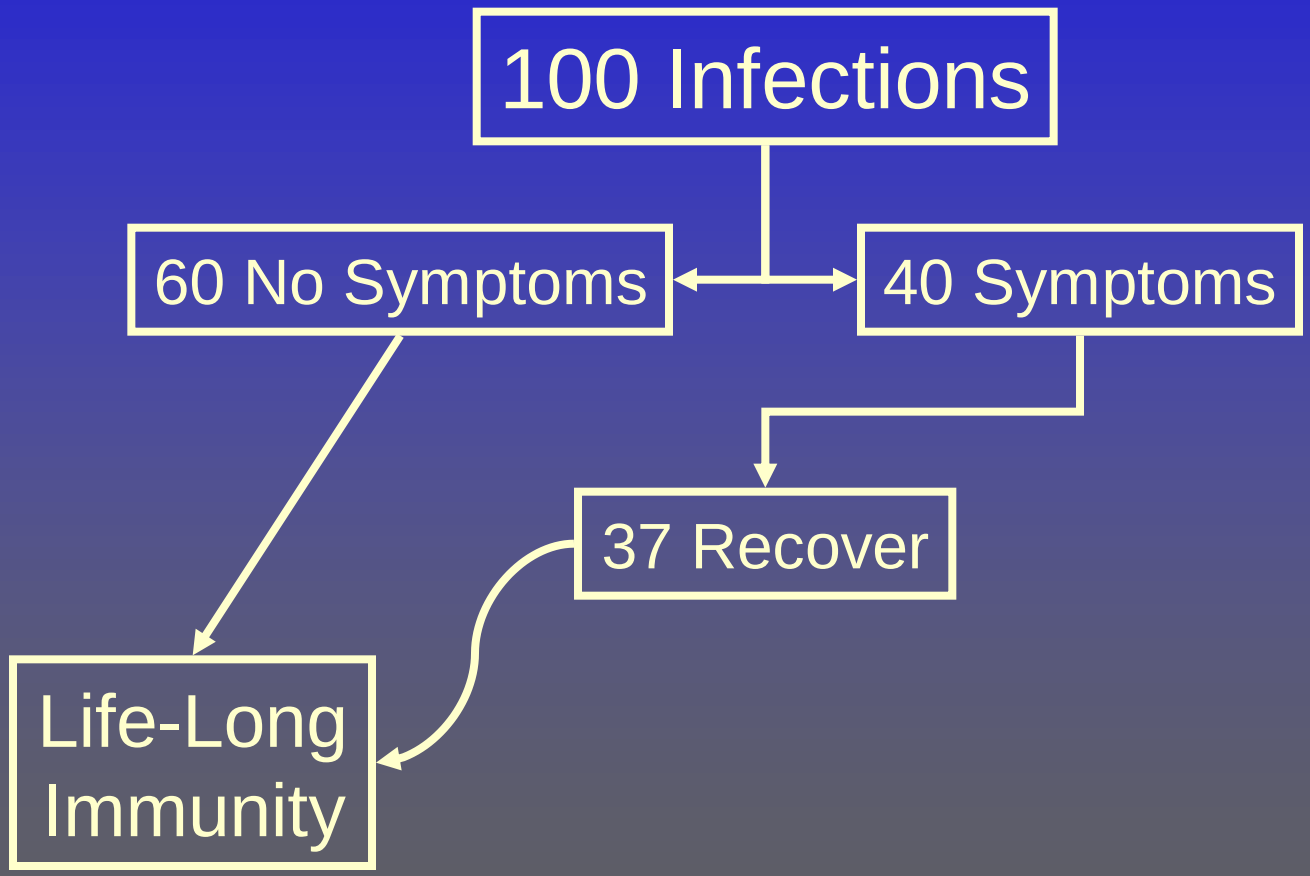
Precision Health in Valley Fever Does Ancestry Matter?

