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Article

The Ocean–Gut–Skin (OGS) Cohort: Baseline Characteristics and Study Protocol for a Prospective Investigation of Marine Environmental Exposure and Dermatological Health in Coastal China

Bo Wan [1, †], Weili Yang [2, †], Qin Fang [3, †], Junxi Mo [1], Ke You [1], An He [4], Yun Zhou [5,*], Xiaoliang Li [2,*]

[1] Department of Aesthetic Medicine, The Third People's Hospital of Zhuhai, Zhuhai 519000, China
[2] Zhuhai Engineering Technology Research Center of Occupational and Mental Health, The Third People's Hospital of Zhuhai, Zhuhai 519000, China
[3] Department of Medical Administration, Zhuhai People's Hospital (The Affiliated Hospital of Beijing Institute of Technology, Zhuhai Clinical Medical College of Jinan University), Zhuhai 519000, China
[4] Department of Dermatology, The Third People's Hospital of Zhuhai, Zhuhai 519000, China
[5] School of Public Health, Guangzhou Medical University, Guangzhou 511436, China
*** Corresponding author:** yunz@gzhmu.edu.cn (Y.Z.), yc47699@um.edu.mo (X.L.)
[†] These authors contributed equally to this work.

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Abstract: Psoriasis is a chronic, immune-mediated inflammatory skin disease with a complex etiology involving both genetic susceptibility and environmental triggers. Accumulating evidence points to a critical role for the gut microbiome in modulating systemic immunity and cutaneous homeostasis—a relationship encapsulated by the "gut–skin axis". However, the potential influence of environmental microbial exposures, particularly those originating from distinctive marine ecosystems, on this axis remains unexplored. We hypothesized that occupational or residential exposure to the marine environment shapes the human microbiome (both cutaneous and intestinal), which in turn modulates the risk and severity of psoriasis. This article presents the study protocol and baseline characteristics of the Ocean–Gut–Skin (OGS) Cohort Study, the first prospective cohort in China dedicated to investigating marine-associated dermatological disorders. The OGS Cohort Study was initiated in January 2023 in Zhuhai, a major coastal city in southern China. The target population comprises 10,000 adults aged 30–70 years, stratified into high and low marine exposure groups. Participants undergo comprehensive health examinations, including dermatological assessment (Psoriasis Area and Severity Index [PASI], Eczema Area and Severity Index [EASI], Dermatology Life Quality Index [DLQI], and transepidermal water loss [TEWL]), collection of stool and skin swab samples for 16S rRNA gene sequencing and shotgun metagenomics, blood sampling for biomarker profiling, and a detailed questionnaire capturing demographic, lifestyle, dietary, medical history, and marine exposure metrics. Participants will be followed biennially for the first 2 years and annually thereafter for a total of 5 years. Baseline recruitment was completed in December 2025, yielding a cohort of 10,245 participants across five study phases. This paper reports the baseline demographic and clinical characteristics of the cohort. The mean disease duration was 8.5 years for psoriasis and 6.2 years for atopic dermatitis (AD). The cohort comprises 2512 psoriasis patients, 2488 AD patients, and 2500 healthy controls, with comprehensive multi-omics data collected at baseline. Follow-up is ongoing. The OGS Cohort Study is uniquely positioned to interrogate the novel "Ocean–Gut–Skin" axis. By integrating deep clinical phenotyping with multi-omics microbiome analyses and rigorous environmental exposure assessment, this cohort will generate robust evidence on how the marine environment may indirectly influence cutaneous health through modulation of the human microbiome.

Keywords: psoriasis; atopic dermatitis; cohort study; gut microbiome; skin microbiome; marine environment; environmental exposure; study protocol

1. Introduction

Psoriasis is a common, chronic, relapsing inflammatory skin disorder that affects approximately 2%–3% of the global population [1]. It is characterized by well-demarcated, erythematous, scaly plaques and is associated with substantial physical and psychological morbidity, as well as an elevated risk of comorbidities including psoriatic arthritis, cardiovascular disease, and metabolic syndrome [1,2]. Similarly, atopic dermatitis (AD) affects approximately 20% of children and 5%–10% of adults worldwide, with a rising prevalence in developing countries [3]. Both conditions impose a disproportionate public health burden owing to their chronic course, high rates of disability, and substantial treatment gaps.

Although genetic factors (e.g., HLA-C06:02 for psoriasis; FLG loss-of-function mutations for AD) confer susceptibility, incomplete concordance among monozygotic twins highlights the critical contribution of environmental factors to disease onset and flares [4,5]. Coastal regions, in particular, present unique environmental exposures that may shape the epidemiology of these disorders. Over the past four decades, China has undergone rapid coastal urbanization and economic development. Nationally representative data indicate that the prevalence of psoriasis in China is approximately 0.47%, whereas AD affects an estimated 4.5% of adults [6]. Notably, coastal provinces such as Guangdong, Fujian, and Zhejiang report higher disease burdens, suggesting potential marine-related environmental influences [7].

