Institute for Global Orthopaedics and Traumatology

Clinical Research Findings from Lesser-Resourced Environments: What Can We Apply to Our Practices?

David Shearer, MD, MPH

Disclosures

Research funded by:

- NIH
- OREF
- OTA
- Heiman
- Wyss foundation
- Doris Duke Foundation

VP, Board of Directors, SIGN Fracture Care International

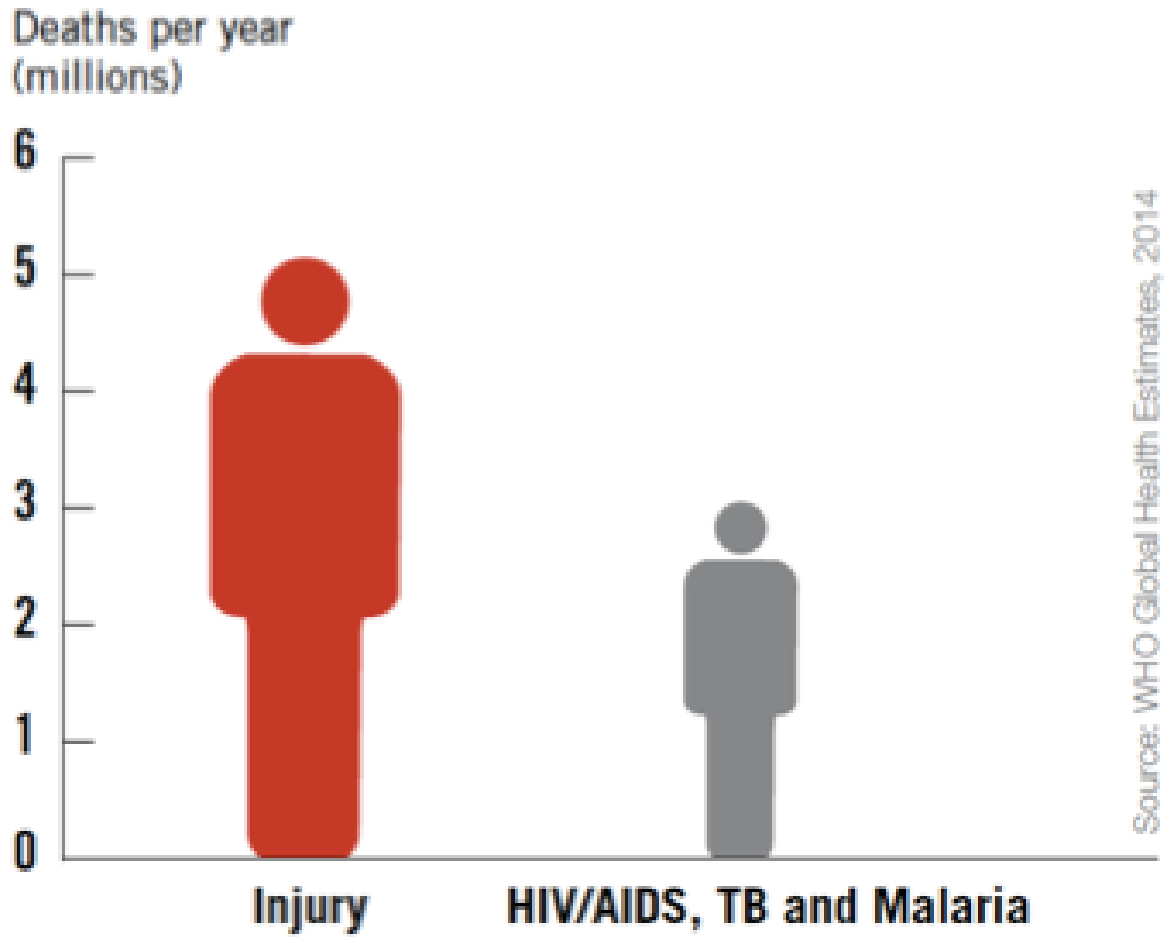
Outline

- Why?
- What can we learn?
- What is the future?

Why?