John N Galgiani MD
Valley Fever Center for Excellence
University of Arizona

Coccidioidomycosis Spectrum of Disease



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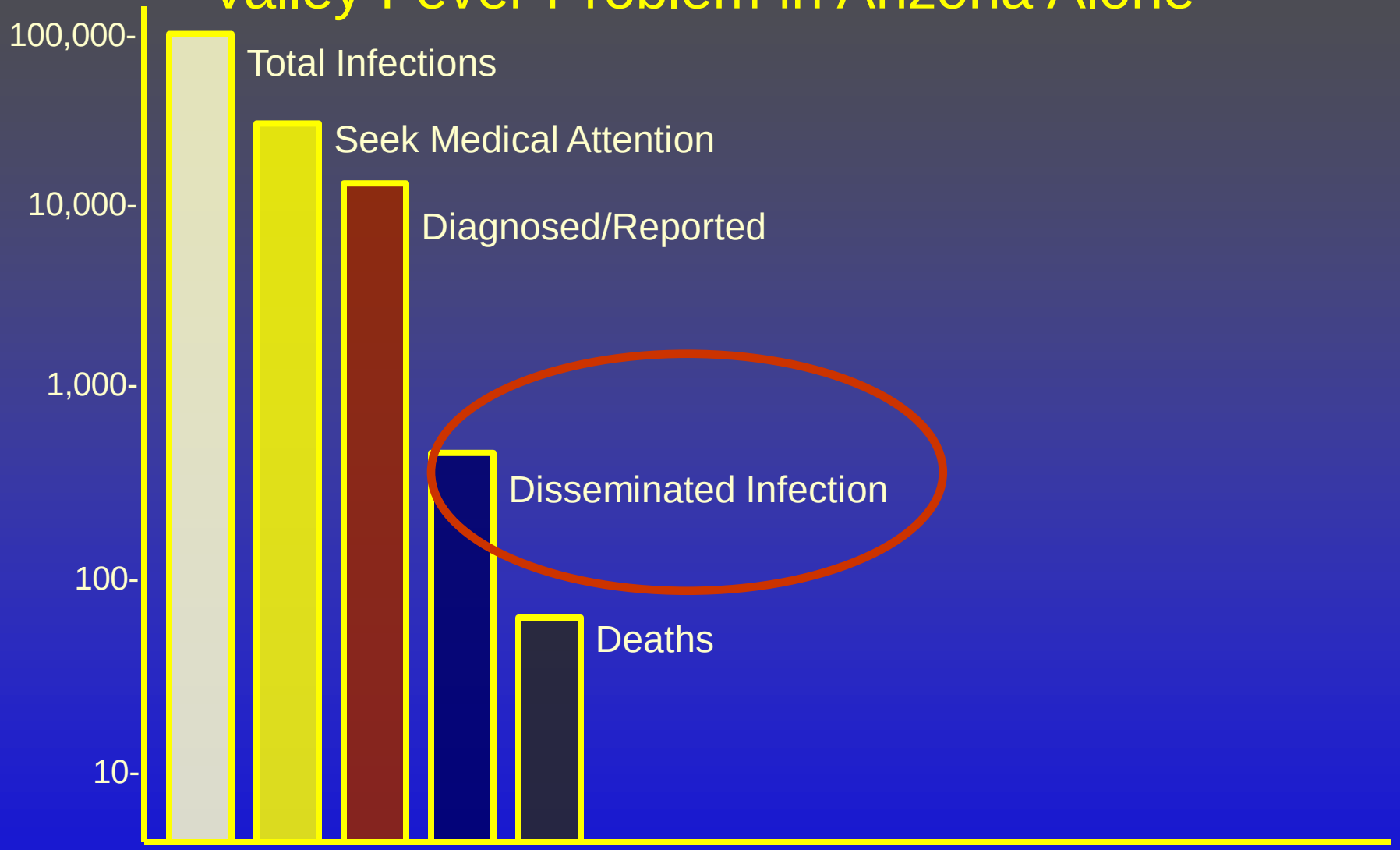
Valley Fever Problem in Arizona Alone



