Reviewing the global burden of acne: how could we improve care to reduce the burden?

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Summary

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Acne (also known as acne vulgaris) remains the most common inflammatory dermatosis treated worldwide, as estimated by global skin disease prevalence studies. Latest reports suggest that the prevalence may be increasing in adolescents and adults, particularly female adults. The concept of 'burden of skin disease' is multidimensional and can be difficult to quantify in light of different healthcare systems across the globe. In acne, the resulting burden may vary according to patient demographics, access to treatments and duration of the disease. The visible nature of acne, symptoms and sequelae all contribute physically and psychosocially to the overall burden of disease, as do the costs required for management. Acne typically presents in adolescence at a time of significant transition. Profound effects on functional status have been demonstrated, along with a strong impact on interpersonal relationships, social functioning and mental health. The high prevalence of acne also presents an economic burden for society. The widespread and prolonged use of antibiotics introduces a potential added burden through resulting antimicrobial resistance. A James Lind Alliance Acne Priority Setting Partnership has identified numerous areas to inform future research, which would help to improve acne management and reduce the burden. The lack of standardized assessments is a major issue in acne trials and challenges the ability to compare treatments and perform meta-analyses. This paper reviews the current literature on burden of acne, identifies areas of treatment uncertainties and summarizes the work of the Acne Core Outcome Research Network as a means of supporting a reduction in the burden of disease.

What is already known about this topic?

- Acne is one of the most common inflammatory dermatoses seen worldwide.
- A number of different factors have been implicated in causing burden related to acne.
- Acne assessments are challenged owing to the lack of standardized approaches.

What does this study add?

- This study provides an up-to-date review of the current state of our understanding of the global burden of acne.
- This review highlights work related to developing agreed standardized tools to improve the assessment of acne.
- We identify areas for future research to complete gaps in our knowledge, which would translate into better care.

Acne is one of the most common inflammatory skin conditions seen globally. The pathophysiology is a complex interplay of hormonally stimulated sebum production, abnormal keratinization of the pilosebaceous duct and an immune response to *Cutibacteria acnes* (formerly *Propionibacterium acnes*) centred around the pilosebaceous unit. The role of innate immunity and inflammation are key factors in all acne lesions and sequelae.[1] The high prevalence and associated clinical and psychosocial sequelae all lead to significant disease burden across the globe.

Diagnosis and assessment

Acne activity is reflected by typical lesions, which include comedones and inflammatory lesions (papules, pustules, nodules). Acne may also manifest as cysts, macular erythema, pigment changes, excoriations or scars. Although acne is easily recognized, clinical assessment remains challenged by the lack of a universally adopted, standardized severity grading tool(s) and agreed minimal diagnostic criteria.[2]

Efforts to develop a single agreed acne severity grading system remain unresolved, with 25 different systems reported in the literature.[3] Both nominal and numerical scales are utilized. These currently reflect global assessments based on descriptive terms/reference photographs and lesion counts. Both systems have aspects of objectivity, but subjectivity remains a challenge.[4] The US Food and Drug Administration recommends both approaches in trials. This leads to discrepancies in outcome measures over the course of the study and challenges comparison across studies and subsequent meta-analyses. Recent developments in digital technology have promoted interest in finding a solution to standardizing assessment; however, further development and validation is required.

A uniform definition of acne and standardized tools to assess severity would enable more accurate evaluation of treatment efficacy and improve future assessment of the burden of acne. The Acne Core Outcomes Research Network (ACORN) is following the methodologies of the Harmonising Outcome Measures in Eczema group to evaluate and/or develop a set of measurement tools to standardize the assessment of acne. To date, seven core outcome domains have been agreed through consensus, and efforts are underway to evaluate existing measurement instruments and/or develop new ones to assess each domain. The development of globally agreed acne assessments will help to assure greater uniformity in acne case definitions in studies and identify the burden of disease moving forward.[5–7]

Epidemiology of acne

Estimates suggest that acne affects 9·4% of the global population[8] and is the eighth most prevalent disease worldwide.[9] A recent systematic review of the epidemiology of acne across the world noted acne prevalence estimates ranging from just over 20% to over 95%. The same review reported a strong association between family history, age, body mass index, skin type and acne severity and presentation.[10]

