The Hereditary Angioedema Center Experience in the United States

Marc Riedl MD MS
Professor of Medicine
Clinical Director – US HAEA Angioedema Center
University of California, San Diego

Creating a Comprehensive Treatment Plan for Hereditary Angioedema

Marc A. Riedl, MD, MS

Immunol Allergy Clin N Am 33 (2013) 471–485

- Evaluation/Diagnosis
- Optimization of Management Plans
- Collaboration with local MDs and specialists
- Dynamic over time

Box 1
Suggested steps in developing a comprehensive HAE treatment plan

Initial Evaluation of Confirmed HAE

- Assess current features of angioedema (frequency, severity, anatomic location, treatment, impact on activities/quality of life)
- Educate patient and family on HAE symptoms, triggers, prodromes, risks, genetics, screening
- Discuss treatment goals for patient
- Discuss required acute treatment plan, comparative medication options
- Discuss option of routine prophylaxis, comparative medication options
- Discuss benefits of early acute treatment
- Discuss unique risks of airway angioedema warranting medical evaluation
- Discuss indications for short-term prophylaxis (surgical, medical, or dental procedures)

Following Selection of Therapeutic Agent(s)

- Determine if candidate for self-administration based on patient and medication factors
- Determine site of treatment (self-administration vs home health provider vs medical facility)
- Provide patient-specific prescription and clinical documentation for processing/payor authorization
- Arrange self-administration training (in office or via home health) as applicable
- Determine plan for reporting use of medication: scheduled office visit, phone, e-communication, home health reports
- Determine plan for communication of treatment plan to local health care providers, integration of care as applicable
- Provide tools for navigating health system: written treatment plan, letter, USB drive, medical alert bracelet
- Provide resources for ongoing education

Periodic Follow-Up Evaluations

- Assess current features of angioedema (triggers, frequency, severity, anatomic location, treatment impact on activities/quality of life)
- Review medication use: frequency and efficacy
- Review medication adverse effects; safety laboratory tests if indicated (androgens: semiannual liver function tests, lipid profile, complete blood count, urinalysis, annual liver ultrasonography; plasma-derived C1INH: consider annual hepatitis B/C, human immunodeficiency virus testing)
- Discuss obstacles to treatment; identify reasons for untreated symptoms that interfered with activity
- Review interactions/communication with other health care providers; integration of care
- Review whether patient goals are achieved with current treatment plan
- Consider treatment adjustments if goals are not achieved (change acute medication or plan logistics, add/remove/titrate prophylactic therapy as clinically indicated)
- Ensure medication refills are provided
- Review benefits of early acute treatment
- Review unique risks of airway angioedema
- Review anticipated indications for short-term prophylaxis

Current medical management of hereditary angioedema: results from a large survey of US physicians

Marc Riedl, MD, MS*; Richard G. Gower, MD†; and Carole Alison Chrvala, PhD‡

Ann Allergy Immunol 2011

Original Article

Current Medical Management of Hereditary Angioedema: Follow-up Survey of US Physicians

Marc A. Riedl, MD, MS[a], Aleena Banerji, MD[b], and Richard Gower, MD[c] *La Jolla, Calif; Boston, Mass; and Spokane, Wash*

J Allergy Clin Immunol Prac 2015

- > 250 physicians treating HAE in U.S.
- ~85% Allergy/Immunology
- > 70% of U.S. patients managed by physician who had experience with <10 HAE patients
- Wide range of variable treatment patterns; inconsistency with consensus guidelines
- Only about 50% of first-degree relatives screened for C1INH-def

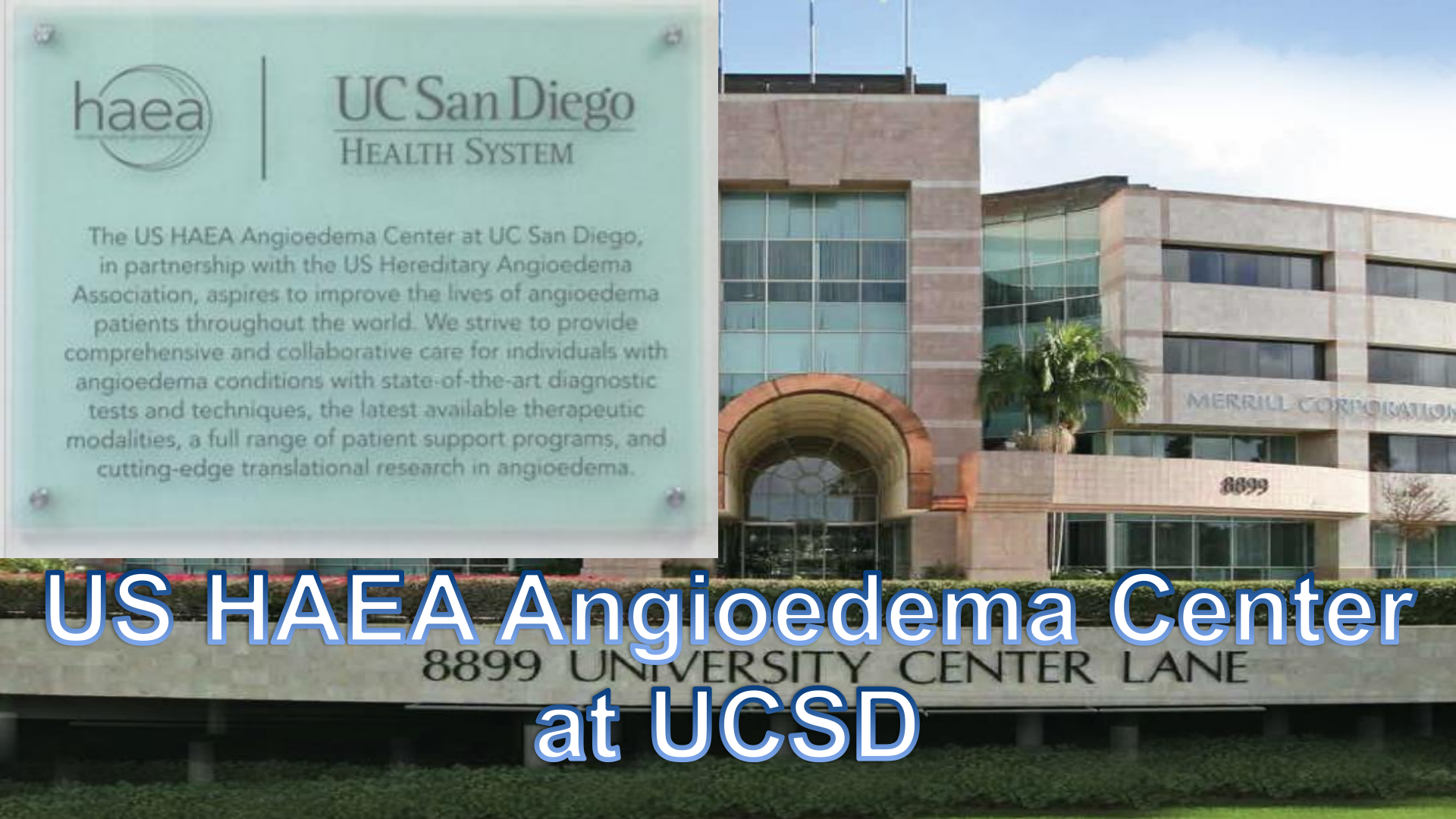
Benefits of HAE Expert Physician Involvement

