# Protective Effects of Propranolol in Adults Following Severe Burn Injury: A Safety and Efficacy Trial

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HSPH Post-Bac Program
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# Agenda

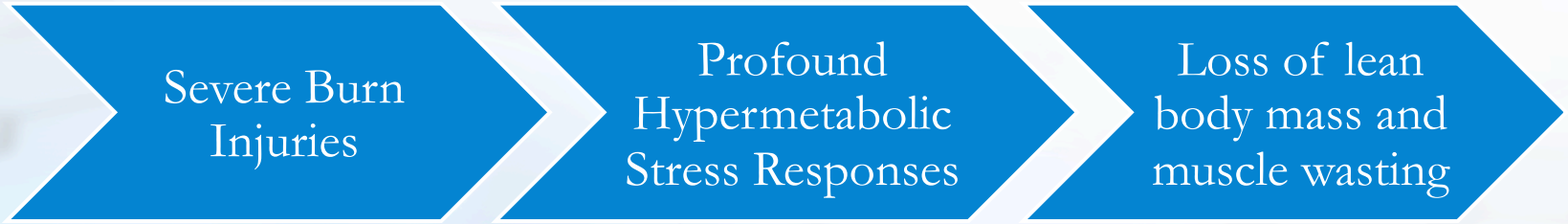
I. The Propranolol Study

II. Data Management

# Background

## I. Severe Burn Injuries

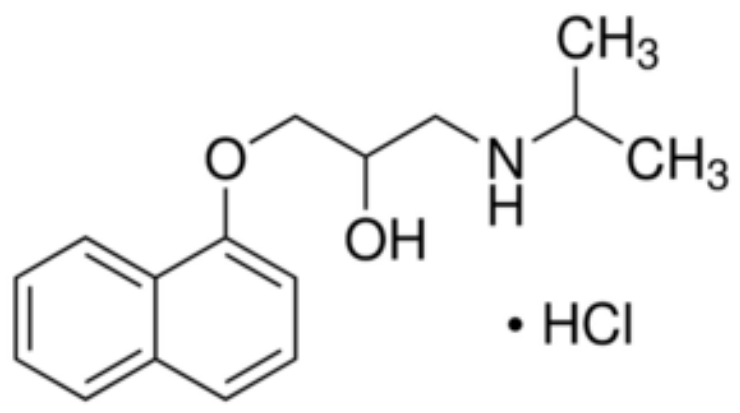
- Burn Injuries Receiving Medical Treatment[1]: 450,000




1. Sources: National Electric Injury Surveillance System-All Injury Project (NEISS-AIP); National Emergency Department Survey (HCUP-NEDS) (2010 Data); National Ambulatory Medical Care Survey.
2. Pruitt BA Jr.: Protection from excessive resuscitation: "pushing the pendulum back".J Trauma. 2000 Sep;49(3):567-8
3. Baxter CR. Guidelines for Fluid Resuscitation. J Trauma, 1981; 21:687-9.

