pathways relevant to skin cancer are diverse[21]; ranging from skin colour (see below), cyclin-dependent kinase inhibitor 2A (CDKN2A/p16INK4a) in familial melanoma, detoxifying cytochromes in basal cell carcinoma, to gap junction communication in keratitis, ichthyosis, deafness (KID) syndrome. In many other disorders, molecular defects leading to internal neoplasia are accessibly manifest in skin.[22]

## Skin colour

Among the most critical genetic adaptations during human history have been those in genes regulating skin and hair colour. In European populations, there is evidence of positive selection for skin colour variants (for example those in the melanocortin 1 receptor (MC1R) which underlie the red hair/fair skin phenotype) probably because fair skin increases ultraviolet (UV)-dependent vitamin D synthesis in northern latitudes.[23] Other skin colour genes include SLC24A5, TYR, and OCA2 and genome-wide analysis has identified more loci.[24,25] Increased UV exposure is, however, also associated with increased skin cancer susceptibility, including melanoma, so it is not surprising that pigmentary loci also influence cancer risk.[26–28] However, susceptibility may not be solely dependent on the pigmentary pathways.[26]

## Summary

During recent decades, discoveries in genetic skin disease have produced insights into the biology of the skin, and in some cases permitted preventive prenatal diagnosis, but application of this knowledge in palliation or cure remains a tantalising prospect.

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# The burden of skin disease: quality of life, economic aspects and social issues


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Doctors looking after patients with skin disease have probably always been aware that the condition can have a devastating effect on many patients' lives. However, the physician-centred view of medicine focused on diagnosis and therapy rather than

on the quality of life (QoL), economic and social impacts of the disease on the patient.

Forty years ago, motivated by a need to improve compensation for work-related skin disease, Sauer proposed a way to measure the effect of skin disease on patients' lives.[1] Robinson also understood this need for measurement.[2] In the late 1960s the impacts of psoriasis on patients, for example embarrassment, were recognised as important factors in an attempt to measure psoriasis severity.[3] Over the next decade there were descriptions of the ways in which people were handicapped by inflammatory skin disease.[4] But crucially the lack of progress in measurement techniques inhibited further understanding.

Quality of life measurement in rheumatology provided the inspiration for the development of the first disease-specific and patient-focused QoL measure in dermatology, the Psoriasis Disability Index.[5] After the creation of other disease-specific measures for acne and eczema, it became clear that all skin diseases affect lives in broadly similar ways. What was needed was a simple measure for use across all skin disease and the Dermatology Life Quality Index (DLQI) was the resulting first attempt.[6] The practical usefulness of the DLQI has been transformed by simple validated descriptor bands, which give meaning to scores.[7] Being able to understand the score has allowed the development of proposed disease-severity definitions encompassing, and therapy guidelines based on, QoL scores.[8,9] The DLQI is now widely used internationally, in over 50 languages.[10] Other well validated dermatology-specific measures, such as Skindex,[11] have also been described.

The ability to measure the impact of skin disease on QoL is useful in clinical care for patient monitoring and to inform or support critical clinical decisions, for example the starting of systemic therapy in inflammatory skin disease. QoL measures are being used as outcome measures in clinical research studies, and in auditing dermatology clinical services. Politically, QoL data provide evidence of the major negative impact of skin disease and the need for appropriate funding.[12,13]

Heightened awareness of the social impact of skin disease has led to attempts to measure its impact on children and on infants with atopic eczema.[14] It is clear that a family member having any skin disease can profoundly affect the lives of partners and others. This wider grouping affected by an individual having skin disease has been termed 'the Greater Patient',[15] and the Family DLQI has been created to measure this secondary impact.

A wide variety of QoL measures for use in dermatology have now been described. Interest is now focusing on clinical aspects; for example what strategies can be created to address patient QoL impairments, and how the use of such measures can assist patients and clinicians. Many methodological issues remain, for example the problem of cultural inequivalence when the same measure is used in different countries.[16] Perhaps the most important outcome of the drive to measure skin disease QoL impairment has been its influence on making clinical dermatology even more patient orientated.

Traditionally dermatological therapy has been relatively low cost, even though needed at some time by a high proportion of the population. Expensive inpatient use has dramatically fallen over the last 50 years. However new techniques, such as laser therapy, now allow effective treatment for previously untreatable conditions and over the last five years very high cost but highly effective 'biologicals' have been used for psoriasis and other indications. This change has been a major impetus to the development of methods to measure direct and indirect costs more accurately as economic evaluation of the overall burden of skin disease and its management is now essential in finitely resourced healthcare systems such as the NHS. Once the true cost of a disease to the patient and to society can be accurately measured, diseases that have often been largely ignored, such as chronic idiopathic urticaria,[17] may become recognised for their true importance. Assessment of overall cost involves calculating the direct costs (drugs, doctor consultations, etc), the indirect costs (travel, days off work, etc) and also less easily defined utility costs (how much the QoL impairment was 'worth').[18] Various techniques have been created to try to capture these utility costs, such as time trade-off (including QALIs) and willingness-to-pay.[19]

Many attempts have been made over the last 50 years to determine the costs of skin disease,[20] but systematic reviews of the socio-pharmaco-economic impact of atopic dermatitis and acne reveal few high-quality publications and with widely ranging results.[20,21] There will continue to be a need to refine cost-effectiveness assessment techniques as new therapies become available.

The last 50 years have seen a dramatic shift in dermatology from being a doctor-centred specialty to being patient centred, with recognition of the wider importance of quality of life and economic issues.

## Competing interest

AYF is joint copyright owner of the PDI, DLQI, CDLQI and FDLQI. His department gains income from their use.

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