US Hereditary Angioedema Association Medical Advisory Board 2013 Recommendations for the Management of Hereditary Angioedema Due to C1 Inhibitor Deficiency

Bruce L. Zuraw, MD[a,b], Aleena Banerji, MD[c], Jonathan A. Bernstein, MD[d], Paula J. Busse, MD[e], Sandra C. Christiansen, MD[a,f], Mark Davis-Lorton, MD[g], Michael M. Frank, MD[h], Henry H. Li, MD[i], William R. Lumry, MD[j], and Marc Riedl, MD[k] *La Jolla, San Diego, and Los Angeles, Calif; Boston, Mass; Cincinnati, Ohio; New York and Mineola, NY; Durham, NC; Chevy Chase, Md; and Dallas, Tex*

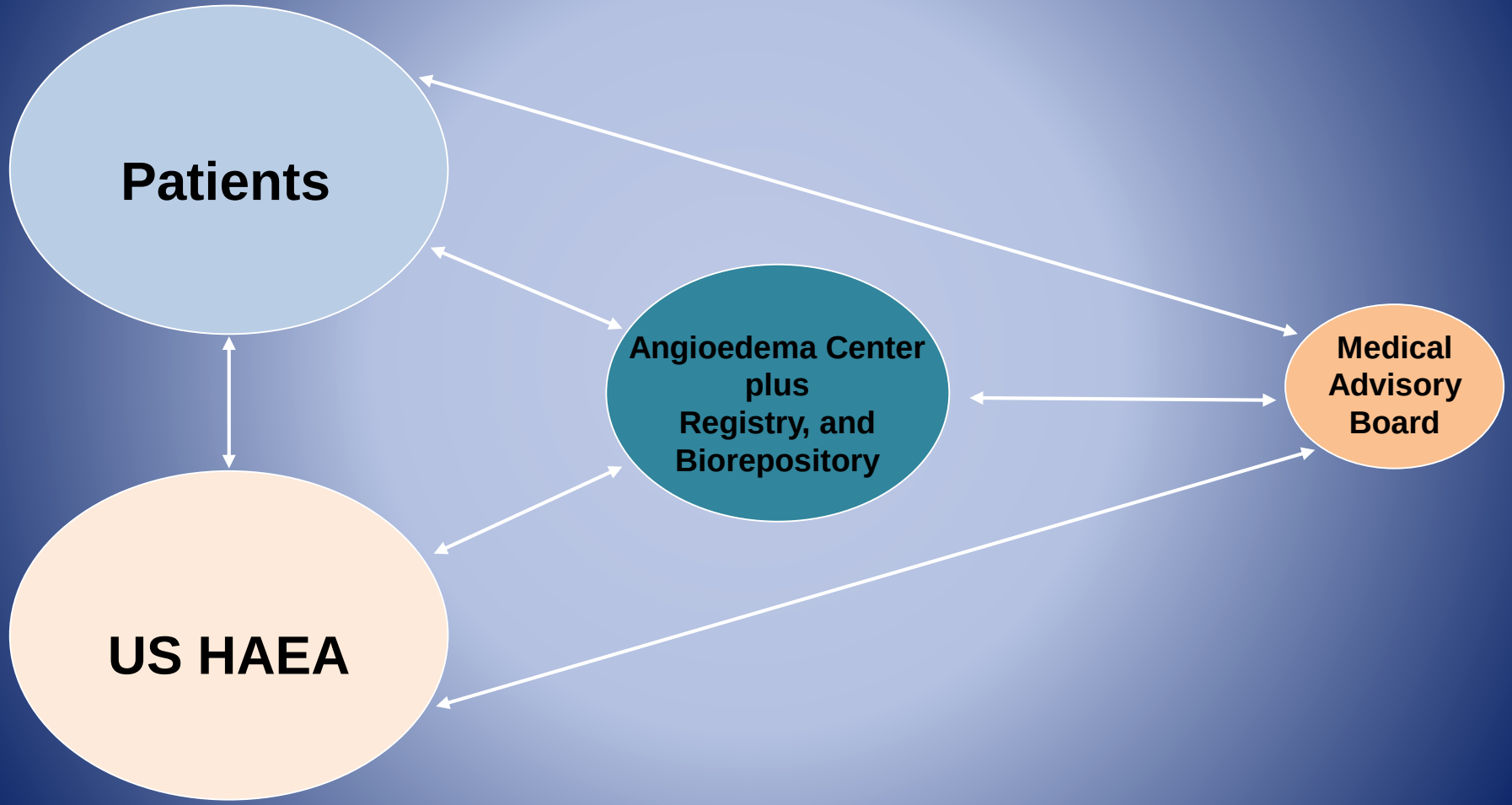
J Allergy Clin Immunol Prac 2013

- National referral centers or networks
- Collaborative care with local physicians
- Optimal patient education regarding condition and treatment options
- Iterative process to adjust/adapt treatment plan over time



US HAEA Angioedema Center at UCSD

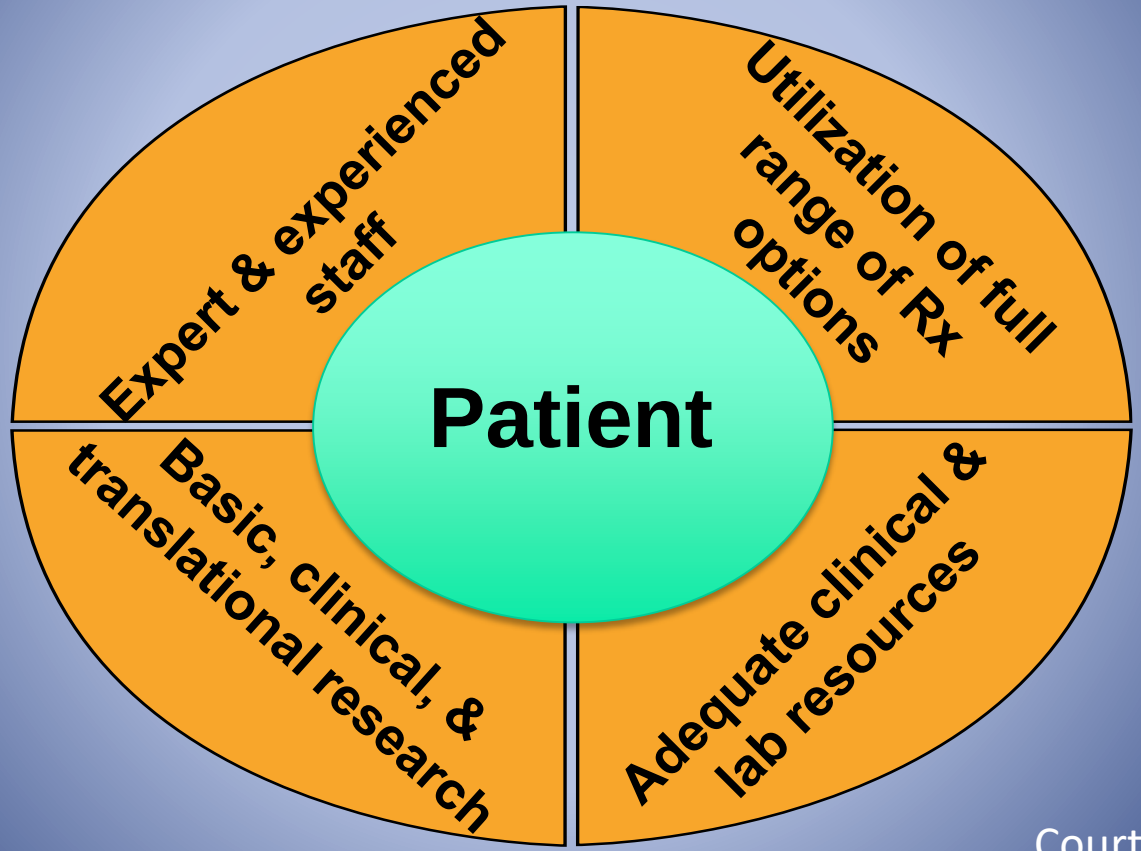
Angioedema Center: Where Does It Fit?



The US HAEA Angioedema Center: A Collaborative Effort

- Vision and impetus from Anthony Castaldo
- Negotiations with the University of California, San Diego
- Recruitment of Physicians
- Outreach to Donors
- Collaboration from Medical Advisory Board
- Building the Center
- Developing staff expertise
- Development of shared vision and mission for the future

The Angioedema Center Model



Courtesy of B. Zuraw

Clinical Operations: Designing the Patient Experience

- High-touch personal approach
  - Office design
  - Scheduling
  - Travel assistance/funding
  - Medical record collection
  - Physician Consultation
  - Nursing support
  - Prescription authorization
  - Implementation of management plan
  - Collaboration with local physicians
  - In-person/teleconference/remote follow-up

Patient Experience

- Staffing Model
  - UCSD
    - Nurse Navigator
    - Clinical Nurses
    - Administrator/Visit authorizations
    - Medical Assistant/Medication authorizations
    - Clinical Study Coordinator
  - US HAEA
    - Health Advocates
    - Patient Advocates

Patient-Centric Care

- Physician consultation – 90 minutes
- Nursing support – knowledgeable regarding condition, medications, self-administration
- Shared-decision making - discussion of all treatment options available to determine optimal individual management plan

