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Photodiagnostic Services in the UK and Republic of Ireland: a British Photodermatology Group Workshop Report

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Conflict of Interest Statements:

Harry Moseley was retained as an expert witness by Biofrontera

John Ferguson received grant funding from the British Skin Foundation and Vitiligo Society and consultancy fees from Genesis Care Radiotherapy Company

Sally Ibbotson received honoraria and financial support for attendance and presentation at meetings from La Roche Posay, UCB Pharma and Galderma UK Ltd, grant funding from British Skin Foundation and royalties for book chapter writing from Davidson's Principles & Practice of Medicine

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Abstract

Background: Photodiagnostic investigations are essential for the accurate diagnosis of abnormal cutaneous photosensitivity and provide important information for the management of patients with photodermatoses (cutaneous photosensitivity disorders). Although photodiagnosis has been undertaken since the early 1970s, specialist services in the United Kingdom (UK) and Republic of Ireland are limited and there is no formal guidance on diagnostic approach. Indeed, there is a limited literature in this area of methodology and diagnostic practice.

Objectives: The primary objective was to undertake a British Photodermatology Group (BPG) Workshop to review the role and activities of specialist centres in the UK and Republic of Ireland in order to ascertain whether there were consensus practices. Secondary objectives were to identify key priorities for service, training and research.

Methods: An initial detailed survey review of current activities was undertaken prior to the Workshop and data from this survey were used to inform discussion at the Workshop, which was attended by key photodermatology experts from the UK and Republic of Ireland.

Results/Conclusions: We have undertaken a detailed review of current Photodiagnostic Services in the UK and Republic of Ireland and report on our findings from the 12 centres and we have identified key areas of consensus practice. This is an important step in the process of standardising and optimising procedures and protocols and defining minimum clinical standards for photodiagnostic investigations, which are of such diagnostic importance in Dermatology.

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Introduction

The value of Specialist Photodiagnostic Services was demonstrated through pioneering early work.[1-6] In 1992, a British Photodermatology Group (BPG) Workshop reviewed photodiagnostic facilities in the UK, with relevance for general dermatologists and the potential for standardisation in mind.[7]

The conclusions were that phototesting was under-utilised and that availability of services and relevant expertise was limited. The importance of collaboration with medical physicists was emphasised. As no further review has been undertaken for almost 30 years, this was the focus of the current Workshop as a step towards optimisation of procedures and defining minimum clinical standards.

Methods

The BPG, supported by the British Association of Dermatologists (BAD), hosted a Workshop in 2019 to review existing photodiagnostic services in the UK and Republic of Ireland and experts from these multidisciplinary teams (consultant dermatologists, medical physics clinical scientists and technologists and nurses) were invited to participate. The objectives were to review existing practices based on literature review, expert opinion and clinical experience. This process included a survey (Appendix 1) completed by participants in advance of the Workshop and subsequent discussion and analysis at the Workshop. The main objectives were to:

- Define the availability and scope of photodiagnostic centres
- Identify the nature of patients referred
- Review investigations, equipment and methodologies
- Review assessment and interpretation
- Review training and educational opportunities
- Define service, research and educational priorities

The Workshop sought to identify areas of consensus and priorities for future development.

Results

Photodiagnostic service availability

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Twelve centres provided photodiagnostic services in the UK and Republic of Ireland, with variation in size, nature and geographical reach (some local, others contracted over wide areas). There was one centre in each of Northern Ireland, the Republic of Ireland, Scotland and Wales plus services in England as shown in Figure 1. Contact details are provided in Appendix 2.

Staffing

There was at least one named Consultant Dermatologist at each centre and either dedicated or collaborative photophysics input, which the Group recognised as essential for photodiagnostic services. Additionally, dedicated specialist clinical technologist and/or nursing input was present at larger centres and considered highly desirable.

Multidisciplinary team working and collaboration was also considered essential to provide the necessary skills and expertise, for example, as with the collaboration within the NHS England Highly Specialised Xeroderma Pigmentosum Service and the European Reference Network (ERN-Skin). Access to Psychology services was identified as a priority given the high psychological burden of severe photosensitivity, although dedicated psychology input was not available at the photodiagnostic centres.[8] A Photodermatology multidisciplinary team (MDT) was also highlighted as important for sharing expertise and opinion relating to diagnosis and management of patients with photosensitivity diseases.

