Epidemiological Assessments of Skin Outcomes in the Nurses' Health Studies

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Objectives. To review the contribution of the Nurses' Health Studies (NHSs) to identifying epidemiological factors associated with multiple skin diseases, including skin cancer, psoriasis, and other inflammatory and autoimmune skin diseases.

Methods. We carried out a narrative review of NHS articles published between 1976 and 2016.

Results. The NHSs have identified environmental and lifestyle factors related to psoriasis, supporting obesity and smoking as psoriasis risk factors; associations between psoriasis and diabetes, myocardial infarction, and Crohn's disease, supporting psoriasis as a systemic disorder; and associations of pigmentary traits, ultraviolet radiation, and lifestyle factors such as citrus consumption with risk of skin cancer. Genetic studies have identified novel genetic loci for skin pigmentation (e.g., *IRF4*, *SLC24A4*, *NID1*, and *EDNRB*) and skin cancer (e.g., *TET2* and *HERC2-OCA2*). Work continues on highly prevalent but less studied skin conditions such as rosacea, acne, and atopic dermatitis. The NHS results have influenced public health policies on indoor tanning devices.

Conclusions. The NHSs have provided invaluable resources on skin disease population science and contributed to the etiological understanding of multiple skin disorders. (*Am J Public Health.* 2016;106:1677–1683. doi:10.2105/AJPH.2016.303315)

Skin is the largest human organ. Skin conditions combined rank as the fourth leading cause of all human diseases, affecting almost one third of the world's population.[1] In addition to direct costs, skin diseases involve extremely high indirect costs and quality-of-life losses; for example, in 2004, these diseases accounted for a total economic burden of approximately $96 billion in the United States.[2] The burden of skin diseases highlights the need to strengthen research on their epidemiology and causes, which will promote disease prevention and treatment.

We gathered detailed data on skin-related outcomes collected through the Nurses' Health Studies (NHSs), including the NHS (initiated in 1976), the NHS II (initiated in 1989), and most recently the NHS3 (initiated in 2010). We had access to comprehensive data on multiple skin diseases, including, predominantly, skin cancer and major inflammatory and autoimmune skin diseases, skin phenotypes, and exposures related to skin conditions. Numerous epidemiological studies on skin outcomes based on the NHSs have been conducted since the 1980s, leading to more than 100 publications and contributing significantly to the dermatoepidemiology field. Here we narratively review the major data the NHSs have collected and the primary findings and contributions based on the NHS cohorts.

PSORIASIS

Psoriasis is a chronic inflammatory skin disorder with an estimated prevalence in the United States of 2% to 3%.[3] Psoriatic arthritis (PsA), an inflammatory musculoskeletal disorder that occurs in 6% to 42% of individuals with psoriasis, affects an estimated 520 000 individuals in the United States.[4]

Data Collection

In the NHS and NHS II, participants were asked whether they had ever been diagnosed by a physician as having psoriasis and, if so, when (Table 1). Among participants reporting a psoriasis diagnosis, Dominguez et al. used the validated Psoriasis Screening Tool questionnaire[5] to confirm the diagnosis. On the basis of multiple a priori hypotheses, scoring algorithms (with 99% sensitivity and 94% specificity) were developed to assign a diagnosis according to the participant's response. A total of 1611 psoriasis diagnoses have been confirmed in the NHS thus far, resulting in a 93.1% confirmation rate. In the NHS II, 1593 cases have been confirmed, and the confirmation rate for these diagnoses is 89.3%. Validation of self-reported psoriasis cases for the 2009 and 2013 follow-ups has begun.

