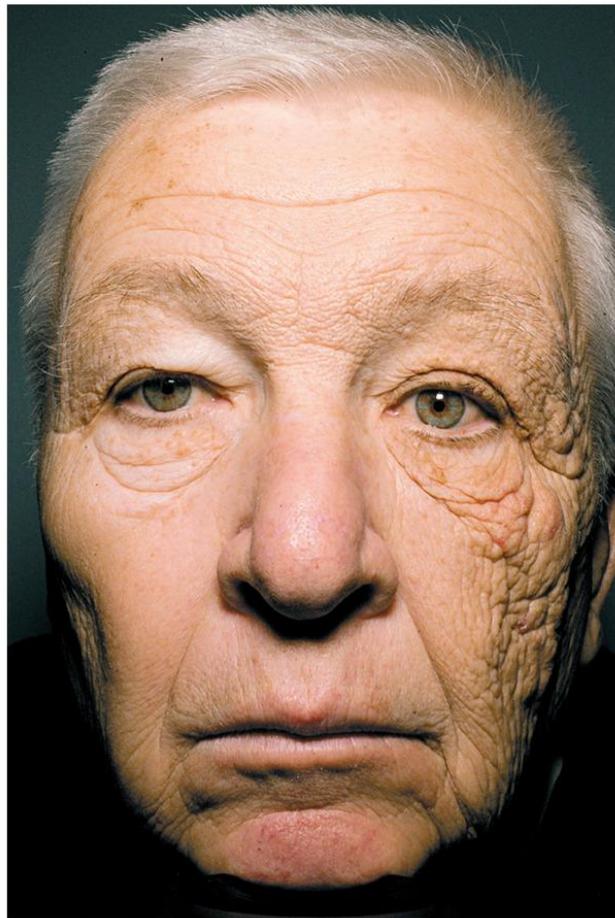




**British Association of Dermatologists
Elective Prize/Project Grant
Summer 2019**

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Understanding the Prevalence of Different Skin Ageing Phenotypes
Z Ali, Dr A Langton, Prof C Griffiths, Prof R Watson



Foreword

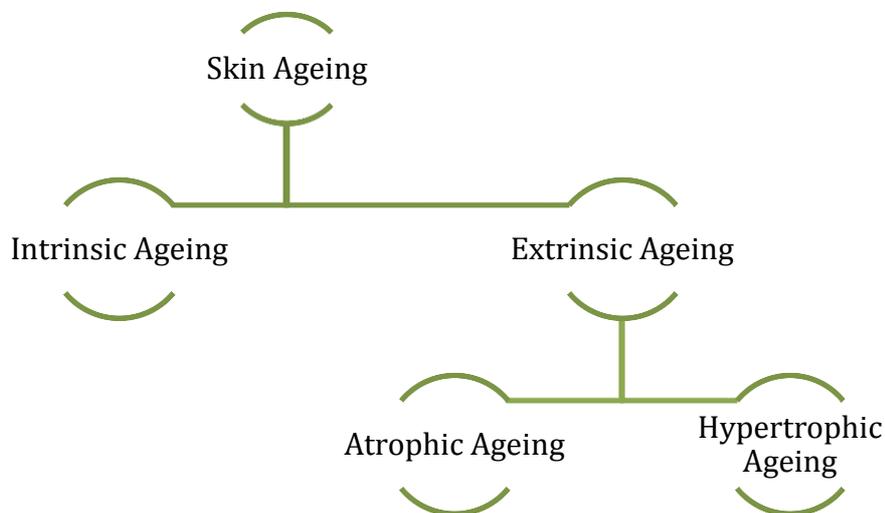
This summer I was fortunate enough to receive an award from the British Association of Dermatologists supporting the research project I carried out during my elective. I conducted an observational study determining the prevalence of different skin ageing phenotypes alongside Professor Christopher Griffiths, Professor Rachel Watson, and Dr Abigail Langton of the University of Manchester. I would like to thank all of the above for their fantastic mentorship and continued support, and also the BAD for facilitating my time with the team.

Why dermatology?

During my fifth year at Cambridge University, I completed a six-week placement in dermatology, which was both enlightening and educational. The experience affirmed my desire to pursue dermatology as a career. Realising the importance of clinical research in the advancement of medicine, I have already been involved in various research projects. My elective allowed me to consolidate this interest and immerse myself in the world of academic dermatology.

I was afforded the opportunity to pursue a dermatology specific elective in my home county of Cheshire. Impressed and inspired by the work of Professor Griffiths at Salford Royal Hospital, I contacted him and he invited me to join his skin ageing research group for the summer.

