Case-control study evaluating competing risk factors for angioedema in a high-risk population

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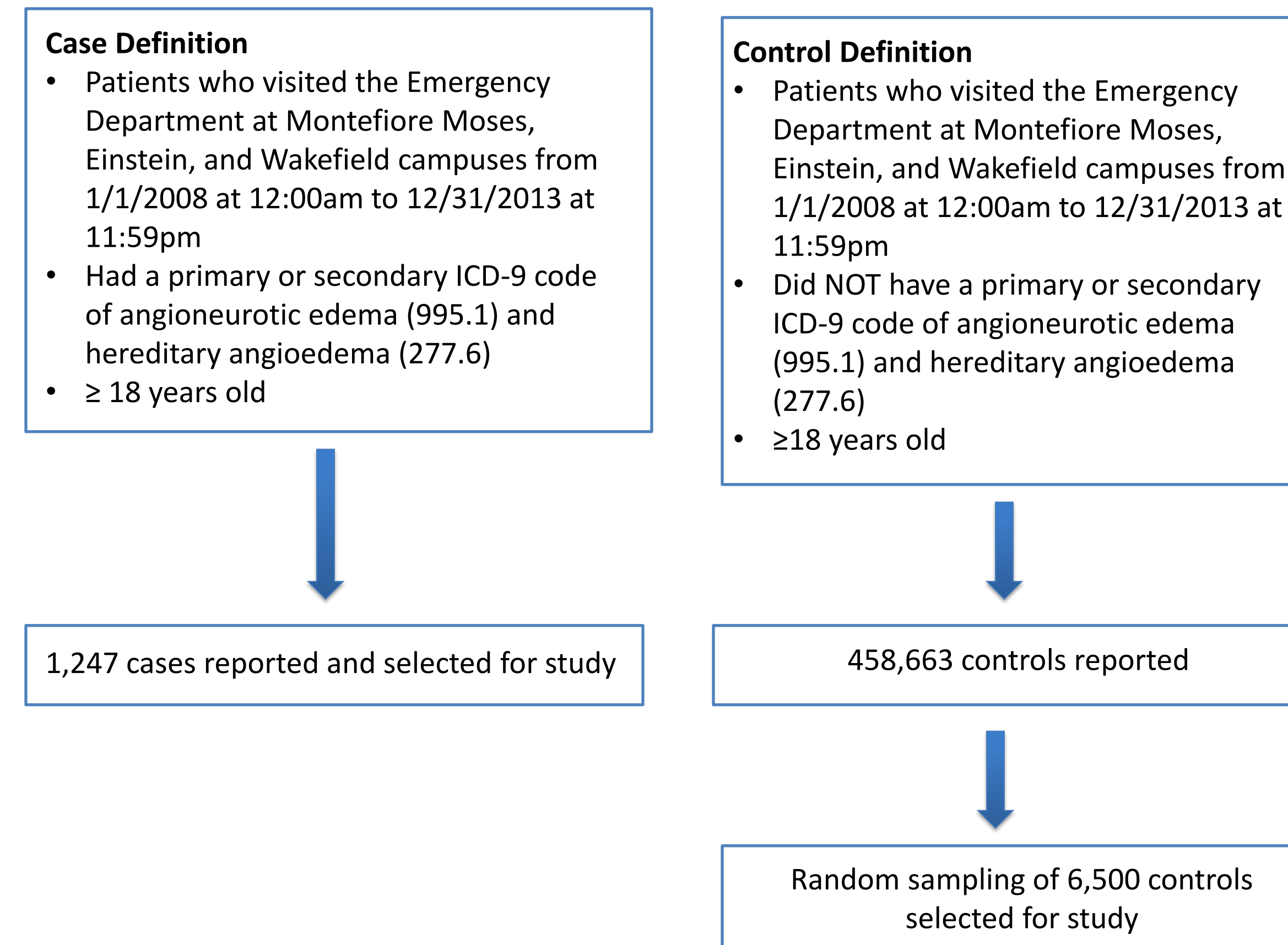
Introduction

- Black race and ace-inhibitor (ACE-I) use are known risk factors in the development of angioedema
- We hypothesized that Black race and ACE-I use were synergistic risk factors
- Our aim was to determine the relative influence of different risk factors in the development of angioedema in the largely Hispanic and Black population of the Bronx

