Contents lists available at ScienceDirect



Review

International Journal of Women's Dermatology



Dermatology on the global stage: The role of dermatologists in international health advocacy and COVID-19 research



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ARTICLE INFO

Article history: Received 21 July 2021 Revised 13 October 2021 Accepted 14 October 2021

Keywords: Global health infectious disease COVID-19 neglected tropical diseases scabies health policy women's dermatology

ABSTRACT

Background: Over the last decade, there has been a surge in interest and funding for global health dermatology. Skin conditions are now recognized as the fourth leading cause of nonfatal disease burden worldwide in disability-adjusted life years. Dermatologists are uniquely positioned within global health because skin conditions are often the presenting sign of severe illnesses, such as neglected tropical diseases and COVID-19.

Methods: We review four major areas of work by dermatologists within global health: i) characterization of global burden of skin disease, ii) advocacy for dermatologic therapies on the World Health Organization's Model List of Essential Medicines, iii) advancements in global programming for skin-related tropical diseases, and iv) the role of dermatologists during the COVID-19 pandemic. For each area of work, the significance and impact on the health of women and girls is briefly highlighted.

Results: Dermatologists have led the efforts to quantify and evaluate the global burden of skin disease, the burden of which is disproportionately shared by women. The dermatology community has also championed global efforts to eliminate skin-related neglected tropical diseases, such as scabies. Through national and international policy advocacy, dermatologists have pushed for more dermatologic therapies in the World Health Organization's Model List of Essential Medicines, helping to secure better care for patients with skin disease throughout the world. Since 2020, the dermatology community has worked collaboratively in the fight against COVID-19, establishing a worldwide registry for cutaneous manifestations of SARS-CoV-2 and pursuing research that has allowed colleagues in the house of medicine to better understand this landmark disease.

Conclusion: Through the study and promotion of global health, dermatologists have an important role in the house of medicine.

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https://doi.org/10.1016/j.ijwd.2021.10.003

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What is known about this subject in regard to women and their families?

- Globally, women share a greater burden of total skin and subcutaneous diseases compared with men, as well as a greater burden of the two highest contributing skin diseases to global disability-adjusted life years: acne and dermatitis.
- Women can be disproportionately affected by skinrelated neglected tropical diseases due to greater exposure in endemic areas and sociocultural stigma compared with men.

What is new from this article as messages for women and their families?

- More work needs to be done to quantify and characterize disparities in skin disease in women and girls.
- Improving access to dermatologic essential medicines has the potential to improve the social, mental, and economic well-being of women in resource-limited settings throughout the world.

Introduction

The field of dermatology has historically been underprioritized by the international health community, traditionally receiving smaller amounts of funding for research, education, and development of the field compared with other medical specialties (Hagstrom et al., 2015; Morrone, 2007; Seth et al., 2017). Over the last two decades, however, there has been a considerable surge in interest, programming, and funding, congruent with the number of academic achievements within the international dermatologic community (Kingman, 2005). Skin conditions are now recognized as the fourth leading cause of nonfatal disease burden worldwide in disability-adjusted life years (DALYs; Karimkhani et al., 2017). Hence, the dermatology community has played a prominent role in setting the global health agenda for conditions ranging from HIV to neglected tropical diseases (NTDs) in recent years. Dermatologists are also increasingly recognized as uniquely positioned in the healthcare landscape, given that skin conditions are often the presenting face of severe systemic illnesses, such as HIV and, more recently, COVID-19 (Mosam et al., 2004; Visconti et al., 2021).

Although small in number, dermatologists worldwide have successfully provided and advocated for novel, cost-effective, and practical approaches to rapidly address old and emerging problems in health. From the implementation of new dermatologic training sites globally to effectively steering the priorities of governing health institutions, the efforts of dermatologists to relieve outsized levels of human suffering have been widely successful (Hay and Marks, 2004; Hay, 2012). This section of the issue on House of Medicine and Dermatology will showcase four major areas of work for dermatologists within global health: i) characterization of global burden of skin disease, ii) advocacy for dermatologic therapies on the World Health Organization (WHO)'s Model List of Essential Medicines (WMLEM), iii) advancements in global programming for skin-related tropical diseases, and iv) the role of dermatologists during the COVID-19 pandemic. Each section will also briefly highlight how each area of work has significant implications for the health of women and their families worldwide.