Consensus statement

The consensus was that tertiary photodiagnostic services should be consultant-led and that multidisciplinary staff knowledge, skills and input was essential, particularly with respect to dedicated photophysics expertise.

Patient referral pathways

All the photodiagnostic services accepted referral of patients from secondary care for further investigation and management, with three also accepting referrals directly from primary care. There was no published guidance with respect to patterns of referral but

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after Workshop discussion a consensus was agreed with respect to patient referral criteria:

- For suspected or confirmed photosensitivity
- For advice regarding management of such patients
- If the diagnosis is unclear
- If photosensitivity needs to be excluded

These criteria were deliberately broad, with the knowledge that photosensitivity may not be clinically obvious and that phototesting may be invaluable even with low suspicion.

Clinical Assessment

There was variation in the clinical assessment undertaken, with less than half of the centres using standardised templates for assessment and reporting. Potential benefits of a standardised template included detailed phenotyping to facilitate comparison between centres and identification of novel diagnostic groups, together with enhanced scope for research.

The average new: return patient ratio reported was 1.4:1, although this varied from 3:1 to 0.4:1. Approximately 72% of patients referred were phototested, again with variation between centres, ranging from 35% to 99% dependent on local arrangements. Clinical assessment and follow up without phototesting was undertaken for the minority, with some patients triaged in clinic to determine whether phototesting was required. For example, if the diagnosis of PLE was clear on clinical assessment, formal phototesting may not be required.

Consensus statement

The Workshop group agreed on broad criteria for patient referral and that standardisation of clinical assessment would be of benefit in terms of facilitating deep phenotyping of patient groups, identification of new diagnostic entities and collaboration between centres. Further work is required to establish minimum standards for these assessment tools.

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Investigations

Investigations and methodologies had evolved based on local expertise and availability, due to a lack of published evidence to guide best practice.

Narrow waveband phototesting

All the centres reported use of narrow waveband phototesting as the "Gold Standard" photodiagnostic investigation. A broadband optical source (xenon arc lamp) combined with a diffraction-grating monochromator or optical bandpass filters was used to achieve narrow waveband irradiation. There was variation in protocols, including:

- Central wavelengths and bandwidths applied
- Radiant Exposure ("Dose", also known as "fluence") ranges tested
- Dose increments
- Adaptation for use in children
- Duration of testing and number of visits

Typically testing was undertaken over two or three days, across UVB and UVA wavebands and into the visible spectrum (300 nm to 600 nm). Centres either tested across all wavelengths or only tested above 400 nm if there was sensitivity at 400 nm or if porphyria or solar urticaria (SU) were suspected. In the absence of objective evidence, both were considered appropriate, although further studies are indicated. Small-increment fill-in phototesting and more extensive dose ranges were used in two centres. There was variation in the central wavelengths and bandwidths used (Table 1).

All centres used the endpoint of minimal perceptible erythema, as assessed by minimal erythema dose (MED).[5] The 24h time-point after irradiation was used by all to define the delayed MED at each waveband. One centre also undertook readings seven hours after irradiation if drug photosensitivity or porphyria were suspected.

Comparison with normal population MED ranges across the tested wavebands in the relevant patient population is key to interpreting phototesting. Most centres had not established their own local population reference ranges and used published normal ranges for predominantly skin phototype I to III populations for comparison.[4, 9] There

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are no data available for normal population MED data for patients of skin phototypes IV to VI and this was considered a priority to develop. Moreover, it is known that visual assessment of MED underestimates UV-erythemal sensitivity in darker skin, with scope for further development of detection technology.[10] In addition to MED values, the degree of erythema and morphology of reactions were also assessed in some centres (Table 2).

All centres additionally assessed for immediate urticaria on phototesting and, if present, used the endpoint of minimal urticaria dose (MUD). Phototesting was used to objectively assess the effect of antihistamines and other therapies for SU at two centres[11]. Further investigation with respect to whether standard practice could be developed would be helpful.

It was agreed that phototesting should ideally be undertaken on clear skin and that topical corticosteroids and systemic immunosuppressants should be avoided where feasible. Topical corticosteroids can suppress UV-induced erythema and prednisolone, even at 10mg orally, may suppress CAD photosensitivity and is best avoided for at least a week prior to testing.[12-15] The effects of other immunosuppressants on phototesting are unknown, although it seems prudent to avoid immunosuppression where possible. In practice this needs to be balanced against the risk of skin flares. Furthermore, interpretation of readings must be with caution if undertaken within 4-6 weeks of sun exposure at test sites due to risk of false negative reactions.