Three large community studies conducted in China (n = 17 345),[11] Germany (n = 90 880)[12] and Egypt (n = 8008)[13] demonstrated point prevalence rates of 8·1%, 3·9% and 5·4% and a rapid increase and peak age range of 16–20 years. Further studies in Taiwan (East Asia), Western Europe and South Asia corroborated the highest prevalence of acne in those aged 15–19 years.[14]

Acne is rare in those aged under 10 years, unusual (1·6%) at age 10 years, peaks at 15 years of age and demonstrates a rapid increase by age 19 years, suggesting a rising incidence of acne across the globe in late adolescence defined as ages 15–19 years.[14]

An earlier puberty onset in girls triggers a higher incidence of acne in the younger age ranges compared with boys, regardless of a country's economic level. Acne is rare in those over 50 years of age. In the late teens and twenties acne appears to be more prevalent in men and in those over 30 years it appears to be more prevalent in women. This may reflect increased reporting and consulting rather than true increased prevalence. Persistent acne in women occurs more commonly than true late-onset acne defined as first presentation at age > 25 years.[15]

Most prevalence studies have concentrated on facial acne; however, the chest and back can be independently affected. The prevalence rates for truncal acne vary; those who have investigated for association suggest that 50–60% of cases with truncal acne also have some facial acne, with inconsistent severity across the sites.[16,17]

Truncal acne has been reported more frequently in male patients.[16–18] Moreover, in one study of 965 patients, the back was more frequently and severely affected than the chest.[16]

Prevalence studies are challenged by the inclusion of inconsistent definitions of acne, variable grading techniques, small sample sizes, different settings, varying populations and self-reported vs. clinician-reported outcomes.

The Global Burden of Disease studies

In 2010, the Global Burden of Skin Disease study analysed the prevalence and impact of skin disease for 187 countries and ranked acne in the top 10 across high- and low-income countries.[9]

An update from the Global Burden of Disease study in 188 countries demonstrated that the burden from acne as measured by disability-adjusted life years (DALYs), years lived with disability and years of life lost, is greatest in Western Europe, high-income North America and Southern Latin America and continues to cause the greatest global skin burden. The greatest burden of acne globally is between the first and third decade of life.[19]

Studies have examined the burden of acne in specific countries.[14,20,21] Collectively in Iran and 15 neighbouring countries, acne alongside dermatitis caused the greatest burden; however, burden in Iran was lowest when compared with neighbouring countries. This variation in burden within the same geographical region may reflect better access to

treatments in some countries, highlighting potential inequalities and the need to support equitable healthcare policies.[20] In Canada, a comparison of the burden of skin disease between 1990 and 2017 demonstrated that the all-age DALY counts and age-standardized DALY rates per 100 000 for acne had increased by 47% and 33%, respectively. The acne all-age prevalence rate and the age-standardized prevalence rate per 100 000 had increased over this period by 12% and 33%, respectively. This suggests a steady increase in the burden.[14] Lynn *et al.* analysed data from the 2010 Global Burden of Disease Compare study over specific regions for individuals aged 15–19 years. The results demonstrated an upward trajectory for all regions except sub-Saharan Africa. There was a clear separation in both prevalence and rate of incline between more wealthy regions (traditionally Western Europe, high-income Asia Pacific, the USA and Canada) compared with poor socioeconomic regions (sub-Saharan Africa, Oceania, Latin America and the Caribbean).[14] Improved recording and increasing demand for treatment may account for some of the increase in numbers. Whitsitt *et al.* identified acne to be the most Googled skin disease term globally and suggested that those with more burdensome disease are likely to seek out information about their condition.[22]

Acne presents at a young age and the protracted course results in prolonged burden of disease over the course of a lifetime. In addition to age-related distribution, the burden demonstrates some geographical variation,[23] which emphasizes the need to work towards more equitable healthcare access and economies for people with acne.

An analysis of the number of systematic reviews and protocol topics in the Cochrane Database of Systematic Reviews measured by DALYs from the Global Burden of Disease 2010 project demonstrated that acne was under-represented. This has informed subsequent systematic reviews and most have identified the need for further research.[24] Acne research remains poorly resourced; a comparison of cutaneous research funded by the US National Institutes of Health with the US skin disease burden demonstrated that acne was underfunded in relation to the disease burden.[25] The global impact of acne confirms the need for further investigation and supports fostering international collaborations when conducting future research.