Global burden of skin disease

Skin disease greatly contributes to the overall global burden of disease, especially in resource-limited areas of the world. Over the

last decade, data published by the Global Burden of Disease (GBD) project has been an essential tool in measuring the impact of dermatologic disease worldwide. The GBD project is a collaborative effort of thousands of health experts, coordinated by the Institutes of Health Metrics and Evaluation (IHME) and funded by the Bill and Melinda Gates Foundation. It provides access to high-fidelity and comprehensive global mortality and morbidity estimates in DALYs for a broad range of diseases, including those that affect the skin (IHME, 2019). Indeed, per the GBD project, illnesses that directly affect the skin were found to be the fourth leading cause of nonfatal disease burden worldwide (Boyers et al., 2014). The most recent GBD project data released in 2019 also revealed that the global number of DALYs attributable to skin or subcutaneous diseases approximated >42 million.

Dermatologists have been instrumental in leading the efforts to quantify global skin disease in the last decade, both in collaboration with the IHME and through independent research efforts. Notably, dermatologists such as Drs. Roderick Hay and Robert Dellavalle have led or contributed significantly to the publication of many of the highest-impact papers analyzing and estimating the overall global burden of skin disease (Hay et al., 2014; Karimkhani et al., 2014; 2017). Recently, Laughter et al. (2021) presented data from the GBD project for the first time on atopic dermatitis and revealed that it ranked 15th among all nonfatal diseases measured by DALYs between 1990 and 2017 (Flohr and Hay, 2021; Laughter et al., 2021). Lastly, with initiatives such as the Grand Challenges in Global Skin Health launched by the International League of Dermatological Societies (ILDS), the dermatology community has declared its commitment to making skin health a realizable global objective, starting with data collection and analysis that will improve our understanding of the worldwide burden of skin disease (Hay et al., 2015).

Efforts to quantify skin disease throughout the world have been crucial to identify diseases that disproportionately affect women and girls. For instance, the 2019 GBD project data show that women overall tended to have a higher burden of skin disease than men (22.8 million vs. 20.0 million DALYs; confidence intervals [CIs] overlap). Additionally, of all DALYs experienced by women, a higher proportion are due to skin and subcutaneous disease than in men (1.91% vs. 1.48%; Table 1). Since 2013, the global percentage of DALYs attributable to skin and subcutaneous diseases have steadily increased from 1.59% to 1.68% in 2019, with women accruing a greater amount of DALYs over time (593 vs. 515 per 100,000). Diseases such as dermatitis and acne have continued to account for the largest amount of DALYs, with women sharing a greater burden in both acne (2.7 million vs. 2.2 million DALYs; CIs overlap) and dermatitis (5.8 million vs. 4.3 million DALYs; CIs overlap; IHME, 2019).

Given the evident contribution of skin conditions to the overall global burden of disease, more work needs to be done in quantifying their scope and impact, as well as understanding how and why these diseases affect women disproportionately.

Model List of Essential Medicines and dermatology

In addition to helping quantify disease globally, dermatologists have also researched and advocated for better access to treatments that would alleviate the burden of dermatologic conditions worldwide. In 2021, the WHO released its update of the WMLEM, which recommends the most efficient, safe, and cost-effective therapies that meet the minimum needs of a health system. The WMLEM is used globally by high- and low-income countries to assist in the development of local lists of essential medicines. The list is