It may be impossible to diagnose or rule out photosensitivity without phototesting.[16] Whilst there is limited evidence, cohort studies characterising photodermatoses and including narrow waveband phototesting, support use of this Gold Standard investigation.[6, 17-22] Additionally, repeated phototesting over time allows objective changes to be monitored, with respect to natural history and treatment effects.[17, 18] Controlled clinical trials of potentially phototoxic drugs can also be evaluated in photosafety studies employing narrow waveband phototesting.[23, 24] If narrow waveband phototesting is not available, important diagnostic information may not be ascertained through broadband phototesting as outlined below.

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Consensus statement

Narrow waveband phototesting is important to objectively characterise photosensitivity and can be essential in establishing a diagnosis and as a guide to management and disease course. The delayed MED and, where present, the MUD were accepted endpoints for assessment. The Group agreed that it was a priority to establish normal population MED ranges for patients of skin phototypes IV to VI.

Photoprovocation testing

In addition to narrow waveband phototesting, larger area iterative provocation testing was available in eight centres. Seven centres undertook provocation using broadband UVA only and/or used a "solar simulator", while one centre also offered UVB provocation testing.[25] Five of the eight centres used a "solar simulator" for provocation testing or small area broadband phototesting. It was discussed that the spectral emissions of these sources vary and may not truly represent natural daylight exposure.[26] The value of solar simulator phototesting was recognised in provoking many conditions, including SU.[20]

Broad waveband band phototesting complements narrow waveband phototesting with its use conferring a higher detection of photosensitivity.[27] Consideration was also given to the possible role of inclusion of infrared radiation with respect to increased yield of photodermatosis provocation and this warrants further study.[28]

Whilst photoprovocation employs larger area repeated exposures (often approximately 4x4cm field) than narrow waveband testing, there is a lack of published evidence to guide this and the Workshop Group highlighted the importance of standardisation of photoprovocation methodology and of assessment and grading of reaction patterns as a priority for further study.

Photoprovocation is generally used to induce a condition on a body site where it is most readily provoked with natural exposure.[29-31] Repeated provocation, up to 3 consecutive days, with broad waveband UVA, enhances PLE provocation.[32] Whilst

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provocation is not usually required in classical PLE, it is helpful when there is diagnostic uncertainty and in severe disease, as it may be predictive of risk of provocation during phototherapy. Photoprovocation may also be useful in suspected cutaneous lupus, actinic prurigo or hydroa vacciniforme.[19, 21, 33] The ease of provocation will depend on diagnosis, severity and individual and in practice, the limitation is often the number of days available for testing.

Relatively strong evidence exists for the use of provocation testing in suspected cutaneous lupus, using repeated exposures at increasing doses, although there is potential for induction of non-specific changes if an overly intensive regimen is used. Lehmann and colleagues collected data between 1990-2000 on 405 patients with lupus and 54% reacted to provocation, 42% to UVB only, and 34% to UVA only.[34] Again, there is no consistent practice and the reaction may require multiple provocations and have delayed onset weeks post-provocation. However, only the minority of patients with lupus require phototesting if there is diagnostic doubt as otherwise it is assumed that lupus will be photoaggravated. Provocation may also be of value in other photoaggravated conditions, such as psoriasis.[35]

Provocation testing to compact fluorescent lamps was available in one centre and was typically used in SU, CAD or lupus.[36-39]

Consensus statement
There is a clinical need to standardise broadband photoprovocation testing methodologies and assessment of reaction patterns. The Workshop Group identified photoprovocation testing as a priority area for further investigation.

Patch and Photopatch Testing
Patch and photopatch testing are essential investigations that should be accessible via a photodiagnostic service, eg. the majority of CAD patients have positive patch and/or photopatch testing.[40-42] A case-series of 157 photosensitive children who had photopatch testing performed as part of their photodiagnostic investigation indicated this can also be beneficial in childhood.[43] Sunscreens are the commonest photoallergens

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in the UK and photopatch testing enables detection of these as a cause/contributor of photosensitivity and is pivotal in allowing recommendations on suitable photoprotection for photosensitive patients.[44, 45] UVA doses as low as 0.5 J/cm^2 may successfully activate photocontact allergens in CAD.[42] All of the UK photodiagnostic services reported access to patch/photopatch testing, with five centres undertaking this in-house and the remainder through access to local contact allergy services. Photopatch testing methodologies are reported elsewhere.[45-48]

Consensus statement

Patch and photopatch testing are essential investigations that all specialist photodiagnostic centres should undertake or have access to.

