

## REVIEW ARTICLE

# Burden of Disease: The Psychosocial Impact of Rosacea on a Patient's Quality of Life

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**Background:** Rosacea is a chronic skin disorder that adversely affects patients' quality of life. Current studies focus on the therapies that treat the clinical signs and symptoms of rosacea, but the impact of this disease on patients' emotional health and quality of life is often overlooked.

**Objectives:** To describe the disease burden of rosacea and the psychosocial implications on patients' quality of life and to review the current understanding of the disease and the available therapies.

**Discussion:** The facial skin manifestations of rosacea have significant implications on patients' well-being and social and emotional health. The 4 clinical subtypes of this disease include erythematotelangiectatic, papulopustular, phymatous, and ocular, and patients may present with more than 1 subtype. Patients with rosacea have reported a negative burden of their disease, such as low self-esteem, low self-confidence, and decreased social interactions. Improvement of the clinical symptoms of rosacea improves the patient's emotional well-being and quality of life. Several topical medications and 1 oral medication have been approved for the treatment of rosacea. Although current therapies do not cure the disease and do not treat the facial erythema associated with it, they do treat the papules and pustules associated with this condition. Proper management of the signs and symptoms of rosacea has been shown to improve patients' quality of life.

**Conclusion:** The self-perception of disease severity varies among patients with rosacea, so physicians should carefully consider each patient's concerns when prescribing a treatment regimen. Although no cure exists, effective treatment options aid in the management of signs and symptoms of rosacea. New therapies that treat the broad range of rosacea symptoms are needed.

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Rosacea is a common and chronic skin disorder with characteristic signs and symptoms, including flushing, facial erythema, inflammatory papules and pustules, telangiectasia, edema, and watery or irritated eyes.<sup>1</sup> Four clinical subtypes of rosacea have been characterized, including erythematotelangiectatic, papulopustular, phymatous, and ocular.<sup>2</sup> It is common for patients to present with more than 1 subtype.

The erythematotelangiectatic subtype of rosacea has been described as the most difficult subtype to treat.<sup>3</sup> The clinical features of this subtype include flushing and persistent central facial erythema, and telangiectasia may also be present (Figure 1).<sup>3</sup>

The papulopustular subtype of rosacea has been sometimes described as resembling acne vulgaris. The

clinical features of this subtype include persistent central facial erythema and transient papules and pustules, and facial edema may be present (Figure 2).<sup>3</sup>

The phymatous subtype of rosacea, which is more common in men, includes thickening skin and irregular surface nodularities (Figure 3). Rhinophyma is the most common type of phymatous rosacea.<sup>3</sup>

Although no exact prevalence data exist, the symptoms and signs of the ocular subtype of rosacea are estimated to affect nearly 60% of patients with rosacea.<sup>3</sup> The clinical features of this subtype include watery or bloodshot eyes, telangiectasia of the conjunctiva and lid margin, and lid and periocular erythema (Figure 4). The common clinical presentations of this subtype include blepharitis, conjunctivitis, and keratitis. Patients with ocular rosacea experience discomfort in the eye including foreign body sensation, light sensitivity, and blurred vision.<sup>3</sup>

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**Figure 1** Subtype 1: Erythematotelangiectatic Rosacea



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**Figure 2** Subtype 2: Papulopustular Rosacea



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**Figure 3** Subtype 3: Phymatous Rosacea



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**Figure 4** Subtype 4: Ocular Rosacea



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### Epidemiology and Triggers of Rosacea

Rosacea is more prevalent in fair-skinned people of Northern European and Eastern European descent, but it has also been reported in people of other ethnicities.<sup>3-5</sup> Women are more frequently affected than men, with onset of this condition generally occurring between the ages of 30 and 50 years, although rosacea has been reported in the teenaged years.<sup>6,7</sup>

Heredity has also been implicated as a factor leading to the development of rosacea.<sup>8</sup> A National Rosacea Society survey of 600 patients with rosacea showed that

nearly 52% of survey respondents also had a family member with the disease, and 42% reported that they were of Irish, German, or English descent.<sup>8</sup>

The factors that are believed to trigger or to exacerbate rosacea include sun exposure, stress, hot and cold weather, the consumption of hot beverages or alcohol, and eating spicy foods.<sup>3</sup>

Rosacea affects more than 16 million people in the United States.<sup>1</sup> Between 1990 and 1997, there were approximately 1.1 million outpatient visits, annually, for rosacea in the United States.<sup>9</sup> Based on data compiled by Galderma Laboratories, LP, on office visits for rosacea, between October 2011 and September 2012 there were 1.67 million office visits in the United States, with 75% of the visits conducted with dermatologists.<sup>10</sup> Although this is a relatively small patient population, patients with rosacea seek treatment because of the burden of their disease and their poor quality of life.