Table 1

Skin-related disability-adjusted life years by percent of global burden in 2019*

| Skin or subcutaneous disorder † | Men | | Women | |
|--|------|-----------|-------|-----------|
| | % | 95% CI‡ | % | 95% CI‡ |
| Total | 1.48 | 1.04-2.10 | 1.91 | 1.37-2.63 |
| Dermatitis | 0.32 | 0.19-0.47 | 0.48 | 0.30-0.72 |
| Acne vulgaris | 0.16 | 0.10-0.25 | 0.23 | 0.14-0.34 |
| Scabies | 0.18 | 0.11-0.28 | 0.20 | 0.12-0.30 |
| Viral skin diseases | 0.18 | 0.12-0.26 | 0.19 | 0.13-0.27 |
| Urticaria | 0.12 | 0.08-0.16 | 0.19 | 0.14-0.25 |
| Psoriasis | 0.13 | 0.10-0.17 | 0.15 | 0.11-0.18 |
| Fungal skin diseases | 0.12 | 0.05-0.25 | 0.13 | 0.05-0.26 |
| Bacterial skin diseases | 0.08 | 0.05-0.10 | 0.09 | 0.07-0.11 |
| Alopecia areata | 0.02 | 0.01-0.02 | 0.03 | 0.02-0.05 |
| Pruritus | 0.03 | 0.01-0.04 | 0.04 | 0.02-0.07 |
| Decubitus ulcer | 0.02 | 0.01-0.02 | 0.02 | 0.02-0.03 |
| Other skin and subcutaneous disorders | 0.13 | 0.06-0.22 | 0.16 | 0.08-0.28 |

CI, confidence interval.

* Source: Institute for Health Metrics and Evaluation, 2019.

[†] Does not include skin cancers (e.g., melanoma, basal cell carcinoma).

[‡] Overlapping CIs.

Table 2

Topical dermatologic therapies on the World Health Organization Essential Medicines List, 8th Edition (World Health Organization, 2021)

| Category | Adult medications | Pediatric medications |
|--|------------------------|------------------------|
| Antifungal | Miconazole | Miconazole |
| | Sodium thiosulfate | Terbinafine |
| | Selenium sulfide | |
| | Terbinafine | |
| Anti-infective | Mupirocin | Mupirocin |
| | Potassium permanganate | Potassium permanganate |
| | Silver sulfadiazine | Silver sulfadiazine |
| Anti-inflammatory and antipruritic | Betamethasone | Betamethasone |
| | Calamine | Calamine |
| | Hydrocortisone | Hydrocortisone |
| Skin differentiation and proliferation | Calcipotriol | Calcipotriol |
| | Benzoyl peroxide | Benzoyl peroxide |
| | Coal tar | Coal tar |
| | Fluorouracil | Podophyllum resin |
| | Podophyllum resin | Salicylic Acid |
| | Salicylic Acid | Urea |
| | Urea | |
| Scabicide/pediculicide | Benzyl benzoate | Benzyl benzoate |
| | Permethrin | Permethrin |

updated every 2 years and dermatologic therapies have been updated periodically. The most up-to-date WMLEM published in June 2021 recommended a total list of 19 dermatologic therapies for adults and 16 for children (Subsection 13), categorized into antifungal, anti-infective, anti-inflammatory/antipruritic, skin differentiation and proliferation, and scabicide/pediculicide (Table 2; WHO, 2021). Although the presence of the 19 adult and 16 pediatric therapies is significant among the total of 460 medications listed in the 2021 WMLEM, advocacy for more dermatologic treatments on the list is ongoing. Over the last decade, the global dermatology community has been working collaboratively to propose amendments with the goal of reducing the global burden caused by skin disorders.

Dellavale et al. recently compared the WMLEM with the crucial medicines for dermatologic treatment listed by *Treatment of Skin Diseases*, the globally used text detailing 136 first-line treatments for dermatologic conditions. They found that, of these 136 treatments, only 32 were a first-line dermatologic indication on the WMLEMS (Rundle et al., 2021). Given that current recommendations are based primarily on expert opinions, dermatology experts have called for a more evidence-supported list of first-line treatments based on rigorous peer-reviewed research. A few proposed modifications to the list have included the addition of biologics and methotrexate for the treatment of psoriasis, alongside the already-listed coal tar, salicylic acid, betamethasone valerate, and hydrocortisone. This year, the ILDS put forward two applications to update the WMLEM, including calcipotriol for psoriasis and hydroxychloroquine for dermatologic diseases (ILDS, 2020). Calcipotriol was successfully added to the recently published 2021 edition of the WMLEM (WHO, 2021).

It should be noted that access to essential medicines has salient effects on the health of women and their families. Access to dermatologic medications is of great importance in societies where gender norms may disproportionately impact socioeconomically disadvantaged women (Germain et al., 2021; WHO, 2016). Disability and changes in appearance resulting from dermatologic conditions can limit women's employment prospects and marriageability, impacting their mental and social wellbeing (Vlassoff et al., 2000). It is also possible for women and girls to suffer disparate socioeconomic consequences if they are expected to take time away from school or work secondary to the stigma of dermatologic disease. Hence, improving access to dermatologic medications has significant ramifications, especially for the most marginalized and disadvantaged women globally.

