid positive/negative reporting	Density is protocol-dependent [15,20,21]	Strong
7	Keep terminology precise: increased density (measurement), demodicosis (diagnosis), and *Demodex*-associated rosacea (interpretation) are not synonyms	Commensal carriage in controls; overlapping distributions [5-10]	Strong

TABLE 3: Practice recommendations for Demodex testing in cutaneous rosacea

Recommendations are practice points derived from a narrative appraisal and are not formal GRADE-based guideline statements.

GRADE: Grading of Recommendations Assessment, Development and Evaluation; SSSB: standardized skin surface biopsy

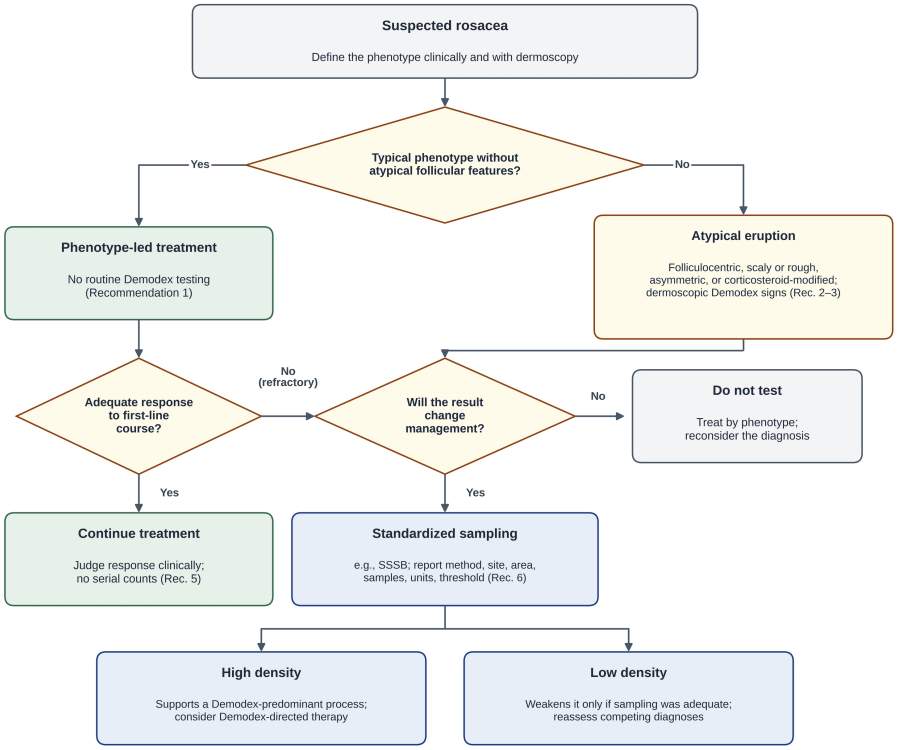


FIGURE 2: Decision pathway for Demodex testing in suspected rosacea

Management of a typical phenotype is phenotype-led without routine testing. Testing is reserved for atypical or refractory eruptions in which the result will change management; dermoscopy is used to select patients for standardized sampling, and every result is reported with its protocol and interpreted within the phenotype. This is an original schematic designed by the authors from the evidence summarized in this review. It was drawn in Python (matplotlib) using AI-assisted plotting code and verified by the authors; no image-generation model or previously published material was used (Table 3).

SSSB: standardized skin surface biopsy; Rec.: recommendation

Limitations

This review has important limitations. It is a narrative rather than a systematic review: the search relied on PubMed, Google Scholar, and citation chasing rather than multiple bibliographic databases; study selection and data extraction were performed by a single author; no protocol was registered; and the restriction to English-language publications may have omitted relevant studies. Evidence-strength labels were assigned by structured judgment rather than formal GRADE methodology, and no study-level risk-of-bias tool was applied. Relevant studies may therefore have been missed, and the categories should be interpreted as qualitative judgments rather than certainty ratings. These limitations are partly offset by the consistency of the central findings across methods and settings, but they underline the need for the comparative studies outlined below.