# II. Propranolol

- A non-selective beta blocker
- To treat hypertension, anxiety, and panic



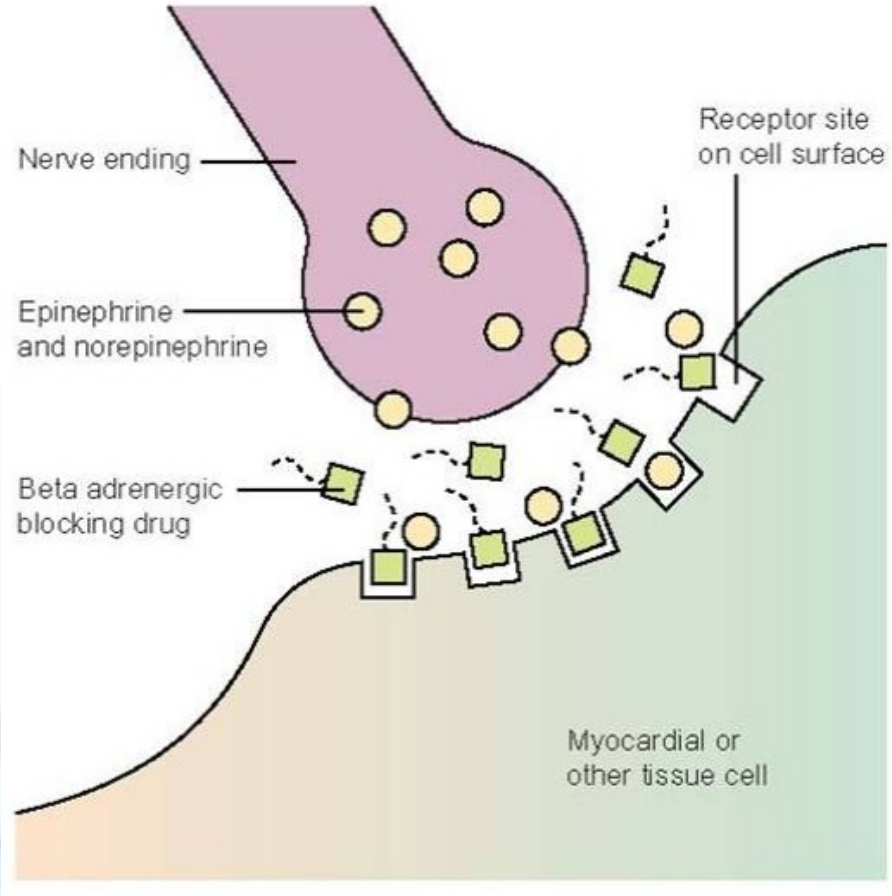




Figure left: http://www.sigmaaldrich.com/catalog/product/sigma/p0884?lang=en&region=US
Figure right: http://marianuniversitysciencеblog.wordpress.com/2010/10/15/beta-blockers-function-and-effects/

# III. Beneficial Effects of Propranolol


NCBI Resources How To

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Burns. 1989 Dec;15(6):376-80.

**Pulmonary embolism in burned children.**

Desai MH[1], Linares HA, Herndon DN.

Author information

Abstract

There are occasional reports in the literature concerning the incidence of pulmonary embolism in the postburn population, but reports of burned children are ... complicatio... review of al... embolism i... pulmonary ... calculated ... pulmonary ... immobile fo... pulmonary ...

PMID: 26246...


BURNS

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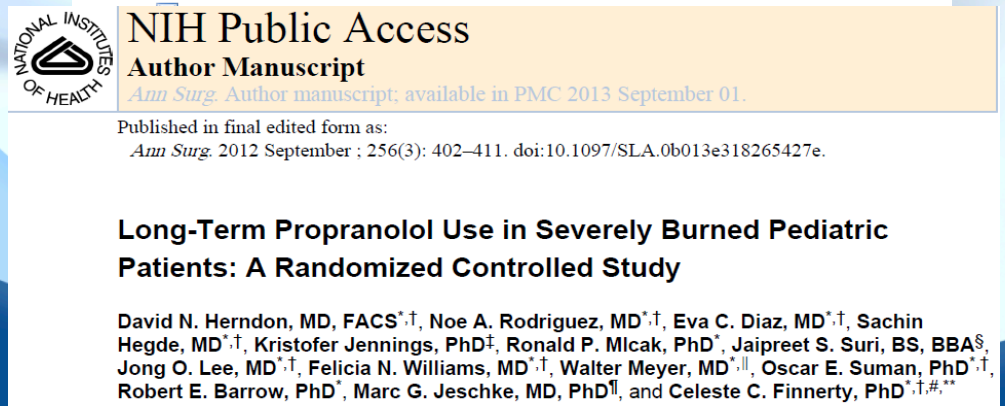
Burns
Volume 30, Issue 6 , Pages 591-593, September 2004

Analysis of deep vein thrombosis in burn patients


NIH Public Access
Author Manuscript
*Ann Surg*. Author manuscript; available in PMC 2013 September 01.

Published in final edited form as:
*Ann Surg*. 2012 September ; 256(3): 402–411. doi:10.1097/SLA.0b013e318265427e.

