



COVID-19 and the Research Response

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AAAS

Novel Human Virus? Pneumonia Cases Linked to Seafood Market in China Stir Concern

By Dennis Normile

PLANTS

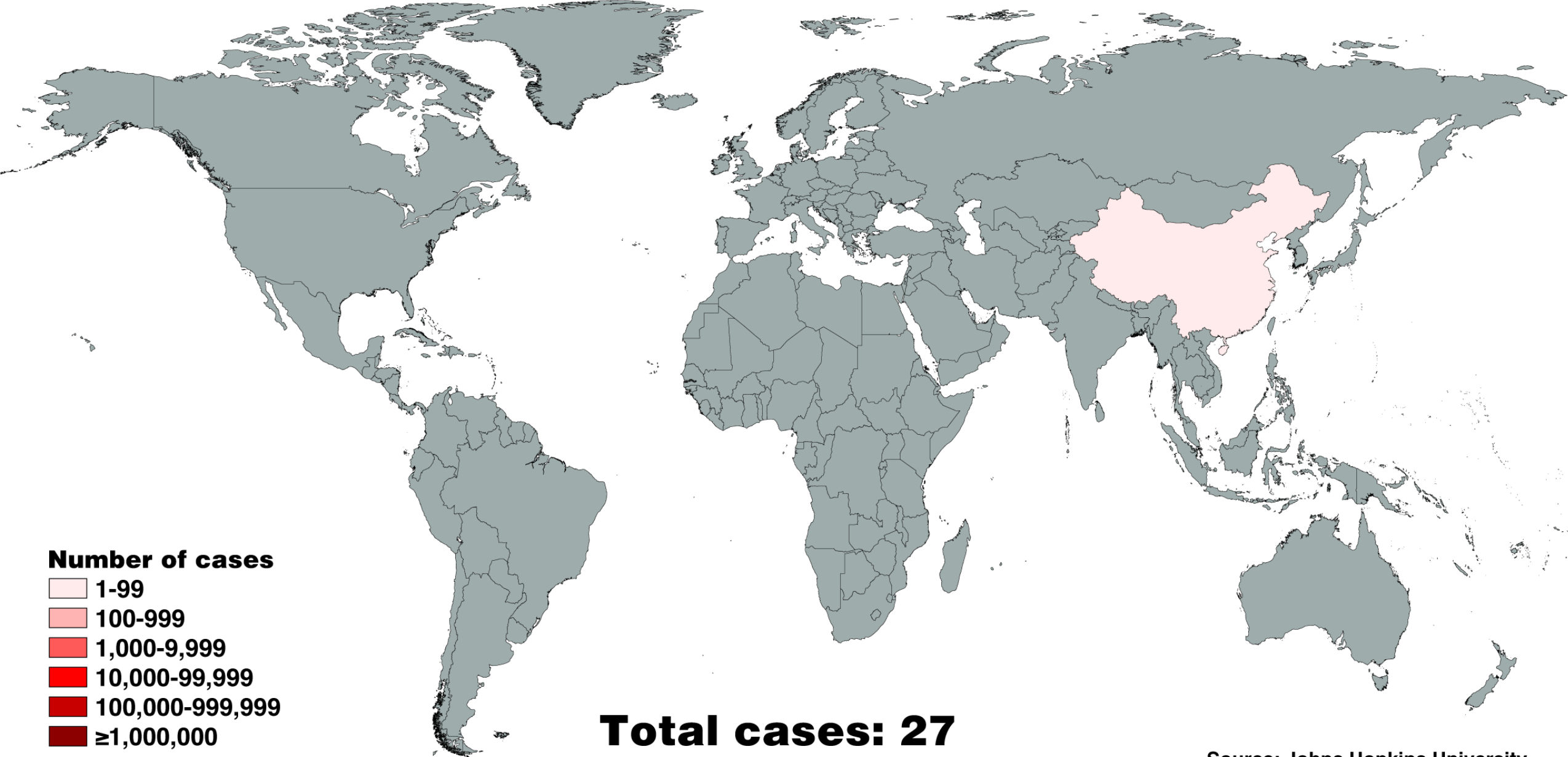
Convoluted shapes
from simple rules pp. 24 & 91

The Washington Post

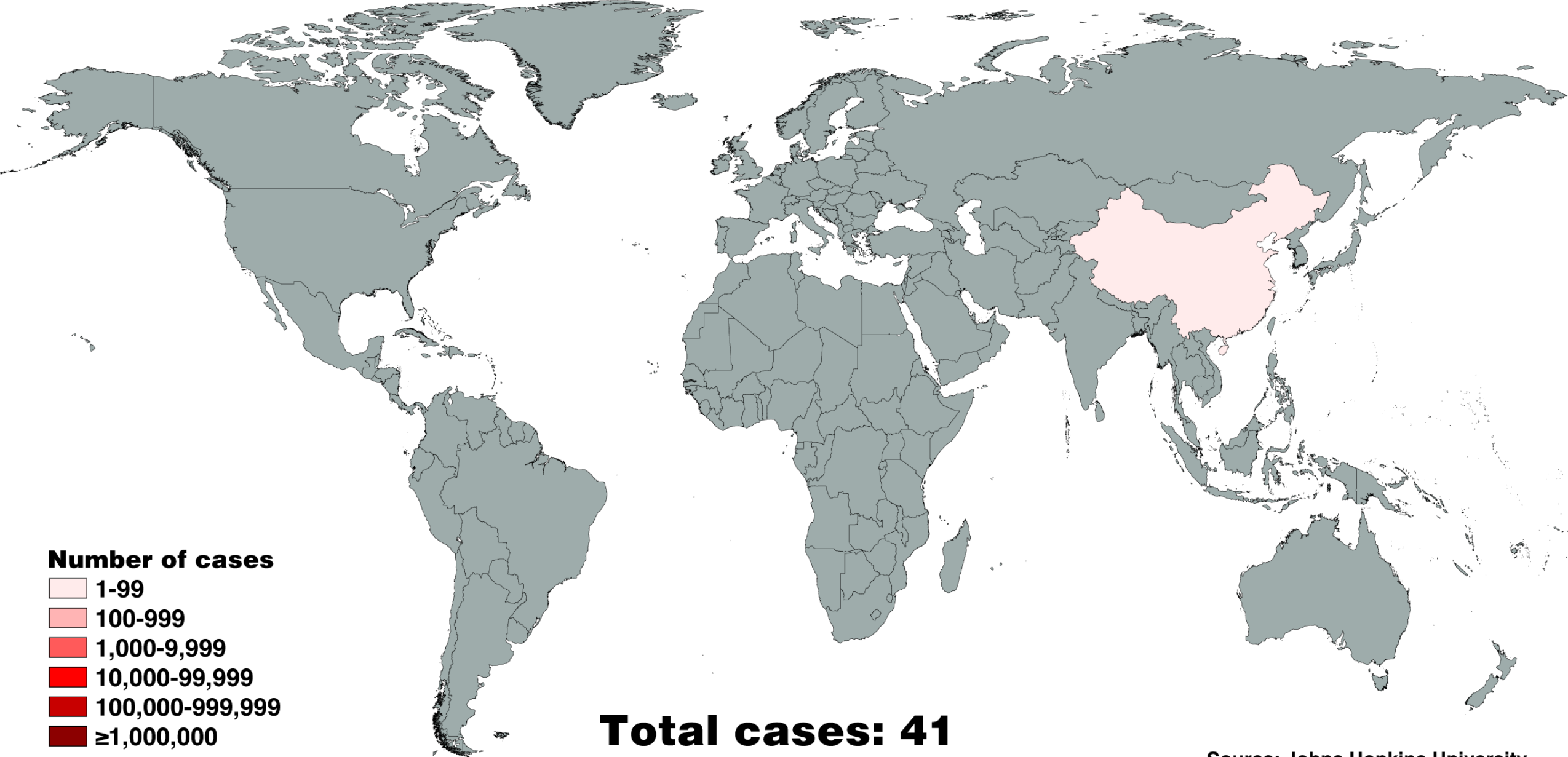
January 9, 2020

China Identifies New Strain of Coronavirus as Source of Pneumonia Outbreak

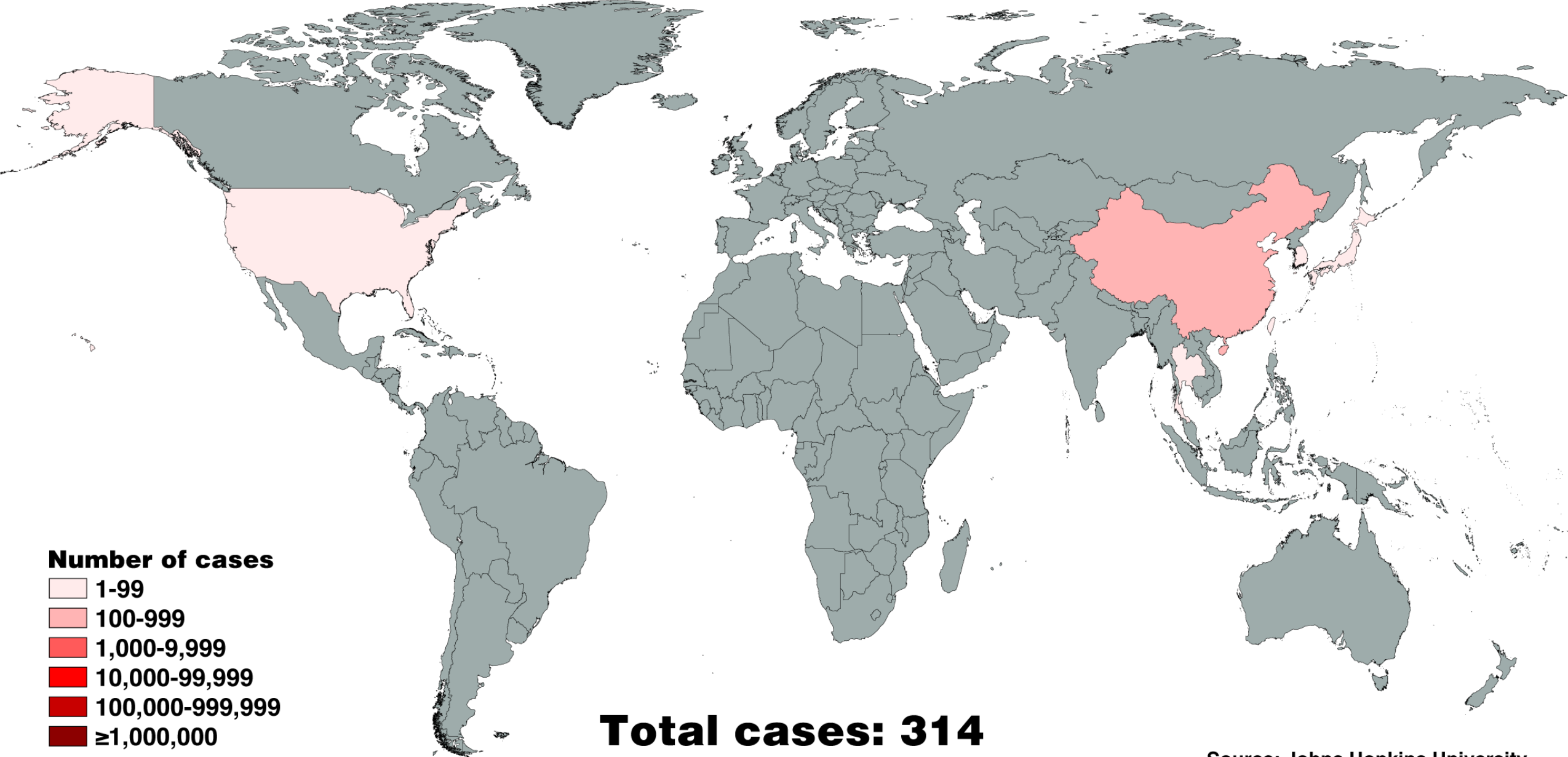
Global Spread of COVID-19 – Dec. 31, 2019



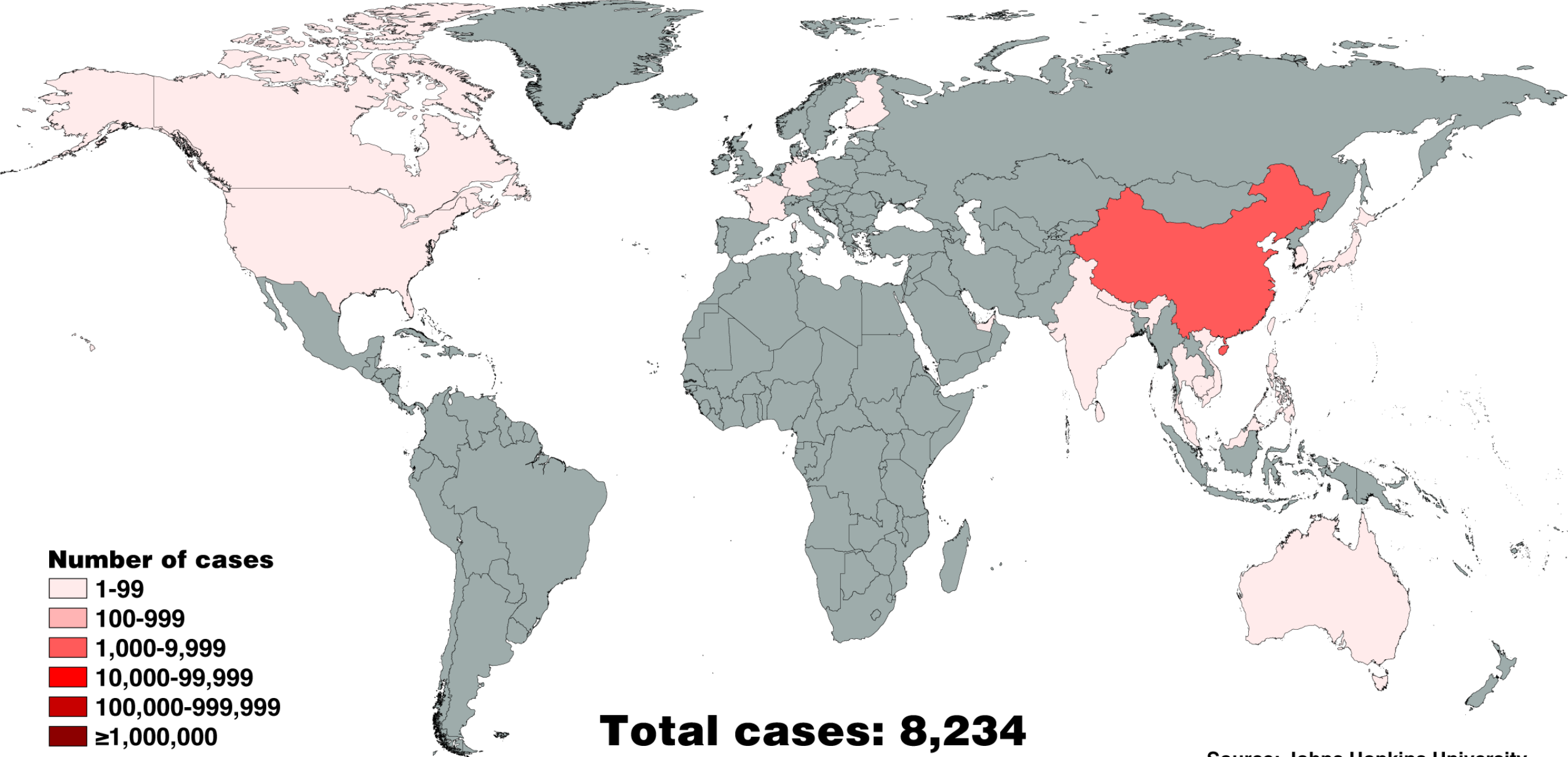
Global Spread of COVID-19 – Jan. 10, 2020



