The Circulation Improving Resuscitation Care Trial (CIRC)

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Conflict of Interest

- Dr. Herken employed by ZOLL Medical Corp.
- Trial funded by ZOLL
  - ZOLL and Principal Investigator developed the trial protocol with
    - Site Investigators
    - Staff at Data Coordinating Center
    - Statistical consultants
- Investigators' institutions received funding from ZOLL

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AutoPulse/LDB Research

- Shown to improve hemodynamics*
- Pre-hospital survival studies conflict
  - 3 retrospective studies found improved outcome ‡
  - 1 RCT (ASPIRE) stopped early#
    - No difference in 4 hour survival
    - Cerebral performance worse at discharge

*Ikeno F 2006; Duchateau FX 2010; Timerman 2004; Halperin 2004
‡Casner 2005; Ong 2006; Krep 2007;
#Hallstrom 2006

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CIRC Trial Objectives

- Compare iA-CPR vs. M-CPR
  - Primary endpoint:
    - Survival to hospital discharge
  - Secondary endpoints:
    - ROSC to ED
    - 24 hour survival
  - Neurologic endpoint:
    - mRS score

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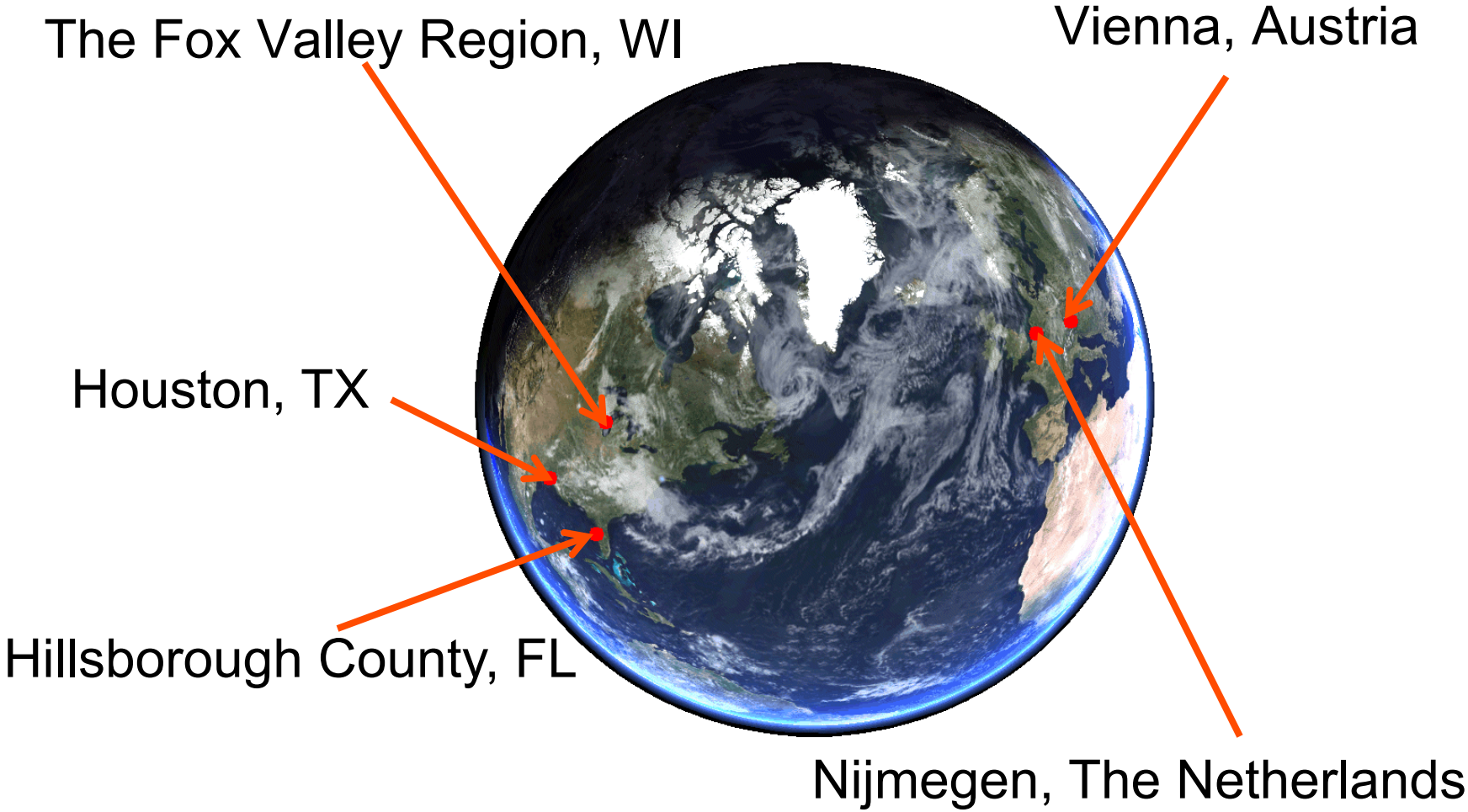
Setting