**Long-Term Propranolol Use in Severely Burned Pediatric Patients: A Randomized Controlled Study**

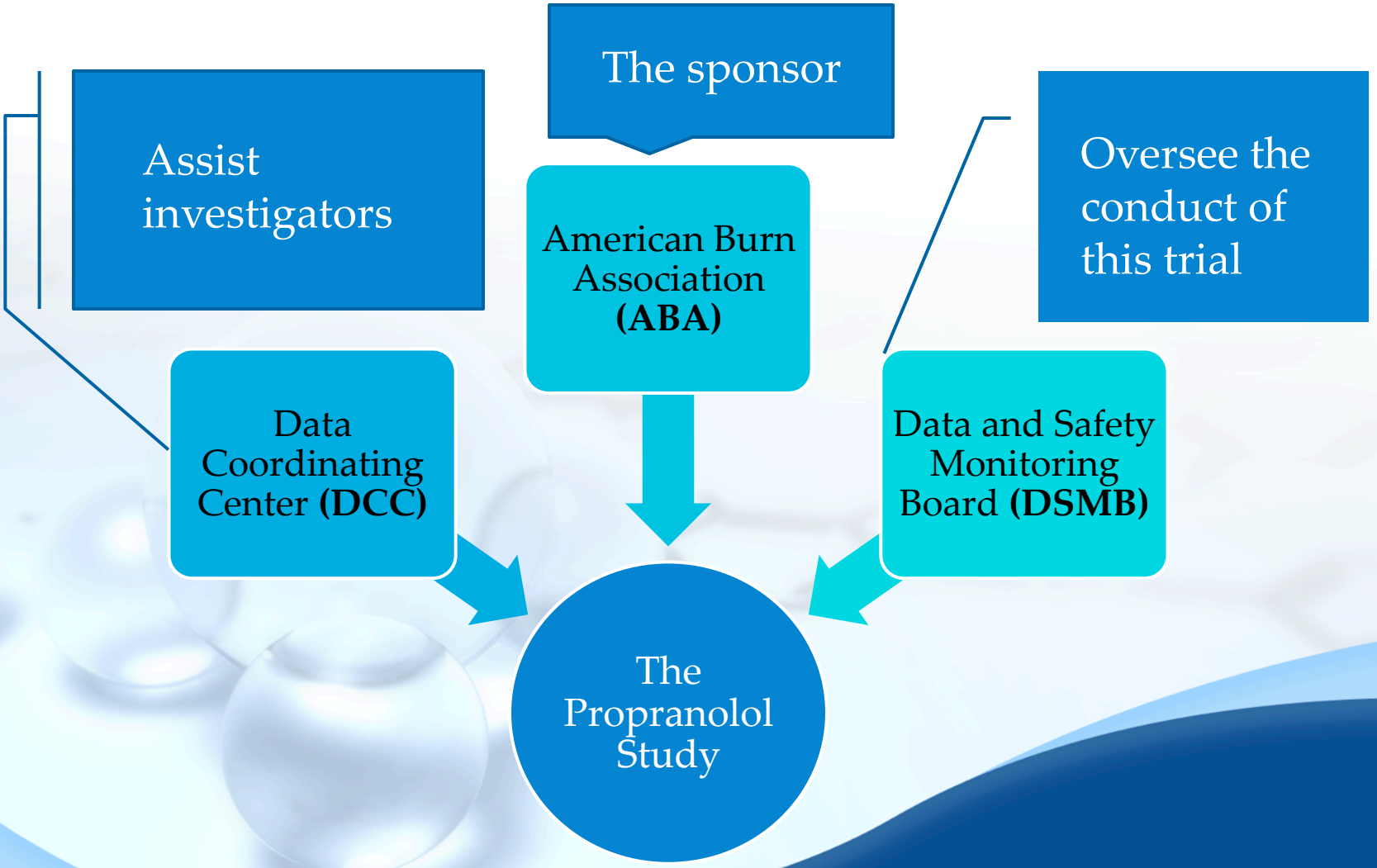
David N. Herndon, MD, FACS[*,†], Noe A. Rodriguez, MD[*,†], Eva C. Diaz, MD[*,†], Sachin Hegde, MD[*,†], Kristofer Jennings, PhD[‡], Ronald P. Mlcak, PhD[*], Jaipreet S. Suri, BS, BBA[§], Jong O. Lee, MD[*,†], Felicia N. Williams, MD[*,†], Walter Meyer, MD[*,‖], Oscar E. Suman, PhD[*,†], Robert E. Barrow, PhD[*], Marc G. Jeschke, MD, PhD[¶], and Celeste C. Finnerty, PhD[*,†,#,**]