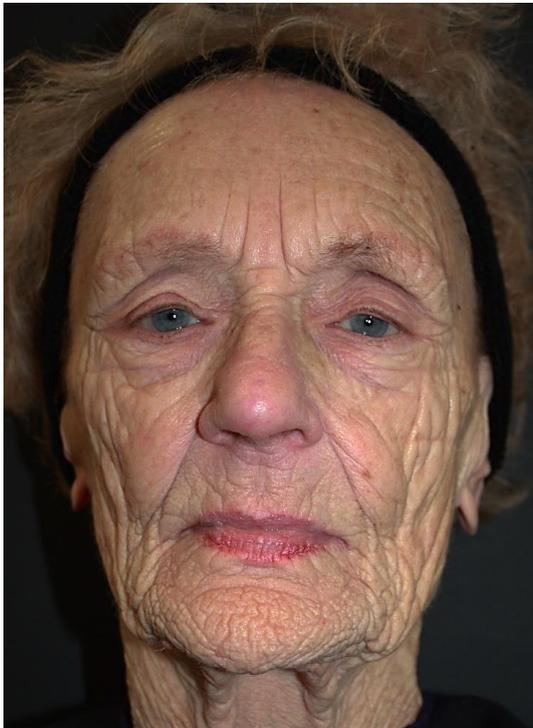
What do we know about skin ageing?



Skin ageing is a process involving intrinsic and extrinsic mechanisms.¹ Observable markers of skin ageing include an increasingly roughened texture and thinning of the skin. This occurs due to the tendency of aged skin to be drier and to lose dermal collagens, elastic fibres, and proteoglycans.³ Although ageing of the skin is a complex process, intrinsic ageing usually encompasses the 'natural' course of skin ageing whereas extrinsic ageing is reliant on UV exposure and other external factors such as environmental pollution.² Histologically, extrinsic ageing causes changes in pigmentation and the development of deeper wrinkles. It is a largely preventable and treatable entity that is readily distinguishable from intrinsic ageing.

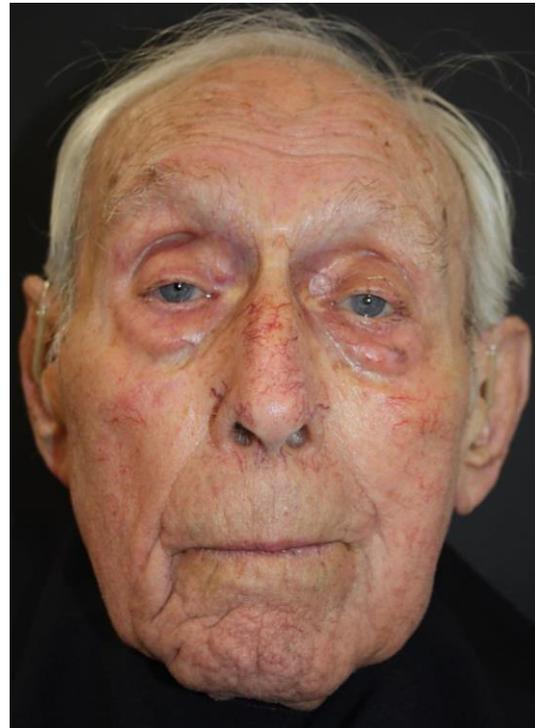
There are numerous factors that contribute to extrinsic skin ageing. Of all external factors, UV exposure is the most prominent variable in accelerating skin ageing. Photodamage results from three distinct factors: cumulative sun exposure; lack of intrinsic and extrinsic protection (e.g. melanin pigmentation, use of protective clothing, sunscreens); and inherent susceptibility to damage, which includes the efficiency of an individual's repair mechanisms.²

Extrinsic ageing often goes unrecognised clinically and can be mistaken for an accelerated form of intrinsic ageing. It has recently been recognised that there are two phenotypes of extrinsic ageing; hypertrophic and atrophic skin ageing. Hypertrophic photoageing presents with a sallow complexion, coarse wrinkles, elastoidosis, and dyspigmentation. Atrophic photoageing presents with shiny, glossy, translucent skin with telangiectasia, minimal wrinkling and an increased frequency of actinic keratoses and keratinocyte cancers.^{4,5} The latter subgroup has only recently been described. Thus while a photonumeric scale for grading hypertrophic skin ageing has long been established, a scale for atrophic skin ageing has only newly been developed.⁶



Hypertrophic Ageing

Coarse wrinkling, rough texture, mottled pigmentation, sallow complexion



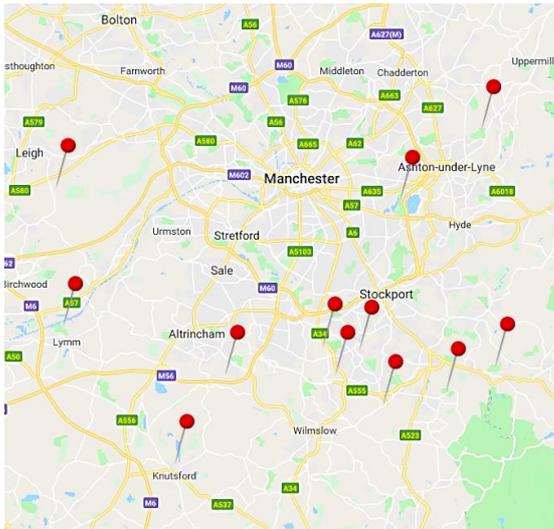
Atrophic Ageing

Minimal wrinkling, thin skin, shiny complexion, telangiectasia

As a newly described subgroup, published comparisons of the hypertrophic vs atrophic conditions have so far only been described in cohorts recruited from dermatology outpatient appointments. We wished to conduct the first study examining the relative prevalence of the hypertrophic and atrophic phenotypes in the general population. It is important to establish the atrophic subgroup and its prevalence in the population as this phenotype denotes an increased susceptibility of keratinocyte carcinoma.⁵ As this form of photodamage is readily preventable, our research has clear clinical relevance. We hope to promote recognition of this phenotype and a reduction in keratinocyte skin cancer by early assessment via the scale.

