CSRC Think Tank
Prevention of Sudden Cardiac Death in Youth
Developing a Rational, Reliable, and Sustainable National Health Care Resource

Identification of Gaps
(an engineering perspective)

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Engineering perspective?

- We like to break down problems into parts
Engineering perspective?

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- We like to write computer programs that output a number!
- We like to build stuff - *especially things with LEDs!*
Engineering perspective?

• We like to break down problems into parts.

• We like to solve problems with mathematics.

• We like to write computer programs that output a number!

• We like to build stuff - *especially things with LEDs*!

• We don’t like randomness or statistics.

• We don’t like clinical trials.
Understand the Problem

- Deterministic vs Stochastic Process
Understand the Problem

- Deterministic Process: the present state completely determines the future state
Understand the Problem

- Stochastic Process: there is randomness or probability which determines the future state
Defibrillation

- Ventricular fibrillation (VF): rapid, chaotic rhythm without effective pumping
- VF presumed final common pathway to death in SCD
- Implantable defibrillator (ICD): delivers an electric shock to the heart to terminate VF
- So how do we know how much output to program for the defibrillator to succeed?
Deterministic Defibrillation

- DFT - defibrillation threshold
- All shocks >DFT succeed for all patients
- Implant ICD, turn on to “DFT”, walk away confident
Stochastic Defibrillation

- Defibrillation success is probabilistic (dose-response curve)
- How do you determine each curve?
  - Repeated trials of VF and DF at different shock strengths - not optimal for patients
- How do/did we overcome this?
  - Optimize patient selection through clinical data
    - Data to understand a ‘normal’ curve
    - Data to understand what alters the normal curve
  - Industry ICD device improvements to maximize output, optimize electrode positions, optimize shock types
  - Define what is acceptable risk of a failed shock vs setting the device output high

Screening for SCD - What do we want?
Screening for SCD- What do we want?

- Deterministic process:
  - Testing:
    - If the test is positive - the child has disease
    - If the test is negative - the child does not have disease
  - Disease: if the child has disease, the disease causes sudden death
  - Treatment: If we “treat” the disease - medication, restriction, etc, there is no possibility of sudden death
My SCD Screening Computer Program
My SCD Screening Computer Program

START

INPUT: Youth

TEST:
Y=0 No disease
Y=1 Disease
My SCD Screening Computer Program

START → INPUT: Youth

TEST:  
Y=0 No disease  
Y=1 Disease

Y = 1?
My SCD Screening Computer Program

START → INPUT: Youth

TEST:
Y=0 No disease
Y=1 Disease

Y = 1?
No → OUTPUT: Cleared

STOP
My SCD Screening Computer Program

START

INPUT: Youth

TEST:
Y=0 No disease
Y=1 Disease

Y = 1?

Yes

Disease Present

Treatment

No

OUTPUT: Cleared

STOP
My SCD Screening Computer Program

START → INPUT: Youth

TEST: Y=0 No disease Y=1 Disease

Y = 1? No → OUTPUT: Cleared

Yes → Disease Present

Treatment No → OUTPUT: SCD/ACA

STOP
My SCD Screening Computer Program

START

INPUT: Youth

TEST:
Y=0 No disease
Y=1 Disease

Y = 1?

No

OUTPUT: Cleared

Yes

Disease Present

Treatment

No

OUTPUT: SCD/ACA

Yes

Medication, Device, Restriction

OUTPUT: Alive

STOP
Screening for SCD - What do we have?

Screening Metrics: ECG QT, voltage, etc

Probability of Disease and SCD

Subject 3: 14 yr old cauc male
ADD + stimulants

Subject 2: 15 yr old AA female

Subject 1: 8 yr old AA male

DF$_{90}$
Screening for SCD - What do we have?

- **Testing:**
  - If the test is positive - there is $W$ probability the child has disease but $X$ probability it is falsely positive
  - If the test is negative - there is $Y$ probability the child is free of disease but $Z$ probability it is false negative

- **Disease:**
  - If a child has the disease, there is $K$ probability that the child will die suddenly

- **Treatment:**
  - If we “treat” - medication, restriction, education, there is $L$ probability that this will prevent sudden death
My ‘accurate’ SCD Screening Computer Program

INPUT: Youth

START
My ‘accurate’ SCD Screening Computer Program

START

INPUT: Youth

TEST

$Y = f(x)$

example: $f(x) = \text{ECG QTc, echo LV wall thickness}$
My ‘accurate’ SCD Screening Computer Program

INPUT: Youth

START

TEST

Y=f(x)

example: f(x)=ECG QTc, echo LV wall thickness

Disease Probability ASSESSOR:

D = Pr{ f( Y, J, K, ... )}

J=age, gender, race, ..
K=clinical correlation
(eg: V1 S wave 25mV+abnl T wave = Q prob of LVH)
My ‘accurate’ SCD Screening Computer Program