The goal of current therapies is to manage the clinical signs and the physical symptoms of rosacea, but the impact

## KEY POINTS

- Rosacea is a chronic facial skin disorder that affects patients' emotional health and quality of life, but these factors are often overlooked in the management of symptoms.
- The pathophysiology of rosacea is not fully understood but is believed to be an inflammatory disorder.
- The 4 clinical subtypes of rosacea include erythematotelangiectatic, papulopustular, phymatous, and ocular; the clinical manifestations include flushing, facial erythema, inflammatory papules and pustules, telangiectasia, edema, and watery or irritated eyes.
- Although there is no cure for this disorder, current treatments can aid in the management of some signs and symptoms and improve patients' quality of life.
- Available therapies do not address the persistent facial erythema associated with rosacea; ongoing research is focused on this symptom.
- Physicians need to consider the patient's self-perception of rosacea when prescribing a treatment regimen.

of rosacea on patients' emotional health and quality of life is sometimes overlooked. It is important for physicians to consider each patient's self-perception when prescribing a treatment regimen for this chronic condition.

### The Pathophysiology of Rosacea

The pathophysiology of rosacea is poorly understood, and many mechanisms have been implicated in this disease.<sup>11</sup> Multiple intrinsic and extrinsic factors, such as climatic exposure, vasculature, dermal matrix degeneration, chemical and ingested agents, pilosebaceous unit abnormalities, genetic susceptibility, and interactions with microbial organisms, may play a role in the pathogenesis of this disease.<sup>12</sup>

Inflammation is believed to be one of the main underlying factors leading to the signs and the symptoms of rosacea.<sup>13,14</sup> Antimicrobial peptides, processing enzymes, and toll-like receptors may be involved in the promotion of inflammation.<sup>15</sup> Elevated epidermal serine protease activity and the deposition of cathelicidin-derived peptides in the skin have been identified in inflammatory lesions of rosacea.<sup>16</sup> A proposed mechanism of action for inflammation in rosacea may involve the production of neuropeptides, which may play a role in generating and maintaining inflammation.<sup>1,15</sup> Some of these neuropeptides have been found to be in higher amounts in the skin of patients with rosacea.<sup>17,18</sup>

Rosacea may be a vascular disorder because of its association with flushing, redness, and visible blood vessels. The supportive data suggest that mast cells may participate in a complex multifactorial process to promote localized vasodilation, angiogenesis, and tissue fibrosis.<sup>15</sup> Physicians have also speculated that flushing may involve the nervous system, because rosacea is often either triggered or aggravated when patients are under emotional stress.<sup>19-21</sup>

The microscopic mite *Demodex folliculorum* has been considered a potential contributor to the pathogenesis of rosacea.<sup>22,23</sup> *D folliculorum* are normal inhabitants of the human skin that consume cast-off cells. They reside predominantly in the lumina of sebaceous follicles and use sebum for nourishment.<sup>24</sup> These mites were found to be substantially more common in patients with rosacea than in control individuals.<sup>25-27</sup> The treatment of rosacea with systemic retinoids inhibited the production of sebum and the number of mites was subsequently reduced.<sup>28,29</sup>

### Psychosocial Impact of Rosacea

The clinical severity of rosacea does not correlate with the level of psychosocial distress experienced by the patient. This psychosocial impact has been documented with studies reporting increased depression rates among patients with rosacea.<sup>30,31</sup> One analysis revealed that 65.1% of patients with rosacea who had a comorbid psychiatric diagnosis also had a diagnosis of depression.<sup>31</sup> This is a much higher proportion than the 29.9% prevalence of depression reported for all psychiatric patient visits.<sup>31</sup>