Research agenda

The decisive study has not yet been performed: a comparison of a prespecified *Demodex*-test-guided pathway with phenotype-guided care [12]. Such a trial should define the phenotype and competing diagnoses before testing, standardize sampling, prespecify thresholds and linked actions, and measure patient-centered outcomes. A complementary design would stratify patients by standardized baseline density and randomize acaricidal versus non-acaricidal therapy to test the treatment-by-biomarker interaction directly. Until such evidence exists, the role of testing is selective and decision-oriented rather than routine.

Conclusions

Evidence on *Demodex* testing in rosacea follows a clear gradient: it is strongest for association and measurement properties and progressively weaker for thresholding, treatment prediction, monitoring, and patient-outcome utility. The threshold of more than 5 mites/cm^2 is not a universal disease boundary, baseline density is not a validated treatment-selection biomarker, and serial mite reduction is not a validated surrogate for clinical benefit. Current evidence does not support routine testing in typical rosacea,

although this reflects an absence of comparative outcome data rather than proof that testing cannot help. Testing has its clearest role when an atypical, folliculocentric, scaly, asymmetric, corticosteroid-modified, or refractory eruption makes demodicosis a meaningful differential diagnosis and when the result will change the next decision. In that setting, a high count obtained with a standardized protocol supports a *Demodex*-predominant interpretation and may justify a *Demodex*-directed regimen, whereas a low count weakens that interpretation only if sampling was adequate and should not by itself exclude demodicosis or withhold ivermectin. Dermoscopy is a simple, non-invasive bedside step: *Demodex* tails and follicular openings raise pretest probability and help select patients for confirmatory sampling, but they neither establish nor exclude demodicosis on their own. The practical standard is simple: test only when the result has a defined purpose, report the protocol with the number, and interpret the number within the phenotype rather than in isolation.

Appendices

Ref	Study	Design	Population / n	Sampling or detection method	Threshold/comparison	Principal finding relevant to this review	Domain
5	Chang and Huang (2017)	Systematic review and meta-analysis	23 case-control studies; 1,513 patients	Various	Rosacea vs controls	Greater frequency of *Demodex* infestation in rosacea; considerable heterogeneity	Association
6	Forton and Seys (1993)	Case-control	49 rosacea (13 ETR, 3 SR, 33 PPR) and 45 controls	SSSB	>5 mites/cm² (98% specificity for PPR)	Higher *D. folliculorum* density in rosacea than controls	Association