In Children:

- Decrease infections
- Increase wound healing
- Improve cardiac work, hypermetabolism, and survival

IN ADULTS?

# The Role of Players



# The Study

**Aim:**

- To determine the safety and efficacy of propranolol relative to placebo in a cohort of severely burned adults

**Design:**

- A multi-center, phase 2a/b, investigator-initiated, randomized trial

**Population:**

- A group of 250 patients who are admitted to one of the participating burn centers within 72 hours of injury with a burn injury ≥ 20% total body surface area (TBSA)

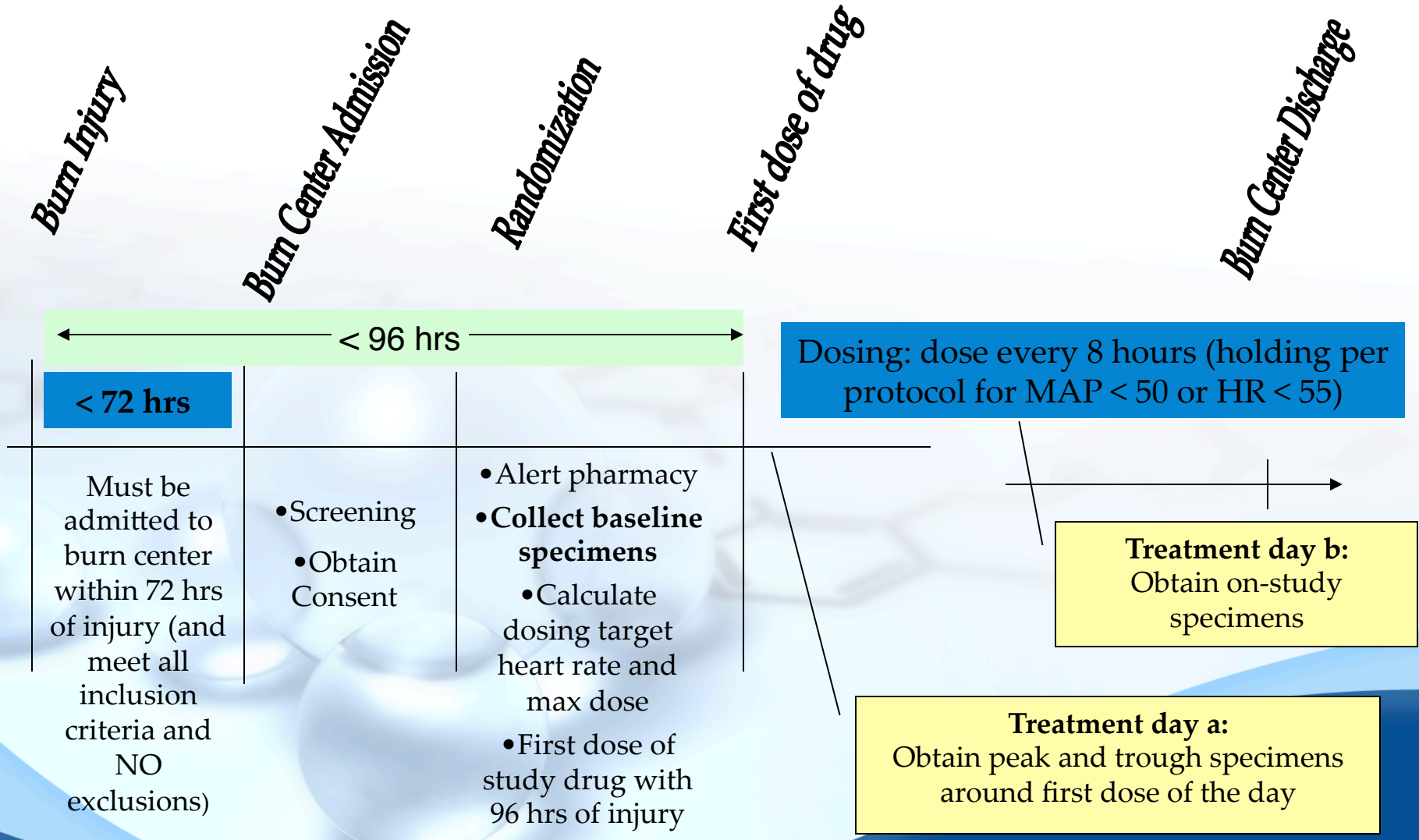