In addition, again via the Psoriasis Screening Tool, participants were asked about the body surface area where psoriasis was at its worst. PsA diagnoses were confirmed with the Psoriatic Arthritis Screening and Evaluation questionnaire, which includes a 7-item symptom scale and an 8-item function scale.[6,7] Details on instrument design and pilot studies have been provided elsewhere.[6,7]

Psoriasis Risk Factors

Both genetic and nongenetic factors are involved in the onset and progression of psoriasis. The NHS cohorts showed that a number of environmental and lifestyle factors are associated with risk of psoriasis. Specifically, these studies provided the first prospective evidence linking obesity,[8] smoking,[9,10] alcohol intake,[11] and lack of physical activity[12] to risk

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TABLE 1—Data on Major Skin Outcomes Collected in the Nurses' Health Study (NHS) and the NHS II

	NHS		NHS II		
Skin Outcome	No. of Cases	Data Collection Period or Year(s)	No. of Cases	Data Collection Period or Year(s)	NHS3: No. of Cases
Skin cancer					
Melanoma[a]	1 216	Biennially	494	Biennially	236
Squamous cell carcinoma[a]	2 353	Biennially	546	Biennially	771 (keratinocyte carcinomas)
Basal cell carcinoma	23 720	Biennially	8 918	Biennially	
Keratinocyte carcinoma	15 413	2004	6 528	2005	NA
Inflammatory skin diseases					
Psoriasis[b]	1 611	2008	1 593	2005, 2009, 2013	1 263
Psoriatic arthritis[b]	212	2008	348	2005, 2009, 2013	. . .
Rosacea	. . .	. . .	6 689	2005	. . .
Severe acne	. . .	. . .	2 762	2013	. . .
Severe adolescent acne	. . .	. . .	8 114	1989	. . .
Eczema	. . .	. . .	9 706	2009, 2013	5 441
Pigmentation disorder					. . .
Vitiligo	625	2012	793	2011	. . .
Other diseases					. . .
Systemic lupus	1 220	1982, 1984, 1986, 2002, 2004, 2006, 2008, 2010, 2012	1 392	1993, 1997, 1999, 2001, 2003, 2005, 2007, 2009, 2011	185
Alopecia areata	402	2012	707	2011	. . .
Shingles	10 877	2012	7 664	2013	. . .

[a]Outcome confirmed through a review of pathological records.
[b]Outcome confirmed through use of supplementary questionnaires.

of psoriasis (see Appendix A, available as a supplement to the online version of this article at http://www.ajph.org, for related NHS and NHS II publications). Since the first provocative report on obesity and risk of psoriasis in 2007,[8] the NHS investigators have published several articles on similar themes, providing more evidence linking major components of obesity and metabolic syndrome to psoriasis risk. Measures of both overall and central obesity have been associated with increased risk of psoriasis.[8] The association appears even stronger for psoriasis with concomitant PsA.[13]

Li et al. also found an interaction between overall and central obesity and *IL12B* genetic polymorphism with respect to psoriasis risk.[14] Both hypertension and hypercholesterolemia are clinical predictors of elevated risk of subsequent psoriasis independent of obesity. Li et al. and Setty et al. found a significant association between smoking and increased psoriasis risk, a trend toward an elevated risk with increasing cumulative measures of smoking, and a graded reduction in risk with increasing time since quitting smoking.[9,10] Independent from smoking, excessive alcohol intake, particularly intake of nonlight beer, may increase the risk of psoriasis.[11] The association for smoking and alcohol intake appeared stronger for psoriasis with concomitant PsA.[15,16] Lack of physical activity is another major risk factor for psoriasis.[12]

In addition, the NHSs have linked rotating night shift work, depression, periodontal bone loss, gallstones, and snoring and obstructive sleep apnea–hypopnea syndrome with increased risk of psoriasis. The NHS investigators have found null associations between psoriasis and coffee, caffeine, and vitamin D intake and use of nonsteroidal anti-inflammatory drugs. However, use of long-term acetaminophens and nonsteroidal anti-inflammatory drugs may still be associated with an increased risk of PsA.

Psoriasis Comorbidities

Lindegård's pioneering cross-sectional study on associations between selected conditions and psoriasis revealed excessive rates of obesity, diabetes, cancer, and myocardial infarction among women.[17] Epidemiological studies focusing on the association between

psoriasis and a spectrum of other comorbidities have been increasing in frequency in recent years, promoting recognition of psoriasis as a systemic disorder.