7	Erbağci and Ozgöztaşi (1998)	Case-control	38 rosacea patients (25 PPR, 13 ETR) vs 38 age/sex-matched healthy controls	Standardized skin surface biopsy (cyanoacrylate glue, Marks & Dawber technique); 3 facial sites (cheek, forehead, nose); light microscopy x100/x200	>5 mites/cm2 threshold evaluated: 10/38 rosacea vs 5/38 controls exceeded it (not significant, p>0.05); sensitivity 0.26, specificity 0.86	Mean mite count significantly higher in rosacea (6.684) vs controls (2.868), p<0.05; but >5/cm2 threshold did not significantly discriminate groups; authors concluded density threshold alone is not an adequate diagnostic criterion	Association
8	Georgala et al. (2001)	Case-control	Papulopustular rosacea; n=92 vs 92 matched controls	-	Mite prevalence 90.2% (rosacea) vs 11.9% (controls); density 2.03 vs 0.16 mites/field	Increased *D. folliculorum* density; evidence of delayed hypersensitivity	Association
9	Moravvej et al. (2007)	Case-control	75 rosacea patients (cases) vs 75 discoid lupus erythematosus + 75 actinic lichen planus patients (two control groups)	Facial skin biopsy (mite presence/prevalence assessed histologically)	Prevalence comparison across 3 groups (no numeric density threshold reported)	*Demodex* prevalence significantly higher in rosacea (38.6%) vs discoid lupus erythematosus (21.3%) and actinic lichen planus (10.6%), p<0.001	Association
10	Casas et al. (2012)	Multicentre prospective case-control study	50 rosacea (18 ETR, 32 PPR) and 48 controls	Quantitative PCR	Rosacea vs controls	*D. folliculorum* detected in 96% of rosacea vs 74% of controls; density 5.7x higher in rosacea; link to innate immune activation	Association
14	Ríos-Yuil and Mercadillo-Perez (2013)	Retrospective case-control	Skin biopsies; equal-sized rosacea and control groups	Histopathology of skin biopsies	Presence/absence of mites on histopathology	Detection 80% (rosacea) vs 30% (controls); OR 9.33; density 1.908 vs 0.718 mites/HPF (p=0.0001)	Association
15	Forton and De Maertelaer (2017)	Diagnostic accuracy study	1,044 patients (retrospective)	2 consecutive SSSBs	1st SSSB >5 mites/cm² OR 2nd SSSB >10 mites/cm² (combined criterion)	Sensitivity 98.7%, specificity 95.5% in a combined rosacea/demodicosis framework; second sample reclassified some patients	Method; threshold
16	Aşkin and Seçkin (2010)	Method comparison	37 patients with suspected demodicosis (23 diagnosed, 62%)	SSSB vs DME	>5 mites/cm^2	SSSB yielded far higher counts than DME (all: 22.9±5.9 vs 2.2±0.8, p=0.001; diagnosed subgroup: 36.5±8.3 vs 3.4±1.2, p=0.0001); SSSB identified more demodicosis cases	Method
17	Yun et al. (2017)	Retrospective method comparison	35 patients with demodicosis (retrospective, Dec 2011-Jun 2015)	SSSB vs DME	>5 mites/cm² (high-density cut-off)	DME yielded higher density than SSSB across subtypes; rosacea-type: DME 12.4±3.5 vs SSSB 3.6±1.2 mites/cm² (84.6% vs 23.1% high-density)	Method
18	Huang et al. (2020a)	Method development	40 papulopustular rosacea patients and 35 acne vulgaris controls	Superficial needle scraping	>=3 mites per 5 pustules	PPR density 5.6+/-4.2 vs acne 0.3+/-1.0 (p<0.001); 78% sensitivity, 97% specificity, AUC 0.89 vs SSSB; concordant with SSSB in ~50%	Method