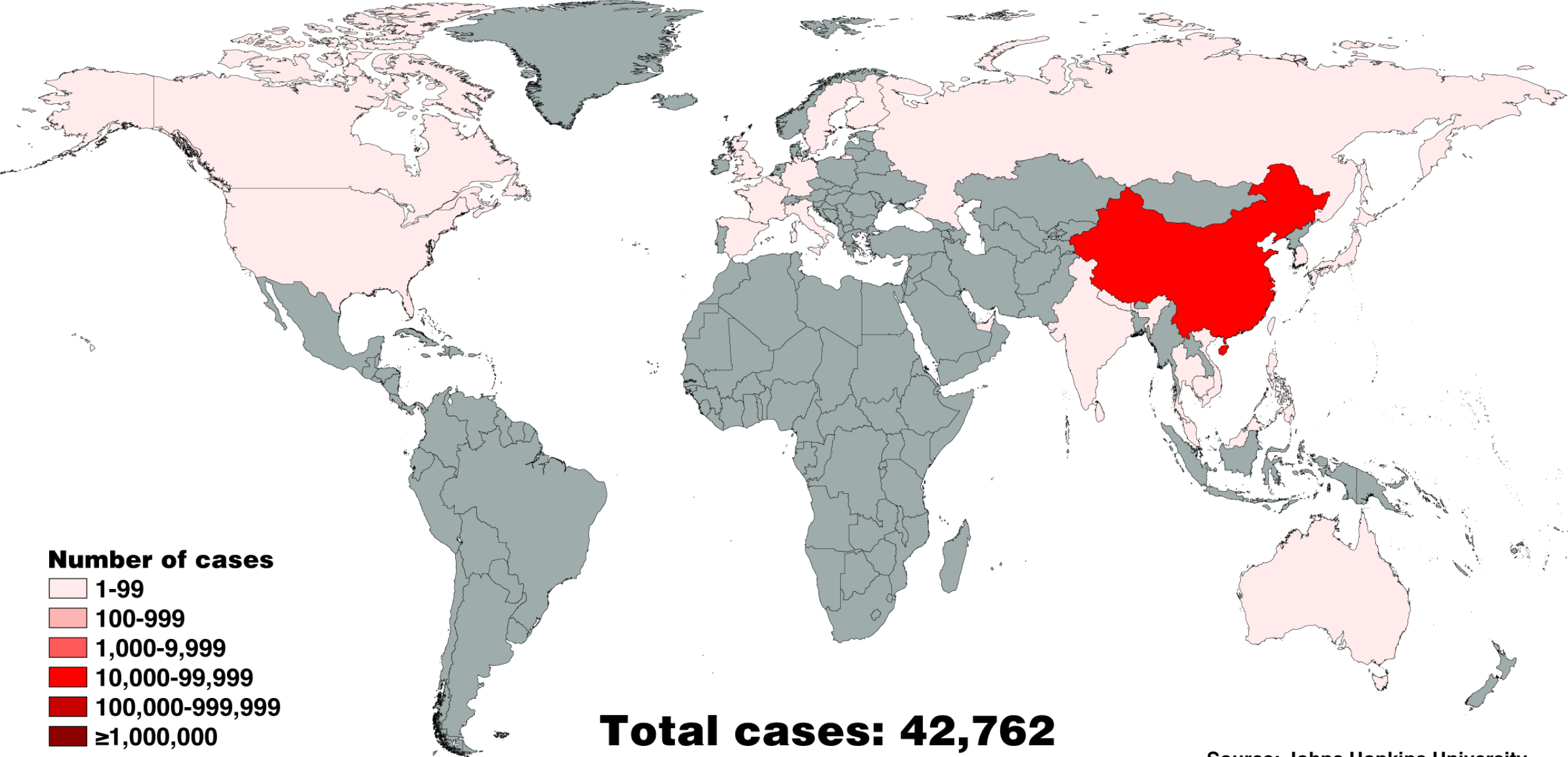
Global Spread of COVID-19 – Jan. 21, 2020



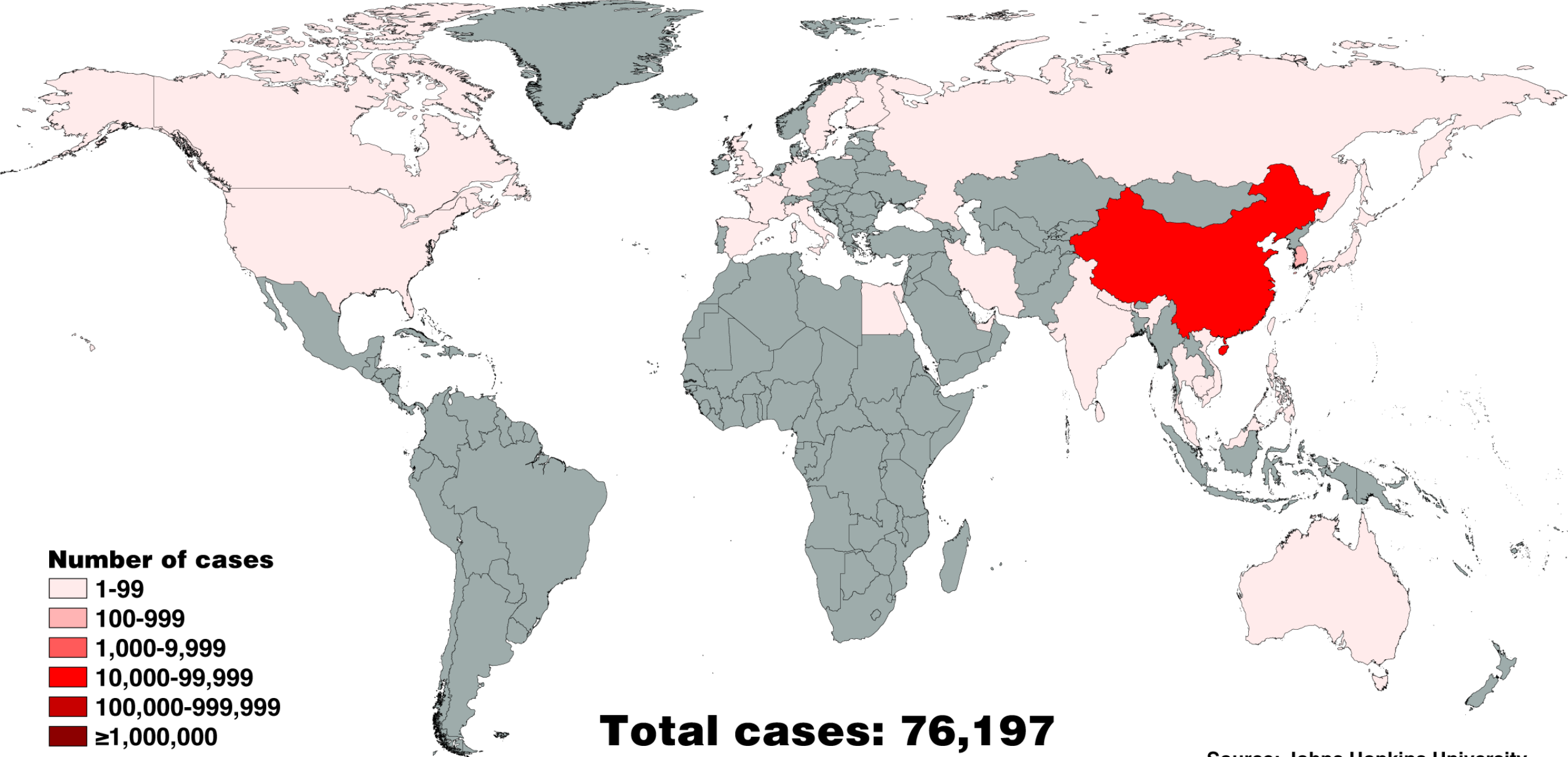
Global Spread of COVID-19 – Jan. 30, 2020



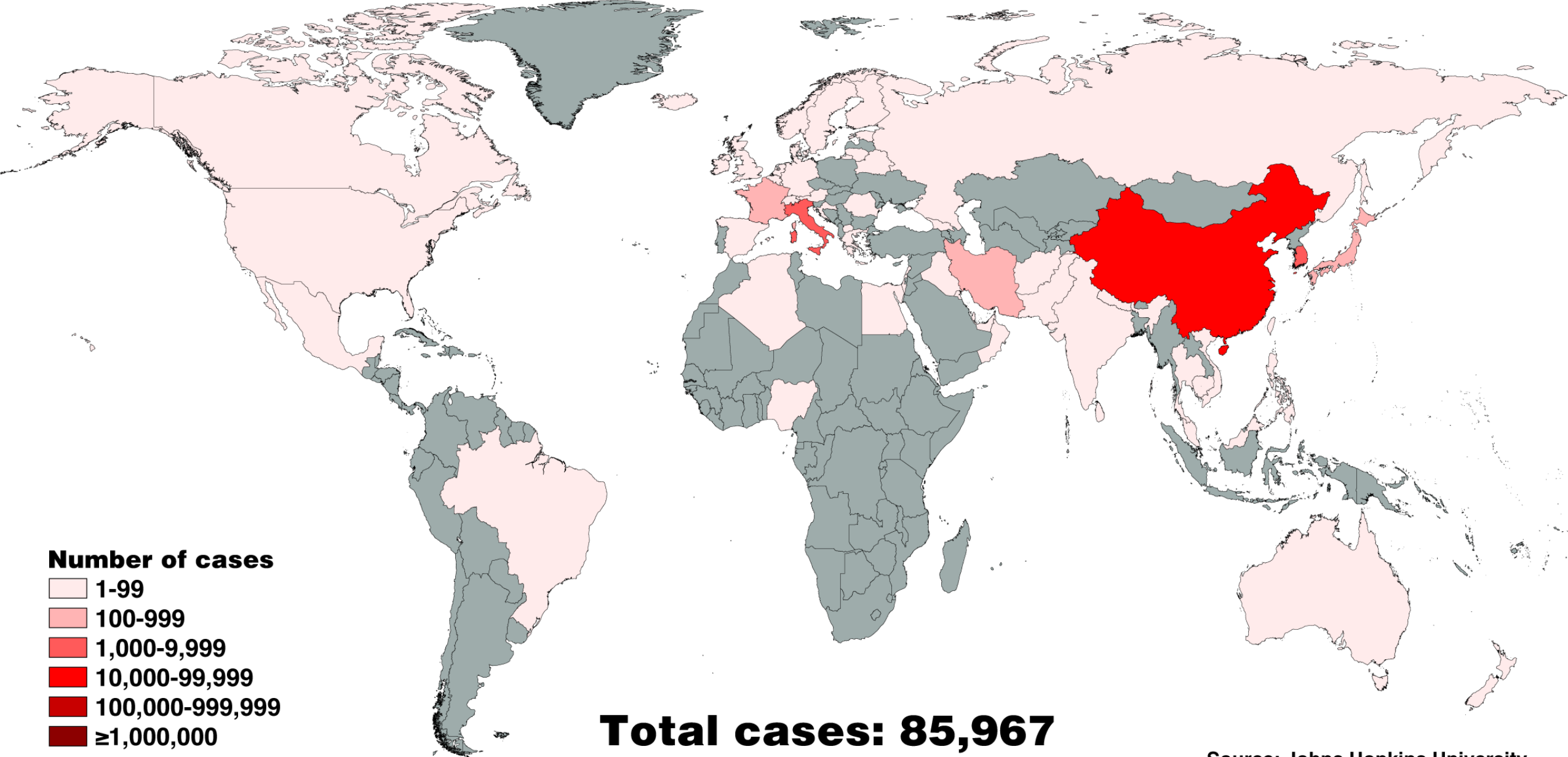
Global Spread of COVID-19 – Feb. 10, 2020