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High Quality CPR

- 4 hour standardized initial training
  - Pit Crew deployment strategy
  - Maximize CPR fraction
- Regular refresher training

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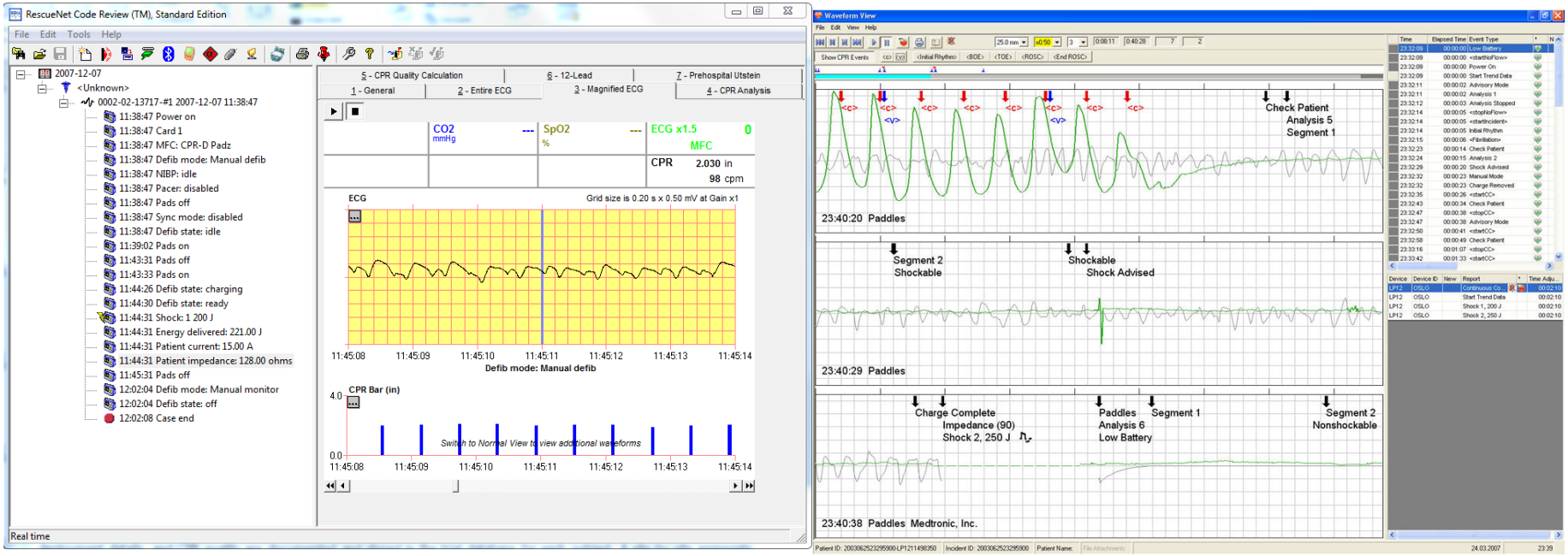
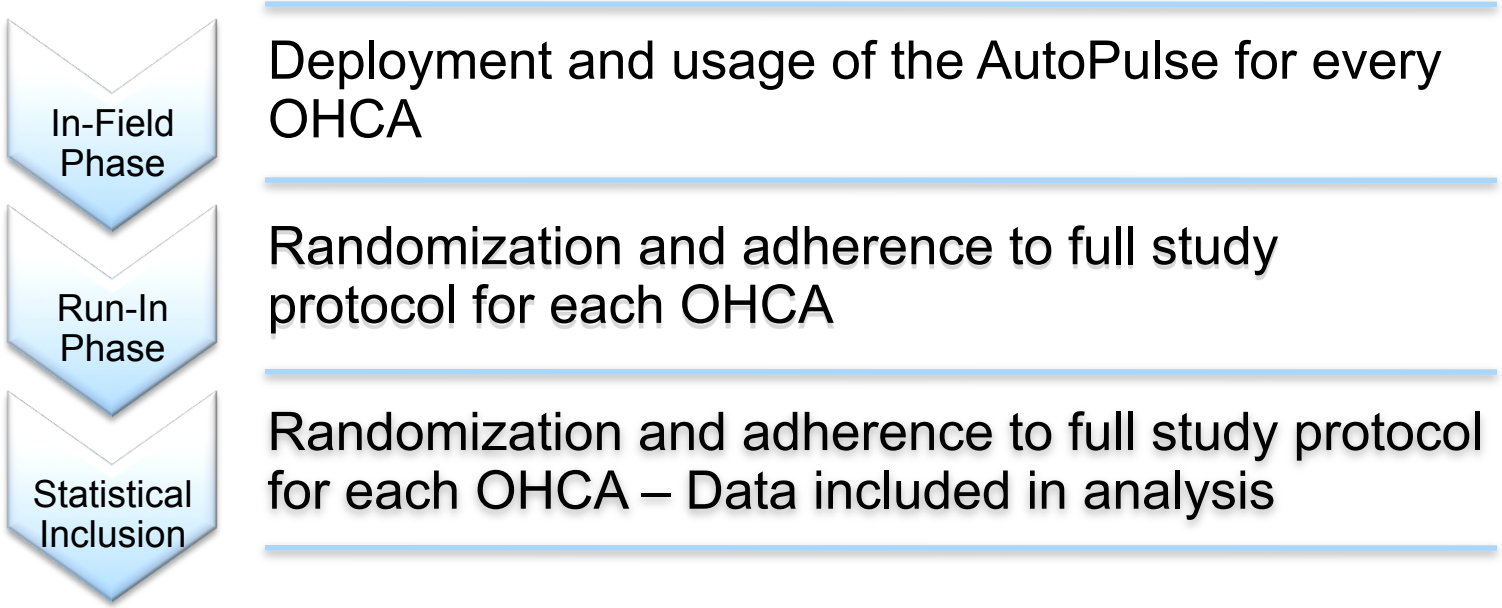
Monitor CPR Quality