Recent research has revolutionized our understanding of host-microbe interactions, revealing that the trillions of microorganisms residing in and on the human body play fundamental roles in immune education and homeostatic maintenance [8]. Dysbiosis has been linked to a wide array of diseases, including inflammatory skin conditions such as psoriasis and AD [9]. The concept of a "gut–skin axis" has gained considerable traction, whereby alterations in the gut microbiota can precipitate systemic inflammation that manifests cutaneously [10]. Likewise, the skin microbiome is a key mediator of local immune responses and barrier function [11].

However, existing studies have focused predominantly on internal (gut) and local (skin) microbial communities. The potential impact of the vast external microbial world—specifically from unique, biodiverse ecosystems such as the ocean—on the human microbiome and subsequent health outcomes remains a frontier of investigation. Marine environments introduce specialized microbial communities through direct contact (e.g., swimming, occupational exposure), dietary intake (seafood consumption), and aerosol pathways [12]. Recent studies have shown that marine-derived bacteria such as Vibrio species can modulate host immune responses [13] and that skin microbiome profiles differ significantly between coastal and terrestrial populations [14]. Notably, the American Academy of Dermatology Annual Meeting highlighted marine-associated pathogenesis in chronic kidney disease-related pruritus [15], wherein κ-opioid receptor agonists showed promise in alleviating systemic itching via neuroimmune modulation. Melanoma studies have also revealed that histopathologic regression after sentinel lymph node biopsy correlates with favorable survival outcomes [16], suggesting that tissue-level microbial dynamics may influence disease progression.

To better understand how marine environmental factors influence dermatological disorders, numerous studies have investigated microbiome profiles in relation to skin diseases. For instance, alterations in the skin microbiome of AD patients, including reduced abundance of Staphylococcus epidermidis and increased colonization by S. aureus, have been observed and found to correlate with disease severity [17]. Experimental studies further support a causal role for these microbial changes, as topical application of S. aureus can induce AD-like inflammation in mouse models [18]. Similarly, a clinical study reported significant differences in the composition and diversity of the gut microbiome between psoriasis patients and healthy controls [19]. Following treatment with biologics, significant changes in the phylum Bacteroidetes were observed, and receiver operating characteristic analysis demonstrated that Bacteroidetes abundance could effectively discriminate treatment responders from nonresponders [20].

Despite growing evidence linking the microbiome to dermatological disorders, most clinical studies are cross-sectional, thereby limiting causal inference and failing to capture dynamic changes over the disease course [21]. Additionally, several population-based cohorts focused on the gut microbiota have been established both domestically and internationally [22], alongside large-scale cohorts centered on skin diseases [23]. However, existing research predominantly relies on single-modality or limited omics approaches, with most cohorts constructed independently around isolated aspects of the gut microbiome, skin microbiome, or clinical phenotypes. Such designs lack systematic integration of multi-system biological information within the same individuals and a unified temporal framework.

Current research gaps include: (1) a lack of longitudinal tracking of microbial adaptation processes in coastal populations; (2) insufficient integration of marine exposure metrics with multi-omics data; (3) limited understanding of seasonal fluctuations in marine microbiome impact; (4) the absence of large-scale prospective cohorts examining the "Ocean–Gut–Skin" axis; and (5) a lack of validated biomarkers for early diagnosis and treatment response prediction in marine-associated dermatoses.

To overcome this critical bottleneck, we established the Ocean–Gut–Skin (OGS) Initiative, the first cohort in China systematically focused on marine-associated dermatological disorders, encompassing psoriasis, AD, and healthy controls. To date, the OGS cohort has integrated multidimensional data from over 10,000 individuals, encompassing standardized clinical symptom ratings (Psoriasis Area and Severity Index [PASI], Eczema Area and Severity Index [EASI], Dermatology Life Quality Index [DLQI]), marine exposure assessments, skin and gut microbiome profiles (16S rRNA sequencing and shotgun metagenomics), serum biochemical indicators (TNF-α, IL-17A, IgE, oxidative stress markers), and longitudinal follow-up data, all collected within a unified clinical and temporal framework. (**Figure 1**).