The NHS investigators have conducted prospective studies on the associations between psoriasis and incident risk of multiple chronic diseases.[18–21] Li et al. found, for example, a significantly increased risk of type 2 diabetes associated with psoriasis, particularly among younger women and those who develop psoriasis at an early age.[18] Another study showed that the presence of psoriasis was associated with an increased risk of nonfatal cardiovascular disease, particularly myocardial infarction.[19] Specifically, those with an earlier onset or longer duration of psoriasis had a higher risk of myocardial infarction.[19] Li et al. conducted the first prospective study providing evidence of an association between psoriasis and increased risk of Crohn's disease,[20] as well as increased risk of gout.[21] In support of a bidirectional relationship between psoriasis and depression, the NHS investigators also found an increased risk of depression among women with psoriasis.

All of the associations just described appeared stronger among people with psoriasis who reported concomitant PsA. Recently, Li et al. (2016) examined the association between psoriasis and risk of cancer and found positive associations for melanoma and kidney cancer.

SKIN CANCER

Cancer of the skin (keratinocyte carcinoma [KC] and melanoma combined) results in estimated annual treatment costs of $8.1 billion in the United States. Melanoma is the most serious type of skin cancer.[22] KC, which comprises basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) and is often referred to as nonmelanoma skin cancer, is the most common cancer in the United States.[22]

Data Collection

In the NHSs, participants have reported diagnoses of melanoma, SCC, and BCC biennially since the inception of the cohort (Table 1). When a diagnosis is reported, related medical records are requested with the participant's permission and reviewed by dermatologists to confirm the diagnosis. Pathology reports are reviewed according to established criteria. For melanoma and SCC, only cases pathologically confirmed according to medical record reviews are documented as outcomes. Confirmation rates for melanoma and SCC are 93% and 97%, respectively.

The NHSs have information available on body site for melanoma and SCC and information on major histopathological variables for melanoma. Although the investigators did not seek to obtain medical records for all BCC cases, previous studies have indicated high levels of validity for self-reports (above 90% in some cases). The NHSs also collected information on cumulative number of KCs (Table 1), with a validation study conducted among 200 patients who reported KCs showing a confirmation rate of 92%.

Constitutional and Environmental Risk Factors for Skin Cancer

The NHSs collected information on pigmentary traits. Data on sun exposure and indoor tanning were collected for different lifetime periods. The erythemal ultraviolet (UV) index at birth, age 15 years, and age 30 years and cumulative UV flux in adulthood, based on state of residence, have been developed to estimate solar UV radiation.[23,24] The NHSs collected detailed information on environmental, lifestyle, and host characteristics. Since 1991, recall bias has been found in assessments of tanning ability in NHS participants with melanoma, and these analyses have revealed the limitations of case–control study designs. Primarily in prospective analyses, epidemiological studies have examined major risk factors associated with skin cancer.

Pigmentary traits. Major pigmentary traits, including natural red or blonde hair, increased number of melanocytic nevi (moles), high numbers of sunburns, burn or blistering skin reactions to the sun, and poor tanning tendency, have been associated with an increased risk of melanoma, SCC, and BCC in the NHS cohorts,[25–27] along with incremental risks of multiple KCs and a higher number of KCs. In the late 1980s, Bain et al. and Weinstock et al. published the earliest skin outcome–related studies on mole counts and melanoma risk based on NHS data.[28,29] Increasing mole counts have been differentially associated with 3 types of skin cancer, with higher effect magnitudes for melanoma than for SCC or BCC.[30] Associations with pigmentary traits may differ by body site, a possibility supported by evidence that a history of blistering and painful sunburn is more strongly related to upper-extremity melanoma and that mole count is more strongly related to trunk melanoma.[31] However, no differential associations with melanoma have been observed according to mole body sites.[29]