The clinical signs and symptoms of rosacea occur predominantly in the facial region and therefore affect the patients' physical appearance. It has been observed in other dermatologic conditions that patients can suffer from emotional stress if the areas that are affected are visible.<sup>32</sup> Physical appearance as perceived by patients with rosacea can negatively influence their emotional health, resulting in psychological comorbidities such as anxiety disorders and social phobias.<sup>33</sup> A survey conducted by the National Rosacea Society with more than 400 patients with rosacea revealed that 75% of respondents reported that their rosacea had lowered their self-esteem.<sup>34</sup> In addition, the majority of respondents reported that their rosacea made them feel embarrassed (70%) and frustrated (69%). More than 50% of respondents reported that they felt robbed of pleasure or happiness because of their rosacea.<sup>34</sup>

Patients with rosacea have also reported having depression and anxiety because of their disease.<sup>33</sup> The effect of rosacea on quality of life was described to be similar to leg ulcers, vitiligo, and occupational contact dermatitis.<sup>35</sup>

Body dysmorphic disorder is a psychiatric condition that describes the preoccupation with a defect in physical appearance.<sup>36</sup> Symptoms of body dysmorphic disorder can



significantly disrupt daily function and have been reported in patients with acne.<sup>36</sup> Although body dysmorphic disorder has not been examined in patients with rosacea, this may also be applicable to patients with rosacea based on the similarities between the symptoms of acne vulgaris and the symptoms of rosacea in some patients and should be considered when evaluating patients with rosacea.

Patients with rosacea are affected by emotional and social stigmas, including being viewed as abusers of alcohol or as having poor hygiene.<sup>14</sup> One survey conducted by Kelton Research evaluated patients' self-perception and the perception of others regarding patients with rosacea.<sup>37</sup> This online "perception survey" contrasted images of women with and without rosacea.<sup>37</sup> More than 1000 members of the general population and 502 women with rosacea completed the online survey between October 29, 2009, and November 9, 2009. Women with rosacea were perceived to be more insecure, not as healthy, not as intelligent, and not as successful as women with clear skin. Overall, respondents with and without rosacea had negative first impressions of women with rosacea.<sup>37</sup>

### Burden of Disease

Collectively, skin diseases are one of the top 15 groups of medical conditions for which prevalence and health-care spending increased the most between 1987 and 2000.<sup>38</sup> The economic burden of skin disease on the US healthcare was approximately \$96 billion in 2004.<sup>38</sup>

Willingness to pay is a monetary- and preference-based measurement that is used to evaluate an individual's burden of disease by focusing on the amount of money that patients would be willing to pay for a hypothetical cure. In addition to evaluating the burden of disease, willingness to pay is a measure that has been used to indirectly evaluate quality of life in patients with skin diseases.<sup>39-41</sup>

In one study by Beikert and colleagues, data from questionnaires completed by 475 patients with rosacea were analyzed and willingness to pay was examined.<sup>42</sup> This population consisted of 79.9% women with a mean age of 56.3 years. When asked to pay a percentage of their monthly income for a complete healing (relative willingness to pay), more than half (60.3%) of the patients reported that they would invest 0% to 10% of their monthly income, 28.3% would invest 10% to 20% of their monthly income, and 11.4% would invest more than 20% of their monthly income.<sup>42</sup> Women between the ages of 21 to 30 years showed the greatest relative willingness to pay. Beikert and colleagues reported that patients in this study showed a "moderate willingness to pay"; according to the authors, this suggests that these patients perceived their disease to be a major burden affecting their quality of life and that they were willing to pay for their treatment.<sup>42</sup>

A retrospective claims database study sponsored by Galderma Laboratories, LP, using the IMS LifeLink health plan claims database, which encompasses more than 79 managed care health plans covering more than 70 million lives, examined patients with at least 1 diagnosis of rosacea.<sup>43</sup> The 99,894 patients included in this study were at least 29 years of age and had continuous eligibility for medical and pharmacy services for 12 months after an initial prescription for a drug to treat rosacea. Most patients (73.2%) were women with a mean age of 52.4 years. The all-cause mean annual total cost was \$6707, of which \$4510 was for medical costs and \$2197 was for pharmaceutical costs.<sup>43</sup> The mean total rosacea-related cost was \$347 (5.2% of all-cause costs), with a mean annual rosacea-related medical cost of \$56 (1.2% of all-cause medical costs) and a mean annual rosacea-related pharmacy cost of \$291 (13.3% of all-cause pharmacy costs).<sup>43</sup> The patients averaged 1.1 physician visits annually, and 58% of them saw a dermatologist during the 12-month study period.<sup>43</sup>