Global Spread of COVID-19 – Feb. 20, 2020

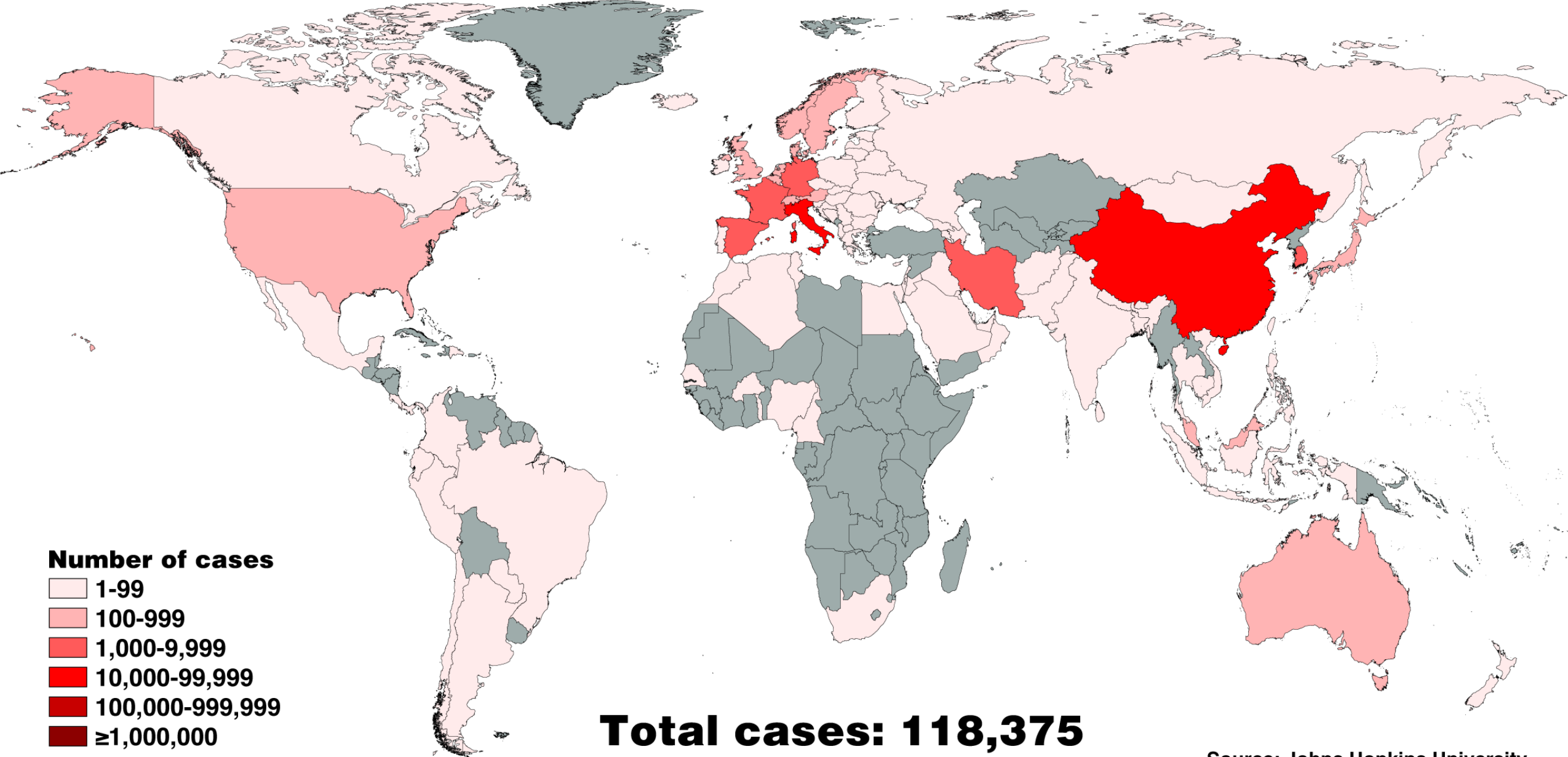


Global Spread of COVID-19 – Feb. 29, 2020



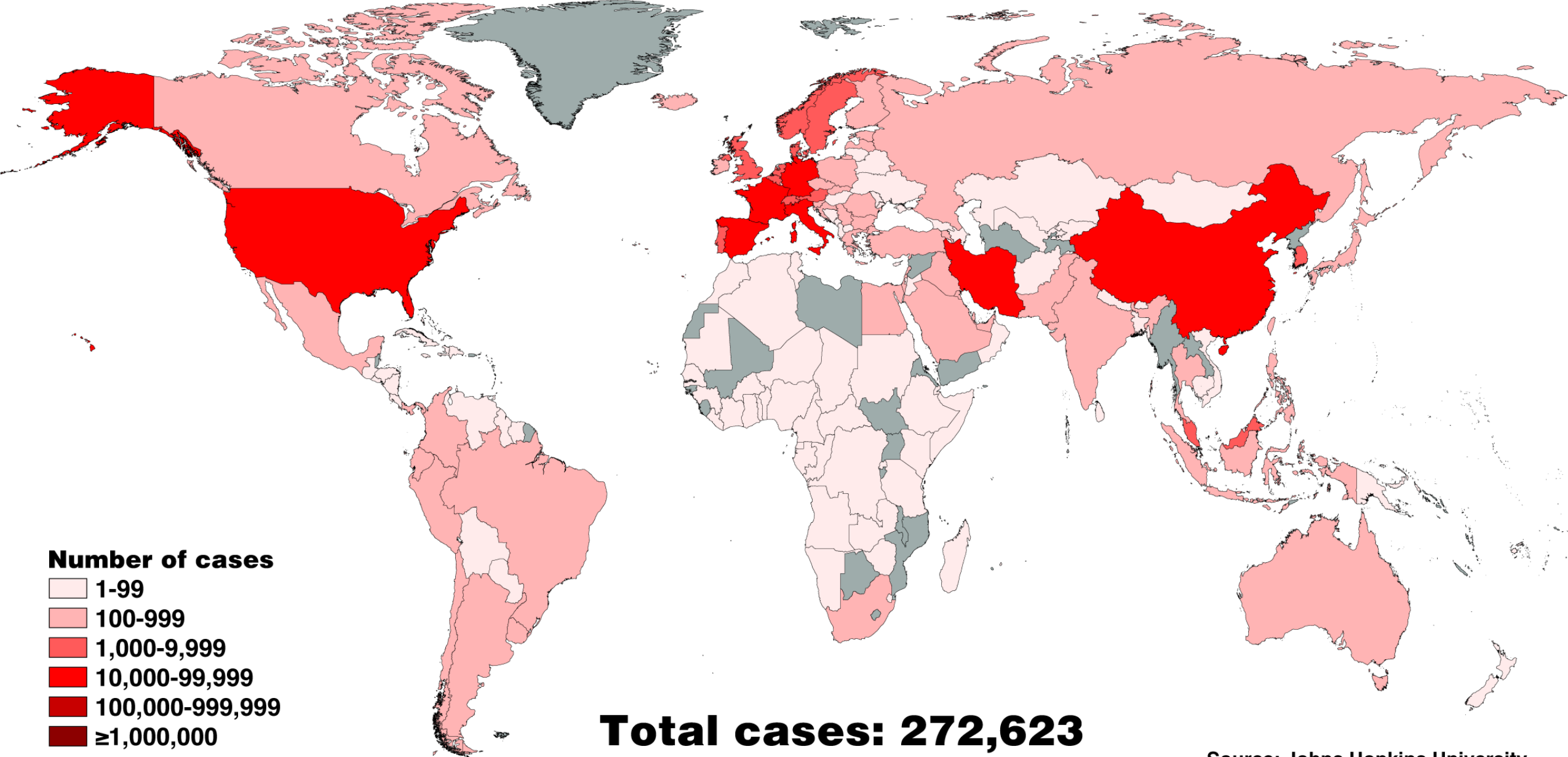
Source: Johns Hopkins University

Global Spread of COVID-19 – Mar. 10, 2020

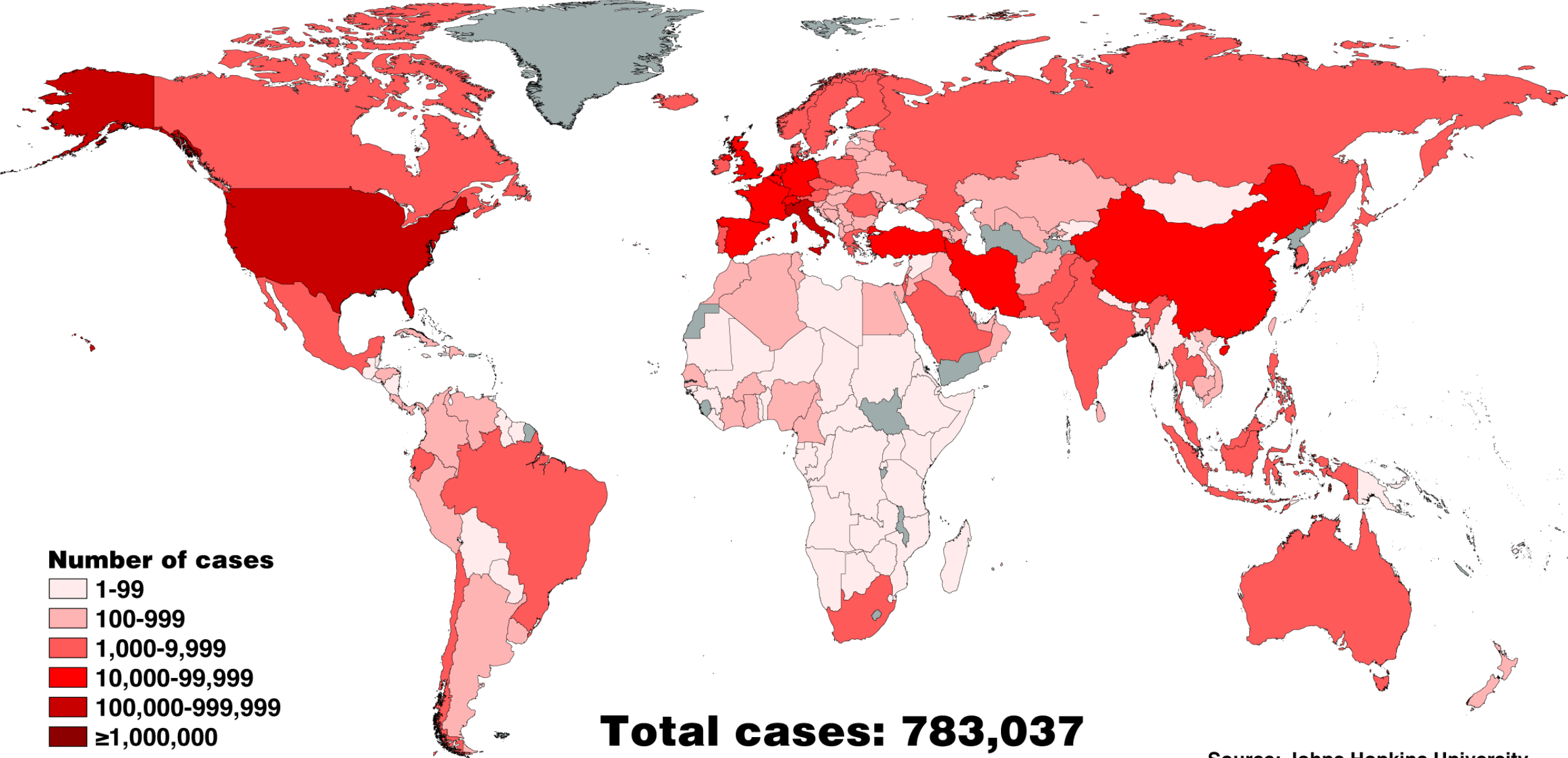


Source: Johns Hopkins University

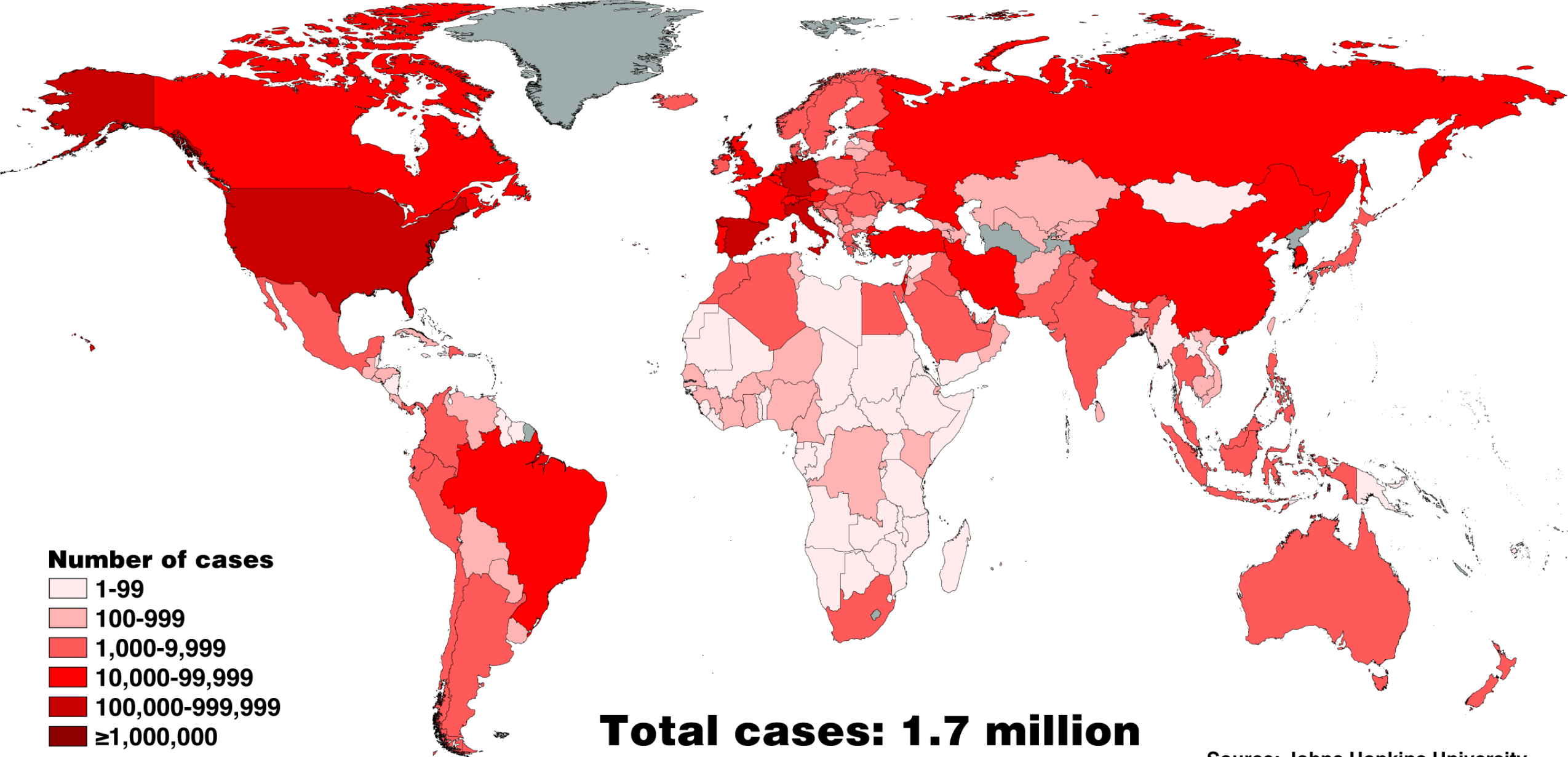
Global Spread of COVID-19 – Mar. 20, 2020