Sun exposure and ultraviolet correlates. Sun exposure is the most recognized skin cancer risk factor, and it has been the primary area of focus since the earliest NHS skin outcome–related studies. In 1989, a nested case–control study showed that a history of blistering sunburns and a more equatorial latitude of residence had a stronger association with melanoma risk among those aged 15 to 20 years than among those older than 30 years, supporting the hypothesis that sun exposure at early ages is more closely linked to melanoma risk.[32] Another study showed that bikini use among young women aged 15 to 20 years may not be a major risk factor for trunk melanoma[33]; in the NHS, not all women with frequent sun exposures had an augmented risk of melanoma, presumably because sun-resistant women develop a photo-protective tan.[33]

Qureshi and colleagues have comprehensively examined the associations between risk of skin cancer and UV radiation based on residential history, and the results support heterogeneous associations between sun exposure and risks of different types of skin cancer.[23,24,27] Two studies revealed that gradient of adulthood UV index scores did not markedly change the risk of invasive melanoma or melanoma in situ.[23,34] Another 2 studies showed that high cumulative UV flux was not associated with an increased risk of melanoma.[24,27] By contrast, risk of KC was found to be independently affected by residence in locations with medium and high UV indexes or higher cumulative UV flux; the effect magnitude was stronger for SCC, which corresponds with the recognition that sustained sun exposure results in a higher risk of SCC than BCC.[23,24,27] In addition, consistent ambient UV exposures among those residing in states with medium and high UV indexes may increase the risk of KC development later in life.

Furthermore, level of plasma vitamin D, which reasonably reflects long-term sun

exposure, has been positively associated with risk of KC. Although lifetime (both adulthood and early life) sun exposure is essential for the development of KC, melanoma risk has been predominantly associated with sun exposure in early life.[23,27] Our data suggest that higher UV indexes at birth and age 15 years and increased numbers of blistering sunburns at age 15 to 20 years are associated with an increased risk of melanoma.[23]

Indoor tanning with artificial UV radiation may be contributing to the relentless rise in skin cancer incidence. Our data supported a significantly increased risk of KC associated with frequent indoor tanning and early life exposure to indoor tanning and also showed suggestive evidence of an increased risk of melanoma in a dose-dependent manner.[35,36]

Citrus and other dietary factors. Earlier NHS publications on dietary intake and skin cancer have basically reported null findings, and these results do not support the hypothesis that dietary intake of vitamins, folate, or specific carotenoids plays a protective role against the occurrence of KC. Researchers in a later study did not find an inverse association between dietary intake of vitamins and risk of melanoma; by contrast, they reported an increased risk of melanoma associated with high intakes of dietary vitamin C and orange juice but not supplemental vitamin C.[37] Given the preferential toxicity of vitamin C for melanoma cells, the effect is likely due to other components (e.g., photoactive compounds such as furocoumarins) of foods rich in vitamin C.[37]

Wu et al. recently found that increased consumption of citrus products, which are rich in psoralens and furocoumarins with known potential photocarcinogenic properties, was associated with an increased risk of melanoma.[37] The association appeared strongest for grapefruit. Consistent with a potential synergistic effect between psoralens and UV radiation, the association appeared to be stronger among those with a higher susceptibility to sunburn as children or adolescents, those with more blistering sunburns, and those who spent more time in direct sunlight.[37] The authors found positive associations between citrus consumption and risk of KC as well.

Alcohol, coffee, and caffeine intake were also examined with respect to their association with skin cancer. Alcohol intake has been associated with an increased risk of BCC. Increasing caffeine intake and caffeinated coffee consumption have been associated with a decreased risk of melanoma and BCC.

Potential androgen basis of melanoma and other lifestyle factors. The NHS results showed that men had a higher risk than women of developing melanoma, particularly on the head or neck and trunk.[31] In addition to the effect of sun exposure, Li et al. hypothesized a potential androgen basis of melanoma to explain the gender distribution[38]; these authors reported an increased risk of melanoma but not KC associated with a personal history of prostate cancer in the Health Professionals' Follow-up Study (HPFS).[38] Supporting this hypothesis,[35] Zhang et al. (2015) recently reported that women with a history of severe adolescent acne had higher midlife plasma free testosterone levels and were at increased risk for melanoma.