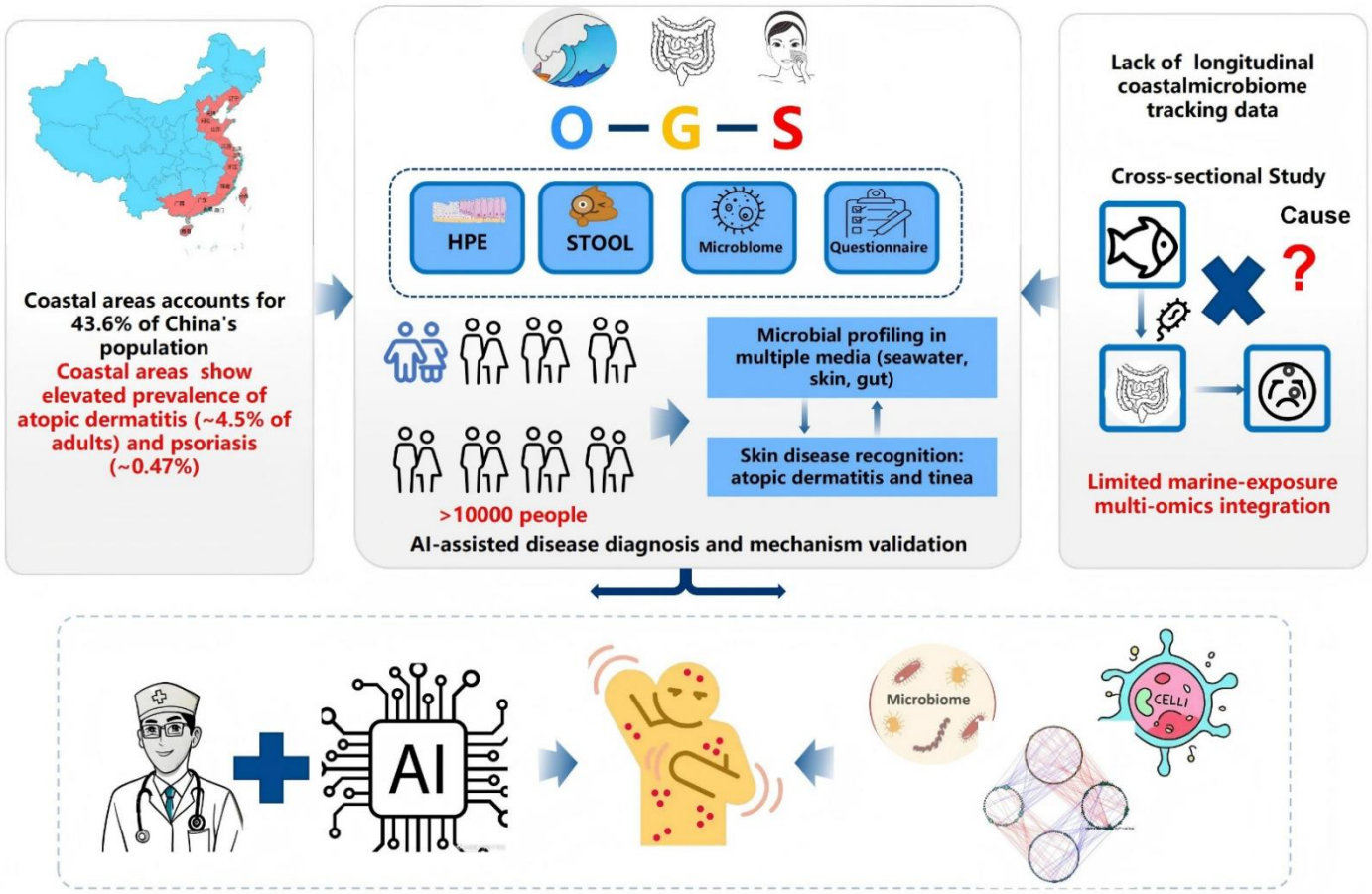

Figure 1. Overview of the Ocean-Gut-Skin (OGS) cohort. The figure depicts the disproportionate burden of AD (~4.5% of adults) and psoriasis (~0.47%) in China's coastal areas, which account for 43.6% of the national population. Current research limitations, including a lack of longitudinal coastal-microbiome tracking and limited marine-exposure multi-omics integration, hinder mechanistic understanding. The OGS cohort integrates microbial profiling across multiple media (seawater, skin, gut), standardized clinical phenotyping, and longitudinal follow-up data from over 10,000 participants.

2. Methods and Design

2.1. Cohort Overview

The OGS study is a longitudinal cohort investigation conducted in five distinct phases, each targeting specific dermatological populations and employing tailored data collection strategies (**Table 1**). The protocol was developed in accordance with the SPIRIT 2013 Statement guidelines [24].

Sample Size and Power Calculation

The sample size was determined based on the estimated 5-year incidence of psoriasis in coastal populations of southern China (approximately 0.5%, derived from local health registry data). To detect a hazard ratio of 1.5 for incident psoriasis or AD comparing high versus low marine exposure groups, with 80% power at a two sided alpha of 0.05, a minimum of 2500 participants per exposure group is required, assuming a 5-year event rate of 2% in the low exposure group. Accounting for an anticipated 20% loss to follow-up over 5 years, we targeted 3000 participants per

group. The final enrolled sample (N = 10,245) exceeds this requirement, providing adequate power for secondary analyses, including subgroup and mediation analyses.

Table 1. OGS substudies and corresponding objectives and participant cohorts.

Group	Measures	Sample	Data collection					
		Number of Subjects	Clinical & DLQI	Marine Exposure	Skin Swab	Fecal	Blood	Follow-up
Phase A	Longitudinal (Psoriasis)	2500 (800)[a]	✓	✓	✓	✓	✓	Yes
Phase B	Longitudinal (AD)	2500 (750)[a]	✓	✓	✓	✓	✓	Yes
Phase C	Cross-sectional (Psoriasis + AD)	1000	✓	✓	✓	✓	✓	No
Phase D	Longitudinal (High marine exposure)	2500 (1000)[a]	✓	✓	✓	✓	✓	Yes
Phase E	Cross-sectional (Healthy controls)	2500	✓	✓	✓	✓	✓	No

Abbreviations: AD, atopic dermatitis; DLQI, Dermatology Life Quality Index. [a] Baseline subject number (follow-up subject number).