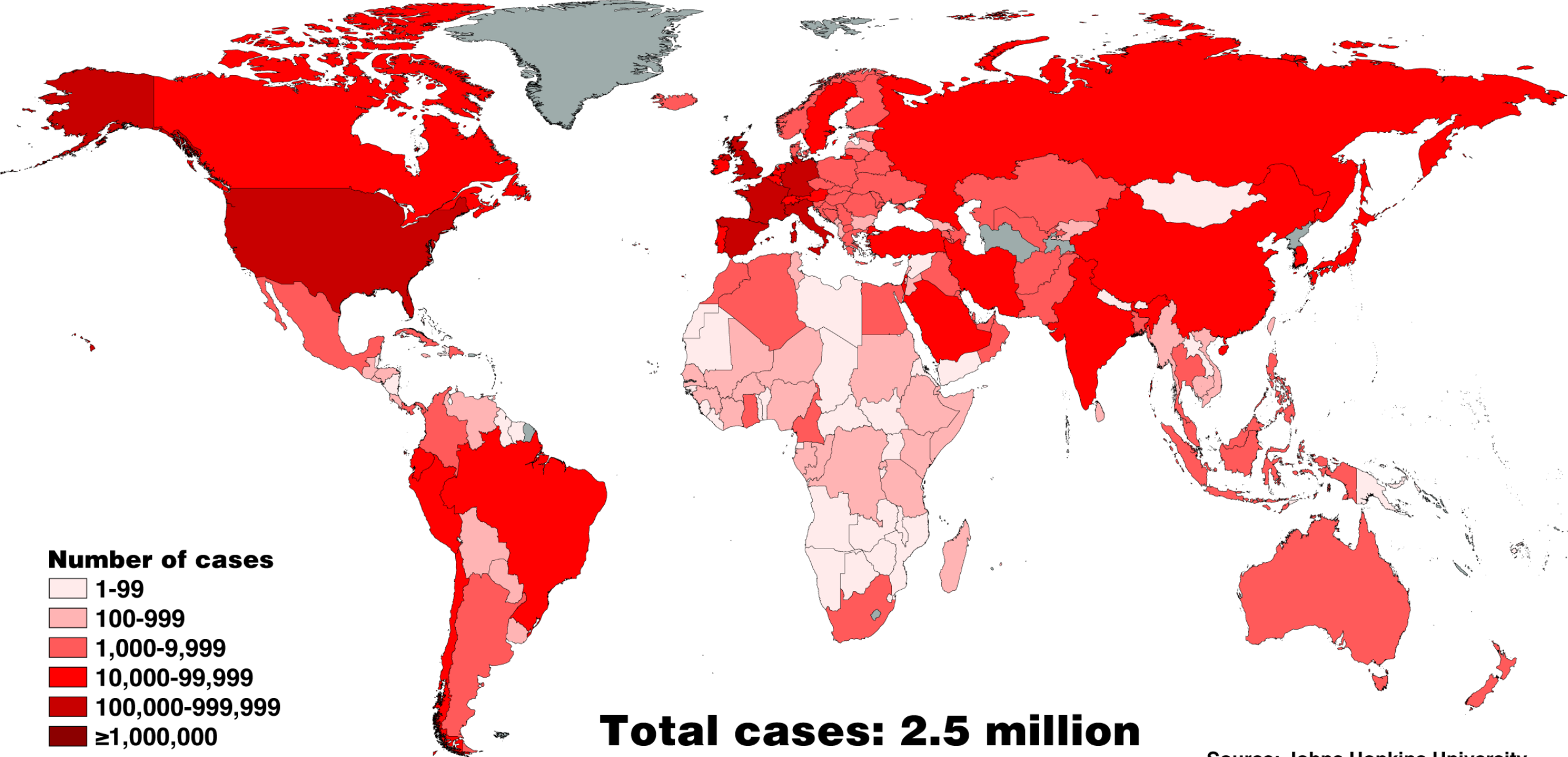
Global Spread of COVID-19 – Mar. 30, 2020



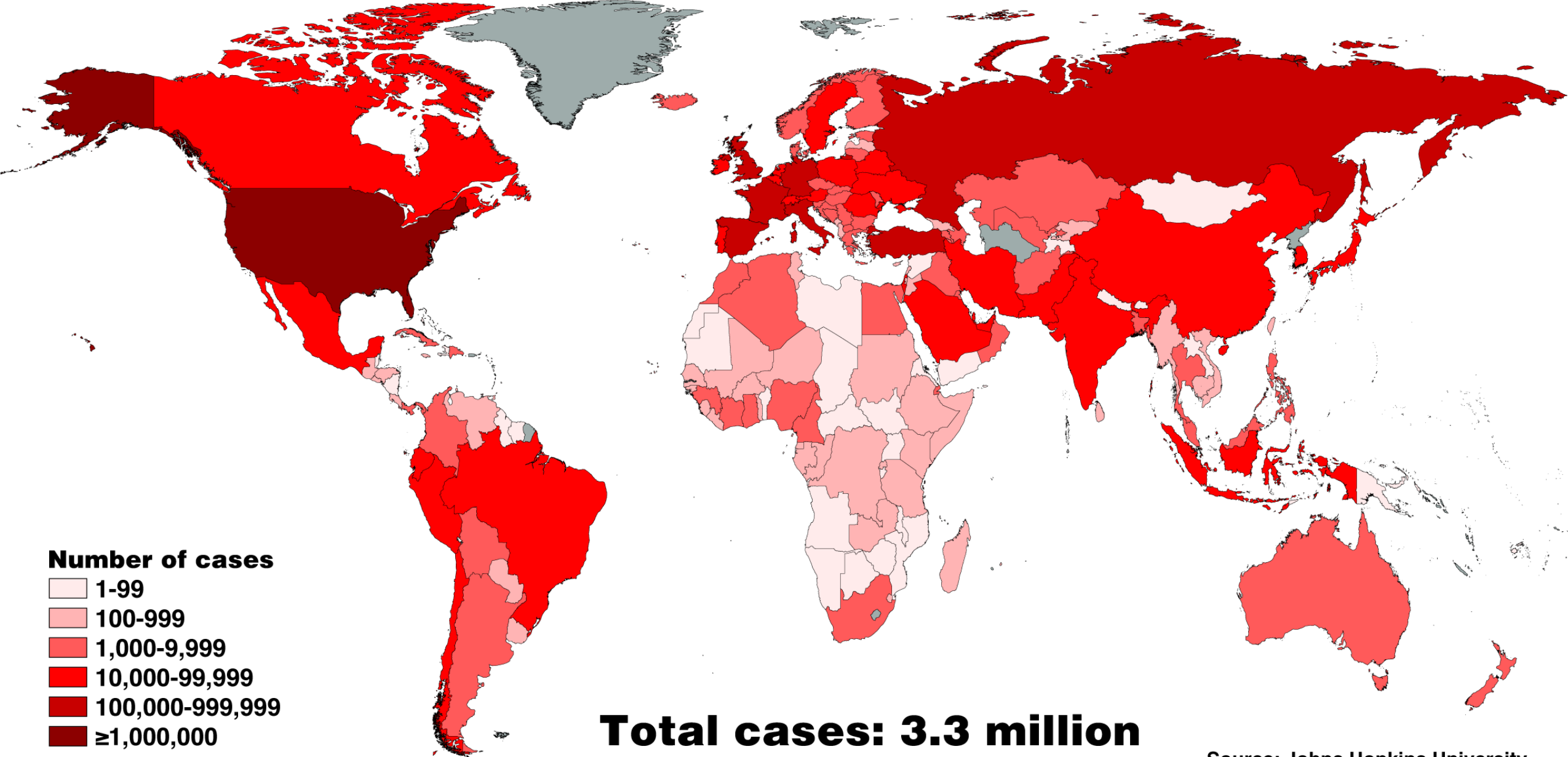
Global Spread of COVID-19 – Apr. 10, 2020