The NHS investigators examined other lifestyle factors and risk of skin cancer. Both smoking and duration of rotating night shift work were independently associated with decreased melanoma risk. Night shift work was also inversely associated with risk of KC. Among premenopausal women, current oral contraceptive use was associated with an increased risk of melanoma.

GENETIC STUDIES

Genetic studies based on the NHSs span from the candidate genetic era more than 10 years ago to genome-wide association studies (GWASs) and post-GWAS research, including studies on individual genetic variations and pathways as well as genetic and expression profiles.

Candidate Gene Studies

Since 2004, a number of NHS-based candidate gene studies on skin cancer have been published (Table A, available as a supplement to the online version of this article at http://www.ajph.org). Starting from the initial studies on DNA repair genes, multiple genetic variants in cell growth, telomere maintenance, oxidative stress, inflammatory response, and pigmentation genes have been associated with pigmentary traits and skin cancer risk. Although most studies have focused on germ-line genetic variants, one investigation examined somatic mutations of *BRAF* and *NRAS*.

Genome-Wide Association Studies

GWASs have greatly advanced the identification of low-penetrance genetic loci. Several GWASs based on in silico analyses of the NHS and HPFS genome data have been conducted (Table 2), including those just detailed.[39–42] In other GWASs, NHS and HPFS data have served as a major part of the discovery set. These studies have identified a number of novel genetic loci, such as *IRF4*, *SLC24A4*, *NID1*, and *EDNRB* for skin pigmentary traits and *TET2* and *HERC2-OCA2* for melanoma, contributing significantly to the genetic architecture of skin pigmentation and skin cancer (Table 2).

Pathway analyses help identify biological pathways that might be missed in standard GWAS approaches. One traditional pathway analysis identified 4 pathways associated with risk of BCC through assigning genetic variants to their physical location. In another study, information on quantitative trait loci was integrated into the BCC assessment, and the pathway analysis identified the JAK-STAT pathway associated with risk of BCC.

In terms of post-GWAS research, candidate gene analyses of skin cancer have incorporated GWASs focusing on other phenotypes to identify unrevealed genetic susceptibility in standard investigations (Table A). GWAS meta-analyses and pooled analyses integrating GWAS data from the NHS and other resources increase levels of statistical power, helping to identify low-penetrance loci.

Telomere Length and Skin Cancer

Shorter relative telomere length in peripheral blood leukocytes has been associated with fewer moles and a decreased risk of melanoma.[43] By contrast, telomere length in peripheral blood leukocytes may not play a substantial role in SCC or BCC. Nan et al. (2011) have provided evidence for the contribution of genetic variants in the telomere-maintaining genes to melanoma susceptibility but not to SCC or BCC risk.

Expression Profiling

The genomic structure of skin cancer was also explored in NHS-based investigations through evaluations of the entire genome mRNA expression profiling of melanoma tissues. One analysis showed

TABLE 2—Major Genome-Wide Association Studies (GWASs) Incorporating Nurses' Health Study (NHS) Data