Laboratory Testing

All centres undertook other testing as directed by clinical assessment and these included lupus serology (Antinuclear Antibodies (ANA) and Extractable Nuclear Antigen Antibodies (ENA)), porphyrin analysis, total immunoglobulin E, Human Leukocyte Antigen (HLA) DR4 subtyping, vitamin D status (25-hydroxyvitamin D levels), specific genetic testing and skin biopsy where indicated. If DNA excision repair disease was suspected then skin biopsy samples were sent to the Molecular Genetics, Genome Damage and Stability Centre at the University of Sussex for fibroblast culture and functional studies, with blood sent to the NHS England Xeroderma Pigmentosum Service in London for genotyping (Appendix 2).

Consensus statement

Other investigations may be required on a case-by-case basis and access to such investigations should be available through photodiagnostic services.

Equipment

There was some variation between centres in the equipment used for photodiagnosis. This reflected, in part, a lack of commercially available equipment for phototesting. Several of the photodiagnostic centres had evolved their techniques to suit clinical needs

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by manufacturing bespoke equipment or repurposing commercial products. Details of equipment used are listed in Appendix 3.

It is essential that the characteristics of any light sources used are well understood, emphasising the need for close medical physics input. The methodologies described by O'Mahoney *et al.* are informative with respect to enabling optical radiation emissions to be characterised and used appropriately.[26]

It is also essential, as part of a wider quality assurance program, for equipment used in phototesting to have scheduled quality control checks with documented results and actions. The frequency of such checks should be determined locally and be based upon experience of equipment reliability. Performance levels can be specified based upon equipment performance and clinical need. Establishing performance Action Levels can help identify equipment where performance is deteriorating, and preventative maintenance can be planned for a future date; Critical performance Levels should highlight when a major equipment issue has arisen requiring the system to be removed from clinical use. The Quality Assurance program should include not only the phototesting equipment but also all ancillary equipment that might influence the patient's received dose (for example UV radiometers). New equipment will require more regular checks until reliability of performance can be established

Consensus statement
There is clinical need for evidence supporting standardised irradiation parameters to facilitate the supply of commercial optical radiation phototesting equipment compliant with appropriate regulations.

Interpretation and reporting
Visual assessment of just perceptible erythema was used by all centres as the basis of defining threshold erythemal sensitivity (MED) on narrow waveband testing. Grading and interpretation of larger area iterative provocation testing was more variable and this was highlighted as an area for further study, to establish a standardised grading system. Assessment of patch and photopatch testing was undertaken using the standard ICDGR

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methodology, with relevance assessed by COADEX.[47] The Group emphasised interpretation of investigations in the clinical context. Individual centres employed their own methods of data collection and analysis, including in-house databases, but processes were not standardised between centres.

Whilst photodiagnostic investigations were undertaken by specialist nursing or technical (medical physics or science backgrounds) staff, reading and interpretation of testing was undertaken by clinical staff at all centres, with the exception of one where readings were performed by nursing staff and interpreted at a later date by the clinician. However, the Workshop consensus was that clinician input was essential for accurate interpretation and clinical relevance of findings. Use of an appropriately lit environment and of minimising patient movement during testing and assessment was also emphasised. Patients are encouraged to provide images of their condition; with sun avoidance or seasonal photosensitivity the condition may not be present at consultations. Expansion of the use of remote consultations and patient images was also discussed and has subsequently become an inevitable consequence of the coronavirus pandemic.

All centres reported to referrer and primary care in written format. Patient information sheets were available at each centre, but the Group highlighted this as an area for standardisation. Approximately one-third of patients were kept under review, typically with repeat phototesting. Email advisory services were specific to individual centres and the importance of Photodermatology MDTs was emphasised.

Consensus statement

The Group recognised that more work was required to standardise photodermatology patient information sheets. Subsequent to the Workshop, the pandemic impact and initial move to remote consultation, may be useful in enabling a longer-term hybrid face-to-face and remote consultation model to enhance service efficiencies, but this will need review and governance.