19	Huang et al. (2020b)	Method development	-	Thumbnail squeezing	Method-specific cut-off	-	Method; threshold
20	Pérez Wilson et al. (2025)	Prospective comparison	61 patients with rosacea	SSSB vs DME	>5 mites/cm²	Median 11 vs 1 mites/cm²; >5 mites/cm² in 64% vs 28%	Method; threshold
21	Ozdemir Cetinkaya et al. (2024)	Prospective cross-sectional	200 rosacea patients (99 ETR, 101 PPR)	SSSB	Density <5 D/cm^2 triggered repeat SSSB (up to 5 attempts)	Detection rose from 62.5% (1st biopsy) to 87% (5th); PPR detection lower than ETR (54.5% vs 70.7%); ETR had higher median density than PPR	Method
22	Trave et al. (2024)	Case-control	20 papulopustular rosacea (17F/3M, mean age 50.45y) and 10 controls (8F/2M, mean age 49.7y)	Microscopy vs PCR	Microscopy vs PCR positivity	Sensitivity at the face approximately 93.8% by PCR vs 50% by microscopy	Method
23	Sattler et al. (2012)	Diagnostic study	25 rosacea patients and 25 matched controls	RCM	Quantitative RCM mosaic (8x8mm and 5x5mm)	Non-invasive in vivo detection and quantification	Method
24	Turgut Erdemir et al. (2014)	Method comparison	48 patients (30F/18M; pityriasis folliculorum n=40, papulopustular rosacea n=7, erythematotelangiectatic rosacea n=1) vs 47 age/gender-matched healthy controls (30F/17M)	RCM vs SSSB	SSSB positivity threshold >5 mites/cm2: 42/48 patients positive (85.7%); RCM identified demodicosis in 48/48 (100%)	Mean *Demodex* density by RCM (409.8+/-209.2) significantly higher than by SSSB (15.33+/-18.1), p<0.001; RCM detected more infested follicles and mites per follicle than SSSB in both patients and controls (p<0.001); RCM concluded superior to SSSB for detection	Method
25	Ünal et al. (2026)	Diagnostic accuracy study	54 patients with rosacea/demodicosis (cross-sectional, Jan-Oct 2023)	UV dermoscopy vs SSSB	SSSB reference	Sensitivity 82.1%, specificity 71.4%, AUC 0.793	Method; dermoscopy
26	Serarslan et al. (2021)	Cross-sectional	30 patients; 83 areas	Dermoscopy vs SSSB	SSSB positivity	*Demodex* tails in 88% of positive samples; more scale and pustules when both species present	Dermoscopy; species
27	Trave et al. (2021)	Comparative observational	60 patients with papulopustular rosacea	Dermoscopy vs SSSB	≥5 mites/cm²	Dermoscopy sensitivity 50%, specificity 77.5% for *D. folliculorum*	Dermoscopy
28	Parra-Cares et al. (2024)	Retrospective intrapatient case-control	64 adults with suspected demodicosis; 256 samples	Dermoscopy vs skin scraping	Tails, follicular openings, dilated vessels; per-field counts	Tails 11-20/field: positive LR 12.10, negative LR 0.32; combined signs: positive LR 7.14, negative LR 0.11	Dermoscopy
29	Yeh et al. (2022)	Rater-blinded randomized split-face trial	Erythematotelangiectatic rosacea with low *Demodex* density; 33 screened, 27 completed	Squeeze method and SSSB at 4 facial sites	Entry below cut-offs (squeeze >11/cm²; SSSB >5/cm²); baseline mean 0.6-0.7 mites/cm²	Equivalent improvement in erythema with metronidazole and ivermectin at 3 months	Prediction
30	Faik et al. (2026)	Case-control	121 patients with facial dermatoses (pityriasis folliculorum 69.4%, rosacea 5.8%) and 121 controls	Dermoscopy and SSSB	SSSB elevated density	Mites on dermoscopy in 73.6% vs 1.7% of controls; elevated SSSB density in 66.9% vs 1.7%	Dermoscopy; method
31	Plozner et al. (2026)	Prospective non-randomized comparative	23 patients with moderate-to-severe papulopustular rosacea	Clinical and dermoscopic assessment	Ivermectin vs metronidazole, 8 weeks	Baseline dermoscopic features associated with optimal ivermectin response; exploratory	Prediction; dermoscopy
32	Kara and Özden (2021)	Observational	23 rosacea patients (17F/6M, mean age 49); 15 with concurrent demodicosis	Dermoscopy	Dermoscopy vs biopsy concordance	Dermoscopic findings of rosacea and demodicosis	Dermoscopy
34	Schaller et al. (2017)	Open-label pilot study	Moderate-to-severe papulopustular rosacea; n=20	-	Topical ivermectin 1%	Ivermectin 1% reduces *Demodex* density and downregulates innate inflammatory mediators (LL-37, IL-8, human beta-defensin 3, TLR4, TNF-alpha): dual anti-inflammatory/anti-parasitic action	Mechanism; treatment
36	Sattler et al. (2015)	Prospective monitoring study	25 patients with facial rosacea	RCM	Before vs after treatment	Density measured before and after treatment	Monitoring
37	Logger et al. (2022)	Prospective monitoring	20 patients with rosacea	RCM	Topical ivermectin	Mite density declined during ivermectin treatment; lesion-level correlation weak; no confocal variable	Monitoring