Methods

- We conducted a case-control study using data collected by the Clinical Looking Glass (CLG) utility
- **Cases** were defined as Emergency Department (ED) visits with primary or secondary ICD9-code diagnoses of Angioneurotic Edema (995.1) and Hereditary Angioedema (277.6) in adults aged ≥18 years from 1/2008-12/2013
- **Controls** were defined as a random sampling of adult ED visits during the same period
- Race-ethnicity was determined by self-identification of race (White, Black, or other) and ethnicity (Hispanic/Latino or not)
- In primary analyses, we tested for interaction between ACE-I use and Black race to evaluate synergy
- Baseline multivariate model adjusted for gender, age, race, facility, and hospital admission within 30 days of ED visit
- Expanded multivariate model adjusted for baseline model variables and ethnicity, diabetes, hypertension, hyperlipidemia, smoking history, asthma, allergic rhinitis, eczema, autoimmune disease, ACE-I and ARB use

Figure 1. Flow-Chart of selection of cases and controls

Case Definition
- Patients who visited the Emergency Department at Montefiore Moses, Einstein, and Wakefield campuses from 1/1/2008 at 12:00am to 12/31/2013 at 11:59pm
- Had a primary or secondary ICD-9 code of angioneurotic edema (995.1) and hereditary angioedema (277.6)
- ≥ 18 years old

Control Definition
- Patients who visited the Emergency Department at Montefiore Moses, Einstein, and Wakefield campuses from 1/1/2008 at 12:00am to 12/31/2013 at 11:59pm
- Did NOT have a primary or secondary ICD-9 code of angioneurotic edema (995.1) and hereditary angioedema (277.6)
- ≥18 years old

1,247 cases reported and selected for study

458,663 controls reported

Random sampling of 6,500 controls selected for study

Results

- 1,247 cases and 6,500 control individuals randomly sampled from a larger control pool
- ACE-I use and Black race were not synergistic (OR 1.10, 95% CI 0.80, 1.51)
- ACE-I use (OR 3.70, 95% CI 2.98, 4.60), HTN (OR 1.88, 95% CI 1.55, 2.29), and Black race (OR 2.25, 95% CI 1.86, 2.72) were the strongest risk factors
- In addition to ace-use, HTN, Black race, only eczema (OR 1.58 [95% CI 1.12, 2.22]), allergic rhinitis (OR 1.38 [95% CI 1.12, 1.70]), female gender (OR 1.18 [95% CI 1.03, 1.37]), and age (OR 1.03 [95% CI 1.02, 1.03]) remained significant in fully-adjusted models

Table 1. Risk factors in the development of angioedema for the entire cohort (n=7,747).

Risk Factor	Baseline Model		Expanded Model	
	OR of Angioedema (95% CI)	p-value	OR of Angioedema (95% CI)	p-value
ACE-I Use	4.73 (3.91, 5.72)	<.001	3.70 (2.98, 4.60)	<.001
Hypertension	2.69 (2.32, 3.13)	<.001	1.88 (1.55, 2.29)	<.001
Black Race	2.39 (2.09, 2.72)	<.001	2.25 (1.86, 2.72)	<.001
Eczema	2.17 (1.59, 2.98)	<.001	1.58 (1.12, 2.22)	.008
ARB Use	2.03 (1.56, 2.64)	<.001	1.25 (0.94, 1.66)	.12
Allergic Rhinitis	1.88 (1.56, 2.26)	<.001	1.38 (1.12, 1.70)	.003
Autoimmune Disease	1.72 (1.14, 2.59)	.01	1.13 (0.73, 1.76)	.59
Female Gender	1.24 (1.08, 1.42)	.002	1.18 (1.03, 1.37)	.02
Smoking History	1.70 (1.38, 2.08)	<.001	1.16 (0.93, 1.46)	.19
Diabetes	1.69 (1.42, 2.02)	<.001	0.85 (0.69, 1.05)	.14
Asthma	1.38 (1.16, 1.65)	<.001	0.97 (0.80, 1.18)	.74
Age[b]	1.04 (1.03, 1.04)	<.001	1.03 (1.02, 1.03)	<.001
Hispanic Ethnicity	0.96 (0.75, 1.22)	.72	0.94 (0.73, 1.21)	.62

a. Baseline multivariate model adjusted for gender, age, race, facility, and hospital admission within 30 days of ED visit. Expanded multivariate model adjusted for baseline model variables and ethnicity, diabetes, hypertension, hyperlipidemia, smoking history, asthma, allergic rhinitis, eczema, autoimmune disease, ACE-I and ARB use.
b. The odds ratio represents the risk of angioedema for each one-year increase in age.
c. Hispanic patients self-identified as any race and Hispanic ethnicity.
d. ACE-I Use – ACE-inhibitor use; ARB use – angiotensin receptor blocker use

Discussion

- Black race and ace-I use were not synergistic risk factors
- ACE-I use, hypertension, and Black race were the strongest risk factors in the development of angioedema
- The relationship between atopic conditions, such as eczema and allergic rhinitis, and the development of angioedema warrants further investigation

Acknowledgments