Patient and Family Education

- US HAEA resources, development of educational modules
- Family testing
  - Angioedema Clinical Epidemiology Testing (ACET): 46 untested first-degree relatives of confirmed HAE-C1INHdef patients
  - 30% confirmed to have C1INH deficiency (Age range 2-60)
  - 64% of newly diagnosed relatives were symptomatic with a mean angioedema attack rate of 2.5 episodes/month

Ried MA, Allergy Asthma Proc, 2015

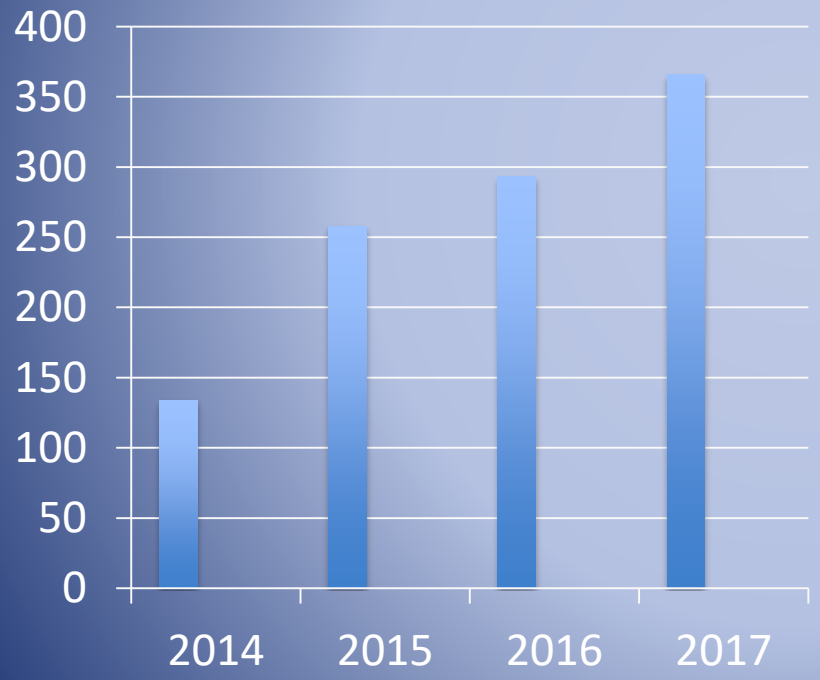
Individualized HAE Treatment Plan

Treatment of Attacks	Laryngeal Attacks	Additional Information
Effective emergency treatment should be given as soon as possible to arrest the attack. There are several effective therapies available, including: 1) C1-inhibitor concentrate by IV injection: -20 U/kg (Berinert), or -1000 U (Cinryze), or -50 U/kg (Ruconest) [max 4200 U] 2) Icatibant (subcutaneous inj) -30 mg in 3 ml (Firazyr) 3) Ecallantide (subcutaneous inj) -30 mg, 3x1ml (Kalbitor)	Because of the risk of asphyxiation during a laryngeal attack and because the effective medicines can take 30-60 minutes to begin to work, physicians should be prepared to emergently intubate the patient or perform a cricothyrotomy. Signs of impending airway obstruction include stridor, inability to swallow, and change in the voice. The airway may be significantly distorted and these procedures should be performed by an expert.	Online: www.haea.org Zuraw BL et al, US Hereditary Angioedema Association Medical Advisory Board 2013 recommendations for the management of hereditary angioedema due to C1 inhibitor deficiency. JACI In Practice 1:458, 2013. Moellman JJ, et al. A consensus parameter for the evaluation and management of angioedema in the emergency department. Acad Emerg Med. 21:469, 2014.