- CPR process monitored throughout trial
  - Accelerometer data
  - Transthoracic impedance data
- Reported to providers in aggregate



Trial Phases

- Three distinct study phases



***Transition based on predefined measures of protocol compliance according to monitoring of the CPR process**

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Randomization Procedure

- Confirm cardiac arrest
- Verify need for CPR
- Start manual compressions
- Determine trial eligibility
- Open randomization envelope
- Treat per randomization card

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Subject Exclusion

- Known or apparent pregnancy
- Do Not Resuscitate orders
- Too big for the AutoPulse
- Prisoner or ward of the state
- Prior application of a mechanical chest compression device
- Randomizing EMS unit arrived >16 minutes after emergency call

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Data Analysis

- Group Sequential Double Triangular Test
- Powered to determine superiority, inferiority, or equivalence
  - Two-sided significance level 5%
  - Power 97.5%
- Equivalence defined as OR 95% CI fully between 0.69 and 1.44

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General Characteristics by Arm

	M-CPR n=2123	iA-CPR n=2099
Age	65.6 ±16.0	65.7±16.4
Male gender	61%	61%
Public location of OHCA	13%	14%
Bystander witnessed	37%	37%
Bystander CPR	49%	47%
Shockable initial rhythm	24%	21%
Response interval [min]	6.6 ± 3.0	6.7 ± 2.9
Prehospital epinephrine	91%	93%
Hospital hypothermia	12%	10%
PTCA/ PCI	6%	4%
Time from arrival to termination/transport [min]	36.1 ± 14.1	37.3 ± 14.3
Initial rhythm VF/ VT average time from defib on to first shock [min]	3.5 ± 4.0	4.6 ± 4.8
Time from defib on to first recorded compression(s)	61 ± 127	65 ± 139

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CPR Process Data*

	M-CPR (n=2,024)	**iA-CPR (n=2,017)**
CPR fraction (mean ± SD)		
at 10 minutes	79.7% ± 10.1%	78.5% ± 9.4%
at 20 minutes	80.2 ± 9.1%	80.4% ± 8.3%
Avg compressions per min (first 10 minutes)	89.2 ± 17.4	66.3 ± 10.7
Avg ventilations per min (first 10 minutes)	8.8 ± 4.7	6.8 ± 3.4

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*Electronic Data available for 96% of study subjects