Global Spread of COVID-19 – Apr. 20, 2020

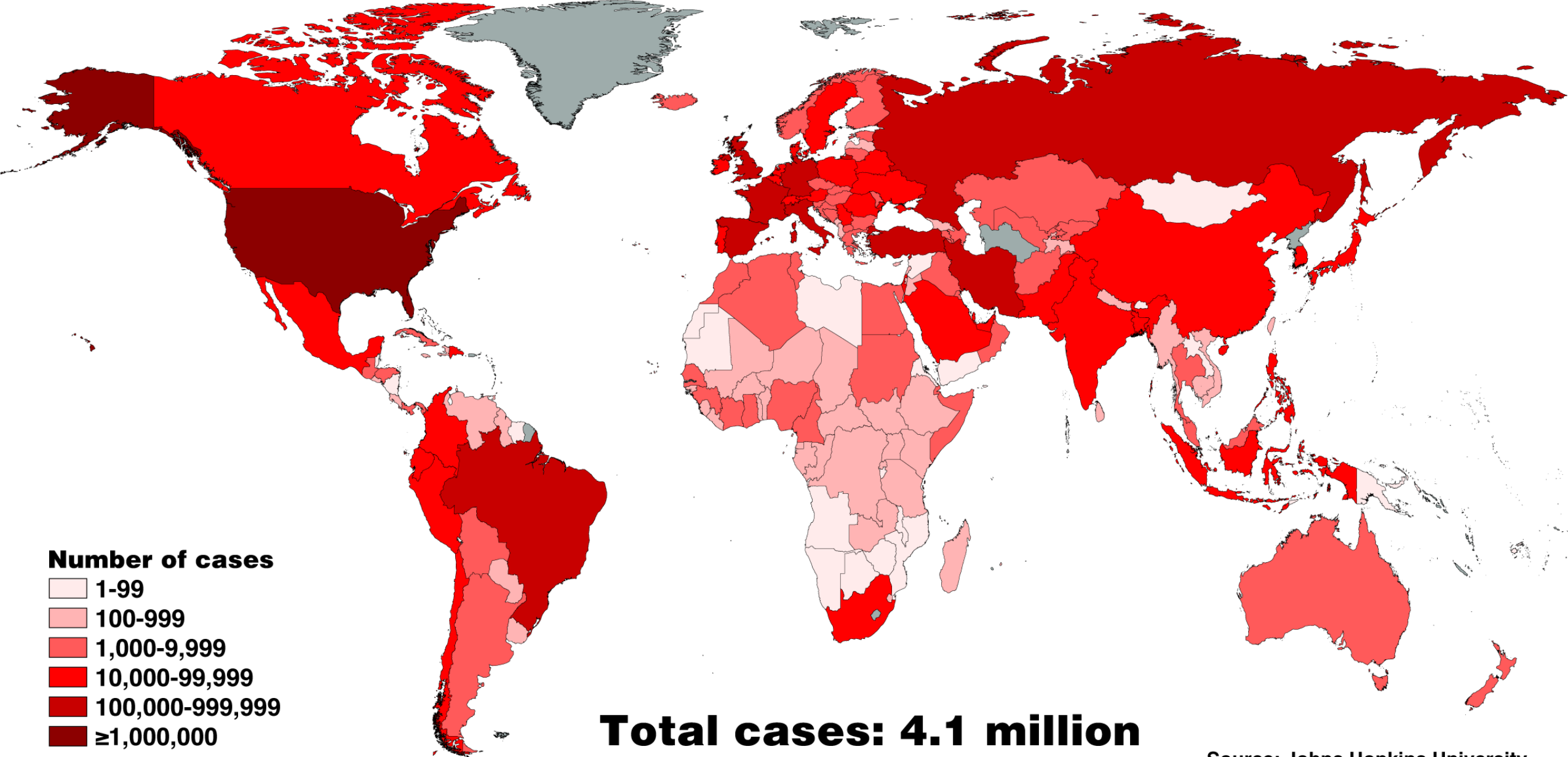


Global Spread of COVID-19 – Apr. 30, 2020

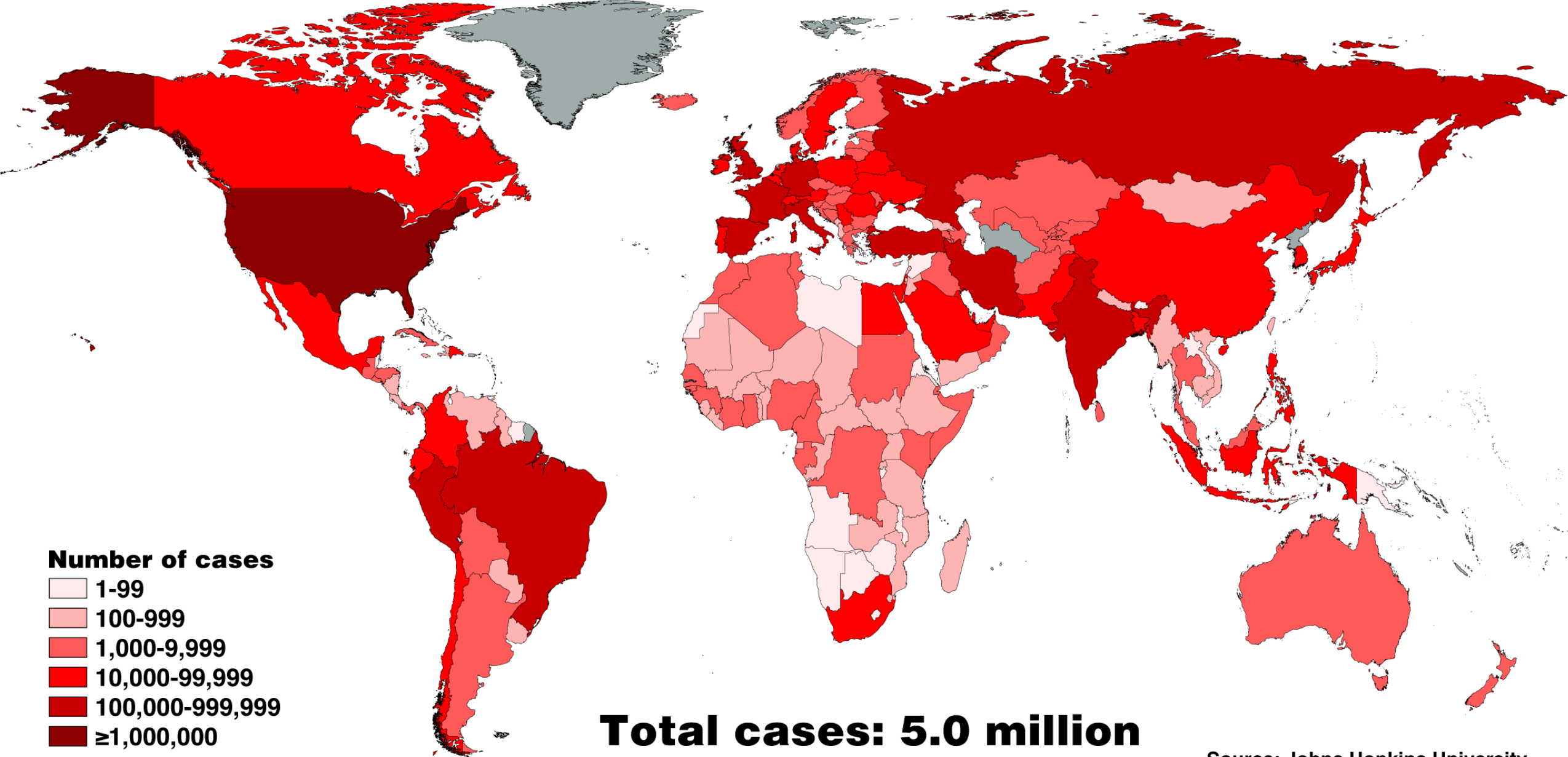


Source: Johns Hopkins University

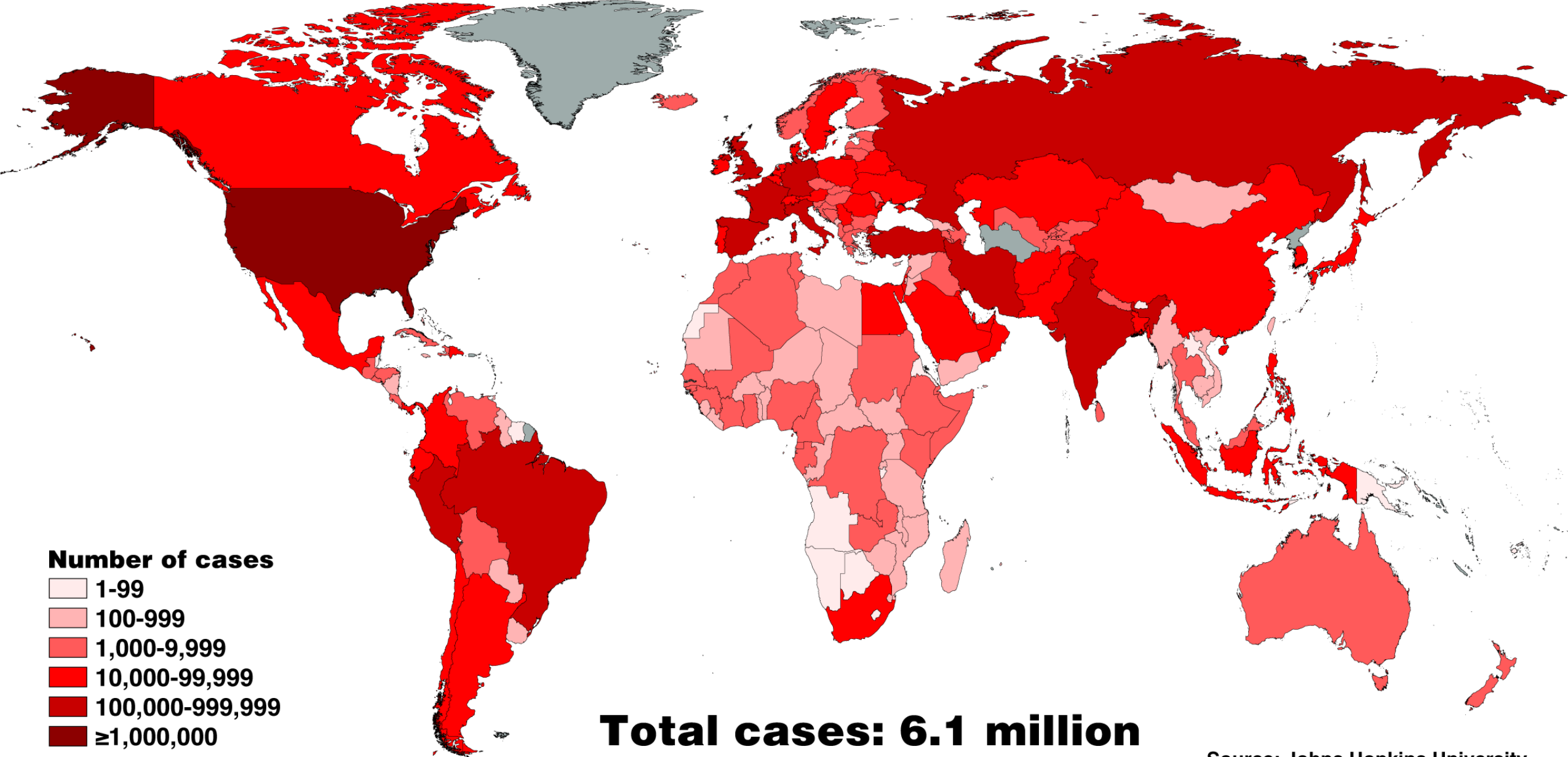
Global Spread of COVID-19 – May 10, 2020



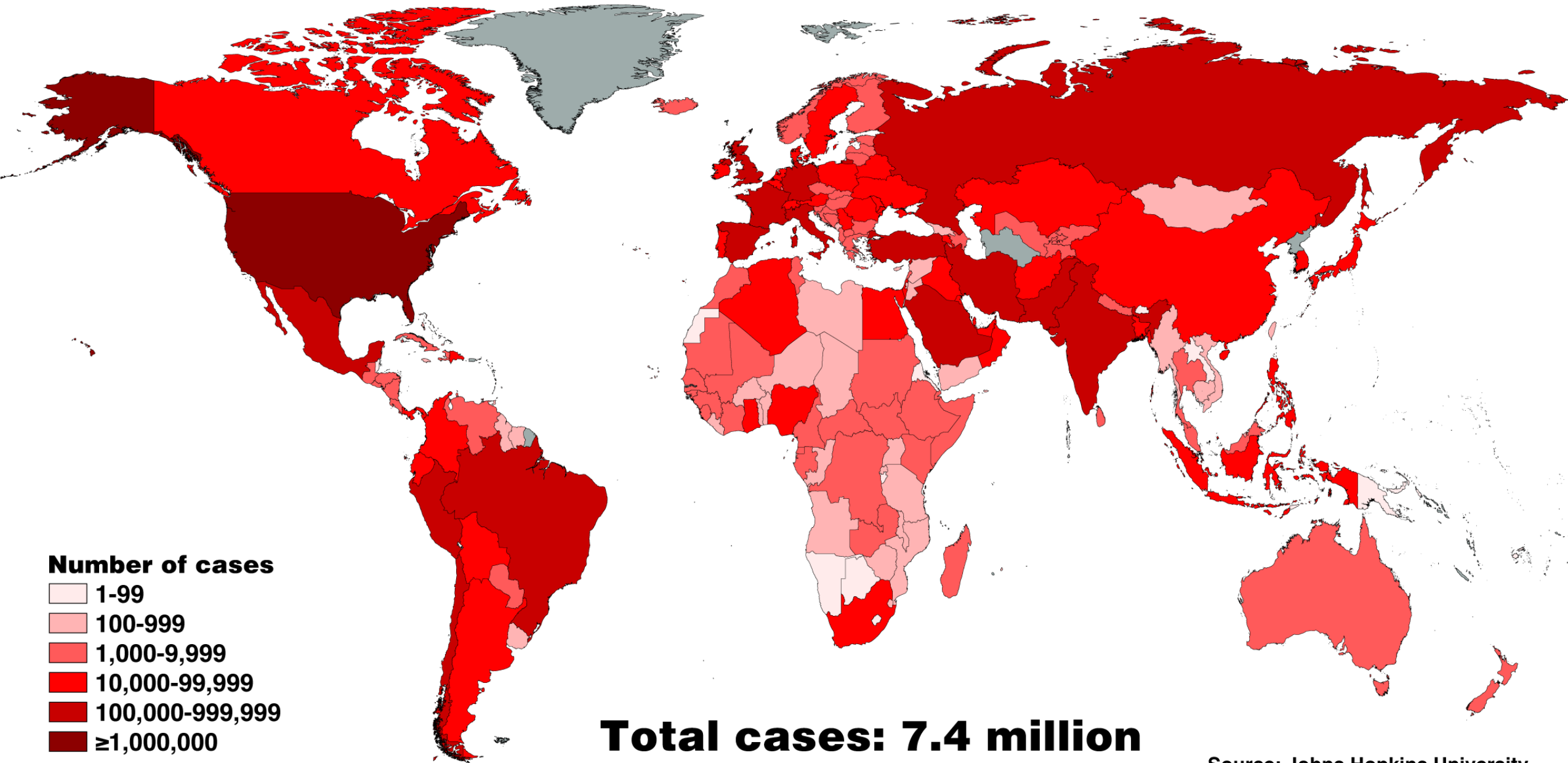
Global Spread of COVID-19 – May 20, 2020