Authors	Phenotype	Major Findings
Han et al.[39]	Hair color, skin color, tanning ability, eye color	This GWAS linked the *IRF4* (6p25-p23) and *SLC24A4* (14q32) loci to human pigmentation for the first time; the study also identified 3 chromosome regions adjacent to the previously known pigmentation genes: *MC1R* (16q24), *OCA2/HERC2* (15q11-q13), and *MATP* (5p13)
Nan et al. (2009)	Tanning ability	This GWAS confirmed the prior known pigmentation genes (*MATP*, *IRF4*, *TYR*, *OCA2*, *MC1R*) associated with tanning ability
Nan et al. (2011)	Number of melanocytic nevi (moles); melanoma only in the post-GWAS candidate gene analysis	This GWAS identified rs3768080 and rs10754833 (NID1, 1q42), associated with nevus count; also, rs10754833 was associated with melanoma risk
Nan et al.[40]	BCC; SCC and melanoma only in the post-GWAS candidate gene analysis	rs1805007 in MC1R showed the strongest association with BCC risk in the discovery set; this study showed that rs12210050 (near *EXOC2*, 6p25) and rs7335046 (near *UBAC2*, 13q32) confer susceptibility to BCC; further candidate gene analysis revealed associations of these 2 SNPs with risk of SCC but not melanoma
Amos et al. (2011)[a]	Melanoma	This GWAS identified novel SNPs in *HERC2/OCA2* (15q13.1) as well as an intergenic region of chromosome 1q21.3 associated with melanoma risk; it also confirmed associations for several previously identified regions: *MATP*, *CDKN2A*, *TYR*, *MC1R*, a broad region in 20q11, and a region of 22q13 encompassing *PLA2G6*
Zhang et al.[41]	Hair color, eye color, number of sunburns, tanning ability, number of keratinocyte carcinomas	A new region downstream of *EDNRB* (13q22) was associated with hair color; Rs3002288 in *VASH2* (1q32.3) was associated with brown eye color; 2 SNPs in the *ITRF4-EXOC2* region (6p25-p23) and 1 SNP upstream of *GNG2* (14q22) were associated with number of keratinocyte carcinomas
Song et al. (2014)	Melanoma	This GWAS identified a novel SNP, rs4698934 (*TET2*, 4q24), associated with melanoma; next-generation sequencing further identified a novel somatic mutation in melanoma
Zhang et al. (2014)[b]	Severe adolescent acne	rs4133274 (upstream of *MYC*, 8q24) revealed the most significant association
Siiskonen et al. (2016)	SCC	This GWAS identified rs8063761 (*DEF8*, 16q24) and several other genetic variants associated with risk of SCC

Note. BCC = basal cell carcinoma; SCC = squamous cell carcinoma; SNP = single nucleotide polymorphism. The studies included are major studies with NHS investigators as the leading (or co-leading) or senior (or co-senior) authors.

[a]NHS data contributed only to the replication stage of this study.

[b]This study did not include the GWAS discovery replication phase.

that the CXCR4 pathway might constitute a novel susceptibility pathway associated with a family history of melanoma.[44]

MAJOR CHALLENGES AND ONGOING EFFORTS

Most previous NHS-related analyses have been high-quality epidemiological studies, with tremendous effort focused on methodological rigor. More recently, the NHS investigators have been integrating epidemiological associations with genomic data and laboratory collaborations to help elucidate the mechanisms underlying the associations observed. For example, *PGC-1B* polymorphisms have been associated with tanning ability and melanoma susceptibility, which, along with basic science data, supports the regulatory role of PGC-1 coactivators in human tanning.[45] Publication of our epidemiological findings on citrus consumption and melanoma[37] has led to further research on furocoumarin levels in citrus fruit and juice and participants' blood samples as a means of confirming the photocarcinogenesis hypothesis.

Future efforts are needed to fill in knowledge gaps, taking advantage of our wealth of questionnaire data and our biospecimen repository as well as emerging new

techniques. The spectrum of comorbidities associated with psoriasis is ever growing, and the mechanistic pathways leading to these comorbidities need to be elucidated. As psoriasis has been associated with lifestyle factors and comorbidities featuring aberrant metabolic characteristics, metabolomic profiling may help in exploring the etiology and networks of the systemic metabolic and inflammatory status underlying psoriasis and its comorbidities.

The incidence of both melanoma and KC is still rising dramatically both in the United States and globally,[22] which calls for further efforts focused on risk factor identification. Most recently, our interest is in the addictive property of frequent indoor tanning and risk of skin cancer; this addictive property is corroborated by our finding of a significantly increased risk of food addiction among frequent indoor tanners (Li et al., unpublished data). On the basis of our decades of epidemiological studies, constructing risk prediction models is warranted for risk assessment and precision management of psoriasis and skin cancer.