Skin-related neglected tropical diseases

Great strides have also been made for dermatology in the broader public health context with respect to NTDs. In 2017, scabies was added to the official WHO portfolio of 20 NTDs, given

Table 3Skin-related neglected tropical diseases

| Neglected tropical disease | Skin involvement* | Example skin findings |
|-----------------------------------|-------------------------|--|
| Buruli ulcer | Skin as primary symptom | Painless singular ulcers with undermined edges commonly involving the limbs (Guarner, 2018; Hospers et al., 2005) |
| Leishmaniasis | | |
| Cutaneous | Skin as primary symptom | Pink papules progressing to nodules with central ulceration and indurated borders (Dowlati, 1996) |
| Postkala-azar dermal | Skin as primary symptom | Erythematous hypopigmented macules progressing to plaques or nodules (Zijlstra et al., 2003) |
| Lymphatic filariasis | Skin as primary symptom | Lymphedema of lower limbs and hydrocele (Pani and Srividya, 1995) |
| Onchocerciasis | Skin as primary symptom | Small, widely scattered pruritic papules (acute papular onchodermatitis; Murdoch et al., 1993) |
| Leprosy | Skin as primary symptom | Well-defined hypopigmented or reddish anesthetic patches (tuberculoid; World Health Organization, 2018b) |
| Mycetoma† | Skin as primary symptom | Painless, indurated, subcutaneous nodules (early finding; Hazra et al., 1998) |
| Scabies and other ectoparasites | Skin as primary symptom | Multiple erythematous pruritic papules with excoriations and burrows (scabies; Chosidow, 2000) |
| Yaws | Skin as primary symptom | Large, pruritic, nontender ulcer forming a honey-brown crust (mother yaw; (Farnsworth and Rosen, 2006) |
| Dracunculiasis (Guinea worm) | Skin as primary symptom | Painful dermal papule usually on the lower extremities (Greenaway, 2004) |
| Chagas disease | Common skin involvement | Unilateral edema of eyelid (Romaña's sign), edematous nodules at inoculation site (chagoma; Bern, 2015) |
| Taeniasis and cysticercosis | Common skin involvement | Painless subcutaneous nodules (World Health Organization, 2021b) |
| Arboviruses (Dengue, Chikungunya) | Common skin involvement | Diffuse macular or maculopapular eruptions (Wilder-Smith et al., 2019) |
| Trypanosomiasis | Common skin involvement | Circinate erythematous macules most prominent on the trunk (Cochran and Rosen, 1983) |
| Schistosomiasis | Common skin involvement | Erythematous pruritic papules (Swimmer's itch; Hoeffler, 1974) |
| Soil-transmitted helminthiases | Common skin involvement | Serpiginous skin lesions and eruptions (Arthur and Shelley, 1958; Jelinek et al., 1994) |
| Trachoma | Common skin involvement | Inward rolling of eyelid due to scarring (entropion; West et al., 2001) |
| Snakebite envenoming | Common skin involvement | Localized edema, ecchymosis, and blistering of inoculation site (Gutierrez et al., 2017) |
| Rabies | Rare skin involvement | Diffuse, nonpurpuric, maculopapular rash (Despond et al., 2002) |
| Echinococcosis | Rare skin involvement | Hyperpigmentation with lichenification (Velasco-Tirado et al., 2016) |
| Foodborne trematodiases | Rare skin involvement | Nonmigratory, indurated, subcutaneous nodule (Kodoma et al., 2014) |

* For the category "Skin as primary symptom," this was defined by WHO listing as a "skin-related NTD" (World Health Organization 2018a).