Other factors contributing to disease burden because of acne

Other ways in which acne may impact on disease burden, include clinical sequelae, psychological aspects, chronicity of acne, economic factors and treatment-related issues including antimicrobial resistance.

Clinical sequelae

Scarring

Inflammatory acne can result in permanent scarring. In a study of 185 patients, Layton *et al.* reported that 95% of patients with acne had some degree of facial scarring and in male patients, scarring on the trunk was recorded in up to 80%.[26] In a larger study of 973 patients, the results were similar, with facial scarring observed in 87% of cases and scarring on the back and chest in 51% and 38%, respectively.[27]

Evaluation of the prevalence, risk factors, clinical characteristics and burden of scars among patients with active acne in Brazil, France and the USA demonstrated that scarring is frequently seen across all cultures and impacts on quality of life, independently of the acne. Scars were a source of embarrassment, frustration, sadness, anger and/or anxiety. Although scarring was more frequent in patients with more severe acne, scars were also associated with mild disease in some cases, which suggests a possible inherent genetic predisposition. The time between onset of acne and effective therapy and/or relapse of acne were risk factors for developing scars.[28,29] Previous studies corroborate the correlation between acne duration and treatment onset, and suggest that early treatment aimed at reducing inflammatory acne would effectively decrease the risk of physical and psychosocial scarring.[26,27] The results of a multinational survey demonstrated that facial acne scars are perceived negatively by society.[30]

Pigment change

Acne is often accompanied by pigmentary changes, which may pose a greater concern for the patient than the acne lesions. Pigmentation problems are often long-lasting; up to 1 year for more than half of individuals affected and 5 years or longer in 22·3%.[31]

Psychosocial impact and psychiatric effects

The World Health Organization (WHO) defines quality of life as 'an individual's perceptions of their position in life in the context of the cultural and value system in which they live and in relation to their goals, expectations, standards and concerns'.[32]

Acne frequently affects teenagers who are undergoing maximum physical and social change as they establish their social identity, rendering them more vulnerable to unacceptable visible changes on their skin; this is compounded by the media promoting perfection in terms of body image and appearance.

The impact of acne on health-related quality of life (HRQoL) across all ages may result in emotional stress, significant psychosocial burden and neuropsychiatric disturbances including depression and suicide. Profound social and psychological effects do not necessarily correlate to acne severity. Even mild disease can impact negatively on work, social interactions and mood. In addition, clinical disease severity does not necessarily correlate with the clinician's perception of the disease.[33]

HRQoL is included in the ACORN consensus-derived core outcome set of domains, but there is currently no universally agreed assessment tool. A recent systematic review on acne impacts has identified several major themes.[34] Bullying and

teasing were an issue that can have devastating long-term effects on mental health, predisposing to anxiety and social phobias.[35] The most common or worst impact was appearance-related distress.[34] Magin *et al.*[36] suggest that all other negative consequences of acne flow from central concern about appearance. Greater self-consciousness of appearance and negative self-concept have been reported in female patients with acne; those over 20 years of age may have greater appearance-related distress than younger individuals. The site of the acne may be relevant, as moderate-to-severe acne on the face has been associated with social self-consciousness of appearance, whereas a similar grade on the back and chest correlates with self-consciousness of sexual and bodily appearance. Ethnicity has also been implicated in appearance-related concern arising from acne.[37]

Acne may be associated with significant psychiatric comorbidities in adolescence. The risk of anxiety, depression and suicidal ideation have been confirmed. Increased risk of mental health problems and suicidal ideation have also been associated with increased self-rating of acne in this age group.[38,39]

A Swedish retrospective cohort study examining oral isotretinoin users over 20 years, reported that the standardized incidence of attempted suicide progressively increased in the 3 years prior to oral isotretinoin use for severe acne, suggesting that the acne itself is a risk factor for attempted suicide.[40]

Using generic and dermatology HRQoL tools, the disease burden of acne has been shown to be comparable with negative effects experienced by patients with other serious debilitating diseases including epilepsy, diabetes, asthma, chronic back pain and arthritis.[41]

Adult patients with acne have reported emotional impact similar to that of patients with psoriasis, and may be more severely and functionally impaired with emotional symptoms than adolescents, possibly relating to the persistent chronic nature of the disease.[42]

Effective treatment can positively impact on psychosocial issues linked to acne or scarring, supporting the need for timely and effective management over the course of the disease duration.