2.2 Study Subjects

2.2.1. Participant Recruitment

Participants were recruited from The Third People's Hospital of Zhuhai and affiliated community health centers in coastal communities of Zhuhai City, Guangdong Province, China. The study was approved by the Ethics Committee of The Third People's Hospital of Zhuhai on January 19, 2023 (approval number: ZHSYSB2023011902) and was conducted in accordance with the latest version of the Declaration of Helsinki (2013). All participants met the following general criteria: aged 30–70 years, permanent residents of Zhuhai City, and provision of written informed consent.

Dermatological diagnoses were determined based on clinical criteria validated through standardized dermatological examinations performed by two board-certified dermatologists; in cases of disagreement, a senior dermatologist confirmed the diagnosis. Psoriasis patients met clinical diagnostic criteria for psoriasis vulgaris, with severity assessed using PASI. Patients with pustular, erythrodermic, or guttate psoriasis were excluded to maintain diagnostic homogeneity. AD patients met the Hanifin–Rajka diagnostic criteria or the Chinese diagnostic criteria for AD, with severity assessed using EASI and DLQI. Patients were categorized based on disease severity (mild: EASI < 7; moderate: EASI 7–21; severe: EASI > 21) and prior treatment history. Healthy controls (HC) were recruited from the same coastal communities via public postings and community health centers. HC participants were required to have no history of dermatological disorders, no family history of psoriasis or AD, no history of chronic inflammatory diseases, and no use of immunosuppressive medications within the preceding six months.

2.2.2. Marine Exposure Categorization

Participants were further categorized based on their marine exposure level. The high marine exposure group comprised individuals with occupational or residential exposure to marine environments, including professional fishermen, aquaculture

workers, seafood processors, residents living within 1 km of the coastline for at least five years, and individuals engaging in sea bathing ≥ 3 times per week during the past year. The low marine exposure group comprised individuals recruited from inland urban districts and rural villages located > 50 km from the coast, with minimal direct contact with marine environments (swimming frequency < once per month, no occupational marine exposure). The 1-km threshold for high marine exposure was selected based on previous environmental health studies demonstrating detectable gradients in airborne marine aerosols, microbial load, and sea salt deposition within 1 km of the coastline [25]. Residential distance to the coast was calculated using ArcGIS Pro (v3.1; Esri, Redlands, CA, USA) with high- resolution (1 m) land use data from the Zhuhai Natural Resources Bureau. A buffer analysis was performed to categorize participants into four distance zones: <0.5 km, 0.5–1 km, 1–5 km, and >5 km. This standardized inclusion framework ensured diagnostic rigor and cohort comparability across clinical groups (**Figure 2**).