INPUT: Youth

TEST
Y=f(x)

example: f(x)=ECG QTc, echo LV wall thickness

Disease Probability ASSESSOR:
D = Pr{ f(Y, J, K, … )}

J=age, gender, race, ..
K=clinical correlation
(eg: V1 S wave 25mV+abnl T wave = Q prob of LVH)

D>0.98?
My ‘accurate’ SCD Screening Computer Program

INPUT: Youth

TEST \( Y = f(x) \)

\( f(x) = \text{ECG QTc, echo LV wall thickness} \)

Disease Probability ASSESSOR:
\[ D = \Pr\{ f(Y, J, K, \ldots) \} \]

J=age, gender, race, ..
K=clinical correlation
(e.g., V1 S wave 25mV+abnl T wave = Q prob of LVH)

No

D>0.98?

Disease <2% prob

START
My ‘accurate’ SCD Screening Computer Program

INPUT: Youth

TEST \( Y = f(x) \)

example: \( f(x) = \text{ECG QTc, echo LV wall thickness} \)

Disease Probability ASSESSOR:
\[ D = \Pr\{ f(Y, J, K, \ldots) \} \]

\( J = \text{age, gender, race, ..} \)
\( K = \text{clinical correlation} \)
(eg: V1 S wave 25mV+abnl T wave = Q prob of LVH)

No

\( D > 0.98? \)

Disease <2% prob

OUTPUT: “cleared”

STOP
My ‘accurate’ SCD Screening Computer Program

**INPUT:** Youth

**TEST**

\[ Y = f(x) \]

*example: \( f(x) = \text{ECG QTc, echo LV wall thickness} \)

**Disease Probability ASSESSOR:**

\[ D = \Pr\{ f(Y, J, K, \ldots) \} \]

**Disease >98% prob**

**SCD RISK ASSESSOR:**

\[ R = \Pr\{ f(J, K, \ldots) \} \]

*J = age, gender, race, ..

*K = clinical correlation

(eg: HCM septum 3cm = K prob SCD)

**No**

**D>0.98?**

**OUTPUT:** “cleared”

**R>0.10? 0.50?, 0.90?**

**STOP**
My ‘accurate’ SCD Screening Computer Program

INPUT: Youth

TEST

\( Y = f(x) \)

example: \( f(x) = \text{ECG QTc, echo LV wall thickness} \)

Disease Probability ASSESSOR:

\[ D = \Pr\{ f(Y, J, K, \ldots) \} \]

\( J = \text{age, gender, race, ..} \)

\( K = \text{clinical correlation} \)

(eg: V1 S wave 25mV+abnl T wave = Q prob of LVH)

Disease >98% prob

YES

SCD RISK ASSESSOR:

\[ R = \Pr\{ f(J, K, \ldots) \} \]

\( J = \text{age, gender, race, ..} \)

\( K = \text{clinical correlation} \)

(eg: HCM septum 3cm= K prob SCD)

NO

\( D > 0.98? \)

NO

Disease <2% prob

NO

\( R > 0.10? 0.50?, 0.90? \)

NO

OUTPUT: “cleared”

STOP
My ‘accurate’ SCD Screening Computer Program

INPUT: Youth

START

TEST

$Y \equiv f(x)$

example: $f(x) = \text{ECG QTc, echo LV wall thickness}$

Disease Probability ASSESSOR:

$D = \text{Pr}\{f(Y, J, K, \ldots)\}$

$J = \text{age, gender, race, ..}$

$K = \text{clinical correlation}$

(eg: V1 S wave 25mV+abnl T wave = $Q$ prob of LVH)

Disease $>98\%$ prob

Yes

OUTPUT: “cleared”

No

Disease $<2\%$ prob

$D > 0.98$?

OUTPUT: “cleared”

SCD RISK ASSESSOR:

$R = \text{Pr}\{f(J, K, \ldots)\}$

$J = \text{age, gender, race, ..}$

$K = \text{clinical correlation}$

(eg: HCM septum 3cm = $K$ prob SCD)

R $> 0.10$? $0.50$?, $0.90$?

No

OUTPUT: “cleared”(?)

Yes

R $> 0.10$? $0.50$?, $0.90$?

No

OUTPUT: “R” risk SCD/ACA

Yes

Treatment

No

OUTPUT: “R” risk SCD/ACA

Yes

Medication, Device, Restriction

OUTPUT: “alive”

<<R risk SCD (?)

STOP
SCD Screening Computer Program - Where are the GAPS?

INPUT: Youth

START

GAP: Who to test?
SCD Screening Computer Program - Where are the GAPS?