Chronic disease

In many cases, acne represents a chronic condition changing in distribution and severity and requiring treatment over a prolonged period. There is evidence that it can persist into adulthood in up to 50% of individuals despite treatment. This course aligns with the WHO definition of chronic disease.[43]

Perception and stigma

People with acne perceive greater stigmatization related to their skin condition than those without acne[44] and this is associated with impaired psychological functioning and impaired HRQoL.[45] People without acne perceive those with acne as unattractive and experience shame upon developing the condition themselves.[46] Studies report

people with acne being subjected to teasing, bullying and social isolation.[47] A more recent study has demonstrated that perceived stigma significantly contributed to HRQoL, psychological distress and somatic symptoms over and above established predictors.[48]

Economic factors

Acne is the most common reason to visit a dermatologist, particularly in women aged 20–34 years. It has been estimated that more than 11 million prescriptions per year are written for the treatment of acne, and that acne therefore imposes a significant burden on healthcare systems and economies. In 2004, the total annual cost relating to acne in the USA was evaluated at $3·1 billion.[49] The direct costs of acne include resources for prescription and over-the-counter medications, cosmetics, clinician visits, medical procedures and hospital visits. The indirect costs reflect changes in productivity, and the intangible costs represent deficits in quality of life.

Direct costs

Pharmacoeconomic studies have the potential to maximize healthcare resources. A recent cost-efficacy study was conducted to facilitate the comparison of current therapeutic options used in the management of acne by assessing cost calculations standardized to 7 months of treatment. This demonstrated drug costs for isotretinoin (excluding laboratory tests) of $1321 to $11 680 and was influenced by patient weight (45–90 kg) and the product used. When laboratory costs and office visit charges were included, the total costs were higher. Other treatments categorized as topical and oral medications ranged in total costs from $339 to $5017 over a similar 7-month period. The authors concede that this does not take into account durable remission and patient preference but provides an indication of costs.[50]

The most expensive agents were topical antibiotics, topical retinoids and topical retinoid combination preparations. The least expensive medication was spironolactone, an unlicensed medication for acne with no robust evidence for use, although clinical trials are being conducted.[51] Oral antibiotics were also less expensive, which may influence their overuse in the management of acne.

Indirect costs

The psychosocial impact of acne also has economic consequences to society through detrimental effects on interpersonal relationships, employment opportunities or ability to work. Patients with severe acne have higher unemployment rates than adults without acne among those aged 18–30 years in the UK.[52] Jowett and Ryan reported that 14% of 30 patients with acne experienced limitations in opportunity, 17% had reported functional difficulty and 45% had recorded interpersonal difficulties at work.[53] As the condition most commonly affects adolescents, parents/carers are often required to take

days off work to bring their children to medical appointments.

Intangible costs: utility costs

Intangible costs reflect the patient's willingness to pay for alleviation of symptoms associated with their acne. Bickers *et al.* found that the intangible cost of acne was $12 billion in the USA in 2004 and demonstrated that in comparison with other leading skin diseases, patients with acne show a much higher willingness to pay than those with atopic dermatitis, herpes simplex or psoriasis.[49]

Treatment-related issues

Treatment guidelines

Despite acne being one of the three skin conditions in the top 10 most prevalent diseases worldwide, the most widely used treatments have changed little in the past 30 years. Most clinical trials of new and existing therapies in acne have been conducted by the pharmaceutical industry. There are over 20 international acne guidelines available worldwide. Many guidelines adopt an evidence-based approach, but the evidence is frequently low and challenged by the paucity of comparative clinical trials. Guidelines are also potentially lacking, as many fail to recognize or include people affected by acne as part of stakeholder engagement.[54]

As a result, relevant questions that people with acne have posed are not considered in recommendations. In 2012, the Acne Priority Setting Partnership was implemented to identify and rank treatment uncertainties by bringing together people with acne and professionals providing care to patients with acne across the globe.[55]

By seeking their views, the key issues of importance were identified to inform future research. A total of 6255 questions were collated into themes and the top 10 treatment uncertainties were prioritized, revealing an extensive knowledge gap about widely used interventions and the relative merits of drug vs. nondrug-based treatments in acne management (Table 1). A number of areas could be addressed in future guidelines including lifestyle issues such as stress management, adequate sleep, healthy diet, with advice on low glycaemic index foods. Guidelines currently fail to advise how to treat acne as a chronic disease. Further information of how and when to escalate therapy would be helpful for prescribers. Specific guidance relating to acne site would also enhance recommendations. Given global disparities in income, information on costs including over-the-counter options and cosmetics would potentially further support the needs of people with acne and healthcare economies.