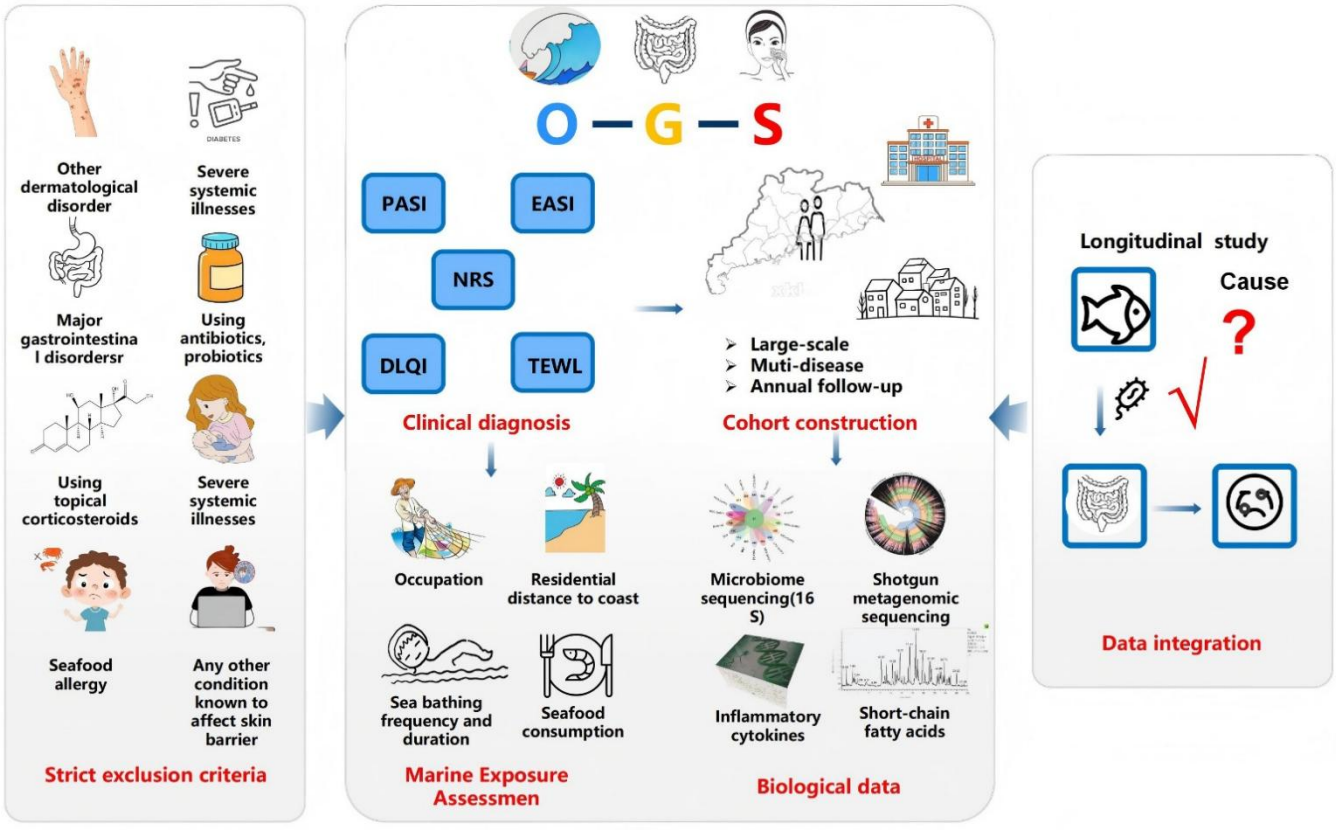

Figure 2. Participant recruitment and study workflow. The figure illustrates the stepwise enrollment process based on strict exclusion criteria (other dermatological disorders, severe systemic illnesses, gastrointestinal disorders, antibiotic/probiotic use, topical corticosteroids, seafood allergy, and conditions affecting skin barrier function). Eligible participants undergo marine exposure assessment (occupation, residential distance to coast, seafood consumption) and clinical diagnosis (PASI, NRS, DLQI, TEWL). Cohort construction integrates microbiome sequencing (16S rRNA gene sequencing and shotgun metagenomics) and host biomarkers (inflammatory cytokines, short-chain fatty acids). The longitudinal study design enables large-scale, multi-disease annual follow-up with data integration from all modules.

2.2.3. Exclusion Criteria

Exclusion criteria were as follows: (a) meeting diagnostic criteria for any other dermatological disorder that could confound analysis (e.g., contact dermatitis, cutaneous lupus, mycosis fungoides); (b) presence of severe systemic illnesses such as uncontrolled hypertension, diabetes, cardiovascular or cerebrovascular disease, malignancy, or any unstable systemic condition; (c) history of inflammatory bowel disease, celiac disease, or other major gastrointestinal disorders; (d) use of antibiotics, probiotics, or immunosuppressive medications within the past three months; (e) use of topical corticosteroids or calcineurin inhibitors on non-lesional skin within the past two weeks; (f) pregnancy or breastfeeding; (g) known history of seafood allergy or anaphylaxis; (h) any neurological or systemic condition known to affect skin barrier function or immune status.

2.3. Data Collection

All baseline data collection was performed during a single visit to the study center. Detailed protocols for questionnaire administration and biological sample collection are as follows.

2.3.1. Questionnaire Survey

General information was collected by trained clinicians and included sex, age, education level, occupation, age of onset, disease duration, past medical history, dietary habits (validated food frequency questionnaire), sleep patterns, smoking status, alcohol consumption, physical activity, and family history of dermatological disorders. Sun exposure was quantified using a validated occupational and recreational sun exposure questionnaire, including: average daily outdoor hours (weekday/weekend), use of sunscreen or protective clothing, and cumulative occupational sun exposure (years × average daily hours). For fishermen, additional information on vessel type, deck versus cabin work, and use of sun protection was collected. Clinical assessment tools included PASI [26], EASI [27], DLQI [28], transepidermal water loss (TEWL; measured using a closed-chamber evaporimeter [VapoMeter, Delfin Technologies, Kuopio, Finland] on standardized sites), and the Itch Numerical Rating Scale (NRS; 0–10 scale assessing average itch intensity over the preceding 24 hours). All assessments were administered by trained, qualified dermatologists who strictly adhered to the guidelines and scoring criteria.

2.3.2. Marine Exposure Assessment

A study-specific module was developed to quantify marine exposure across multiple dimensions: occupation (categorized as high, medium, or low), residential distance to coast (measured in kilometers using geographic information system mapping), sea bathing frequency and duration (assessed via questionnaire), seafood consumption (assessed via a validated food frequency questionnaire quantifying intake of fish, shellfish, crustaceans, and seaweed), and environmental seawater sampling (collected quarterly from participant residential beaches within 1 km for microbiome analysis, including quantitative real-time PCR (qPCR) for key genera: Vibrio, Pseudomonas, Enterococcus).