Personalization

Patient Care Statistics

- Over 700 patient evaluations for angioedema; ~200 HAE patients

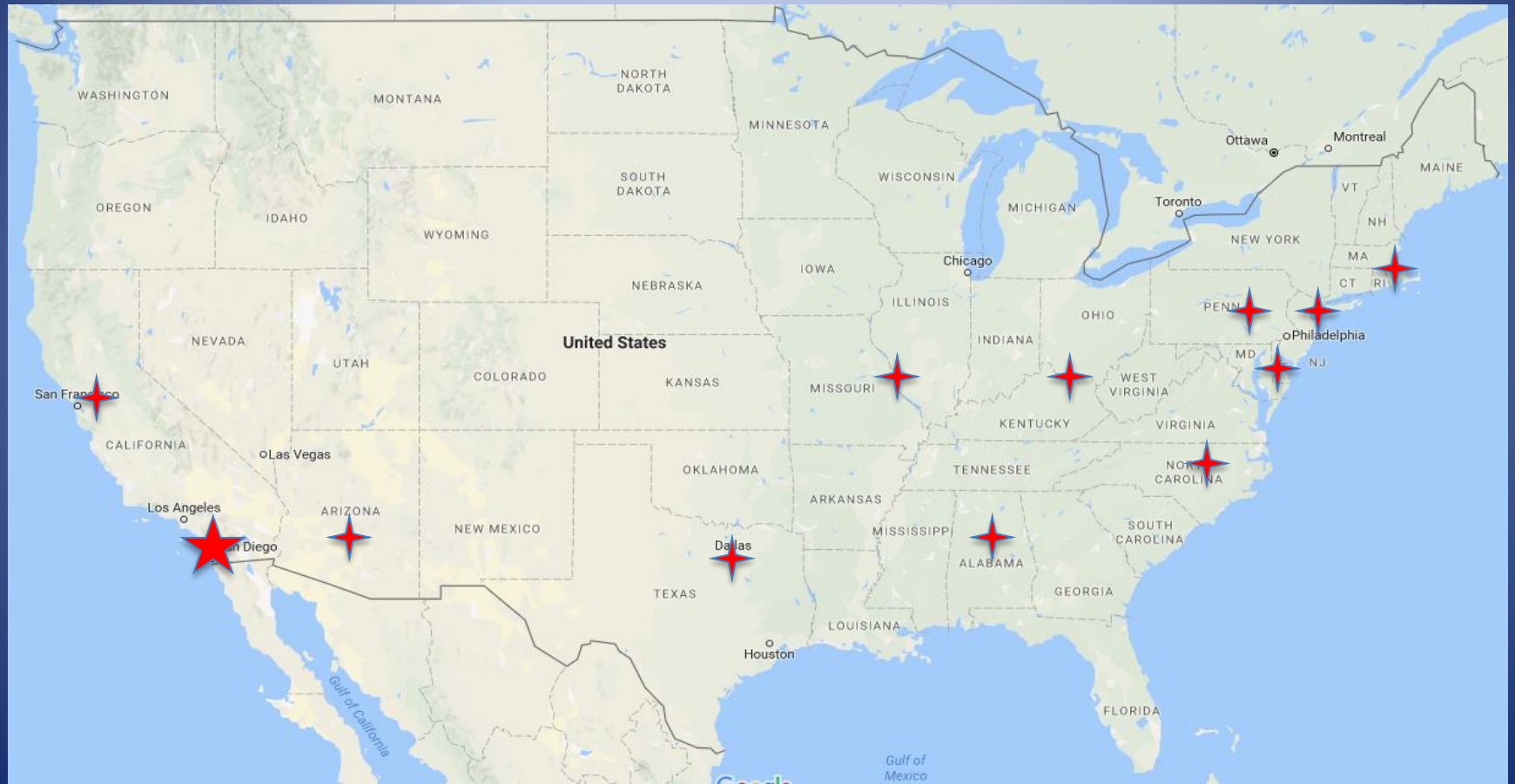


- 95% patients from United States: 35 states
- Patients from Canada, Mexico, Central America, South America, Asia, Africa

Research at the US HAEA Angioedema Center

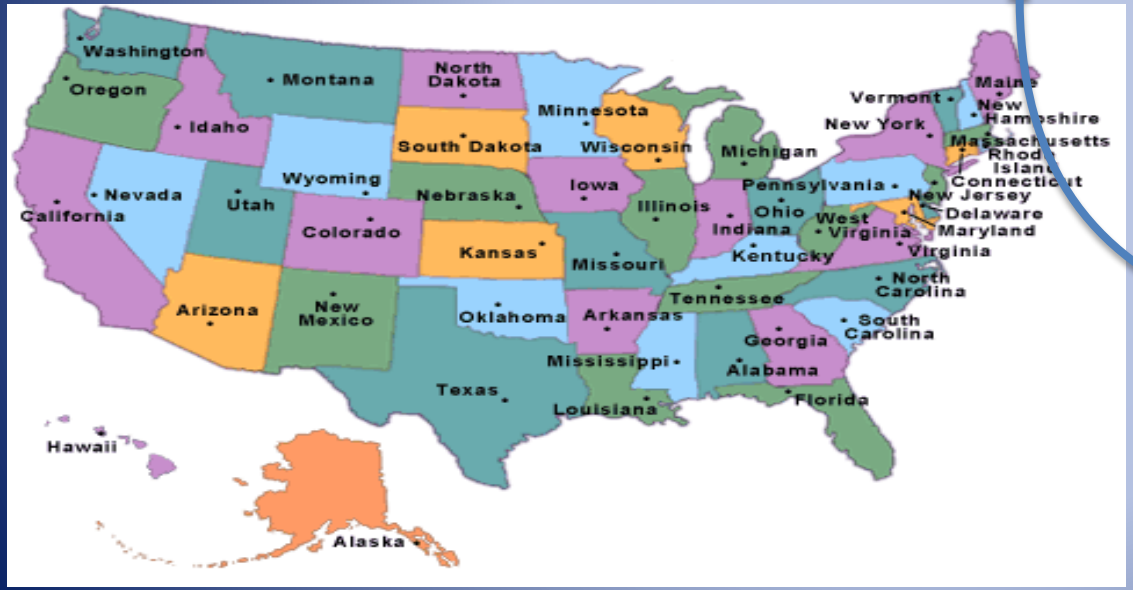
- Clinical studies of investigational drugs for HAE
- Translational and diagnostic studies
  - HAE with normal C1INH
- Patient focused projects
  - HAE and stress
  - HAE and diet
- Recently establishment of US HAEA Research Network for collaborative research efforts

US HAEA Research Network



Patient Registries to Study Rare Diseases

6,000 – 10,000 HAE I/II
??? HAEnlC1INh



Patients → Internet → HAE Registry ← Investigators

US HAEA Registry

- Established February 2005 with GeneLogic and Genetic Alliance
- 909 US HAEA members signed up
  - 801 are active enrollees
  - 3187 DNA samples
  - 821 serum samples, 647 Buccal samples
  - 538 Past medical history, 839 general medical, 1,436 Attack Event and 2,868 completed
  - May 2012: migrated to custom MySQL database
- October 2016: Centered at UCSD
  - Chromogenic assays and sequencing projects planned