Pattern of diagnoses

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There was wide variation in the numbers of patients seen at the Photodiagnostic centres, ranging from 24 to 470 patients per year. There was a broad range of photodermatoses investigated and diagnosed (Figure 2). The most commonly diagnosed were the immunological photodermatoses, particularly PLE, consistent with published experience.[49] However, the Group emphasised that investigation of PLE should be limited to those with severe or atypical disease where there is diagnostic doubt or suspicion of concurrent photodermatoses. The other photodermatoses were represented less frequently and it was recognised that exclusion of photosensitivity is an important contribution to the investigation of some patients.

Training & education

The importance of training and education was emphasised. In the UK, the specialty training pre-Certificate of Completion of Training (CCT) and post-CCT photodermatology curricula clearly state training requirements for dermatologists in training and those wishing to specialise in photodermatology respectively (www.bad.org.uk/healthcare-professionals/education/dermatology-specialty-trainees/curriculum-and-sce; www.bad.org.uk/healthcare-professionals/education/dermatology-speciality-trainees/post-cct-fellowship-curricula).

Postgraduate photodermatology training courses aimed at dermatologists are available in Dundee, London and through the European Society for Photodermatology (www.espd.eu.com). Phototherapy courses are also available (eg.www.newportphototherapytraining.co.uk; www.photonet.scot.nhs.uk; www.photomedicine.org). The European Society for Photobiology (www.photobiology.eu) also offers training aimed primarily at PhD students (non-clinical and clinical) but can accommodate others specialising in the field. We noted a lack of clear educational and training pathways for personnel specifically allied to photobiology, particularly medical physics clinical scientists and clinical technologists. This has resulted in reliance on in-house training or short attachments at other centres of expertise as the main specialist-training routes at present. This was highlighted as a priority area for further development.

Consensus statement

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The need for appropriate photodermatology training pathways was emphasised by the Workshop and whilst structured training is available for dermatologists, this was found to be lacking for clinical scientists and technologists and was identified as a priority for further development.

Conclusions and future priorities

The overall aim of this BPG/BAD Workshop was to review Photodiagnostic Services and identify areas of consensus practice and those for further development. The report outlines the characteristics of these services and emphasises the importance of the consultant-led multidisciplinary team, including dedicated photophysics involvement. We have highlighted areas of importance for clinical service development, governance, research, education and training. We have reported on areas of common practice and variation and emphasised collaboration. This is a step towards optimising procedures and defining minimum clinical standards in photodiagnosis, which we consider is applicable Europe-wide. We anticipate that this will also have an impact on research, to facilitate data sharing, deep phenotyping and better understanding of the photodermatoses.

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Legends

Figure 1*:* The location of Specialist Photodiagnostic Services in the UK and Republic of Ireland. *Service in set up

Figure 2: Representative patterns of diagnoses made in patients assessed through Specialist Photodiagnostic Services

PLE: polymorphic light eruption; CAD: chronic actinic dermatitis; AP: actinic prurigo; SU: solar urticaria; HV: hydroa vacciniforme

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Appendix 1: The in-house survey developed by authors and used to inform Workshop discussion

Appendix 2: Contact details for UK Photodiagnostic Services

Appendix 3: Phototesting equipment used in the UK and Ireland Photodiagnostic Centres

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Table 1: Waveband (central wavelength/half maximum bandwidth, nm) characteristics employed during narrow waveband phototesting at each of the Photodiagnostic centres

Centre*	**Monochromator wavelengths**
Dundee	305 (5) 335 (27) 365 (27) 400 (27) 430 (27) 460 (27) 500 (27) 600 (27) *Drug studies* *295 (5) 300 (5)*
Newcastle	300 (5) 320 (10) 350 (10) 400 (30) *And for SU only:* *450 (30) 500 (30)* *550 (30) 600 (30)*
Leeds	305 (5) 320 (13.5) 335 (27) 365 (27) 400 (27) 500 (27) 600 (27)
Manchester	300 (10) 320 (10) 330 (10) 350 (10) 370 (15) 400 (15) 500 (25) 600 (25)
Birmingham	In set up

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London	300 (5) 307.5 (5) 320 (10) 340 (20) 360 (20) 380 (20) 400 (20) *For SU* *500 (20) 600 (20)*
Southampton	300 (5) 307.5 (5) 320 (10) 340 (20) 360 (20) 380 (20) 400 (20) 500 (20) 600 (20)
Belfast	305 (5) 335 (27) 365 (27) 400 (27) 430 (27) 450 (27)
Dublin	300 (5) 320 (10) 370 (20) 400 (20)