**Hypothesis:**

- Propranolol will provide significant benefit to adults following severe burn injury at doses that are safe and do not increase risk of adverse infections and non-infectious outcomes

**Significance:**

- A pilot study
- Safety and efficacy
- Subpopulations
- Dose levels

# Study Summary Timeline



# Statistical Analysis Plan

## EFFICACY

Cardiac Rate Pressure Product

(RPP aka. cardiovascular product/ double product)

RPP = HR× SBP

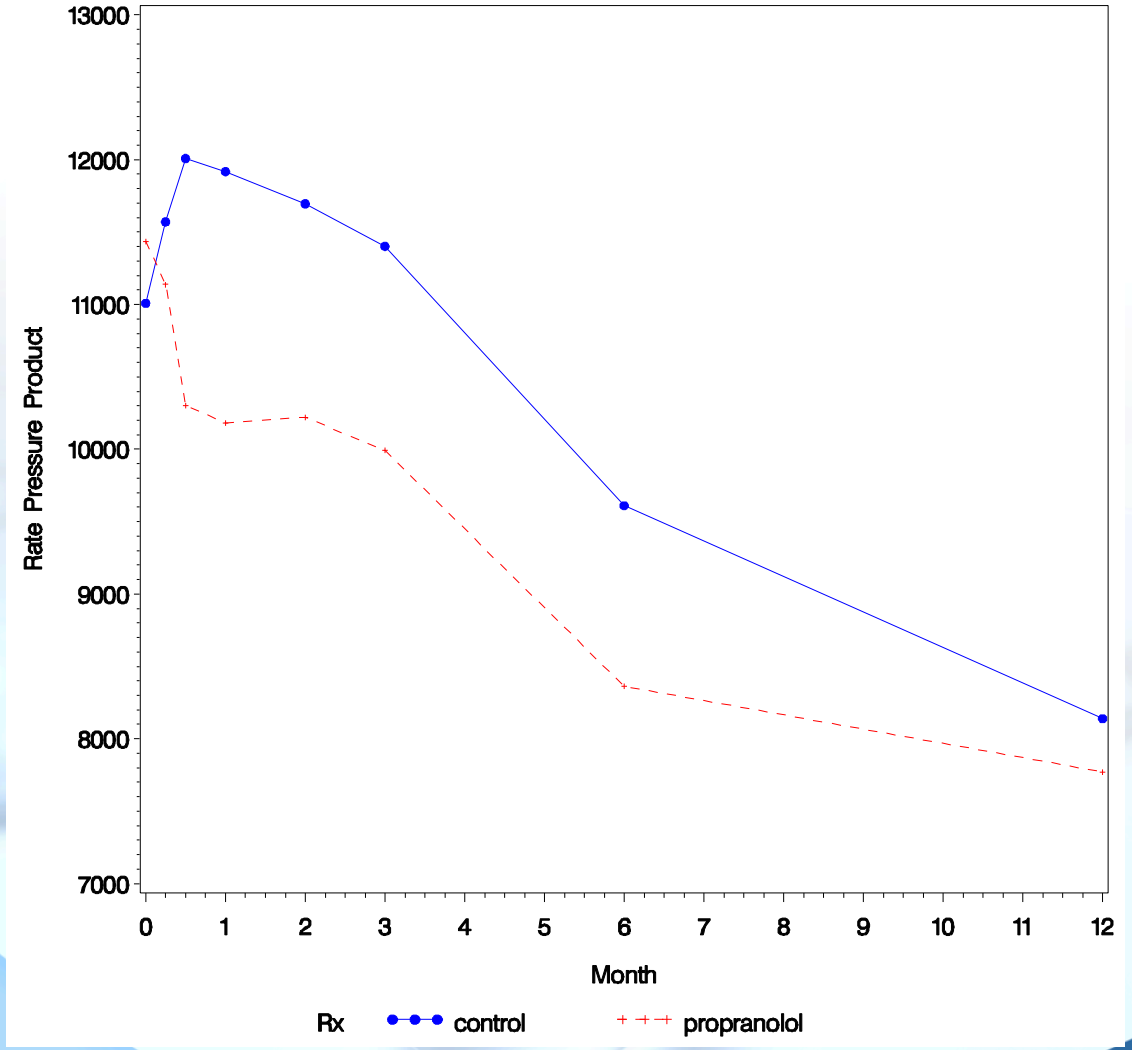
- A piecewise linear random effects model
- Bonferroni correction