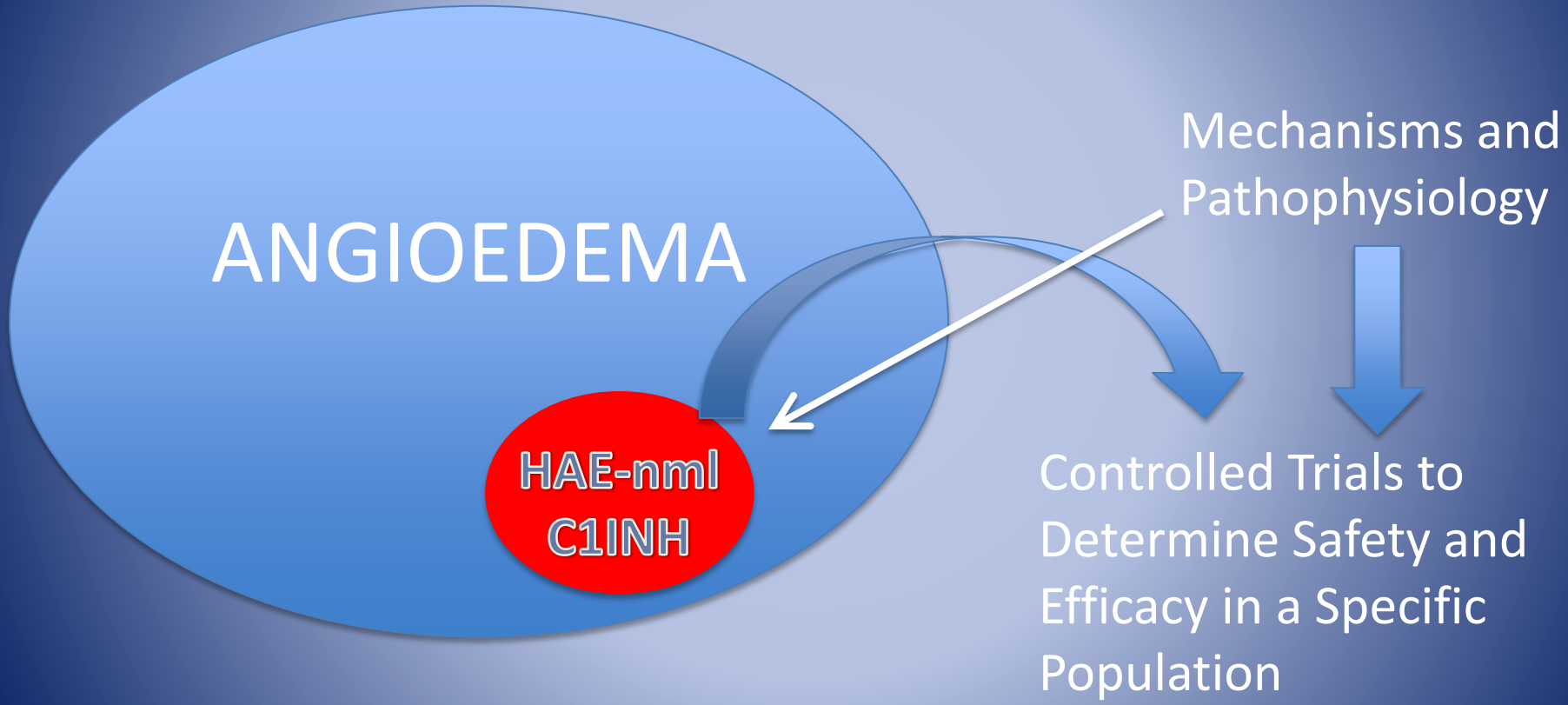
Hereditary Angioedema with Normal C1-INH (HAE Type III)

Hereditary angioedema with normal C1 inhibitor function: Consensus of an international expert panel

Bruce L. Zuraw, M.D.,[1,2] Konrad Bork, M.D.,[3] Karen E. Binkley, M.D.,[4] Aleena Banerji, M.D.,[5] Sandra C. Christiansen, M.D.,[1,6] Anthony Castaldo, M.P.A.,[7] Allen Kaplan, M.D.,[8] Marc Riedl, M.D.,[9] Charles Kirkpatrick, M.D.,[10] Markus Magerl, M.D.,[11] Christian Drouet, Ph.D.,[12] and Marco Cicardi, M.D.[13]

Allergy Asthma Proc 33:S145–S156, 2012

HAE Normal C1INH: Clinical Studies



Blood Drawing – The Key to Success

- Extensive interactions between staff and lab to develop optimized protocols for drawing research blood samples

Angioedema Sample Collection Face Sheet (revised 2/1/16)

Subject Code: _____ Date: _____ Time: _____ MD: _____

Dx: ☐ HAE-C1INH ☐ HAE-FXII ☐ HAE-U [probability: ☐ low ☐ medium ☐ high]
☐ ACE-I AE ☐ Histaminergic AE ☐ Other AE _____ ☐ Control

Currently swelling?: ☐ No ☐ Yes: Date/time of last swelling attack: _____

Samples obtained (check all that apply): ☐ Blood ☐ Urine ☐ Saliva

Meds: (C1INH, Firazyr, Kalbitor, TA, EACA, AH, androgen, progestin) **Date/time last received:**

_____ _____
_____ _____
_____ _____
_____ _____

Samples collected by: _____ Samples processed by: _____

Blood drawing order (please check off confirming that samples were obtained):