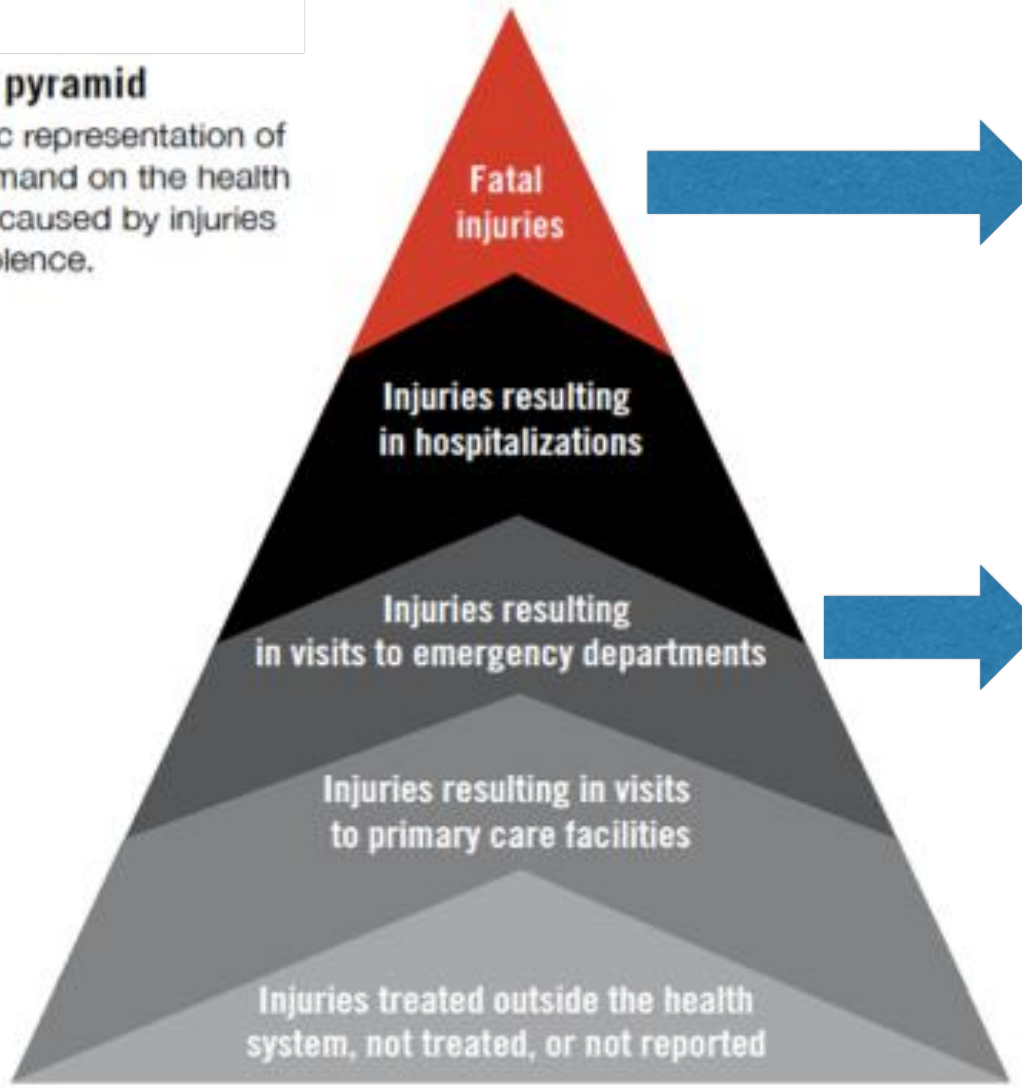
Reason #1 It’s just the right thing to do