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Complications from Coccidioidomycosis

Pulmonary

- Diffuse acute pneumonia
  - ARDS
- Peripneumonic effusion
- Nodules
- Cavities
  - Hemoptysis
  - Rupture
- Chronic firbro-cavitary pneumonia

Disseminated Infection

- Skin
- Subcutaneous abscesses
- Arthritis
- Osteomyelitis
- Meningitis

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Possible Reasons for Complication in Valley Fever

- Infection from lots of fungal spores
  - Archeology dig exposures are hi-inoculum
  - more likely pneumonia but no more likely to have complications
- Some strains more virulent than others?
  - No evidence for this
- Some people are different from others
  - All evidence points to this

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Risk Factors for Coccidioidal Complications

Pulmonary

- Diabetes mellitus
- Cardio-pulmonary or other co-morbidities. (Evidence: “common sense”).

Disseminated Infection

- Deficient cellular immunity
- Males > Females
- Racial background
  - African-American
  - Filipino
- Adults > Children
- Pregnancy

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Coccidioidomycosis in Renal Transplantationn 1970-1979: 18/260 (6.9%)

	Kidney Recipients	Tucson Population
Incidence/yr	3%	1%
Dissemin.	75%	<1%
Mortality	65%	<1%

IM Cohen et al, 1982

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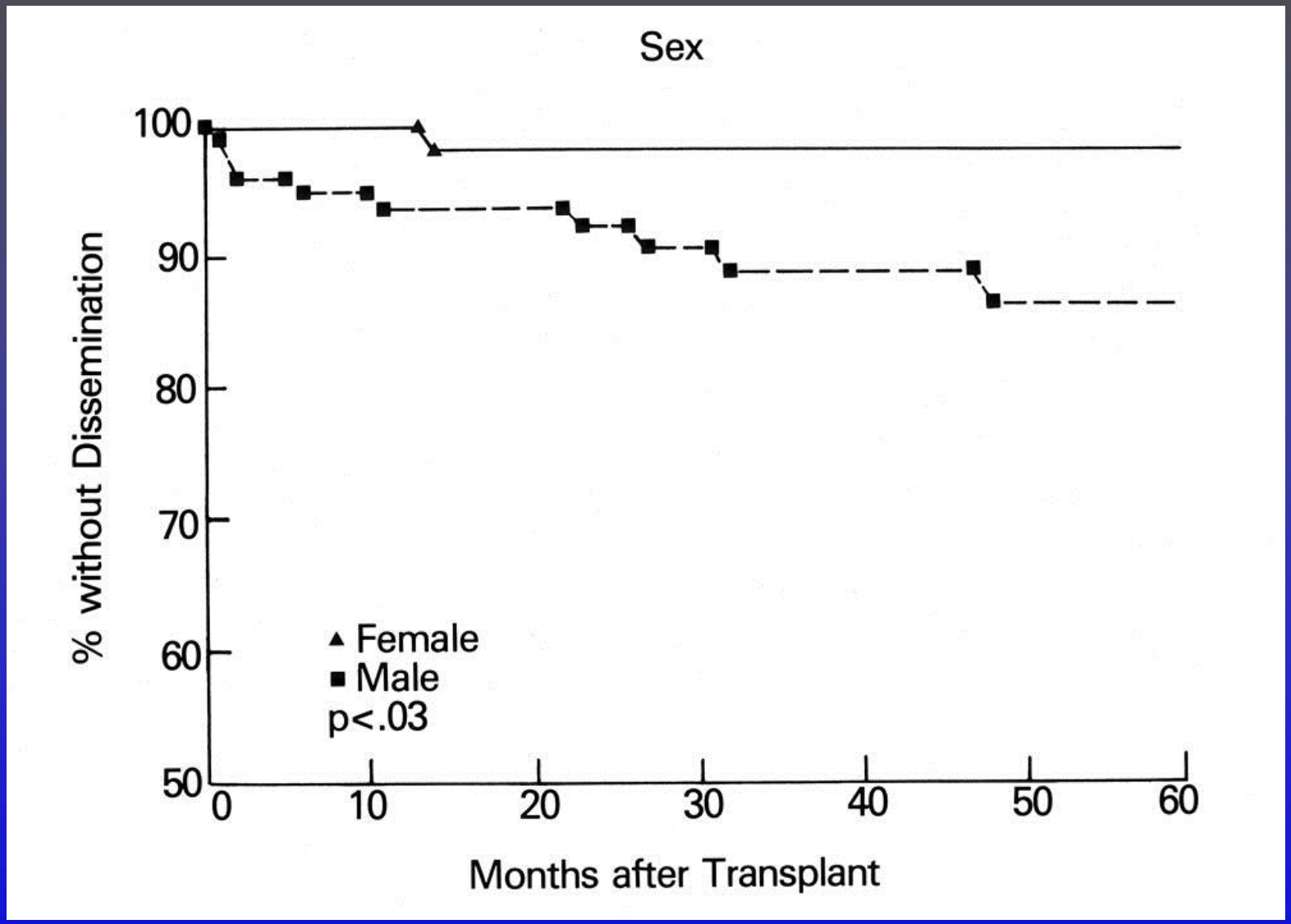