Order	Size	# Tubes	Type	Label Name (# of labels)	Centrifuge	Aliquot	Store	Obtained ☑ # Aliquots
1	10 ml	1	EDTA (Pink)	EDTA (6)	Yes	Yes	Liq Nit	☐ _____
2	4 ml	1	EDTA (Lavender)	DNA (4)	**NO**	**NO**	Refrig	☐ _____
3	2.7 ml	2	Citrate (Lt. Blue)	Citrate (3)	Yes	Yes	Liq Nit	☐ _____
4	2 ml	1	CTI (SCAT)	CTI (3)	Yes	Yes	Liq Nit	☐ _____
5	2.5 ml	1	Tempus	RNA (1)	**NO but shake**	**NO**	Refrig	☐ _____
Red Discard Tube								
6	4 ml	1	Heparin (Dk. Green)	Heparin (3)	Yes	Yes	Liq Nit	☐ _____
7	4 ml	1	Serum (Red)	Serum (1)	**NO**	**NO**	Refrig	☐ _____
8	10 ml	2-8*	EDTA (Pink)	Cells (8)	**NO**	**NO**	Refrig	☐ _____

* Check with lab personnel before drawing

Critical Efforts for Continued Progress

- **Scientific registries**
  - Response to therapies
  - Genetic investigations
  - Long-term safety data
- **Government and regulatory advocacy efforts**
  - Secure access and coverage of effective treatment
- **Research**
  - Development of diagnostic assays
  - Clinical Data on special populations: pediatrics, elderly, pregnancy
  - Developing next generation of HAE treatments
  - Quality of Life improvements
  - Pharmacoeconomics

Educational Efforts

- Clinical rotations for students, residents, fellows
- HAE CME Program to regional medical societies
- Peer-to-peer discussions
- Implementation of “Visiting Scholars” curriculum for physicians

Improving HAE Management

- Efficient and effective acute treatment of attacks for every patient
- Appropriate use of prophylactic treatment
- Minimizing treatment burden
- Maximizing patient activity and function

CLINICAL CARE

- Improved understanding of disease mechanisms (genetics, mediators, triggers): Scientific registries
- Improve diagnostic capabilities
- Studies to investigate new treatments for improved clinical outcomes

RESEARCH

- Offer comprehensive education for patients, families, health care providers

EDUCATION

Current state of hereditary angioedema management: A patient survey

Aleena Banerji, M.D.,[1] Paula Busse, M.D.,[2] Sandra C. Christiansen, M.D.,[3,4] Henry Li, M.D.,[5] William Lumry, M.D.,[6] Mark Davis-Lorton, M.D.,[7] Jonathan A. Bernstein, M.D.,[8] Michael Frank, M.D.,[9] Anthony Castaldo,[10] Janet F. Long,[10] Bruce L. Zuraw, M.D.,[3,11] and Marc Riedl, M.D., MS[3,11]

