**Methods**

***Study Design and Dataset***

The current study was designed as a population-based case-control study aiming to evaluate the risk of having BP among patients previously diagnosed with asthma. In accordance with this study design, only patients in whom the outcome (BP) followed the exposure (asthma) were included in calculating the main outcome measures.

This study was based on the computerized database of Clalit Health Services (CHS), the largest healthcare organization in Israel, providing healthcare services for 4,927,000 enrollees as of October 2018 (57% of the general Israeli population based on the 2019 census). According to the National Health Insurance Law, membership in one of the four healthcare organizations is compulsory for all inhabitants of Israel, thus making the dataset of CHS thoroughly inclusive with complete follow-up. CHS covers a wide array of healthcare services in different settings, including the general community clinics, both primary care and referral centers, and both ambulatory and hospitalized care. The computerized database of CHS is based on continuous real-time data input from clinical, pharmaceutical, and administrative operating systems.

The chronic registry is one of the central parts of the computerized dataset of CHS. It mines data from multiple sources, including from hospital and primary care reports, drug purchases, laboratory analyses, and imaging findings. The accumulated data is then manually validated by the primary care healthcare provider of each patient. Previous studies attributed a high extent of validity for this registry [1]. The study was approved by the institutional review board of Ben-Gurion University.

***Study Population and Definition of Main Variables***

The computerized dataset of CHS was screened for incident cases being given a diagnostic code compatible with the diagnosis of BP between the years 2002 and 2019. The eventual inclusion of BP cases in this study was based on the following criteria: (i) a documented diagnosis of BP registered at least twice by a community board-certified dermatologist, or (ii) diagnosis of BP in hospital discharge letters from dermatological wards. Only cases fulfilling at least one of the aforementioned eligibility criteria were included in the current study. Figure 1 illustrates selection of study population.

The control group consisted of up to 5 individuals per each case of BP. The formers were frequency matched based on sex, age, and ethnicity. Prior to their recruitment, controls were ascertained to be alive and to contribute longitudinal data to the CHS.

The diagnosis of asthma was based on the chronic registry of CHS. Therefore, it was delivered by pediatricians, pulmonologists, or internal medicine specialists, and based on the purchase of asthma-related drugs and is subsequently cross-checked manually by the managing general practitioner.

***Covariates and Sensitivity Analyses***

The outcome measures of the study were controlled for comorbidities as assessed by the Charlson Comorbidity Index, an epidemiological score enabling to assess the extent of comorbid conditions [2]. The latter was found to precisely predict lethal outcomes and is methodologically valid in large data analyses [2].

Aiming to substantiate the validity of our findings, two sensitivity analyses were held. The first sensitivity analysis excluded cases and controls with a diagnosis of asthma within the 2 years prior to the diagnosis of BP and the recruitment, respectively. This analysis aimed to minimize the likelihood of ascertainment bias that may interfere with our findings. The second sensitivity analysis included only BP patients prescribed a BP-related medication for longer than 6 months. These drugs included systemic corticosteroids, topical corticosteroids, or immunosuppressive and immunomodulatory adjuvant agents like methotrexate, azathioprine, mycophenolate mofetil, dapsone, doxycycline, rituximab, intravenous immunoglobulins, and plasmapheresis. The aim of the second sensitivity analysis was to substantiate the validity of the diagnosis of BP.

***Statistical Analysis***

Baseline characteristics are described by means and standard deviations (SD)s for continuous variables, whilst categorical values were signified by percentages. The comparison of sociodemographic and clinical factors between cases and controls was performed using the χ2 test and *t* test, as indicated.

Logistic regression was used to calculate odds ratios (ORs) and 95% confidence intervals (CI)s to compare cases and controls regarding the presence of preceding asthma. In the case-control analysis, the association was calculated based on individuals who developed BP following the diagnosis of asthma, given that a temporal relationship exists between exposure and outcome. While investigating the lifetime prevalence and the epidemiological characteristics of patients with BP and asthma relative to those with isolated BP, all patients with both diagnoses were included, regardless of the sequence of their appearance. Two-tailed *p* values less than 0.05 were considered as statistically significant. All statistical analyses were performed using SPSS software, version 25 (SPSS, Armonk, NY: IBM Corp).

***References***

[1] Rennert G, Peterburg Y. Prevalence of selected chronic diseases in Israel. Isr Med Assoc J. 2001 Jun;3(6):404–8.

[2] Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40(5):373–83.