IM Cohen et al, 1982

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Mycoses Study Group Treatment of Disseminated VF

Publication Date	Antifungals Studied	% Male (n)
1988	Ketoconazole	76% (85)
1990	Itraconazole (Dissem.)	81% (21)
1993	Fluconazole (CNS)	82% (50)
2000	Fluconazole	73% (191)
2007	Posaconazole	65% (20)

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Impact of Disseminated Coccidioidomycosis in Arizona, 2007-2008

Coccidioidomycosis Study Group 55th Annual Meeting April 2, 2011

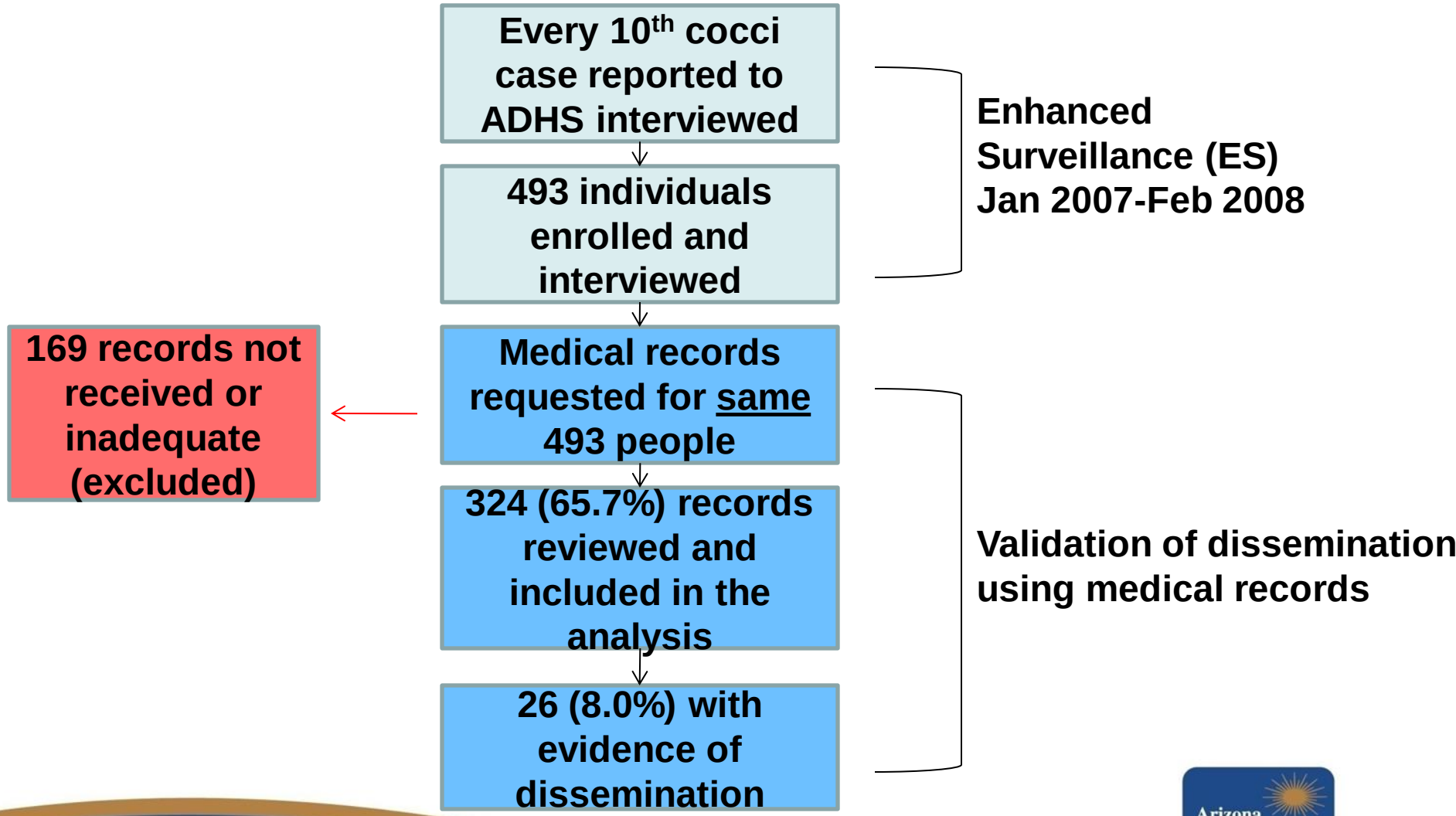
Foley CG, Tsang CA, Christ C, Anderson SM