A national survey conducted in 2006 aimed to gain insight into patients' experiences with rosacea therapies and patients' relationships with their healthcare providers.<sup>44</sup> The patients reported that their relationship with their physicians was important, and that it played a role in the management of their disease.<sup>44</sup> Patient education about the chronic nature of rosacea is also important. Understanding that daily treatment can improve the symptoms of this chronic disease may increase patient adherence to prescribed treatment regimens. Patient education, along with a continued patient-physician relationship, can promote treatment adherence and improve patient satisfaction.<sup>44,45</sup>

### Quality of Life

The Dermatology Life Quality Index (DLQI), which was developed in 1994, was the first dermatology-specific quality-of-life instrument. The DLQI is a validated 10-item questionnaire that has been used to evaluate quality-of-life issues in more than 33 skin conditions. In a study of 308 patients with rosacea, 164 patients completed the DLQI after treatment.<sup>7</sup> The results of this study suggested that rosacea affects quality of life to a moderate extent and that improvement in quality of life after treatment may be related to the patients' sex, type of treatment modality, development of side effects, improvement of rosacea, rosacea severity, and self-reported ease of living with rosacea.<sup>7</sup> In another study, 22 patients with erythematotelangiectatic rosacea completed the DLQI questionnaire before and after 3 pulsed dye laser treatment sessions.<sup>46</sup> A significant improvement was observed in the DLQI score after 3 sessions, and all patients were judged by the investigators to have improved facial erythema.<sup>46</sup>

Currently, no validated rosacea-specific quality-of-life instrument exists. In a preliminary study, one rosacea-specific instrument, RosaQoL, was found to be reliable.<sup>47</sup> This pilot instrument consists of a 21-item rosacea-specific questionnaire.<sup>47</sup> In a large 12-week trial of more than 1400 patients, RosaQoL was used to evaluate their quality of life.<sup>48</sup> This study demonstrated that the impaired quality of life in subjects with rosacea was substantially improved during a 3-month period with effective treatment.<sup>48</sup>

### Treatment Options

Currently, there is no cure for rosacea.<sup>49</sup> Available treatments are aimed at managing the signs and symptoms, which can worsen without treatment. Appropriate treatment can minimize the psychosocial impact of rosacea on the patient. The 3 topical agents approved by the US Food and Drug Administration (FDA) for the topical treatment of rosacea are metronidazole, azelaic acid, and sodium sulfacetamide-sulfur.<sup>49,50</sup>

**It is important to consider the self-perception of rosacea by patients when prescribing a treatment regimen. The impact of rosacea on the patient's emotional health and quality of life has been underestimated or overlooked.**

Currently, doxycycline 40 mg (30 mg immediate-release and 10 mg delayed-release) is the only FDA-approved oral drug indicated for the treatment of the inflammatory lesions (ie, papules and pustules) of rosacea.<sup>50</sup> No approved treatment is currently available for the facial erythema that is associated with rosacea.

Metronidazole gel 1% is a nitroimidazole indicated for the topical treatment of the inflammatory lesions of rosacea. Although the mechanism of action in rosacea is unknown, metronidazole has antioxidant and anti-inflammatory effects. Significant decreases in the inflammatory lesions of rosacea have been reported in multiple clinical studies.<sup>51-54</sup> The most common adverse reactions (incidence, >2%) are nasopharyngitis, upper respiratory tract infection, and headache.<sup>51-54</sup>

Azelaic acid gel 15% is indicated for the topical treatment of the inflammatory papules and pustules of mild-to-moderate rosacea. The exact mechanism of action of azelaic acid gel is also unknown. Several studies indicated that azelaic acid may exert anti-inflammatory effects in patients with rosacea.<sup>55-59</sup> The adverse events reported in a 15-week clinical trial of azelaic acid gel included burning; stinging or tingling; dryness, tightness, or scaling; itching; and erythema, irritation, or redness.<sup>57</sup>

Tetracycline, the mainstay of oral antibiotic therapy, has been used as an off-label treatment for rosacea since the 1950s.<sup>60-62</sup> Tetracycline is believed to affect inflammation, immunomodulation, cell proliferation, and angiogenesis.<sup>60,63</sup> One concern with the long-term use of tetracycline has been antibacterial resistance.<sup>63</sup> The common adverse reactions observed in patients receiving tetracyclines at higher, antimicrobial doses include nausea, vomiting, diarrhea, dysphagia, and inflammatory lesions (with vaginal candidiasis) in the anogenital region.<sup>60,63</sup>