Antimicrobial resistance

Oral antibiotics are prescribed widely for the treatment of moderate-to-severe acne because of their antimicrobial and

Table 1 The top 10 research priorities linked to uncertainties about acne treatment

What management strategy should be adopted for the treatment of acne in order to optimize short- and long-term outcomes?

What is the correct way to use antibiotics in acne to achieve the best outcomes with the least risk?

What is the best treatment for acne scars?

What is the best way of preventing acne?

What is the correct way to use oral isotretinoin in acne in order to achieve the best outcomes with least risk of potentially serious adverse effects?

Which lifestyle factors affect acne susceptibility or acne severity the most and could diet be one of them?

What is the best way of managing acne in mature women who may/may not have underlying hormonal abnormalities?

What is the best topical product for treating acne?

Which physical therapies, including lasers and other light base treatments are safe and effective in treating acne?

How long do acne treatments take to work and which ones are the fastest acting?

Adapted from Layton *et al.*[55]

anti-inflammatory activity. Prolonged use of oral antibiotics remains a significant global concern owing to the increasing numbers of resistant bacteria, not only on the skin, but at all body sites with resident commensal microflora.[56–61]

Studies have shown high rates of skin colonization by antibiotic resistant *C. acnes* in patients with acne referred from the community to dermatology departments and the prevalence of resistance to both erythromycin and clindamycin in the UK isolates of *C. acnes* shows no sign of falling. These data suggest that strains of *C. acnes* resistant to erythromycin and clindamycin may be establishing themselves as members of the resident microflora of patients with acne. This could reflect an ability to outcompete antibiotic susceptible strains, but could also link to a lack of awareness about avoiding antibiotic monotherapy when acne is treated in the community. Analysis of the UK Clinical Practice Research Datalink confirmed that general practitioners prescribe oral antibiotics in one-third of patients with acne at their first consultation. A US retrospective analysis of a claims database confirmed a trend towards increased use of systemic antibiotics by nondermatologists between 2004 (20% of systemic treatment courses per 100 patients with acne were systemic antibiotics) and 2013 (22·5%).[62] These data highlight the need to continue to forge changes in antibiotic prescribing habits in acne management as part of a strategy to reduce antimicrobial resistance.

Treatment adverse effects

Many treatments are advocated for acne management. Topical therapies have potential for irritation, possible photosensitivity and bleaching effects. Oral isotretinoin requires vigilant review owing to reported adverse effects. Even when indicated, regular laboratory testing and a strict pregnancy prevention programme may preclude the use of isotretinoin in some cultures

and populations. There is still a paucity of robust evidence for lasers and light therapies in the management of acne;[63] they are frequently available only in the private sector. Potential adverse effects, lack of availability and resource requirements may all pose challenges and contribute to the burden of acne.

Conclusions

Studies confirm a high prevalence of acne worldwide. The chronic nature of acne and resultant scarring contribute to significant physical, social, psychological, psychiatric and economic burden. Timely treatment should lead to less physical and social scarring emphasizing the need to provide early management with equitable access for all. There are still many uncertainties about treatment and increasing prevalence rates that may relate to earlier onset of puberty, genetic drift or environmental factors including the Western diet, socioeconomic status and changing societal perceptions. The significant disease burden resulting from acne and the continuing use of antibiotics support the need for therapeutic advances and an international approach for standardizing assessments of novel therapies within the context of clinical trials. Appreciating the global patterns associated with the burden of acne has potential to inform the underlying pathogenesis, risk factors and the possible link with comorbidities such as underlying endocrinopathies.

Strategic international approaches to research and sharing of data could contribute to early management supporting the prevention of acne and scarring and should improve the burden for patients, society and economies. The adoption of innovative technology to assess and educate both people with acne and allied health professionals would improve management strategies, lead to better access to treatment and contribute to cost-effectiveness.

Acknowledgments

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