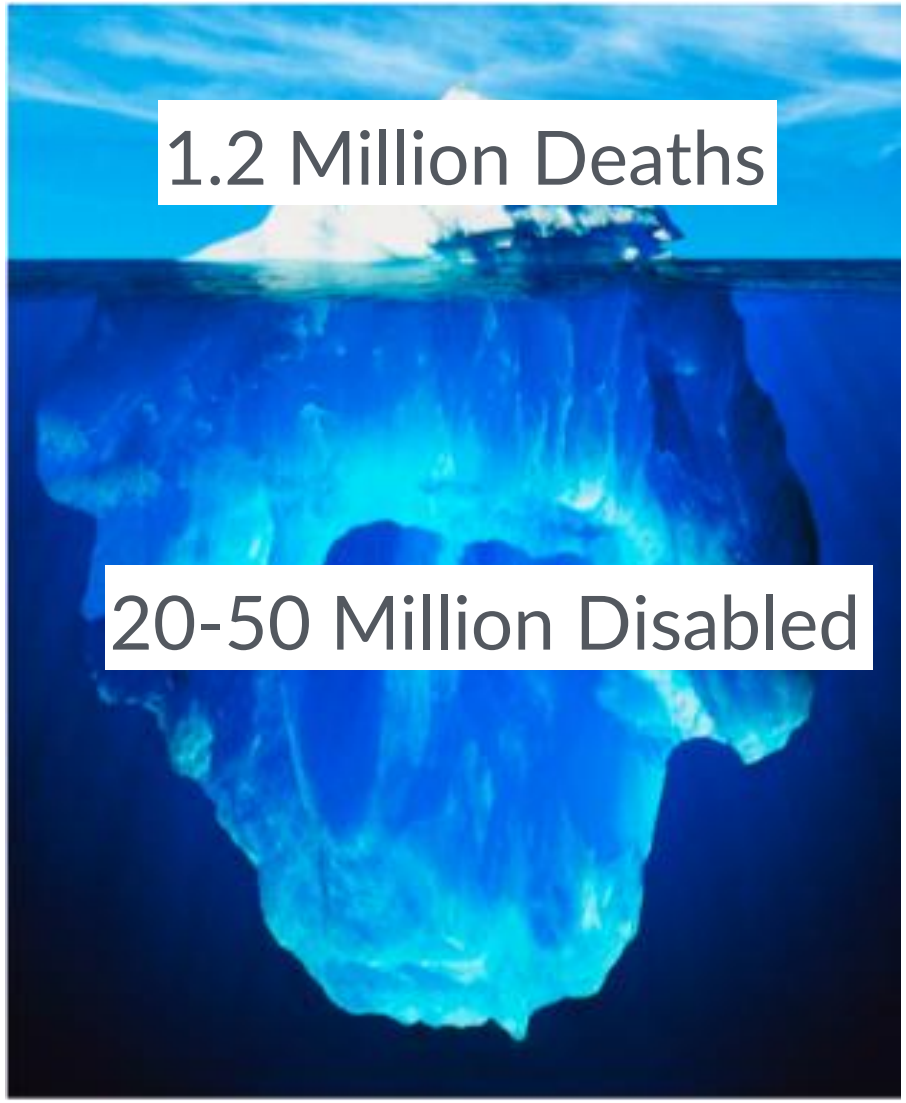
How Do Trauma Deaths Compare?



Injury pyramid

Graphic representation of the demand on the health sector caused by injuries and violence.






Snapdragon

IGOT

Institute for Global Orthopaedics and Traumatology

- Founded in 2006
- Non-Profit departmental initiative
- Emphasis on academic ***partnering***