Global Spread of COVID-19 – May 30, 2020

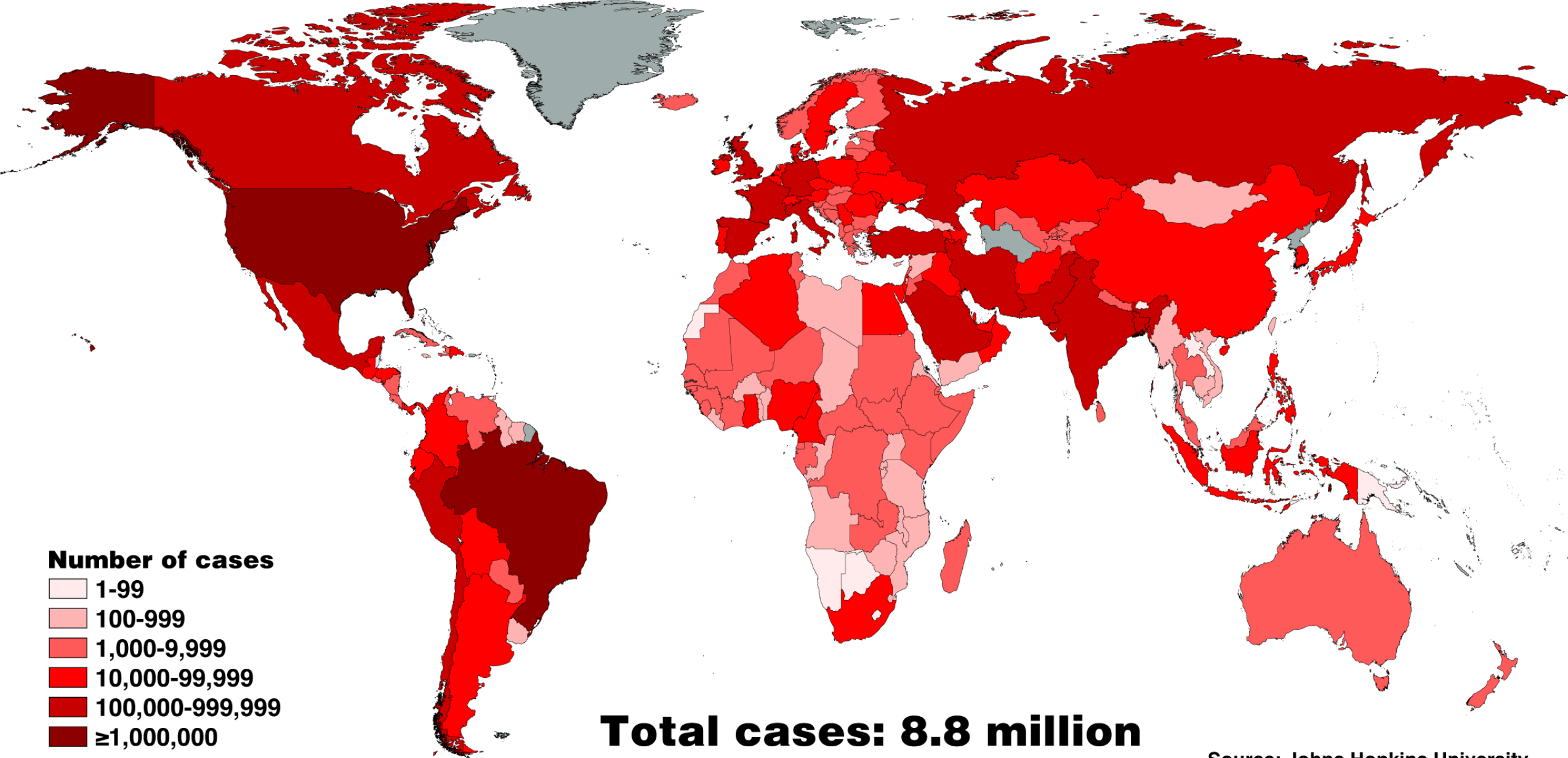


Global Spread of COVID-19 – June 10, 2020



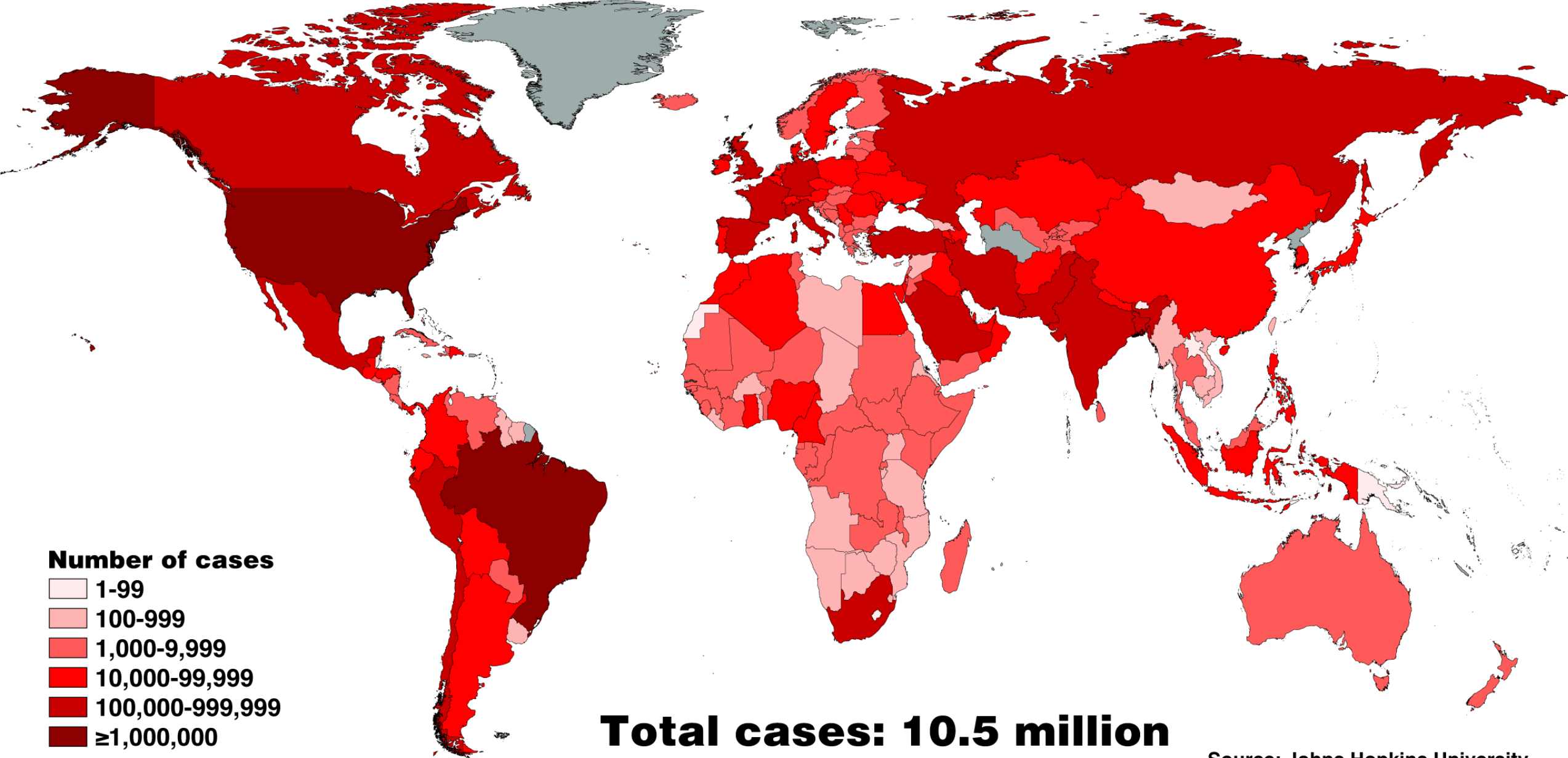
Source: Johns Hopkins University

Global Spread of COVID-19 – June 20, 2020



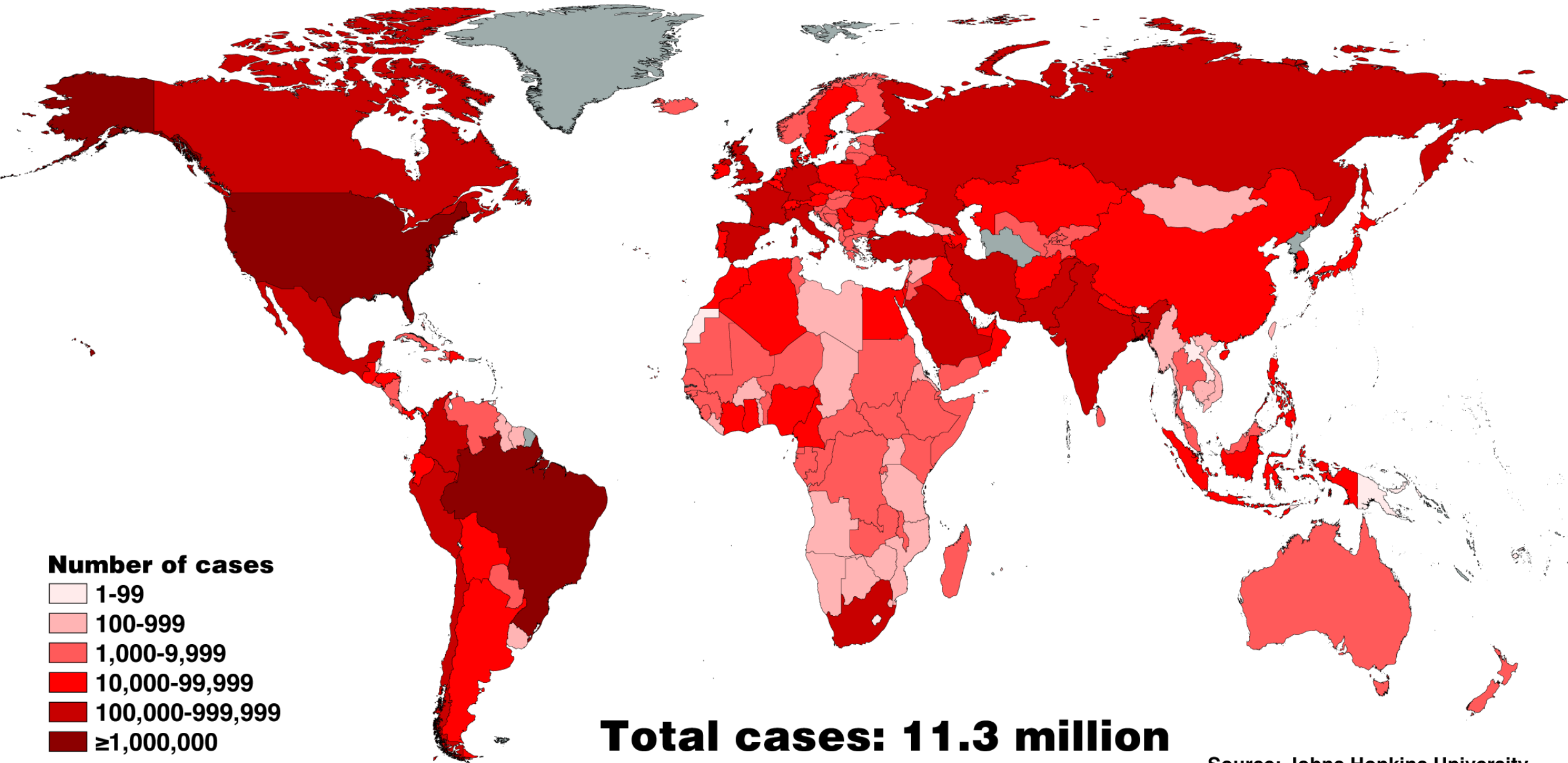
Source: Johns Hopkins University

Global Spread of COVID-19 – June 30, 2020



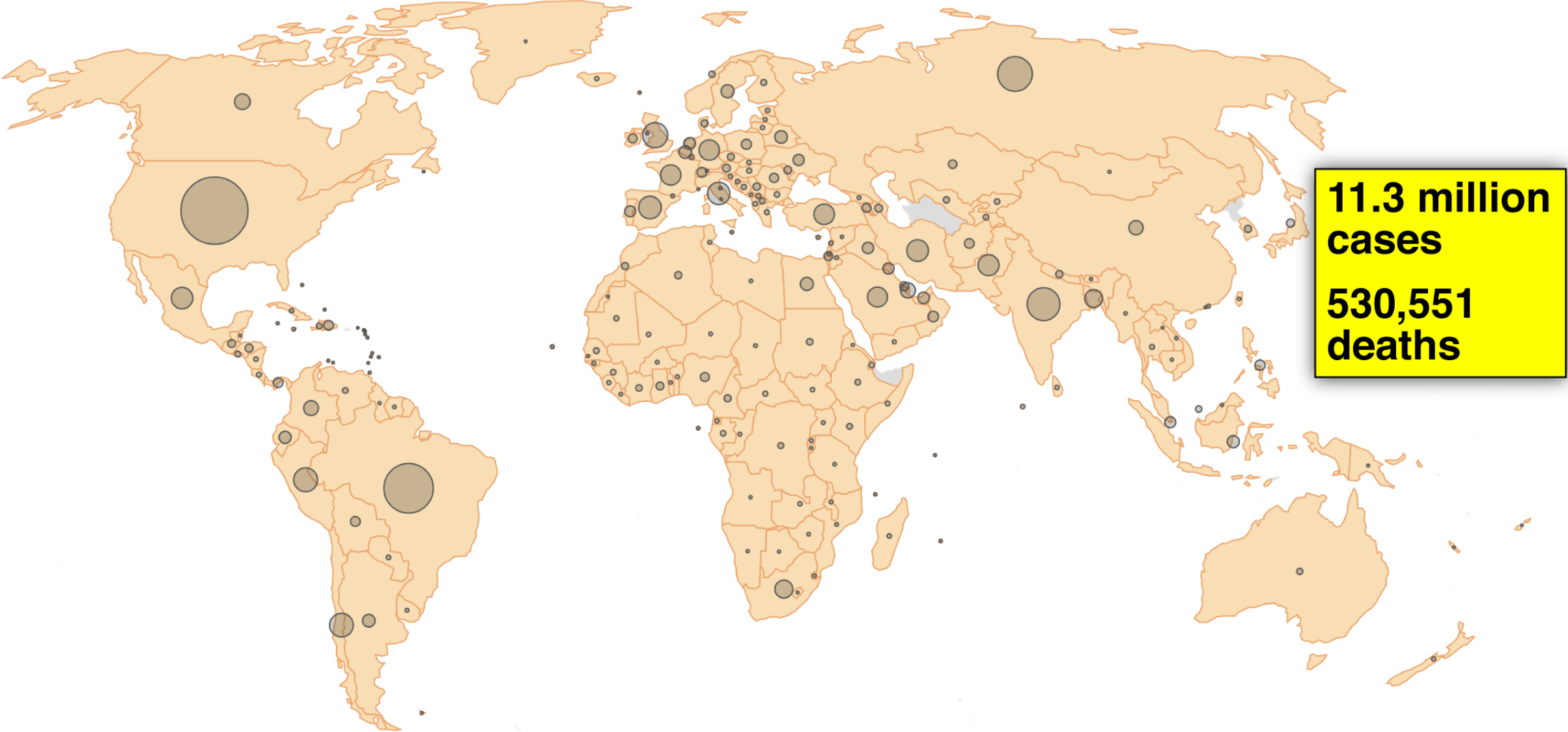
Source: Johns Hopkins University

Global Spread of COVID-19 – July 5, 2020



Source: Johns Hopkins University

COVID-19 Globally: 11.3 Million Cases in 215 Countries and Territories



Sources: NPR.org; Worldometer. Data as of 7/5/2020, 12:00 pm.

JAMA

The Journal of the American Medical Association

Published online
January 23, 2020

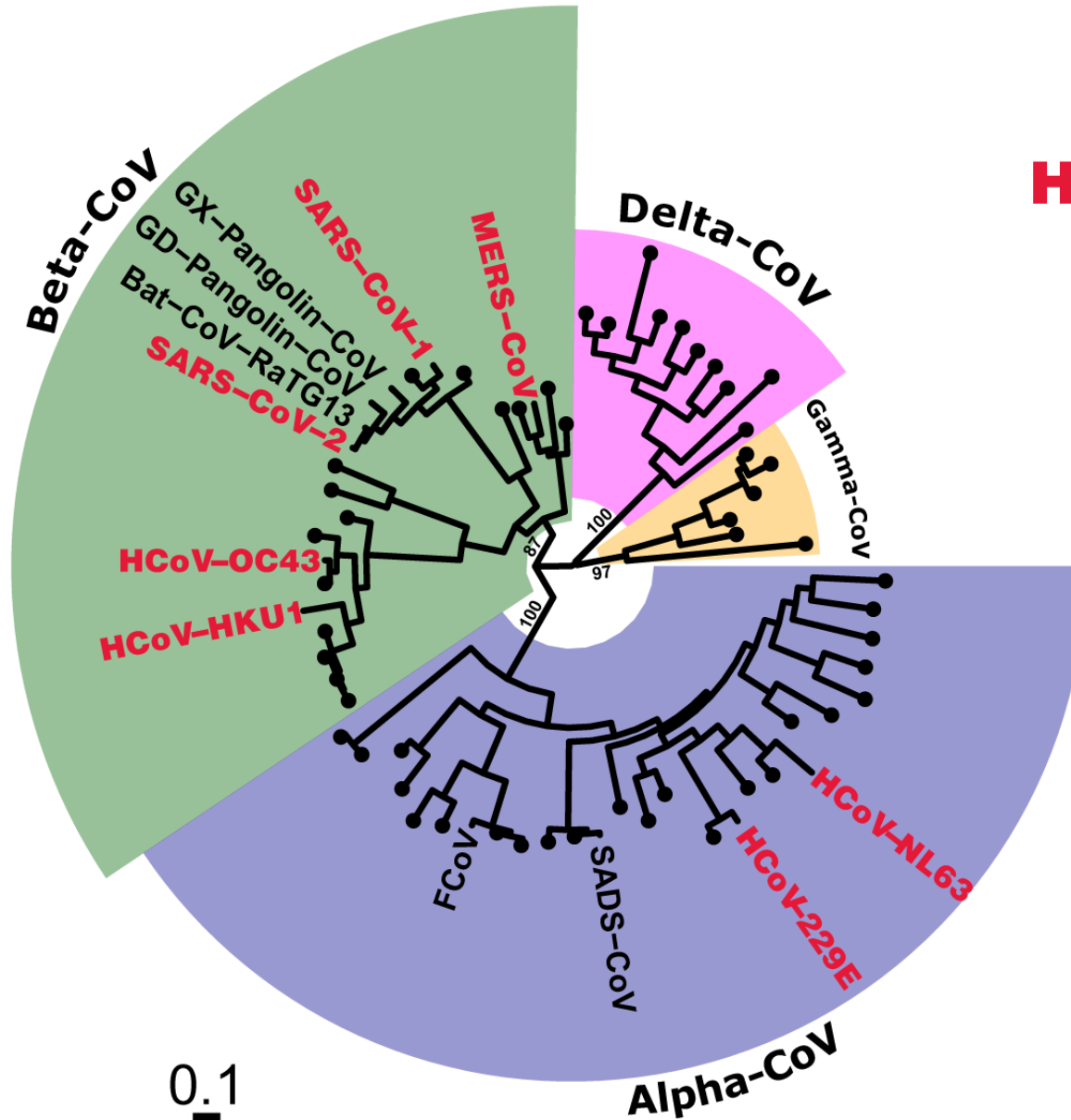
Viewpoint

Coronavirus Infections—More Than Just the Common Cold

CI Paules, HD Marston and AS Fauci

Basic Biology

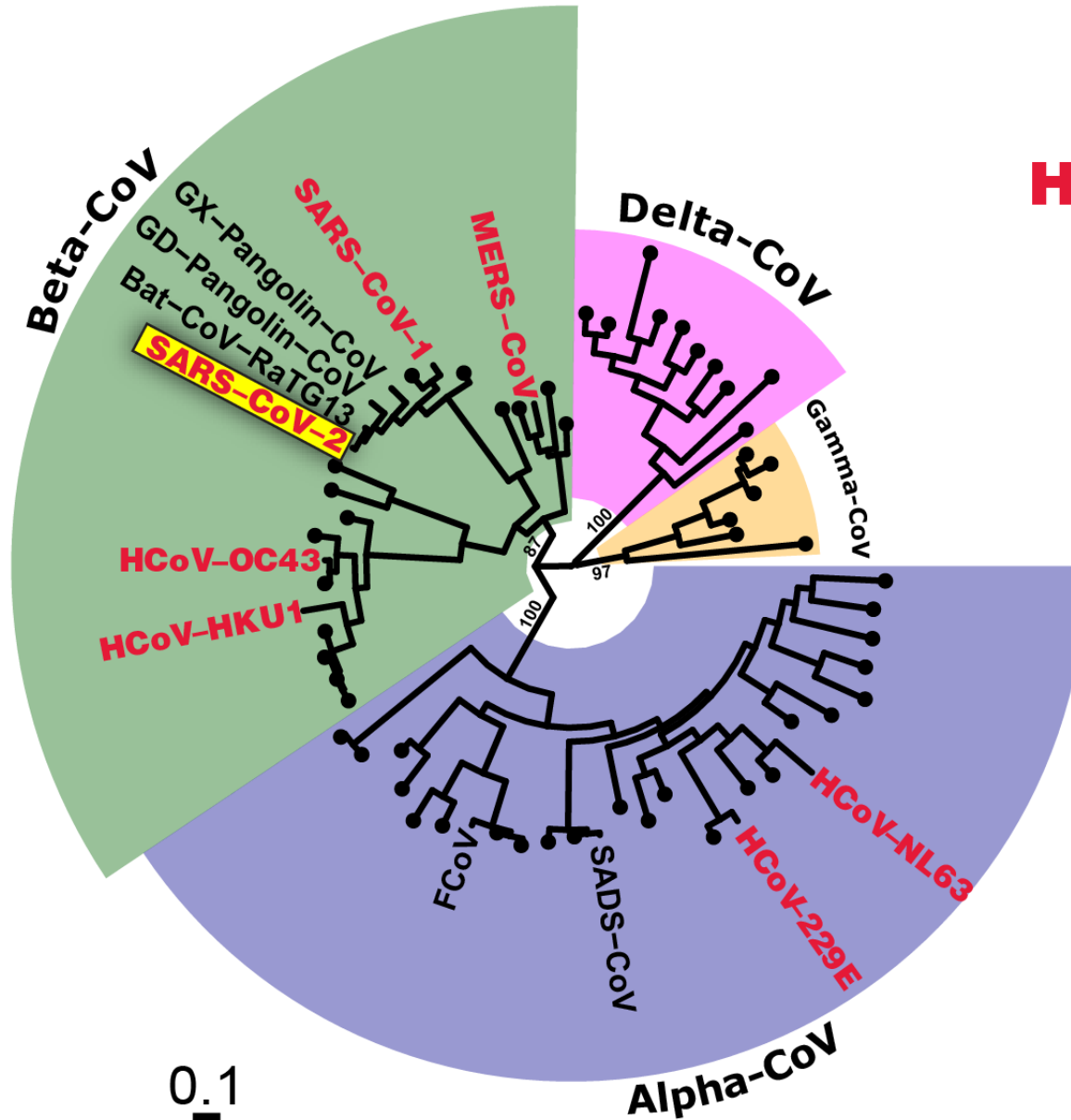
Coronavirus Phylogenetic Tree



Human coronaviruses

Figure courtesy of S.M. Gygli, Ph.D., NIAID. Based on 440 bp nucleotide sequences of RNA dependent RNA polymerase (RdRp).