Doxycycline 40 mg (30 mg immediate-release and 10 mg delayed-release) is indicated for the treatment of only inflammatory lesions (ie, papules and pustules) of rosacea in adult patients. Doxycycline 40 mg provides anti-inflammatory activity at a subantimicrobial dose with a reduced risk of bacterial resistance compared with higher doses of doxycycline.<sup>62-66</sup> It has been demonstrated that administration of this subantimicrobial dose of doxycycline (40 mg) once daily for 9 months did not lead to the development of antibiotic resistance in patients with periodontal disease.<sup>67</sup> The most common adverse reactions reported in clinical trials (incidence, >2%; more common than with placebo) are nasopharyngitis, sinusitis, diarrhea, hypertension, and an increase in aspartate aminotransferase.<sup>64-66</sup>

### Conclusions

Rosacea is a lifelong condition that adversely affects the emotional health and quality of life of patients. Although only a small percentage of patients with rosacea will seek professional advice and treatment, studies and national surveys have indicated that these individuals perceive their disease to be a burden, and they are motivated to address the adverse effects of this condition on their quality of life. Physicians need to be reminded of the psychosocial aspects of rosacea. It is important to consider the self-perception of rosacea by patients when prescribing a treatment regimen.

The impact of rosacea on the patient's emotional health and quality of life has been underestimated or overlooked. Surveys conducted by the National Rosacea Society and by Kelton Research have indicated that people have a negative impression of patients with rosacea.<sup>34,37</sup> Regarding symptoms, including symptoms of persistent erythema predominantly in the central facial region, patients with rosacea have reported avoiding social interactions and their workplace productivity may be impacted. In addition, patients with rosacea are willing to pay for their treatments, suggesting that they perceive their disease to be a burden.

The visible facial erythema and blemishes that are associated with rosacea can negatively affect patients' emotional health. The improvement of the clinical

symptoms of rosacea improves the patients' emotional well-being. Current therapies treat the papules and pustules that are associated with rosacea, but no approved therapies target persistent facial erythema. There is no evidence that current therapies have a direct effect on erythema. This suggests an unmet medical need for treatments that will specifically target the persistent facial erythema associated with rosacea. Nevertheless, the treatment of the papules and pustules characteristic of rosacea by approved therapies improves patient quality of life. New therapies currently in development may be able to treat the broad range of symptoms of rosacea. ■

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## STAKEHOLDER PERSPECTIVE

### The Psychosocial Impact of Skin Disorders: Time for a Closer Look?

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The article by Dr Huynh on the psychosocial aspects of rosacea in this issue of *American Health & Drug Benefits* introduces a topic that is not at the forefront of healthcare concerns for policymakers, payers, or even primary care physicians. However, as this article makes clear, the emotional toll and impact on a patient's quality of life merits a renewed look at this condition.

**PAYERS:** Dermatology is not a clinical area that is top of mind for most payers, particularly for skin conditions that do not require specialty medications. Unlike psoriasis, which is on the payer's radar, with annual treatment costs in the \$30,000 range, treatment options for acne and rosacea may not carry as much priority for payers, or the risk for potentially high costs associated with inappropriate drug use. However, drug therapies for dermatologic conditions, particularly oral therapies, have not been completely off the radar for payers. Increasing numbers of oral and topical medications for dermatologic conditions, including rosacea, have become more costly and can place a financial burden on patients, and eventually on payers. Monthly costs can reach between \$100 and \$900, which can amount to a considerable copayment or coinsurance for some patients, especially for those who are underinsured or who have a large coinsurance amount.

**PATIENTS:** Several studies and patient surveys have zeroed in on the psychological distress, social stig-

ma, and reduced quality of life that are characteristic of patients with rosacea.<sup>1-5</sup> Moreover, a small study has documented 16 patients with dermatologic conditions, including acne and rosacea, who committed suicide after presenting to their physician with skin problems, prominently facial skin disorders,<sup>6</sup> shedding light on the potential for severe depression that could accompany a chronic skin condition, which nevertheless is often being misperceived as mainly a cosmetic problem.

**PROVIDERS:** Providers should consider the psychosocial impact of rosacea on the patient when choosing the best approach to therapy. Various therapeutic options are available today, but cost may become a consideration as well. Providers should work closely with patients, and, if necessary, with payers, to ensure that proper management is available to all patients with this chronic and potentially debilitating disorder.

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