2.3.3. Biological Sample Collection

Skin swabs were collected using sterile rayon-tipped swabs (Copan Diagnostics, Inc., Murrieta, CA, USA) from three standardized sites: lesional skin, non-lesional buttock, and volar forearm. Swabs were immediately placed in DNA/RNA Shield solution (Zymo Research, Irvine, CA, USA) and stored at −80 °C within 2 hours. For longitudinal follow-up, skin swabs are collected monthly from a random sub-cohort (n = 3,000). Fecal samples were collected at home using a sterile collection kit (GP Medical Devices A/S, Holstebro, Denmark), returned to the study center within 24 hours, aliquoted, and stored at −80 °C. Dietary data were obtained using a 3-day dietary recall and food frequency questionnaire. Whole blood samples (10 mL) were collected after an overnight fast, centrifuged, and stored at −80 °C for biomarker analysis. Seawater samples were collected monthly from participant residential beaches using sterile 1-L bottles, filtered, and stored at −80 °C for DNA extraction.

2.3.4. Laboratory Assays

DNA was extracted from skin swabs and fecal samples using the QIAamp PowerFecal Pro DNA Kit (Qiagen, Hilden, Germany). The V3–V4 hypervariable region of the 16S rRNA gene was amplified and sequenced on the Illumina NovaSeq 6000 platform (Illumina, Inc., San Diego, CA, USA). Raw reads were processed using QIIME2 (v2023.5; QIIME 2 Developers, Northern Arizona University, Flagstaff, AZ, USA) and taxonomically classified using the SILVA database (v138; SILVA Team, Leibniz Institute DSMZ – German Collection of Microorganisms and Cell Cultures, Bremen, Germany). For a subset of samples (n = 1,000), shotgun metagenomic sequencing was performed on the Illumina NovaSeq 6000 (30 million paired-end reads per sample), with analysis using MetaPhlAn4 (Huttenhower Lab, Harvard T.H. Chan School of Public Health, Boston, MA, USA/Department CIBIO, University of Trento, Trento, Italy) and HUMAnN3 (Huttenhower Lab, Harvard T.H. Chan School of Public Health, Boston, MA, USA/Department CIBIO, University of Trento, Trento, Italy). Inflammatory cytokines (TNF-α, IL-17A, IL-22, IL-4, IL-13, IL-31) were measured using multiplex bead-based immunoassays (LEGENDplex, BioLegend, San Diego, CA, USA). Total and specific IgE were measured using fluorescence enzyme immunoassay (ImmunoCAP, Thermo Fisher Scientific, Waltham, MA, USA). Oxidative stress markers (superoxide dismutase (SOD), malondialdehyde (MDA), and glutathione peroxidase (GPx)) were measured using colorimetric assay kits (Abcam, Cambridge, UK). Short-chain fatty acids (acetate, propionate, butyrate) were quantified using gas chromatography–mass spectrometry (GC–MS, Agilent 7890B/5977B, Agilent Technologies, Santa Clara, CA, USA).

2.4. Follow-up Plan

Participants will be followed for a total of 5 years. Follow-up assessments are scheduled every 6 months for the first 2 years and annually thereafter until study completion in 2028. Follow-up includes: an updated electronic questionnaire covering health status, new dermatological diagnoses, medication use, changes in lifestyle or marine exposure, and quality-of-life measures; repeat dermatological examination (PASI/EASI scoring and DLQI); repeat collection of skin swabs and fecal samples;

repeat blood sample collection for biomarker analysis; and passive surveillance through linkage with the Zhuhai Municipal Health Insurance Database.

Loss to follow-up will be handled using inverse probability censoring weighting (IPCW) and multiple imputation for missing covariates. We will perform sensitivity analyses comparing complete-case analysis with the imputed data. Retention strategies include annual health feedback reports, reminder calls, and reimbursement for travel expenses.

Adverse events (e.g., serious infections, hospitalization, severe flares requiring emergency care) will be recorded at each follow-up contact and reported to the Ethics Committee of The Third People's Hospital of Zhuhai within 7 days. A Data Monitoring Committee (DMC) comprising independent epidemiologists and biostatisticians will review data annually for safety and data quality. No interim analyses are planned.

2.5. Statistical Analysis Plan

Continuous variables will be expressed as mean ± standard deviation (SD), and categorical variables as counts and percentages. Normality will be assessed using the Shapiro–Wilk test, and homogeneity of variance via Levene's test. Group comparisons will use chi-square tests for categorical variables, independent-sample t-tests or Mann–Whitney U tests for continuous variables, and one-way ANOVA or Kruskal–Wallis H tests for multi-group comparisons. Multiple comparisons will be adjusted using the Benjamini–Hochberg method.

Primary analyses will use Cox proportional hazards models to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between baseline marine exposure level and the risk of incident psoriasis or AD over 5 years. For participants with prevalent disease, linear mixed-effects models will examine the association between exposure and changes in PASI/EASI scores over time. Mediation analysis will assess the extent to which gut and skin microbiome compositions mediate observed associations.

To address potential selection bias from sex imbalance in occupational subgroups (e.g., fishermen predominantly male), we will conduct: (1) propensity score matching stratified by sex; (2) sensitivity analyses restricted to male participants only; and (3) adjusted analyses including sex × exposure interaction terms.