Results: Primary Endpoint

- Equivalent survival to hospital discharge
  - OR 1.06, 95% CI 0.83 - 1.37
    - Adjusted for covariates (age, witnessed arrest, initial cardiac rhythm, and enrollment site) and interim analyses
    - Within pre-defined equivalence region (0.69 - 1.44)
  - Non-inferiority test iA-CPR vs. M-CPR p=0.0003
  - Non-inferiority test M-CPR vs. iA-CPR p=0.008

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Results: Effectiveness Endpoints

	M-CPR (2132)	iA-CPR (2099)	Unadjusted OR (95% CI)	Partially Adjusted OR (95% CI)	Fully Adjusted OR (95% CI)
Survival to Hospital Discharge	11.0%	9.4%	0.84 (0.69 – 1.02)	0.89 (0.72 – 1.10)	1.06 (0.83 - 1.37)
Survival to 24h	25.1%	21.8%	0.84 (0.72 – 0.96)	0.86 (0.74-0.998)	N/A
Sustained ROSC	32.3%	28.6%	0.84 (0.74 – 0.96)	0.84 (0.73-0.96)	N/A

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Results: Neurologic Endpoint

- No difference in mRS scores ≤3
  - Adjusted OR 0.80, 95% CI 0.47 - 1.37 (n.s.)

	M-CPR	iA-CPR
Discharge mRS	(n=233)	(n=196)
Score of 0 -3	48.1%	44.4%
Score of 4 -5	26.2%	25.5%
Unknown score	25.8%	30.1%

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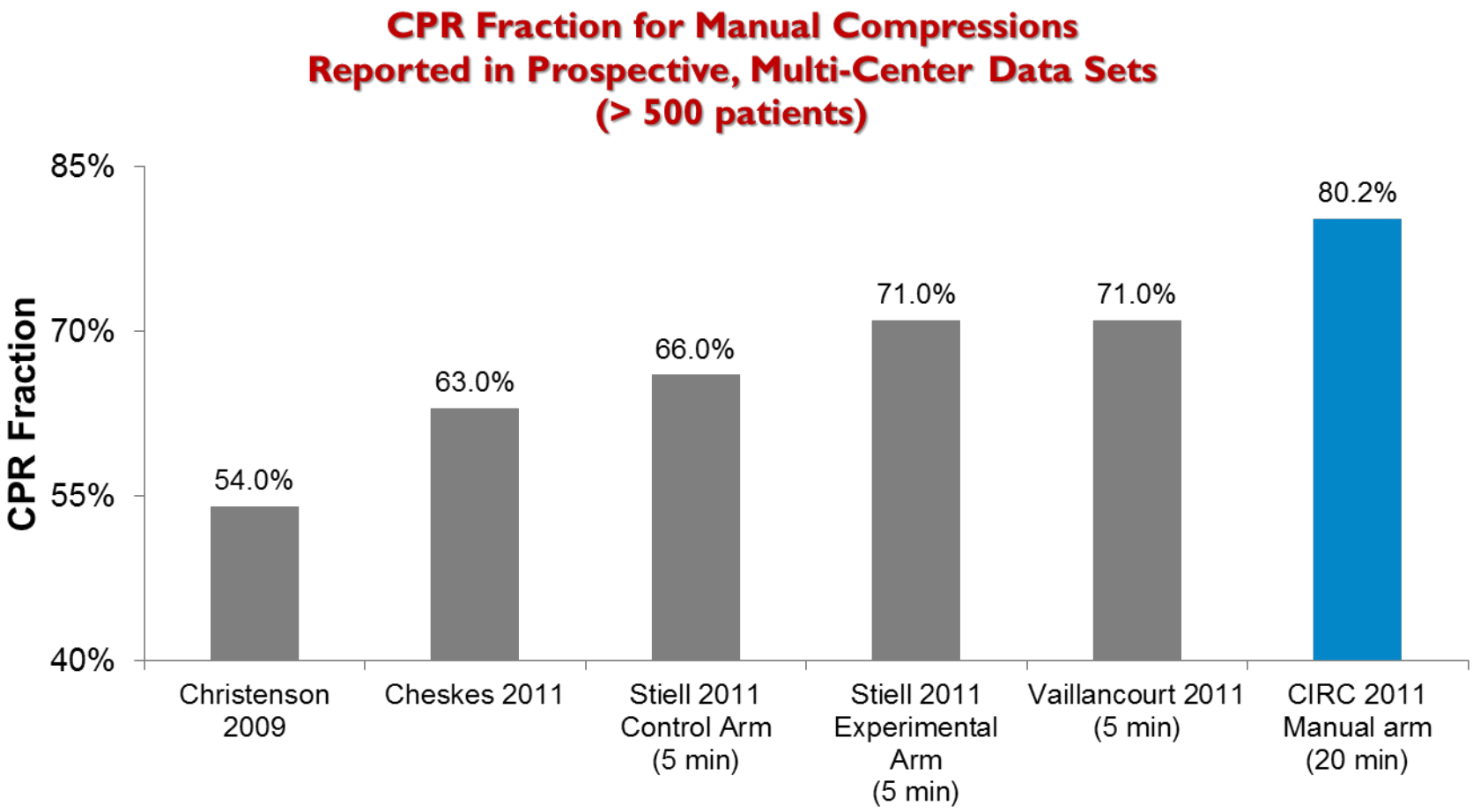
Highest CPR Fraction Reported