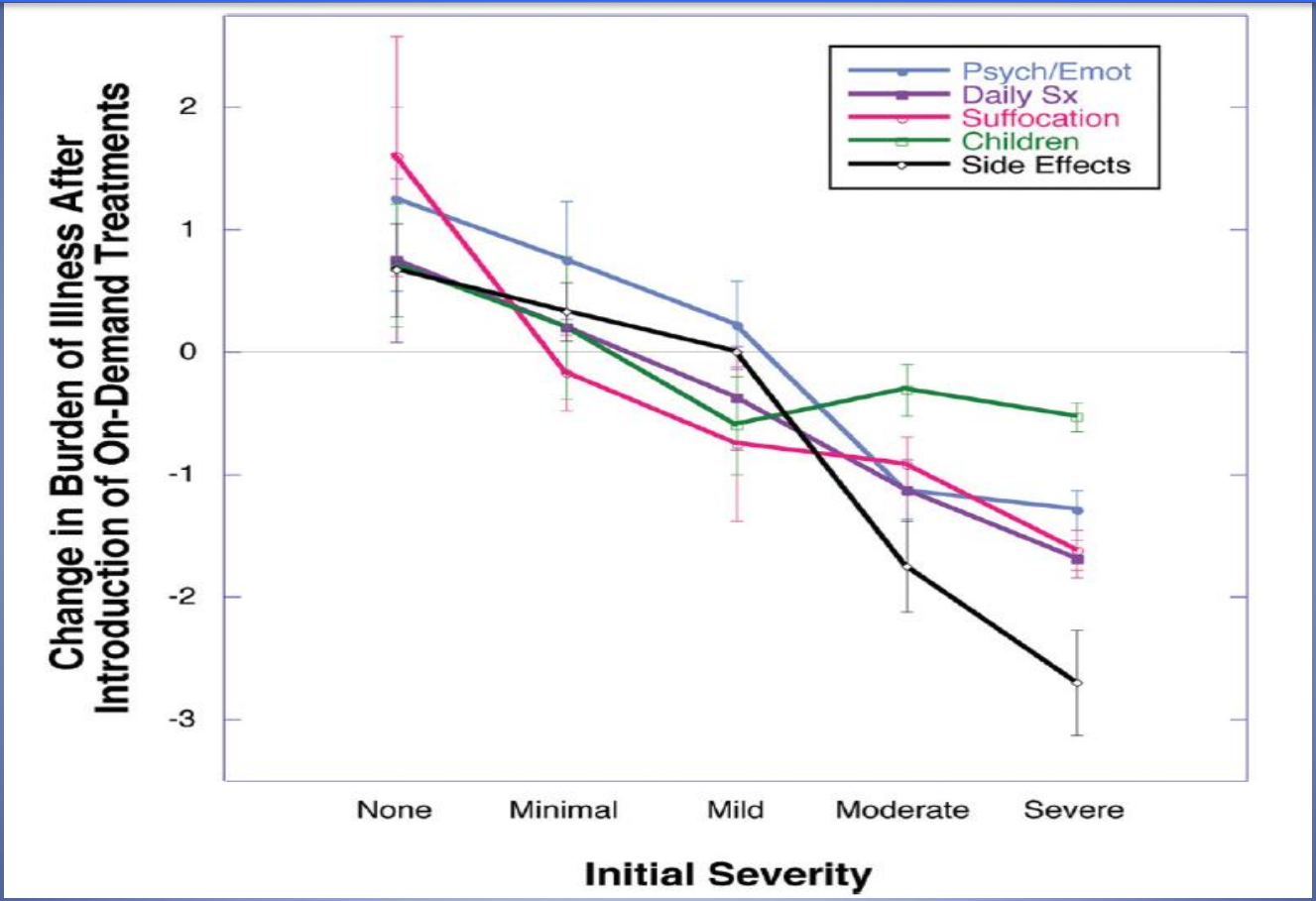
Allergy Asthma Proc 36:213–217, 2015

Before and after, the impact of available on-demand treatment for HAE

Authors: Christiansen, Sandra C.; Bygum, Anette; Banerji, Aleena; Busse, Paula; Li, Henry; Lumry, William; Davis-Lorton, Mark; Bernstein, Jonathan A.; Frank, Michael M.; Castaldo, Anthony; Long, Janet F.; Riedl, Marc; Zuraw, Bruce L.

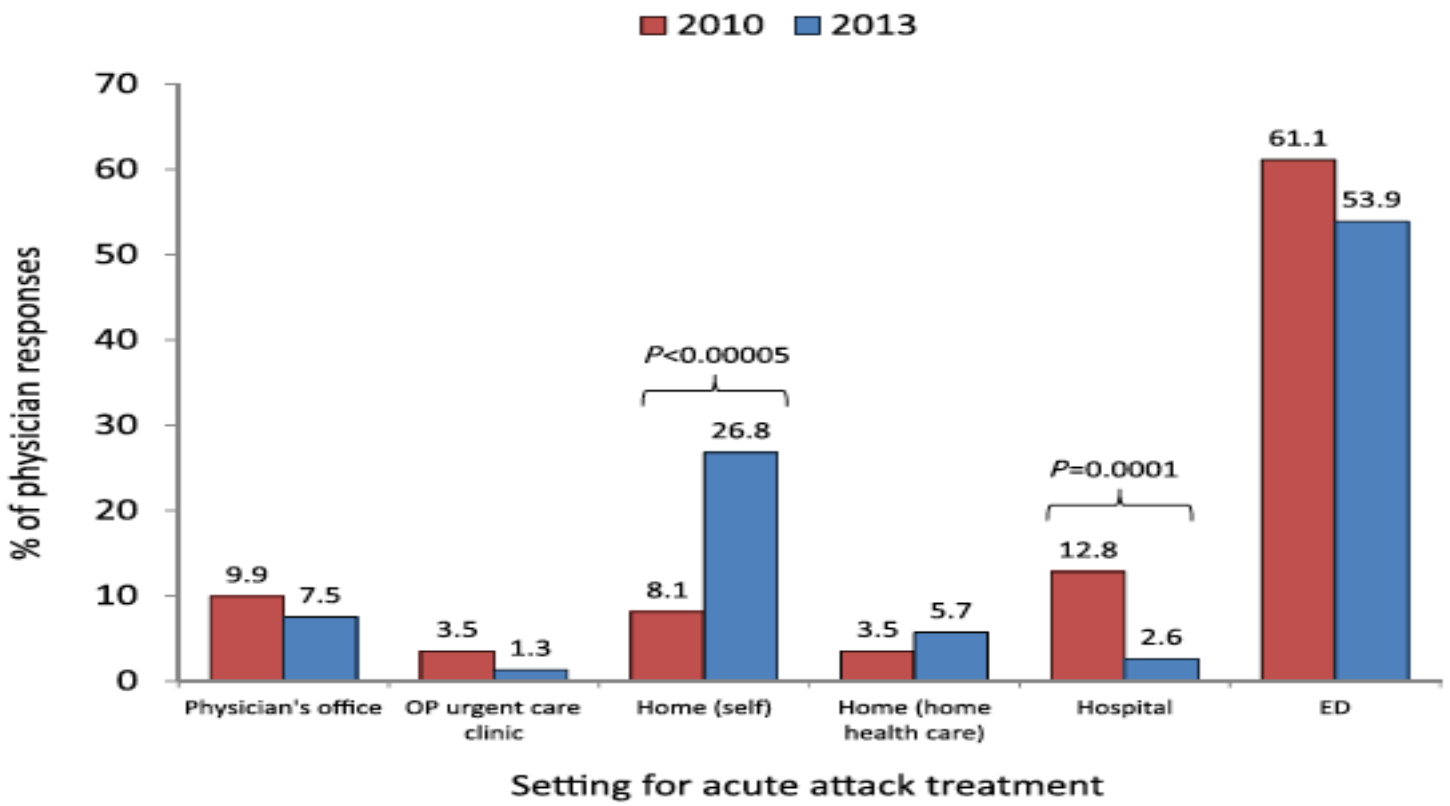
Source: Allergy and Asthma Proceedings, Volume 36, Number 2, March/April 2015, pp. 145-150(6)

Improved Patient-Reported Outcomes



Christiansen, Allergy Asthma Proc. 36:213, 2015

Effects of Improved HAE Care



ED=emergency department; OP = outpatient

Riedl MA, et al. JACI:IP. 2014.

Indications of Success

- Improved diagnostic accuracy
- Access to effective medication
- Rational use of HAE-specific drugs
- Increased self/home-administration; reduced hospital visits
- Increased referrals from payors
- High patient satisfaction scores
- Need for more rigorous outcome measures; cost-effectiveness, quality of life

Questions, Suggestions, Recommendations…..

THANK YOU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