Coronavirus Phylogenetic Tree

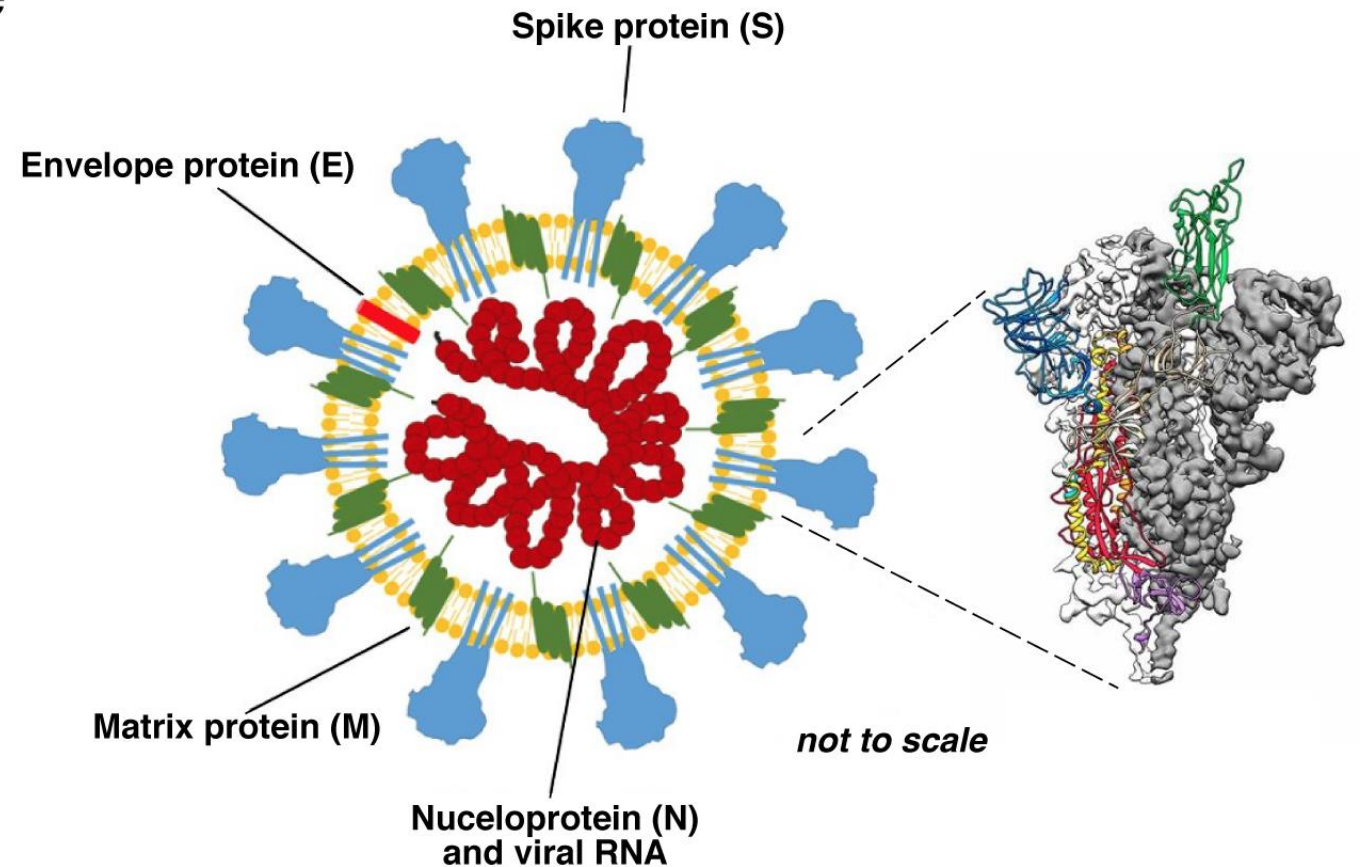


Human coronaviruses

Figure courtesy of S.M. Gygli, Ph.D., NIAID. Based on 440 bp nucleotide sequences of RNA dependent RNA polymerase (RdRp).

SARS-CoV-2 Virology

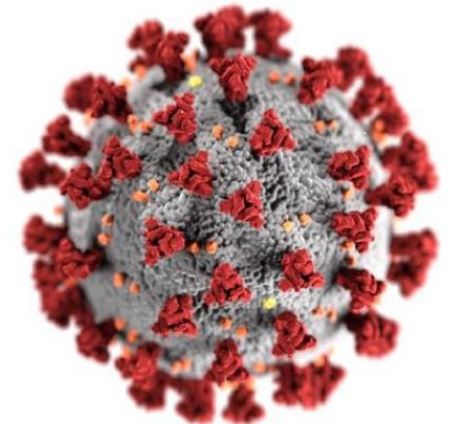
- **Beta coronavirus** in the same subgenus as the SARS virus and several bat coronaviruses
- **Enveloped, positive-sense single-stranded RNA (+ssRNA) virus**
- **Large genome: ~30,000 kilobases**
- **4 structural proteins: S, E, M, N**
- **S protein** allows virus to attach to and fuse with membrane of host cell
- **ACE2** is cellular receptor



Transmission

SARS-CoV-2 Transmission

- **Person-to-person transmission (<6 feet) via respiratory droplets (>5 μ m diameter)**
- **?Aerosols: <5 μ m particles that remain in the air over time and distance**
- **Infected surfaces**
- **Virus found in stool, blood, semen and ocular secretions; role in transmission unknown**
- **Animals (including domesticated) not major source of human infection**



Prevalence of Asymptomatic SARS-CoV-2 Infection

A Narrative Review

DP Oran and EJ Topol

- Data from 16 cohorts, total n= 45,000+
- Asymptomatic persons account for ~40-45% of SARS-CoV-2 infections

Asymptomatic Transmission of SARS-CoV-2



Presumed Asymptomatic Carrier Transmission of COVID-19

Y Bai, M Wang et al.

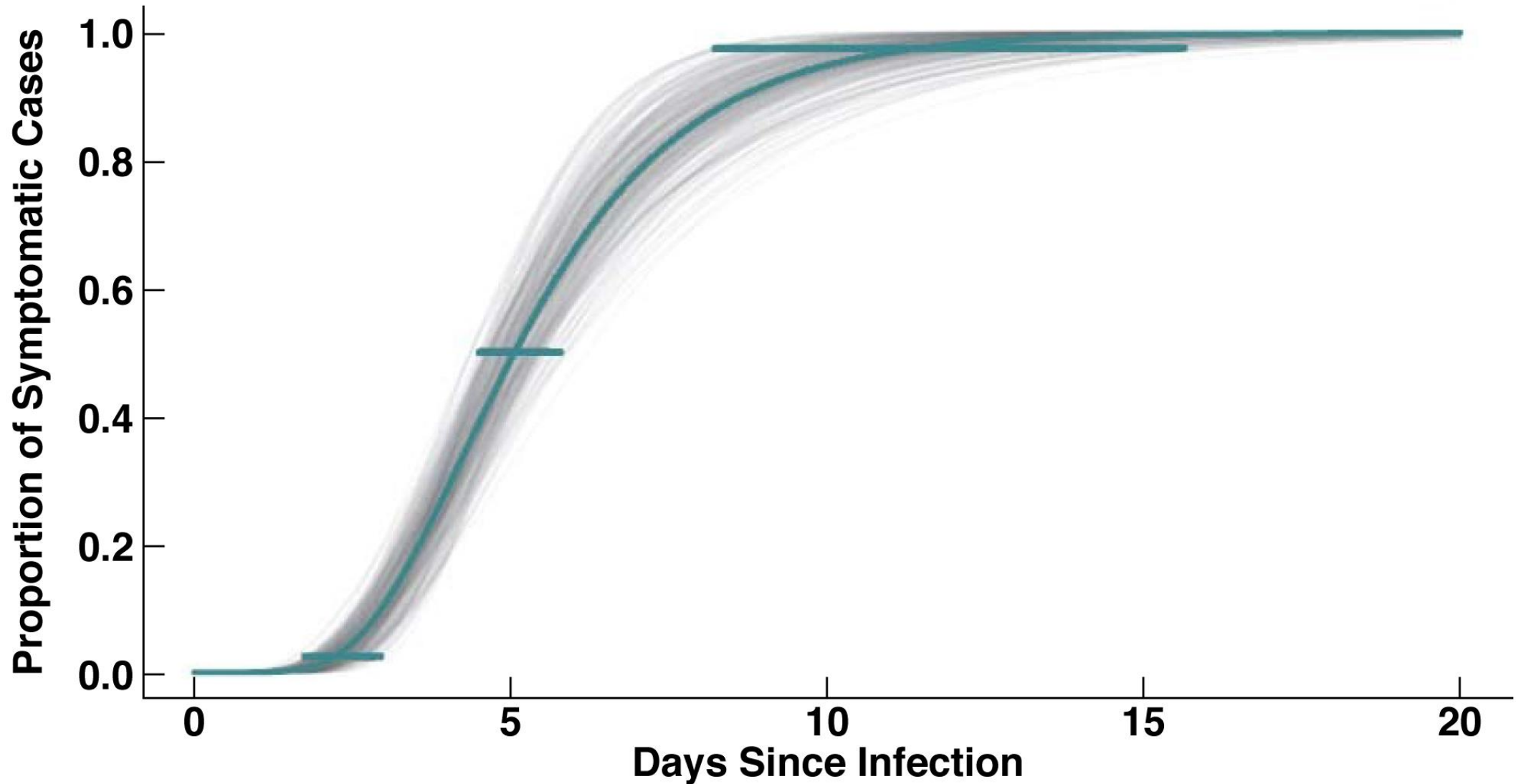


A Familial Cluster of Infection Associated With the 2019 Novel Coronavirus Indicating Possible Person-to-Person Transmission During the Incubation Period

P Yu, Y Han et al.

Clinical Manifestations

Median COVID-19 Incubation Period is 4-5 Days (Range: 2-14 Days)



Sources: CDC; Lauer, *Ann Intern Med* 2020; Xu, *BMJ* 2020; Guan *NEJM* 2020

COVID-19 Clinical Presentation

■ Fever	83–99%
■ Cough	59–82
■ Fatigue	44–70
■ Anorexia	40–84
■ Shortness of breath	31–40
■ Myalgias	11–35

Other non-specific symptoms reported

- Sore throat, nasal congestion, headache, diarrhea, nausea, vomiting. Loss of smell/taste preceding the onset of respiratory symptoms.

COVID-19: Wide Spectrum of Disease

Asymptomatic Illness No symptoms

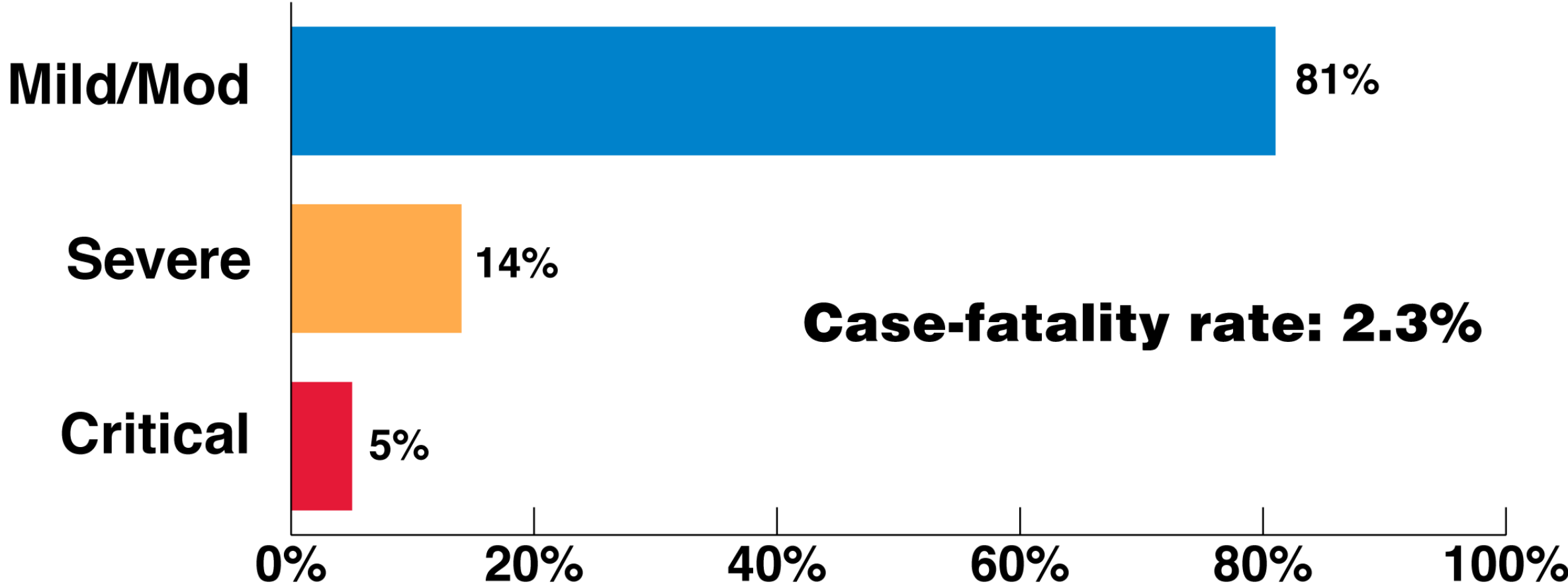
Mild Illness Uncomplicated upper respiratory tract infection

Moderate Disease Pneumonia without the need for supplemental oxygen

Severe Pneumonia Pneumonia plus one of the following: respiratory rate > 30 breaths/min; severe respiratory distress; or SpO₂ $< 90\%$ on room air