Our study

In order to sample an aged population who had likely had a large degree of sun exposure during their lifetime, we arranged to visit a variety of different golf clubs and garden centres in the Greater Manchester and Cheshire area. I collected data on 1568 individuals (M=534, F=639) over the study period. This involved observing those that appeared over 50 and recording their estimated age, their phenotype (atrophic or hypertrophic), and their severity of skin ageing using the atrophic and hypertrophic photonumeric scales.^{4,6} We took this opportunity to interact with the public and provide information about sun safety and skin self-examinations.



Locations for data collection across Greater Manchester and Cheshire



Dr Langton and myself at Hale Golf Club where we educated the members on sun safety



Presentation on sun safety to the general public



Giving out free sunscreen samples and collecting data at a golf club

We found that males were more likely to have the atrophic phenotype (62% atrophic, 38% hypertrophic) and females were much more likely to have the hypertrophic phenotype (25% atrophic, 75% hypertrophic). Previous studies have found that for those over the age of 45, men are 2-3x more likely than women to develop keratinocyte carcinomas.⁷ We also know that those with the atrophic phenotype are more likely to develop these cancers.⁵ Considering these two statements, our results suggest the propensity of males to develop keratinocyte skin cancers may be due to the increased

prevalence of the atrophic phenotype in their gender. If this conclusion is correct, further study into the atrophic and hypertrophic phenotypes could help us understand more about the mechanism of skin cancer and an individual's risk of developing these carcinomas. There are many questions for further study. What determines the skin ageing phenotype an individual develops? Are there biochemical markers of atrophic skin we can identify that cause the increased risk of carcinoma?

Our results have an important public health message. It is important we understand who is at risk of the atrophic skin type as this subgroup has an increased risk of keratinocyte skin cancers. It is also important we have the correct training and tools to be able to recognise the difference between atrophic and hypertrophic skin ageing when it is clinically apparent, as this will allow us to inform a patient of their individual carcinoma risk. Everyone should follow basic sun safety rules, but these atrophic patients should be even more vigilant in avoiding excessive sun exposure, applying sunscreen regularly, and routinely checking their skin for signs of suspicious changes.

Reflections

This project allowed me to immerse myself in the world of academic dermatology, and work within a team of both academic dermatologists and dermatology scientists. Rather than simply handing me a job to do, the team involved me in the project during the entire study timeline. I took part in the initial protocol brainstorming, conducted the majority of data collection and analysis, and I will be involved in the penning of a manuscript for publication. This research also had a public health message; we performed data collection concurrently with educating the public on sun safety and skin health. All audiences were appreciative and engaged, and many remarked they had learnt something new, and would change their sun habits accordingly. This feedback was hugely rewarding to hear, instilling a desire to further pursue opportunities which incorporate education and health promotion into my medical career.

Throughout my time at medical school I have sought opportunities to be involved in research, however it was my time with Professor Griffiths's team that has cemented my desire to pursue a career as an academic dermatologist. I believe the skills I have amassed during my elective will enable me to forge this career path for myself, and I hope to return to Salford Royal and their excellent dermatology program in the future. Thank you again to the BAD for supporting this venture.

References

1. Trojahn C, Dobos G, Lichterfeld A, et al. Characterizing Facial Skin Ageing in Humans: Disentangling Extrinsic from Intrinsic Biological Phenomena. *BioMed Research International* 2015; 2015:1-9.
2. Edwards C, Heggie R, Marks R. A study of differences in surface roughness between sun-exposed and unexposed skin with age. *Photodermatol Photoimmunol Photomed* 2003; 19(4):169-174.
3. Kanaki T, Makrantonaki E, Zouboulis C. Biomarkers of skin aging. *Rev Endocr Metab Disord* 2016; 17(3):433-442.
4. Ayer J, Watson RG, Griffiths TW, Griffiths CEM. A comparison of atrophic and hypertrophic facial photoageing. *J Invest Dermatol* 2015; 135:S32-4.
5. Brooke RC, Newbold SA, Telfer NR, Griffiths CE. Discordance between facial wrinkling and the presence of basal cell carcinoma. *Arch Dermatol* 2001; 137:751-4.
6. Ayer J, Ahmed A, Duncan-Parry E, Beck P, et al. A photonumeric scale for the assessment of atrophic facial photodamage. *Br J Dermatol* 2018; 178(5):1190-1195.
7. Apalla Z, Lallas A, Sotiriou E, et al. Epidemiological trends in skin cancer. *Dermatol Pract Concept* 2017; 7(2):1.