All models will be adjusted for confounders, including age, sex, BMI, smoking, alcohol consumption, diet, genetic risk scores, and cumulative sun exposure (as a continuous covariate). For fishermen, we will additionally include vessel type and deck-based work as covariates. To address seasonal migration of fishermen, GPS tracks from a subset of vessels (n = 50) will be collected over one year to estimate geographic variation in marine exposure; for the full cohort, exposure will be assigned based on primary residence and principal fishing ground, with season included as a fixed effect.

Seasonal effects on microbiome composition will be examined using interaction terms with sampling season. Analyses will be conducted using R (version 4.3.3; R Core Team, Vienna, Austria) and Python (version 3.12.5; Python Software Foundation,

Wilmington, DE, USA). A two-tailed $P < 0.05$ will be considered statistically significant.

2.6. Study Status and Timeline

Baseline recruitment was completed in December 2025. The first follow-up wave is ongoing. The total planned duration of follow-up is 5 years, with the final follow-up anticipated in December 2028.

2.7. Protocol Amendments

Any protocol amendments (e.g., changes to inclusion criteria, outcome measures, or follow-up schedule) will be submitted to the Ethics Committee of The Third People's Hospital of Zhuhai for approval prior to implementation. Approved amendments will be registered on the Chinese Clinical Trial Registry (ChiCTR), and participants will be notified of any changes that affect their informed consent.

2.8. Primary and Secondary Outcomes

Primary outcomes: (1) incidence of psoriasis or atopic dermatitis (AD) during the 5-year follow-up period; (2) change in Psoriasis Area and Severity Index (PASI) score for psoriasis participants and change in Eczema Area and Severity Index (EASI) score for AD participants from baseline to each follow-up visit.

Secondary outcomes: changes in Dermatology Life Quality Index (DLQI), transepidermal water loss (TEWL), Itch Numerical Rating Scale (NRS), serum inflammatory cytokines (TNF-α, IL-17A, IL-22, IL-4, IL-13, IL-31), total and specific IgE, and oxidative stress markers (SOD, MDA, GPx).

Exploratory outcomes: gut and skin microbiome alpha and beta diversity, differential abundance of specific microbial taxa (genus and species level), and short-chain fatty acid (SCFA) concentrations.

2.9. Protocol Registration

This study is registered with the Chinese Clinical Trial Registry (ChiCTR), ID: 307435.

2.10. Data Monitoring and Missing Data Handling

As noted in Section 2.4, a Data Monitoring Committee (DMC) will review data annually. Missing data will be addressed using multiple imputation by chained equations (MICE) with 20 imputed datasets, assuming missing at random. Sensitivity analyses will compare results from imputed data with complete-case analyses.

3. Baseline Characteristics of the OGS Cohort

Over a 3-year period (January 2023–December 2025), we enrolled 10,245 participants. As this is a combined study protocol and baseline data paper, we report the baseline characteristics below. Outcome analyses will be published separately after follow-up completion. Phase A (Psoriasis longitudinal): 2512 participants (1845 males, 667 females; mean age 51.8 ± 9.1 years); Phase B (AD longitudinal): 2,488 participants (735 males, 1753 females; mean age 52.8 ± 8.2 years); Phase C (Cross-

sectional, Psoriasis + AD): 1000 participants (500 psoriasis, 500 AD); Phase D (High marine exposure longitudinal): 2500 participants (primarily fishermen and coastal residents); Phase E (Healthy controls): 2500 participants (1250 from high-exposure areas, 1250 from low-exposure areas). The mean disease duration was 8.5 years for psoriasis and 6.2 years for AD. Detailed baseline characteristics are summarized in **Table 2**.

Table 2. Baseline characteristics of OGS participants (N = 10,245; first 5000 shown)*.

Characteristic	Total (N = 5000)	Psoriasis (N = 2512)	AD (N = 2488)	HC (N = 2500)
Age, years, mean (SD)	52.3 (8.7)	51.8 (9.1)	52.8 (8.2)	52.0 (8.5)
Male, n (%)	2580 (51.6)	1845 (73.4)	735 (29.5)	1250 (50.0)
BMI, kg/m², mean (SD)	24.8 (3.2)	24.5 (3.1)	25.1 (3.3)	24.6 (3.0)
Current Smoker, n (%)	1120 (22.4)	685 (27.3)	435 (17.5)	400 (16.0)
Education (≥ College), n (%)	1850 (37.0)	720 (28.7)	1130 (45.4)	1100 (44.0)
Median Distance to Coast, km (Interquartile range [IQR])	8.5 (1.2–42.0)	0.8 (0.3–1.5)	12.0 (2.0–45.0)	15.0 (3.0–50.0)
Seafood Consumption (times/week), median (IQR)	4.0 (2.0–6.0)	8.0 (6.0–10.0)	3.0 (1.0–5.0)	2.0 (1.0–4.0)
PASI score, mean (SD)	—	12.4 (6.2)	—	—
EASI score, mean (SD)	—	—	15.2 (7.8)	—
DLQI score, mean (SD)	—	8.5 (5.2)	9.1 (5.8)	0.5 (0.8)
TEWL (g/h/m²), mean (SD)	—	18.5 (4.2)	22.3 (5.1)	10.2 (2.5)

*Primary and secondary outcome analyses will be reported in future publications.