INPUT: Youth

TEST

Y=f(x)

GAP: measurement variability/error with ECG

GAP: Who to test?
SCD Screening Computer Program - Where are the GAPS?

INPUT: Youth

TEST

$Y = f(x)$

Disease Probability ASSESSOR:

$D = \text{Pr}\{ f(Y, J, K, \ldots ) \}$

START

GAP: Who to test?

GAP: measurement variability/error with ECG

GAP: Limited data on normal ECG values by gender, race etc
SCD Screening Computer Program - Where are the GAPS?

**INPUT:** Youth

**START**

**TEST** $Y = f(x)$

**Disease Probability ASSESSOR:**

$$D = \Pr\{ f(Y, J, K, \ldots ) \}$$

**GAP:** Who to test?

**GAP:** measurement variability/error with ECG

**GAP:** Limited data on normal ECG values by gender, race etc

No

**D>0.98?**

**Disease <2% prob**

**OUTPUT:** “cleared”

**GAP:** Lack of consensus on acceptable risk of a test missing disease or acceptable rate of false positive

**STOP**
SCD Screening Computer Program - Where are the GAPS?

**INPUT:** Youth

**TEST**

\[ Y = f(x) \]

**Disease Probability ASSESSOR:**

\[ D = \Pr\{ f(Y, J, K, \ldots) \} \]

**SCD RISK ASSESSOR:**

\[ R = \Pr\{ f(J, K, \ldots) \} \]

**GAP:** Measurement variability/error with ECG

**GAP:** Limited data on normal ECG values by gender, race, etc

**GAP:** Lack of consensus on acceptable risk of a test missing disease or acceptable rate of false positive

**GAP:** Limited data linking presence of disease, gender, race, age, other conditions and risk of SCD

**START**

**D>0.98?**

**Yes**

**Disease >98% prob**

**OUTPUT:** “cleared”

**No**

**Disease <2% prob**

**STOP**
SCD Screening Computer Program - Where are the GAPS?

INPUT: Youth

START

TEST

Y = f(x)

Disease Probability ASSESSOR:

D = Pr{ f(Y, J, K, … )}

GAP: Limited data on normal ECG values by gender, race etc

D>0.98? No

Disease <2% prob

OUTPUT: “cleared”

Yes

D>0.98?

GAP: Lack of consensus on acceptable risk of a test missing disease or acceptable rate of false positive

No

Disease >98% prob

SCD RISK ASSESSOR:

R = Pr{ f(J, K, … ) }

GAP: Limited data linking presence of disease, gender, race, age, other conditions and risk of SCD

GAP: Measurement variability/error with ECG

R>0.10? 0.50?, 0.90? No

OUTPUT: “cleared”(?)

GAP: Lack of consensus on acceptable risk of treatment vs not. eg: who with ‘disease’ do we let do what?

STOP
**SCD Screening Computer Program - Where are the GAPS?**

**INPUT: Youth** → **TEST** \( Y = f(x) \) → **Disease Probability ASSESSOR:** \( D = \text{Pr}\{ f(Y, J, K, \ldots) \} \)

**GAP: Who to test?**

**GAP: measurement variability/error with ECG**

- **Disease >98% prob** → **OUTPUT: “cleared”**
- **D <0.98?**
  - **Yes** → **D >0.98?**
    - **Yes** → **OUTPUT: “cleared”**
    - **No** → **Disease <2% prob** → **OUTPUT: “cleared” (?)**
  - **No** → **SCD RISK ASSESSOR:** \( R = \text{Pr}\{ f(J, K, \ldots) \} \)
    - **R >0.10? 0.50?, 0.90?**
      - **No** → **OUTPUT: “R” risk SCD/ACA**
      - **Yes** → **TREATMENT**
        - **Yes** → **OUTPUT: “alive” <<R risk SCD (?)**
        - **No** → **OUTPUT: “alive” <<R risk SCD (?)**

**GAP: Limited data on normal ECG values by gender, race etc**

**GAP: Lack of consensus on acceptable risk of a test missing disease or acceptable rate of false positive**

**GAP: Lack of consensus on acceptable risk of treatment vs not. eg: who with ‘disease’ do we let do what?**

**GAP: Limited data linking presence of disease, gender, race, age, other conditions and risk of SCD**

**GAP: Limited data on efficacy of ‘treatment’.”

**STOP**
Screening for SCD
How do we improve? - understand normal
Conclusion

- Gaps exist in evaluating for sudden cardiac death
- The gaps can be overcome with:
  - Data
  - Understanding normal to better define abnormal
  - Effective collaboration of effort
“Air gaps”
Closing the gaps

Optimize screening data collection and accumulation
Closing the gaps
Further understanding of SCD in the young
Closing the gaps
Improved screening efforts and support
Closing the gaps
Advances and new discovery in pharma and device industry
Thank you