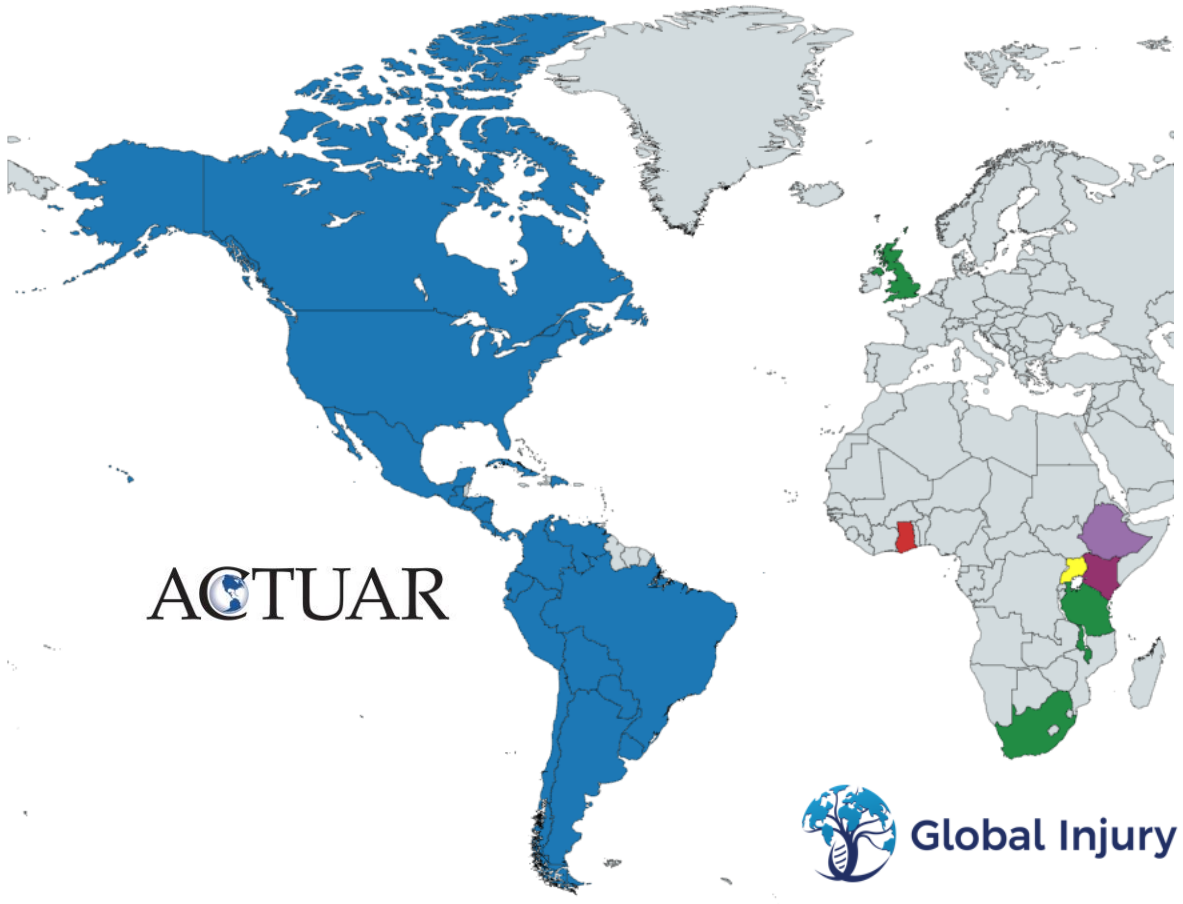
Morshed *CORR* 2013

IGOT Partner Sites

IGOT Research

- Prospective Studies
  - Tanzania
  - Malawi
  - Uganda
  - Ghana
  - Latin America

- Research networks
  - ACTUAR (Latin America)
  - Global Injury Group (Tanzania, Malawi, South africa, UK, US)



IGOT Research

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  - Tanzania
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  - Ghana
  - Latin America

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Why?

Reason #1 It’s just the right thing to do

Addressing Locally Important Questions

IMN more cost-effective than Skeletal Traction in Malawi

IMN is more effective than plating in Tanzania

Why?

Reason #1 It’s just the right thing to do

Why?

Reason #1 It’s just the right thing to do

Reason #2 We all benefit

Shared Problems

Major Extremity Trauma Research Consortium (METRC)

- >$150 million in funding
- 34 clinical trials
- >22,000 participants enrolled

Focus areas:

1. Fixation of open fractures
2. Prevention and treatment of infection
3. Optimization of outcomes following high energy lower extremity trauma – reconstruction, amputation and orthotics/prosthetic

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Orthopaedic Trauma Association

- >3500 active members world-wide (>65 countries)
- ~$750 in research funding awarded annually
- ~ $15 million in research funding since 1990

Focus areas:

1. Open fractures management
2. Infection prevention
3. Soft tissue and bone defect reconstruction

Open Tibia Fractures: Ex-Fix vs. Nail

External Fixator

Medullary Nail

Open Tibia Fractures: Ex-Fix vs. Nail

METRC

- 20 U.S. Trauma Centers
- 7 years
- 260 randomized patients followed for 18 months
- >$2 million dollars
- **$7700/patient**

Modern External Ring Fixation Versus Internal Fixation for Treatment of Severe Open Tibial Fractures

A Randomized Clinical Trial (FIXIT Study)

Major Extremity Trauma Research Consortium (METRC)*

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Modern External Ring Fixation Versus Internal Fixation for Treatment of Severe Open Tibial Fractures

A Randomized Clinical Trial (FIXIT Study)