## SAFETY

Mortality rates, infectious and non-infectious complications

- A mixed model negative binomial regression:
  - fixed treatment effects, log(follow-up time)

# Efficacy Cont.

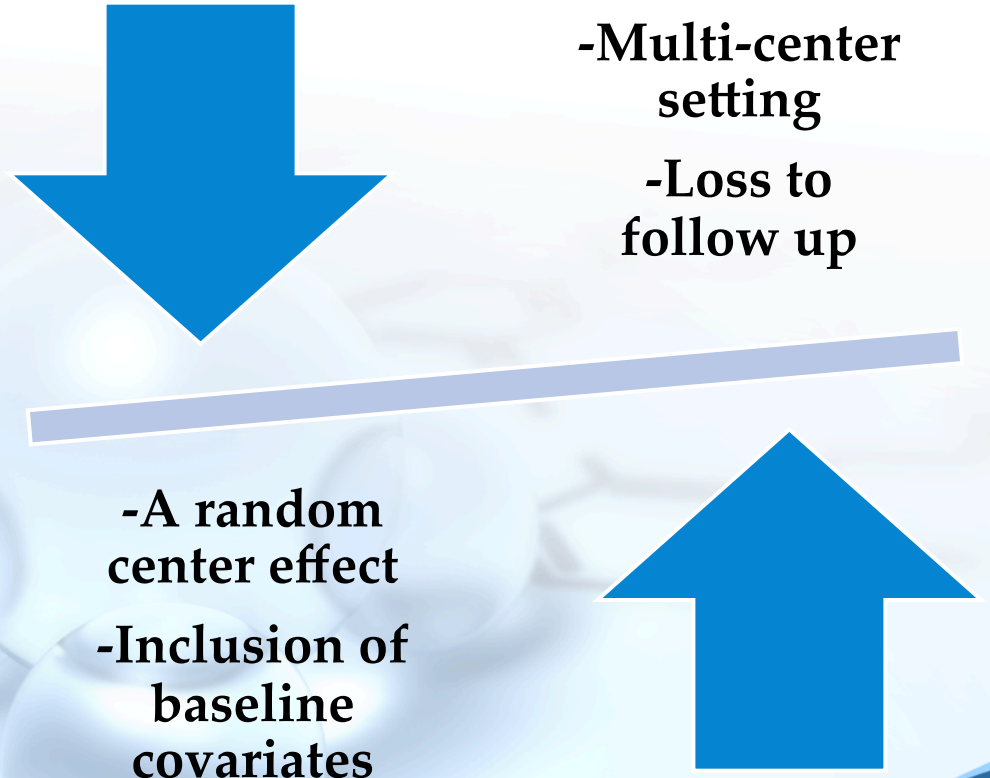



**Two co-primary endpoints:**

- A comparison of slopes over the first 2 weeks
- A comparison of means at 30 days