[†] Includes chromoblastomycosis and other deep mycoses.

its large global prevalence and substantial global burden in DALYs. Additionally, it became increasingly recognized that secondarily infected scabies by streptococcal species had the serious and potentially lethal sequelae of poststreptococcal nephritis and chronic renal failure (Chung et al., 2014). The inclusion of scabies has not only paved the way for a more integrated approach to addressing skin NTDs, but signaled a poignant acknowledgment that dermatologic conditions are a priority on the global health agenda (Engelman et al., 2019). The addition was the result of a longterm collaborative effort by advocacy groups, such as the NTD Network, International Alliance for the Control of Scabies, and individual WHO country offices (WHO, 2017). For at least a decade, these groups worked collaboratively with the global dermatology community in their appeals to the WHO Department of NTDs, conducting widescale studies to map the burden of scabies and its impact on the world's poorest populations and develop strategies for control and management. The appeal eventually met success using the strong foundation of evidence and literature that was largely built by the dermatology community (Engelman et al., 2016; Hay et al., 2012).

Dermatologists are also ideally positioned to aid in the advocacy work of most NTDs, given that most of the 20 NTDs in the WHO portfolio have recognizable skin manifestations (Table 3). New programmatic focus within the organization has been given to skin-related NTDs under the leadership of Dr. Mwelecele Malecela, the head of the NTD Department of the WHO. In a presentation to the International Alliance for Global Health Dermatology (GLODERM), Dr. Malecela discussed the WHO's newly established NTD Roadmap to align the actions of stakeholder groups as a strategic framework for the elimination of NTDs globally over the next decade. A key takeaway from Dr. Malecela is how dermatologists can individually advance NTD work by expanding awareness of NTDs, reporting cases of skin disease, conducting capacity building, and advocating with service organizations (Malecela, 2021). Additionally, the WHO released the Skin NTD training app in July 2020, made in partnership with dermatologists, that quickly allows health care workers and the public to get information about a specific skin NTD's clinical features, management, and geographical distribution (WHO, 2020). Notable dermatologists in the international community leading these efforts include Drs. Claire Fuller and Roderick Hay, who are also helping steer the development of "A Strategic Framework for Integrated Control of Skin-Neglected Tropical Diseases 2030," an adjunct project of the WHO NTD Roadmap (ILDS, 2020).

Advocacy for the prioritization of NTDs on the global health agenda has significant implications for the health of women and girls. NTDs have widely been acknowledged to impact women disproportionately, not only due to disparate levels of exposure compared with men but also sociocultural effects and the stigma of NTD infection (Arakaki et al., 2016). For instance, adult women can be up to four times more likely than men to develop trichiasis because they are more likely to be infected through close contact with children (Courtright and West, 2004). Women and girls are also at much greater risk of developing schistosomiasis because they perform two-thirds of the water collection in endemic areas of the world (WHO, 2009). As previously discussed, disfigurement and disability secondary to dermatologic disease—especially NTDs—often lead to stigma that limits employment, marriageability prospects, and socioeconomic well-being (Hotez, 2009; Vlassoff et al., 2000). Hence, the work by dermatologists to help eradicate NTDs globally serves to substantially improve the health of women and girls globally.

Dermatologists and COVID-19

The last featured area of work by dermatologists includes the recent COVID-19 pandemic and ongoing reporting of cutaneous manifestations of SARS-CoV-2. Since 2020, the pandemic has provided a unique and prominent role for the dermatology community to aid in the early identification of COVID infection among individual patients and, in turn, affect transmission. Unsurprisingly, dermatologists were the first to report skin manifestations as presenting signs of COVID, ranging from pernio-like lesions (i.e., COVID toes) to urticarial rashes and morbilliform eruptions. An international registry aimed at collecting case reports of COVID-19 skin manifestations was developed early in the pandemic from collaborative efforts by the American Academy of Dermatology and the ILDS (Freeman et al., 2020a). The registry allowed the medical community to gather vital prospective data on the timing of patients' symptoms, dermatologic condition details, and other infection-related symptoms that could aid in recognizing early infection. The registry comprises >1000 cases of skin manifestations and a spectrum of >30 different skin conditions (Freeman et al., 2020b). In some states, such as Massachusetts, the registry's realtime data even served as the catalyst for policy change, prompting the addition of skin symptoms to the criteria for early testing (The Commonwealth of Massachusetts Executive Office of Health and Human Services, 2020).