CSTE Council of State and Territorial Epidemiologists

CDC

Arizona Department of Health Services

Overview of Methodology



Demographics

Characteristic	Disseminated 26 (8%)	Non-Disseminated 298 (92%)	p value
Mean Age	49.4 yrs	52.5 yrs	0.44
Male (n=167)	18 (11%)	149 (89%)	0.06
Female (n-157)	8 (5%)	149 (95%)	
White (n=257)	16 (6%)	241 (94%)	
Black (n=20)	5 (25%)	15 (75%)	0.02
Asian (n=12)	0 (0%)	12 (100%)	0.61
Native Am. (n=6)	1 (17%)	5 (83%)	0.40

Risk of disseminated Valley Fever in African-Americans as compared to Caucasians.			
Report	**Year**	**Study type**	**Fold increased risk**
Smith et al	1946	Retrospective	+14.0
Flynn et al	1979	Outbreak, retrosp.	+9.5
Pappagianis	1988	Outbreak, retrosp.	+9.1
Rosenstein et al	2001	Retrospective	+ 7.0
Crum et al	2004	Retrospective	+41.9
Drake et al	2009	Retrospective	+11.0
Foley et al	2011	Prospective	+4.0

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Relation of Race/Ethnicity and Genetics?

- Self-Identified Race/Ethnicity is just that:
  - Social/Cultural affinity and identification.
  - Genetically in the U.S. this is nearly always an **admixture** of various ancestries.
- Approximately 95% of the human genome DNA sequence is not related to any particular ancestral origin.
- However, the remaining 5% is.