Figure: Herndon et al, Long-Term Propranolol Use in Severely Burned Pediatric Patients, Annals of Surgery, Volume 256, Number 3, September 2012,

# Overview of Statistical Issues



# Agenda

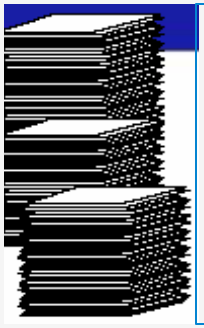
## Data Management

1. Overview of data quality (DQ)
2. Data cleaning framework
3. Using SAS PROC SQL effectively

# DQ

- SCDM definition of DQ in clinical trials:

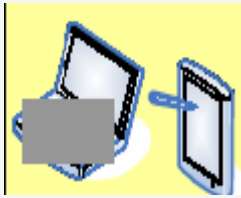
"quality data is data that support conclusions and interpretations equivalent to those derived from error-free data" (Institute of Medicine, Roundtable Report, 1999)



**Study Coordinating Sites**

- Fill in data forms
- Determine if queries are resolvable

Direct feedback



**Studytrax Data Capture System**
Built-in range and logic check

**SAS Generates Spreadsheets for Errors**

Error

**Was Error Previously Non-resolvable / Site?**

If Non-resolvable

If Resolvable

**Spreadsheet Sent Back to Sites for Review**

No

Yes and Keep

Error free

**Further Analysis**

# SAS

## SQL Procedure

- SQL (Structured Query Language) is the universally adopted language for querying a database
- Simple command structure for data definition, access, and manipulation
- Instead of specifying how to do, just say what you want to be done

# Examples: SELECT and CREATE TABLE statements

```
* ========================================== Project Flow ============================================================;
proc sql noprint;
create table work.flow1 as
select ReferenceID, SiteName,
       'Participant Signed Consent but Consent Date is Missing' as problem,
       'Consent' as form, 'Consent-Inclusion-Exclusion' as Timeline
from work.all_wide having SIGNCONS=1 and STARTDT =.;

create table work.flow2 as
select ReferenceID, SiteName,
       'Study Termination Reason is "Other" and Missing Description' as problem,
       'Study Termination' as form
from work.all_wide having TRMRFT =9 and TRMOTHSP='' ;

create table work.flow3 as
select ReferenceID, SiteName,
       'Screening Date after Enrollment Date' as problem,
       '' as form, '' as Timeline,
       'Screening Date: '||put(ScreenDate, MMDDYY10.)||', Enrollment Date: '||put(EnrollDate, MMDDYY10.) as Details
from work.baseline
having .<EnrollDate<ScreenDate;

create table work.flow4 as
select ReferenceID, Sitename,
       "Follow Up Visit Date is prior to Visit 1 Visit Date" as problem,
       'Visit Form' as form,
       'Visit 1 Date: '||put(VISITDT01, MMDDYY10.)||', Follow Up Date: '||put(VISITDT02, MMDDYY10.) as Details
from work.all_wide having .<VISITDT02<VISITDT01 ;
```

# References


1. Vadim Tantsyura, Olive Yuan, and Sergiy Sirichenko: Challenges and Opportunities in Clinical Trial Data Processing
2. Ranjit Singh and Dr. Kawaljeet Singh: A Descriptive Classification of Causes of Data Quality Problems in Data Warehousing
3. Clinical Trial Data Validation: Using SAS PROC SQL effectively, SFBC New Drug Services
4. Van den Broeck et al: Data Cleaning: Detecting, Diagnosing, and Editing Data Abnormalities
5. Propranolol Study Protocol, manual of operation, statistical plans and study training
6. Sources: National Electric Injury Surveillance System-All Injury Project (NEISS-AIP); National Emergency Department Survey (HCUP-NEDS) (2010 Data); National Ambulatory Medical Care Survey.
7. Pruitt BA Jr.: Protection from excessive resuscitation: "pushing the pendulum back".J Trauma. 2000 Sep;49(3):567-8
8. Baxter CR. Guidelines for Fluid Resuscitation. J Trauma, 1981; 21:687-9.

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