Critical Illness ARDS, sepsis, septic shock, multiple organ dysfunction/failure

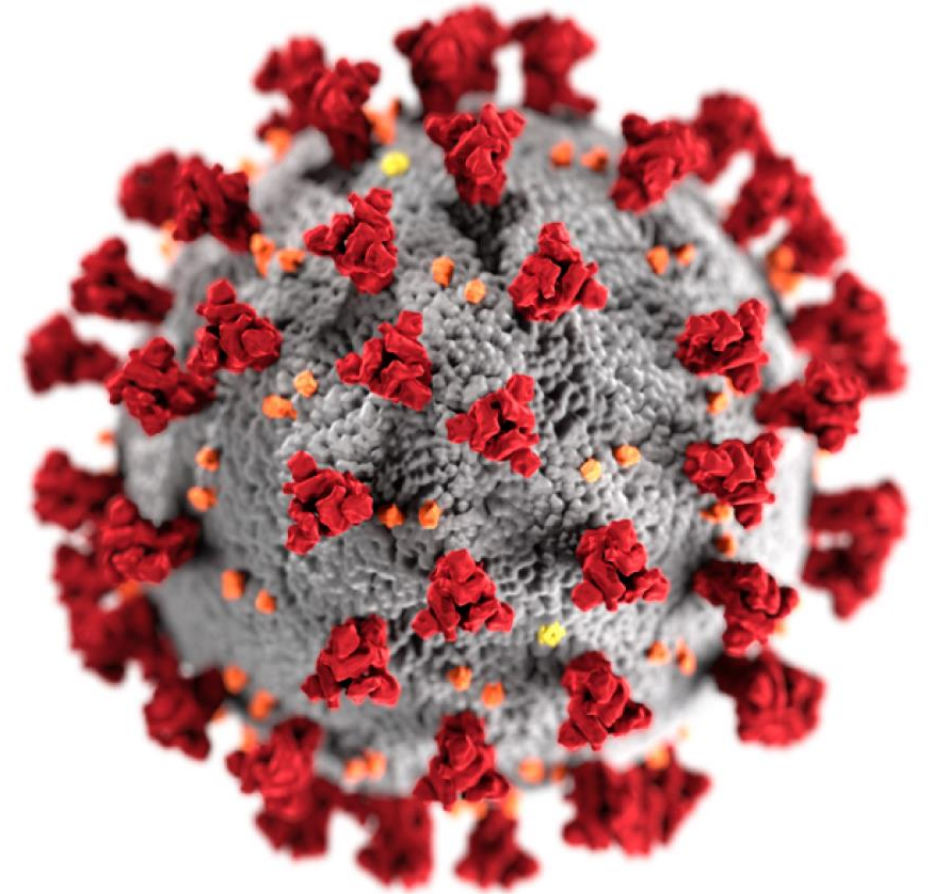
Spectrum of Disease Among 44,672 Individuals with Confirmed COVID-19, China



Source: Z Wu & JM McGoogan, *JAMA* 323:1239, 2020.

People at Increased Risk for Severe COVID-19 Illness

- Older adults
- People of any age with certain underlying medical conditions



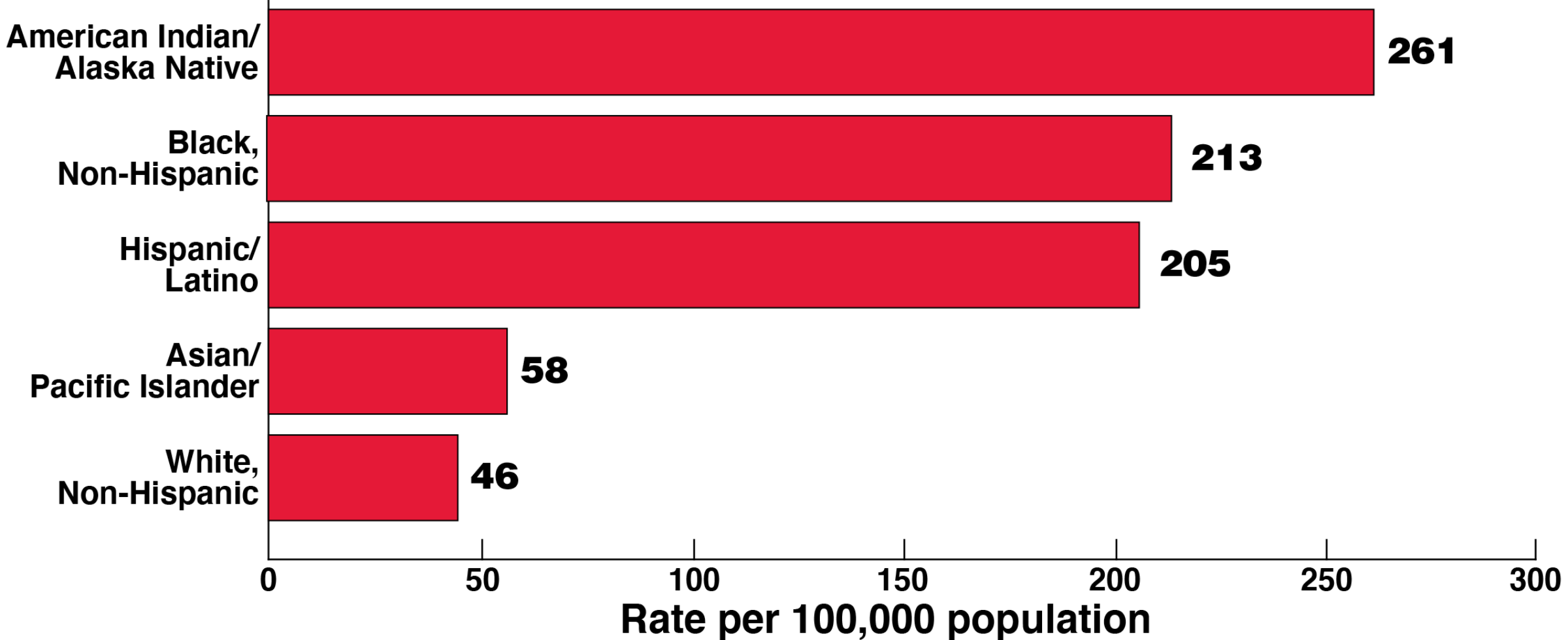
Underlying Medical Conditions Strongly Associated with Increased Risk for Severe COVID-19 Illness

- **Chronic kidney disease**
- **Chronic Obstructive Pulmonary Disease (COPD)**
- **Immunocompromised state from solid organ transplant**
- **Obesity (BMI \geq 30)**
- **Serious heart conditions (e.g. heart failure, coronary artery disease, cardiomyopathies)**
- **Sickle cell disease**
- **Type 2 diabetes mellitus**

Underlying Medical Conditions That May Confer Increased Risk for Severe COVID-19 Illness

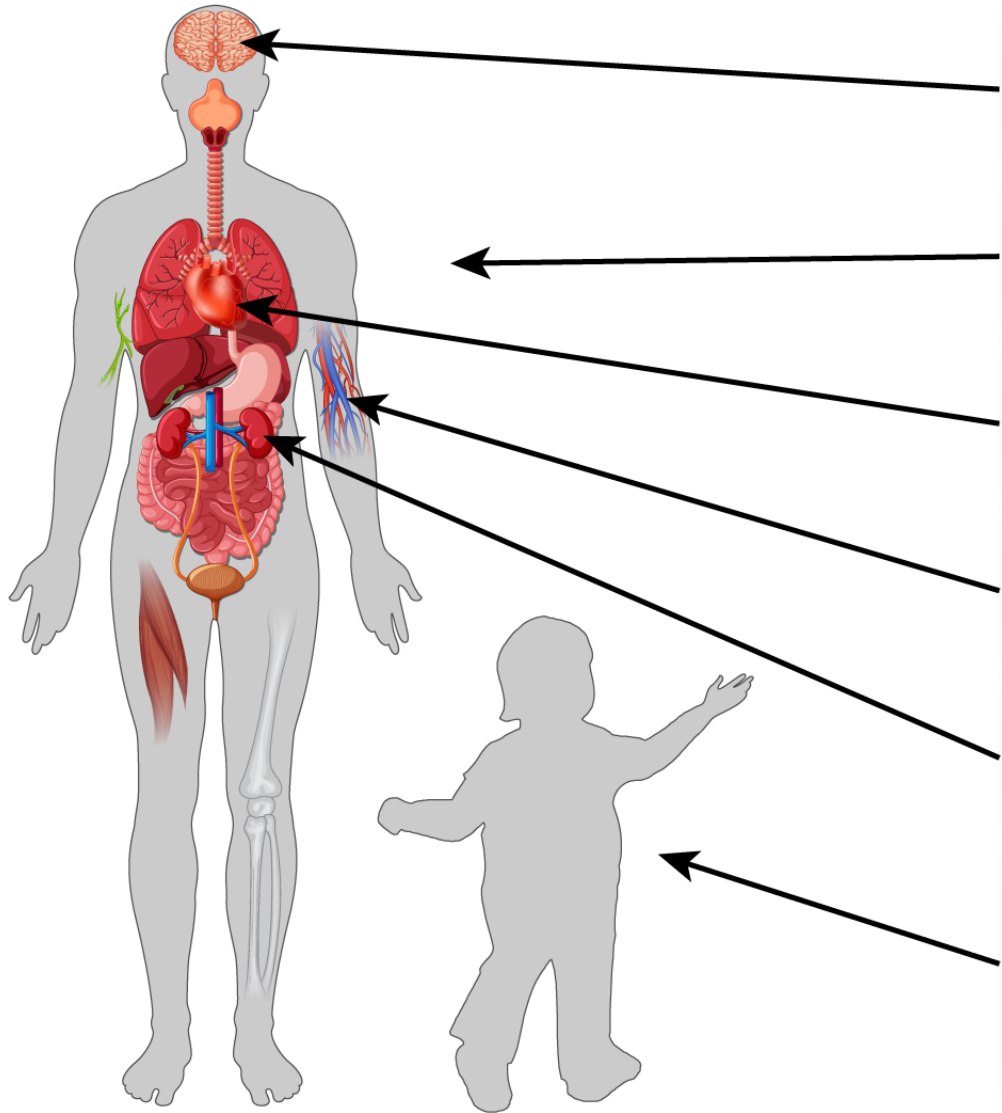
- **Asthma**
- **Cerebrovascular disease**
- **Hypertension**
- **Pregnancy**
- **Smoking**
- **Use of corticosteroids or other immunosuppressive medications**
- **Bone marrow transplantation**
- **HIV**
- **Immune deficiencies**
- **Inherited metabolic disorders**
- **Neurologic conditions**
- **Other chronic lung diseases**
- **Liver disease**
- **Type 1 diabetes mellitus**
- **Thalassemia**

Age-Adjusted COVID-19-Associated Hospitalization Rates by Race and Ethnicity, United States, March 1 – June 27, 2020



Source: CDC COVID-NET. Data from 14 states.

Numerous Non-Pulmonary Complications of COVID-19 Have Been Reported



Neurological disorders

Hyperinflammation

Cardiac dysfunction

Hypercoagulability

Acute kidney injury

Multisystem inflammatory syndrome in children (MIS-C)

Therapeutics

Investigational Therapeutics for COVID-19

- Remdesivir
- Other broad-spectrum antivirals
- Convalescent plasma/hyperimmune immunoglobulin
- Repurposed drugs, e.g. hydroxychloroquine, lopinavir/ritonavir
- Host modifiers/immune-based therapies
- Anti-SARS-CoV-2 monoclonal antibodies
- Others





The
New England
Journal of Medicine

Established in 1812 as THE NEW ENGLAND JOURNAL OF MEDICINE AND SURGERY

published online May 22, 2020

Remdesivir for the Treatment of Covid-19 – Preliminary Report

JH Beigel, HC Lane et al. for the ACTT-1 Study Group Members

- **Patients who received remdesivir had a 32% faster time to recovery than those who received placebo ($p < 0.001$)**
- **Results also suggested a survival benefit**
- **N=1,063 patients from 10 countries in U.S., Europe, Asia**

Effect of Dexamethasone in Hospitalized Patients with COVID-19: Preliminary Report

P Horby et al. and the RECOVERY Collaborative Group

- **RECOVERY trial in UK -- 6,425 patients randomized to receive dexamethasone 6 mg once per day (oral or IV) for up to ten days or usual care alone**
- **Dexamethasone reduced 28-day mortality by 35% in ventilated patients and by 20% in other patients receiving oxygen**
- **No benefit among those patients who did not require respiratory support**

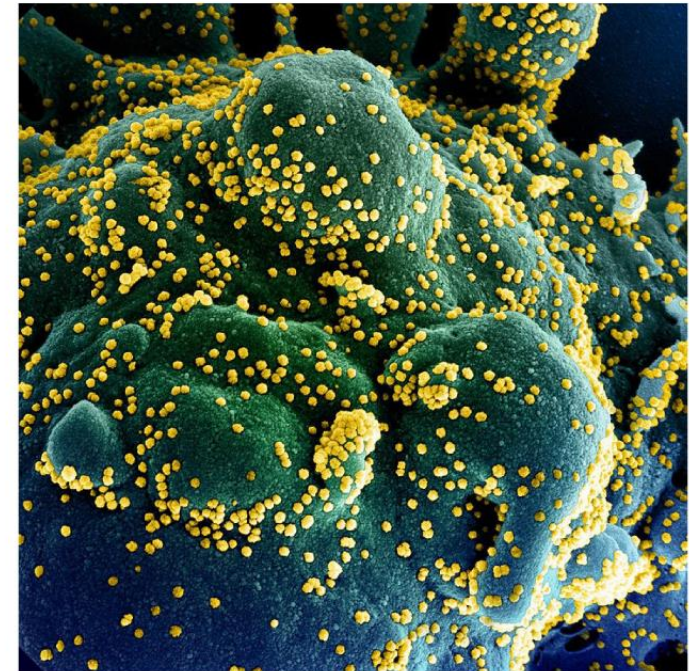


News Release

Expert U.S. Panel Develops NIH Treatment Guidelines for COVID-19

“Living document” expected to be updated often as new clinical data accrue

■ [Covid19treatmentguidelines.nih.gov](https://www.covid19treatmentguidelines.nih.gov)



Vaccines

Published online May 11, 2020








Science

A Strategic Approach to COVID-19 Vaccine R&D

L Corey, JR Mascola, AS Fauci & FS Collins

- **Unprecedented collaboration and resources will be required to research and develop safe and effective vaccines for COVID-19 that can be manufactured and delivered in the scale of billions of doses to people globally.**

Priority COVID-19 Vaccine Candidates

Platform	Developer	Phase 1/2
Nucleic acid		Completed
		Completed
Viral vector		Completed
		7/2020 start
		TBD
Protein subunit		Ongoing
		TBD