Major Extremity Trauma Research Consortium (METRC)*

IGOT

- 1 African Trauma Center (Dar es Salaam, Tanzania)
- 2 years
- 240 randomized patients followed for 12 months
- $50,000
- **$200/patient**

Intramedullary Nailing Versus External Fixation in the Treatment of Open Tibial Fractures in Tanzania

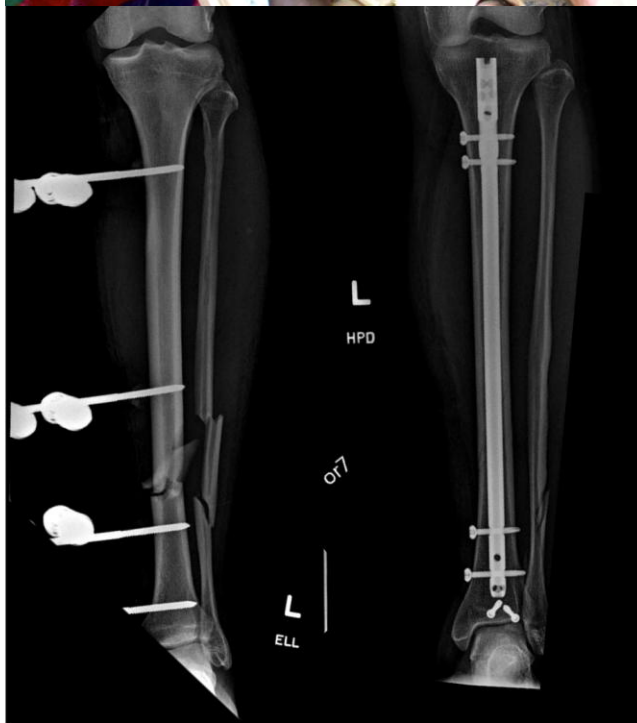
Results of a Randomized Clinical Trial

Billy T. Haonga, MD, Max Liu, AB, Patrick Albright, MS, Sravya T. Challa, BS, Syed H. Ali, BS, Ann A. Lazar, PhD, Edmund N. Eliezer, MD, David W. Shearer, MD, and Saam Morshed, MD, MPH, PhD

Investigation performed at the Muhimbili Orthopaedic Institute, Muhimbili National Hospital, Dar es Salaam, Tanzania, and the University of California San Francisco, San Francisco, California

Open Tibia Ex-fix vs. Nail RCT

- 240 Gustilo Type 1-3A open tibia randomized ex-fix or SIGN nail
- No difference in reoperation
- Secondary outcomes favored IMN
  - Better early quality of life
  - Faster radiographic healing
  - Lower rate of malunion
- Direct costs of IMN outweighed by societal costs from ex-fix