The demand for large sample sizes in genetic studies requires collaborative research. The NHS investigators are working with multiple groups and consortiums worldwide to assess the genetics of psoriasis and skin cancer. For example, a recent international 2-stage meta-analysis of melanoma GWASs led by Law et al. (2015), representing the largest study to date, confirmed all 13 previously reported melanoma-related loci and resolved a pair of likely associations at *CCND1* and *HERC2-OCA2*.

The current level of understanding of the etiology and risk factors for most skin diseases is still limited. The NHS investigators have published several articles on rosacea, acne, vitiligo, and atopic dermatitis (see Appendix B, available as a supplement to the online version of this article at http://www.ajph.org) and have begun to investigate the risk factors for alopecia areata. Although the NHSs have a well-recognized reputation with respect to quality of self-reported data on psoriasis and skin cancer, validation of skin diseases based on supplementary questionnaires completed by participants cannot fully address concerns regarding reporting bias, even given the backgrounds of the participants as health professionals.

Efforts are being made to further improve validation, which will lay the foundation for future research. For example, Qureshi and colleagues are in the process of collecting information on treatment of psoriasis, including use of systemic therapy and psoriasis severity. On the basis of our past work on moles, we are working on validation of atypical nevi. As the NHS participants have aged, the NHS II and NHS3 have collected data on younger populations, covering a wide range of ages relevant to different skin diseases. The NHS3 is collecting data on multiple skin diseases (Table 1), and data will soon be collected on atopic dermatitis, atypical nevi, and hidradenitis suppurativa, which should provide crucial information for future explorations. Particularly in the NHS3, efforts are needed to collect data on other understudied skin outcomes as well, including blistering disorders, keloid scars, stretch marks (striae), and pruritus (itching).

Translating epidemiological findings into clinical and public health practices and policies has always been our primary motivation for research. NHS publications on UV radiation, including prospective studies on early life exposures and long-term follow-ups, helped buttress the decision of the International Agency for Research on Cancer to declare UV radiation and UV-emitting tanning devices as class I carcinogens. These findings also supported the subsequent announcements of the Food and Drug Administration and the Centers for Disease Control and Prevention regarding the risks associated with UV radiation as well as safety measures and regulations for indoor tanning devices. Our publications on psoriasis risk factors and comorbidities have been frequently highlighted by major professional societies (e.g., the National Psoriasis Foundation) and social media, widely raising public awareness and having a positive impact on medical practices.

In summary, the NHSs have provided invaluable resources on skin disease population science, including insights on cancer and inflammatory conditions. Research based on the NHS cohorts has made a remarkable contribution to the etiological understanding of multiple skin disorders. The NHS investigative team is one of the most recognized dermatoepidemiology groups in the country and also has become known worldwide. The collaborations that have resulted with groups in varied disciplines outside dermatology are a crucial part of the past work emanating from these cohorts, further emphasizing the relevance of skin conditions in systemic disease and the overall health of the US population. AJPH

CONTRIBUTORS

W.-Q. Li contributed to conceptualizing the outline for the article and led the writing and revisions. E. Cho and M. A. Weinstock made critical revisions to the article. H. Mashfiq contributed to the writing of the skin cancer section. A. A. Qureshi contributed to conceptualizing the outline for the article and made critical revisions. All of the authors contributed substantially to the concept and design of the study and to the drafting or revision of the article.

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HUMAN PARTICIPANT PROTECTION

The Nurses' Health Studies were approved by the institutional review board of Brigham and Women's Hospital. Participants' completion and return of their self-administered questionnaire was considered informed consent.

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EDITOR'S NOTE

Because of space restrictions and the large volume of references relevant to the Nurses' Health Study, additional references are provided in a supplement to the online version of this article at http://www.ajph.org.