		study				predicted treatment success	
38	Huang et al. (2021)	Retrospective interventional study	39 patients (persistent erythema, high baseline *Demodex* density)	Thumbnail squeezing (serial)	Topical ivermectin ± oral carvedilol	Ivermectin alone or with oral carvedilol reduced erythema and mite density; correlation between changes moderate (rho=0.50, p=0.002)	Treatment; prediction
39	Temiz et al. (2022)	Retrospective treatment monitoring	Rosacea; n=34 (27 women, 7 men)	SSSB (cyanoacrylate, 1 cm^3, cheek)	Before vs 4 weeks after 577-nm pro-yellow laser	Mean density 18.1 ± 10.7 to 10.2 ± 7.9 mites/cm^2 (p = 0.001); decrease not correlated with regression of erythema (p = 0.46)	Monitoring
40	Trave et al. (2022)	Prospective observational cohort	Papulopustular rosacea; n=60 (45 women, 15 men; mean age 57y)	Standardized skin surface biopsy (SSSB), 1 cm^2 of stratum corneum examined at 10x/40x; positive threshold >=5 *Demodex*/cm^2	Ivermectin 1% cream	*Demodex* remission in 87.5% (12.5% relapse); complete clinical response in 70%; global success 54.76%; median time to relapse 140 days	Monitoring
41	Raoufinejad et al. (2016)	Double-blind randomized controlled trial	Papulopustular rosacea; n=20 (within-patient bilateral comparison)	-	Permethrin 5% gel vs placebo	*Demodex* density significantly reduced in both groups; greater reduction with permethrin 5% vs placebo (p<0.05)	Treatment
42	Ebneyamin et al. (2020)	Double-blind controlled trial	Papulopustular rosacea; n=47 enrolled (35 completed; within-patient bilateral comparison)	-	Permethrin 2.5% with tea tree oil	*Demodex* density significantly reduced from week 5 onward (p=0.001) with permethrin 2.5%+TTO vs placebo; improved papules, pustules, erythema, burning, stinging, dryness (p<0.05)	Treatment
43	Forton and De Maertelaer (2020)	Retrospective	394 patients (117 with rosacea; 278 women; mean age 49y)	-	Crotamiton 10% AM + BB 12% PM; BB 12% BID; or BB 20-24% QD (with crotamiton)	Effects on density and clinical symptoms	Treatment; monitoring
44	Trave et al. (2019)	Real-life observational	-	-	Topical ivermectin	Effectiveness, tolerability, and antiparasitic effect	Treatment; monitoring
45	Yang et al. (2023)	Single-center randomized evaluator-blind trial	44 randomized (41 completed: ALA-PDT 20, minocycline 21)	-	ALA-PDT (3-5 sessions) vs oral minocycline 100mg/day x8wk; 24wk follow-up	Comparable lesion reduction and QoL improvement between groups; erythema success lower with ALA-PDT (35% vs 67%); *Demodex* density change comparable between groups	Treatment
46	Turgut Erdemir et al. (2017)	Comparative cross-sectional study	Acne rosacea; n=60 (30 papulopustular, 30 erythematotelangiectatic) + 40 healthy controls	RCM	RCM mean mite count cut-off >=0.17 for infestation	*Demodex* density markedly increased in both PPR and ETR vs controls	Method; association
47	Forton and De Maertelaer (2021)	Retrospective pilot study	n=1044 (844 *Demodex*-positive; 200 *Demodex*-negative)	Two consecutive standardized skin surface biopsies (SSSB1 superficial + SSSB2 deep) from same facial site	*Demodex*+ mean density 263.5 +/- 8.9 D/cm^2 vs *Demodex*- 2.3 +/- 0.4 D/cm^2	Factors associated with *Demodex* proliferation	Biology
48	Aylesworth and Vance (1982)	Biopsy series	Consecutive dermatopathology biopsy series-	Histopathology	10% of biopsies / 12% of follicles positive; prevalence increased with age; facial predominance; *D. brevis* more widely distributed; higher counts in males	Distribution of *D. folliculorum* and *D. brevis* in cutaneous biopsies	Species

TABLE 4: Characteristics of the 39 studies appraised in the review

Reference numbers correspond to the reference list of the main article.

Context-only references (consensus statements [1-4], methodological papers [11,12,33], ocular trial [13], editorial [35], and mechanistic study [49]) are not listed.

ALA-PDT: 5-aminolevulinic acid photodynamic therapy; AUC: area under the receiver operating characteristic curve; DME: direct microscopic examination; ETR: erythematotelangiectatic rosacea; HPF: high-power field; LR: likelihood ratio; OR: odds ratio; PCR: polymerase chain reaction; PPR: papulopustular rosacea; RCM: reflectance confocal microscopy; SR: squamous rosacea; SSSB: standardized skin surface biopsy; UV: ultraviolet; -: detail not extracted for this review

Additional Information

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All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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