Haonga, et al. *JBJS Am*. 2020

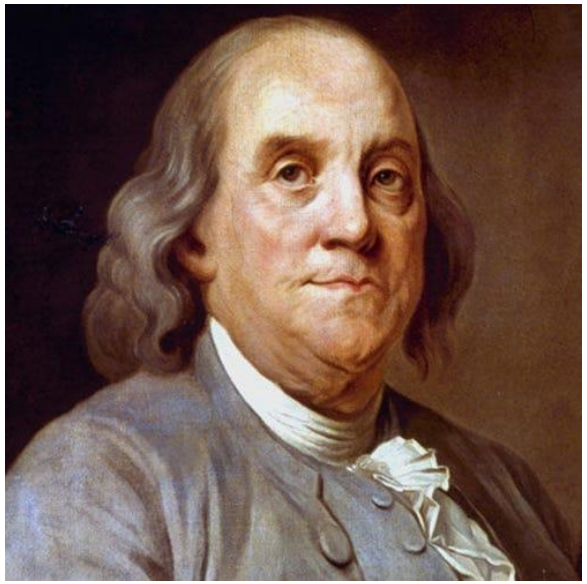
Overall

>

Risk of Infection

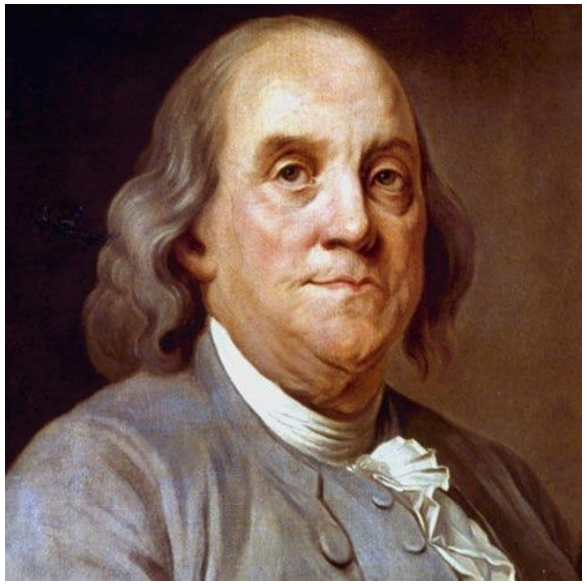
=

12%



"An ounce of prevention is worth a pound of cure"

- Benjamin Franklin



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"What about local antibiotics?"

- Billy Haonga

Local antibiotics

Local Injection of Aminoglycosides for Prophylaxis Against Infection in Open Fractures

Cheryl Reese Lawing, MD, Feng-Chang Lin, PhD, and Laurence E. Dahners, MD

Background: The purpose of this study was to determine the efficacy of local wound cavity injections of aqueous aminoglycosides (gentamicin and tobramycin), in conjunction with systemic antibiotics, to lower the prevalence of infection in patients with open fractures.

Methods: Three hundred and fifty-one open fractures were identified by Current Procedural Terminology codes 11011 and 11012. Data on patient demographic characteristics, injury characteristics, infection, and fracture union were obtained from the electronic medical records. Patients in the control group (183 fractures) received systemic antibiotics only. Patients in the intervention group (168 fractures) received, in addition to systemic antibiotics, a locally administered aminoglycoside (2 mg/mL) at the time of the index surgical procedure. At the discretion of the attending surgeon, some wounds also received postoperative irrigations of aqueous aminoglycoside (n = 34). For wounds that could not be closed and wounds that received postoperative irrigations, negative pressure dressings were used.

Results: The deep and superficial infection rate in the control group was 19.7% (thirty-six of 183 fractures), but it was significantly lower (p = 0.010) in the intervention group at 9.5% (sixteen of 168 fractures). When comparing only the deep infections, the infection rate in the control group was 14.2% (twenty-six of 183 fractures) compared with 6.0% (ten of 168 fractures) in the intervention group (p = 0.011). After multivariate analysis to adjust for possible confounding factors, the administration of local antibiotics was found to be an independent predictor of lower infection rates in both deep and superficial infections (odds ratio, 2.6 [95% confidence interval, 1.2 to 5.6]; p = 0.015) and deep infections only (odds ratio, 3.0 [95% confidence interval, 1.1 to 8.5]; p = 0.034). The use of local antibiotics did not have an impact on nonunion rate (p = 0.881), with a type-I error rate of $\alpha = 0.05$ and 0.8 power.

Conclusions: This study suggests that local aqueous aminoglycoside administration as an adjunct to systemic antibiotics may be effective in lowering infection rates in open fractures; further research with higher-level research designs are needed.

Level of Evidence: Therapeutic Level III. See Instructions for Authors for a complete description of levels of evidence.

TABLE VI Multivariate Analysis

Analysis	Odds Ratio*	P Value
Unadjusted (deep infections)	2.7 (1.3 to 5.8)	0.011
Adjusted (deep infections)	3.0 (1.1 to 8.5)	0.034
Unadjusted (deep and superficial infections)	2.5 (1.2 to 4.9)	0.010
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*The values are given as the odds ratio, with the 95% CI in parentheses.

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- Gentamicin **$0.05** vs Vancomycin $10-100
- Gram negative + staph coverage
- Synergy with IV cephalosporins

Research Question

Will a low-cost, aqueous **Gentamicin** solution injected following wound closure reduce **infection** (FRI) following open tibia fracture in Tanzania?

pilot Gentamicin Open (pGO) Tibia study

- 100 patient pilot study enrolling
  - Adult Open Tibial Fractures
  - Gustilo Type 1-3A
- Randomized to either
  - Intervention: Gentamicin (2mg/mL) injected after wound closure
  - Comparator: Saline placebo injection
- F/u: 1 Year Follow up