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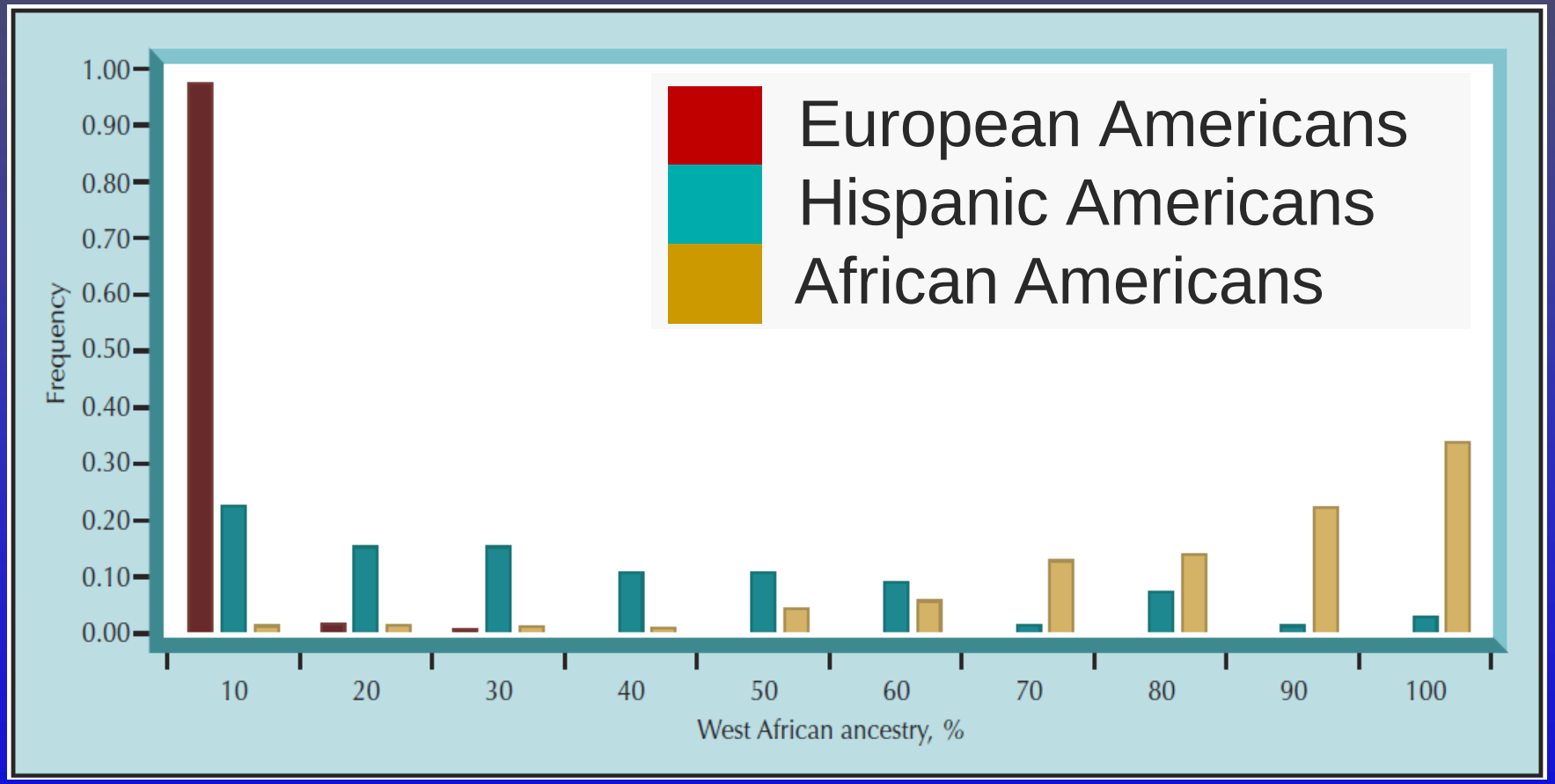
% of Genes of West African Ancestry In 3 Self-Identified U.S. Populations