Dermatologists also demonstrated leadership during the COVID-19 pandemic by recognizing that skin manifestations can be part of long COVID, a condition in which patients experience prolonged symptoms at least 4 weeks after initial SARS-CoV-2 infection. Recent data have suggested that long-COVID symptoms may occur in up to 87% of infected patients (Carfi et al., 2020; Carvalho-Schneider et al., 2021). As such, the dermatology community has been advocating for skin manifestations to be considered as a recognized symptom of long COVID (WHO, 2021a). A study published by our group in *Lancet Infectious Diseases* in January 2021 showed that 6.8% of patient cases of pernio reported to the international COVID registry lasted >60 days, of which two cases were laboratory-confirmed (McMahon et al., 2021a).

The dermatology community has also played a significant role in COVID-19 vaccination efforts and informing public opinion of mRNA vaccine side effects. One common reason for vaccine refusal is fear of side effects, such as adverse skin reactions (Bono et al., 2021), and dermatologists are well-poised to address these concerns. In a multi-institutional study published in May 2021, dermatologists in the United States were among the first to report the morphology and timing of COVID-19 postvaccination reactions early in the vaccine rollout. The study also described the differences in cutaneous reactions between the two vaccine doses, which provided guidance for the medical community regarding vaccine counseling. This study revealed that vaccine reactions were generally minor and self-limited and should not discourage the public from vaccination (McMahon et al., 2021a; Sun et al., 2021). As mass vaccination efforts are underway and vaccine reactogenicity reports continue to surface, dermatologists are poised to keep bridging knowledge gaps in our understanding of the mechanistic relationship between these vaccines and their associated cutaneous side effects.

Recently published data have shed light on the possible sex differences regarding cutaneous manifestations of SARS-CoV-2. A large population-based study in the United Kingdom evaluating the

diagnostic value of skin reactions in COVID-19 infection revealed the self-reported symptoms of >336,000 users of the COVID Symptom Study App. The study showed that, among users who reported testing positive on a swab test, approximately 8.8% had an associated skin rash, and the prevalence of reported body rash was higher among women compared with men (odds ratio: 1.60; 95% Cl, 1.08–2.44; p = .02; Visconti et al., 2021). Other studies examining immune responses to SARS-CoV-2 have shown significant differences in viral loads, antibody titers, and plasma cytokines when comparing male and female patients (Takahashi et al., 2020). For instance, researchers have found higher levels of innate immune cytokines associated with worse disease progression in female patients. Even for COVID-19 and other types of vaccination, women consistently report more frequent adverse effects of the vaccine compared with men, which also holds true for vaccine skin reactions (Fathi et al., 2020; Fischinger et al., 2019). Among 414 early cases reported to the COVID-19 skin registry in February 2021, 90% of all cases were female (McMahon et al., 2021b). As larger population-based studies focusing on SARS-CoV-2 skin changes and vaccine skin reactions continue to emerge, better characterization of sex differences may hold important clues for both our immunologic understanding of COVID-19 and informing public health policy during the pandemic.

Conclusion

Global health has offered the field of dermatology an opportunity to find its place on a worldwide stage. Through national and international policy advocacy, the dermatologic community has championed efforts to eliminate scabies and other skin-related NTDs. Dermatologists helped push for more dermatologic therapies on the WMLEM that will help secure better care for millions of patients suffering from debilitating skin diseases. The COVID-19 pandemic gave dermatologists the opportunity to pursue quality research and data collection with an international focus, changing the way the medical community looked at the evolving landscape of a landmark disease and influencing national policy decisions. Each area of work by dermatologists holds key importance for the health and well-being of women globally.

As evidenced by the work of dermatologists discussed herein, the dermatology community has shown its commitment to further establish research, education, and advocacy initiatives throughout the world. In 2019, GLODERM formed as a partnership between dermatologists to promote skin health worldwide through enhanced access to care, training, advocacy, capacity building, clinical care, and research (Oyesiku et al., 2021). Organizations such as ILDS and GLODERM Alliance are focusing efforts on educating trainees, bringing together the larger global dermatologic community to reduce the burden of both common and neglected skin diseases. Since its founding, GLODERM has grown to include >500 dermatologists, nurses, trainees, and health experts across the world, highlighting the need for and interest in global health opportunities. Dermatologists have much to offer in the advancement of international health, and the field of global health provides the dermatology community with a prominent role in the house of medicine.

Conflicts of interest

None.

Funding

This research was supported by the National Institute of Allergy and Infectious Diseases in accordance with the regulatory requirements of the National Institutes of Health (award numbers

Study approval

N/A

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