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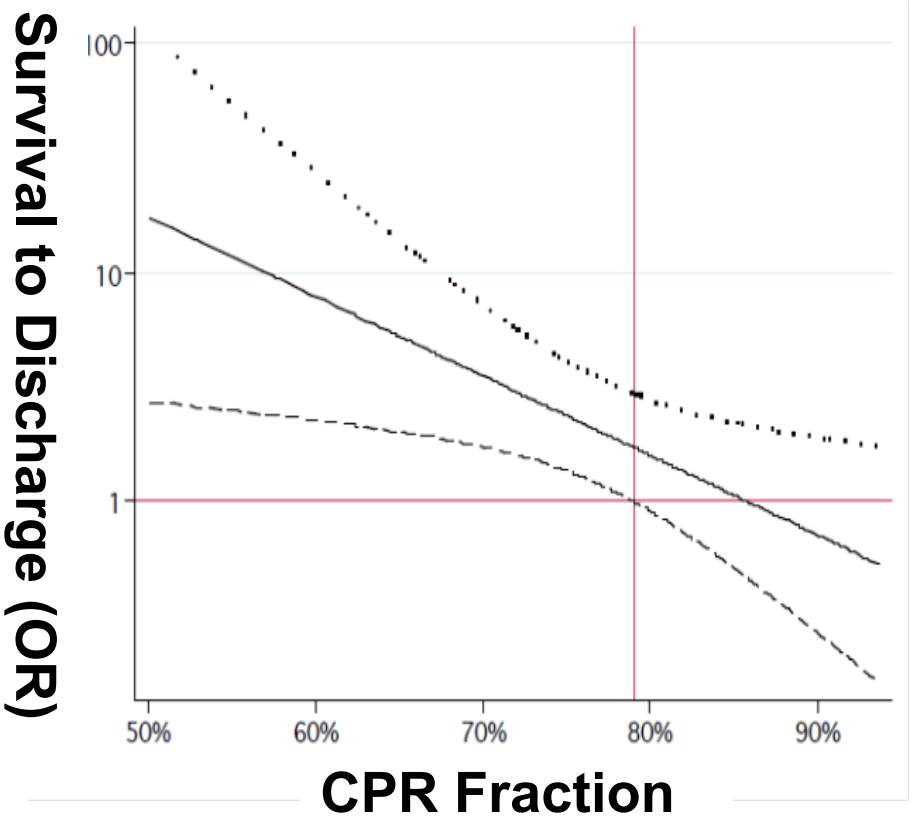
Subgroup Analysis

- Witnessed VF/VT Arrests
- Survival higher for iA-CPR if CPR fraction <78%
- No survival difference with higher CPR fractions.
- Example: CPR fraction 70% OR 3.4, 95% CI: 2–7.4



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Discussion

- Equivalence
  - Powered to show true statistical equivalence
  - At least as good as high-quality M-CPR
- iA-CPR may solve practical problems
  - CPR in confined spaces
  - CPR with limited number of rescuers
  - CPR during transport
    - Rescuer safety
    - Compression efficacy

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Discussion

- CPR fraction
  - ~80% CPR Fraction in both arms
    - Higher than most CPR fractions reported for other large RCTs.
  - High CPR fraction hard to achieve and maintain
  - Secondary analysis: at typical “clinical” CPR fractions iA-CPR better than M-CPR

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Conclusions

- CPR quality good in both arms
- It is possible to achieve high-quality manual CPR
- Compared to high-quality M-CPR:
  - iA-CPR statistically equivalent survival to hospital discharge
  - No difference in neurologic status at discharge

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