*No data available for Oxford or Cambridge

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Table 2: An example of a visual grading system used to interpret phototest reactions

- Just perceptible erythema (Grade 1)
- Well established erythema (Grade 2)
- Erythema with oedema (Grade 3)
- Papular
- Vesicular
- Eczematous
- Pigmented
- Purpuric

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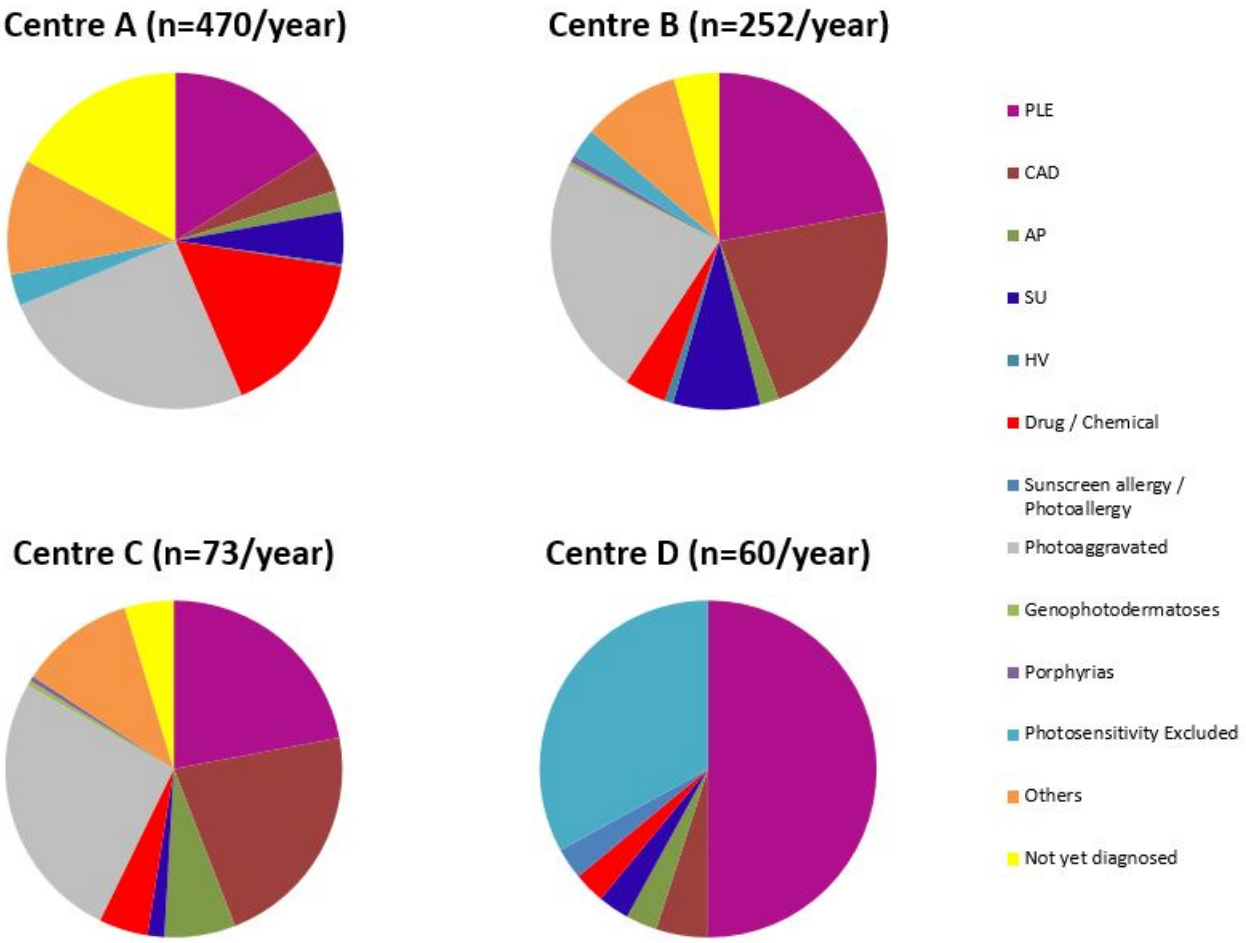

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