4. Discussion

To the best of our knowledge, the OGS Initiative is the first prospective cohort in China dedicated to investigating the "Ocean–Gut–Skin" axis in dermatological disorders. This Study Protocol describes the rationale, design, and methodology of this large-scale investigation, which systematically integrates environmental exposure assessment, deep clinical phenotyping, and multi-omics microbiome profiling within a unified longitudinal framework.

The OGS cohort has several notable strengths. First, it encompasses a wide diagnostic spectrum by systematically enrolling individuals with psoriasis, AD, and healthy controls, enabling both disease-specific and cross-disease analyses. Second, standardized protocols with stringent quality control ensure the collection of comprehensive data, including marine exposure metrics, clinical assessments, microbiome profiles, serum biomarkers, and longitudinal follow-up over a planned 5-year period. This design fills a critical gap in domestic research and overcomes key limitations of previous international studies, such as relatively small sample sizes, single-diagnosis focus, and cross-sectional designs. Third, the integration of multidimensional data offers new perspectives for the early identification, subtype

classification, and precision intervention of marine-associated dermatoses. Fourth, the longitudinal design enables tracking of dynamic changes in microbiome composition and disease activity, allowing assessment of causal relationships and identification of predictive biomarkers.

Hypothesized Mechanisms Linking Marine Microbes to Skin Inflammation

We hypothesize several non-mutually exclusive pathways by which marine environmental exposure may influence psoriasis and AD through microbiome modulation. First, marine bacteria such as Vibrio parahaemolyticus and Pseudomonas aeruginosa produce lipopolysaccharide (LPS) and other pathogen-associated molecular patterns (PAMPs) that activate Toll-like receptor 4 (TLR4) and TLR2 signaling on intestinal and skin epithelial cells, potentially promoting T helper 17 (Th17) differentiation and subsequent cutaneous inflammation [13]. Second, seawater exposure may transiently alter the skin microbiome by introducing halotolerant species (e.g., Halomonas, Marinobacter) while displacing commensals like Staphylococcus epidermidis, thereby compromising skin barrier function [14]. Third, consumption of raw or undercooked seafood introduces marine-derived polysaccharides and bacteria that could modulate gut microbial production of short-chain fatty acids (SCFAs), with downstream effects on regulatory T cells and systemic immune tone. The OGS cohort is uniquely positioned to test these mechanistic hypotheses by integrating multi-kingdom microbiome profiling (bacteria, fungi, viruses) with host inflammatory markers and detailed exposure assessment.

Several considerations were addressed in the study design to minimize bias. The male predominance observed in the psoriasis group (73.4%) likely reflects the occupational demographics of the high-exposure cohort (predominantly fishermen). Propensity score matching will be applied in future analyses to balance sex distributions across exposure groups. Seasonal fluctuations in marine microbial communities will be accounted for through repeated seawater sampling and incorporation of season as a covariate in all models.

This study also has limitations. First, the OGS cohort is currently in a single-center development phase (Zhuhai City), which may affect the external generalizability of results. Coastal populations in southern China may have distinct marine exposure patterns, dietary habits, and genetic backgrounds compared to other coastal regions. Future efforts will expand to multi-center collaborations across coastal cities (Qingdao, Xiamen, Sanya) to enhance geographic and population representativeness. Second, sample sizes remain imbalanced across diagnostic categories, limiting statistical power for some cross-disease comparisons. Third, the cohort has not yet incorporated host genomic information; future integration of whole-genome sequencing will facilitate the construction of a more comprehensive mechanistic model. Fourth, residual confounding by unmeasured lifestyle factors (e.g., sun exposure, skincare product use, stress levels) cannot be excluded. Fifth, although we collected detailed sun exposure metrics, residual confounding by ultraviolet (UV) radiation, particularly relevant for the predominantly male fisherman subgroup, cannot

be fully excluded. Future analyses will incorporate satellite-derived UV index data for the study region to further adjust for cumulative UV dose.

In conclusion, the OGS Initiative establishes a novel framework for investigating marine microbiome–host interactions in dermatology. By integrating environmental exposure data with high-dimensional microbial profiling and clinical phenotyping, this cohort will provide critical insights into pathogenic pathways underlying psoriasis and AD in coastal populations. Future collaborations with marine biology, computational biology, and synthetic biology will further elucidate the complex ecological drivers of coastal dermatological diseases.

Author contributions: X.L. and Y.Z. conceived and designed the study. B.W. and W.Y. had full access to all data and took responsibility for data integrity and accuracy of analysis. B.W. and Q.F. drafted the manuscript. J.M. and K.Y. collected samples. Q.F. and J.M. performed statistical and modeling analyses. Y.Z., A.H., and X.L. contributed to manuscript review and editing. All authors read and approved the final manuscript.

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