Torres and Kittles, 2007

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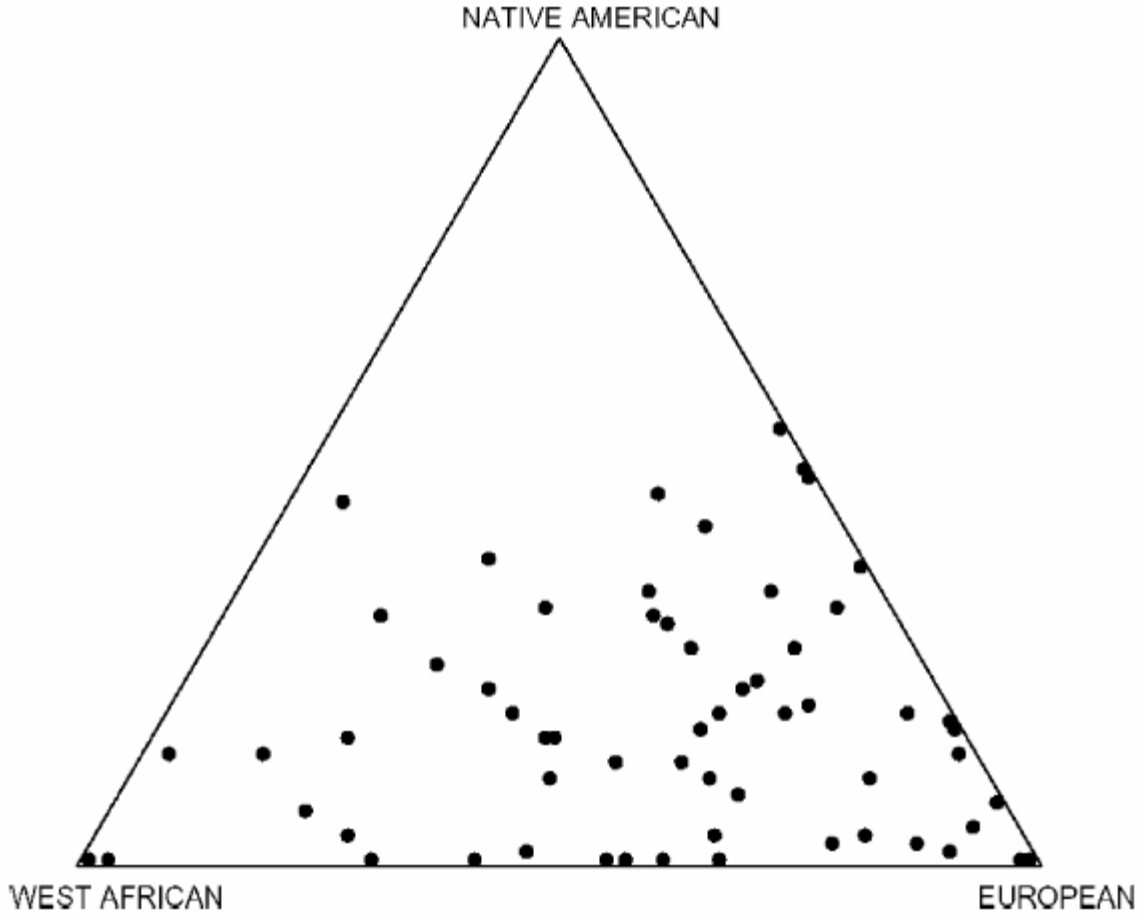

Fig. 1 Triangle plot showing the distribution of individual admixture estimates obtained by using a maximum likelihood approach in the population of Puerto Rico. Each of the three founder populations constitutes a *vertex* of the triangle. Each *circle* represents an individual and its position in the graph depends on the ancestry proportions of the subject

Bonilla et al, 2004

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Two Genetic Studies Now Open

NIH Study (Dr. S Holland)

- Any person with disseminated Valley Fever and normal immunity.
- UA is enrolling for this study; involves collecting a blood specimen.
- Some subjects could be seen at the NIH Clinical Center in Bethesda.

Valley Fever Center Study

- Any person self-identified as African American with normal immunity.
- Involves collecting saliva for DNA and optionally a blood specimen.
- All studies will be conducted in Arizona.

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Thank-you

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