Results - Feasibility

Enrollment

199 screened, 100 enrolled 9-months = 11.1/month

Excluding 1-month COVID pause: **12.5/month**

Retention: 84% completed 1 year f/u or primary event

Data Completeness: >95% at all follow up time points

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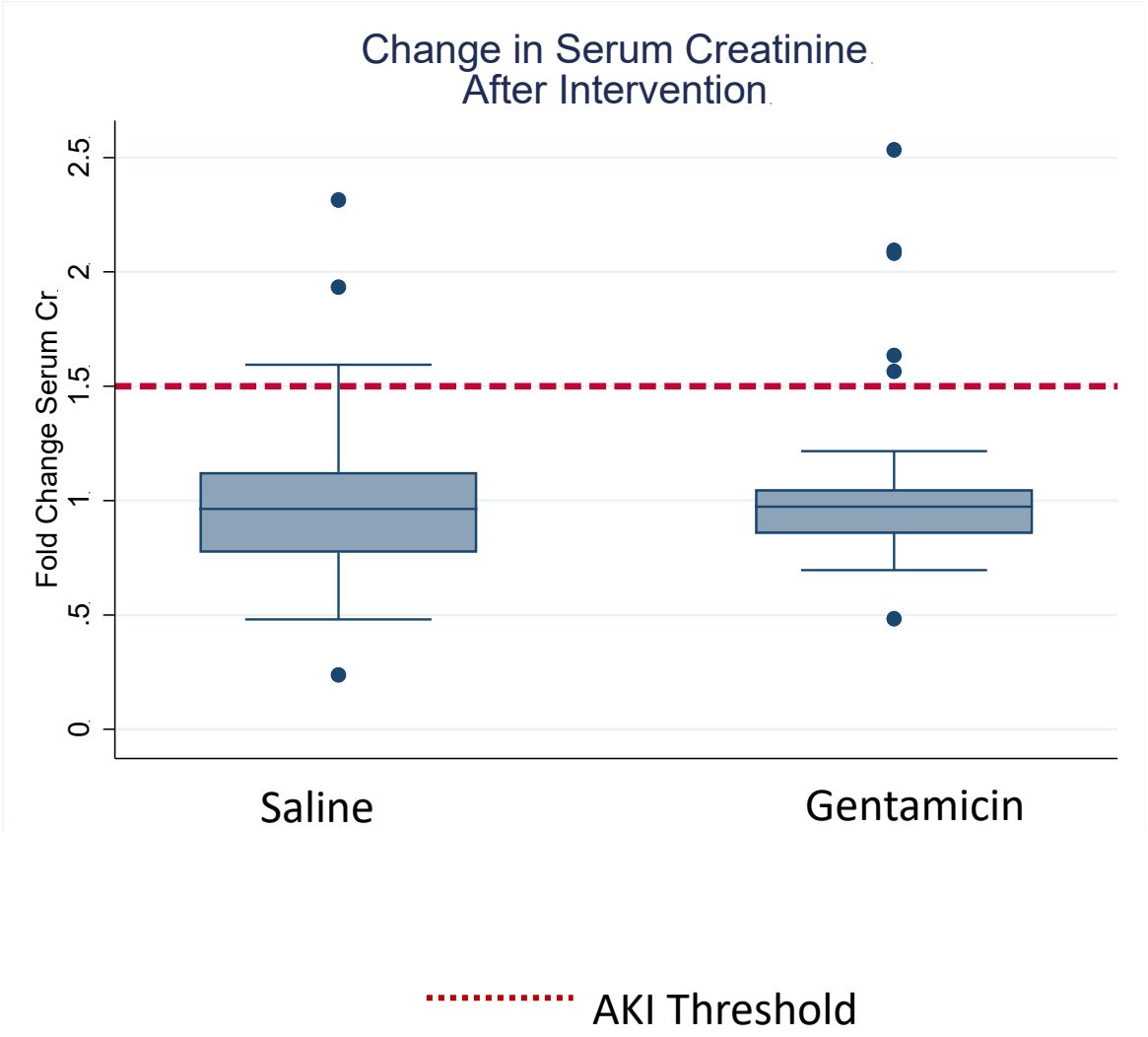
Results - Safety

- No severe or persistent kidney injury

- Mild/Moderate AKI
  - Gentamicin 5/45 (11%)
  - Saline 4/55 (7.3%)

- Mild hearing loss
  - Saline: 1 case



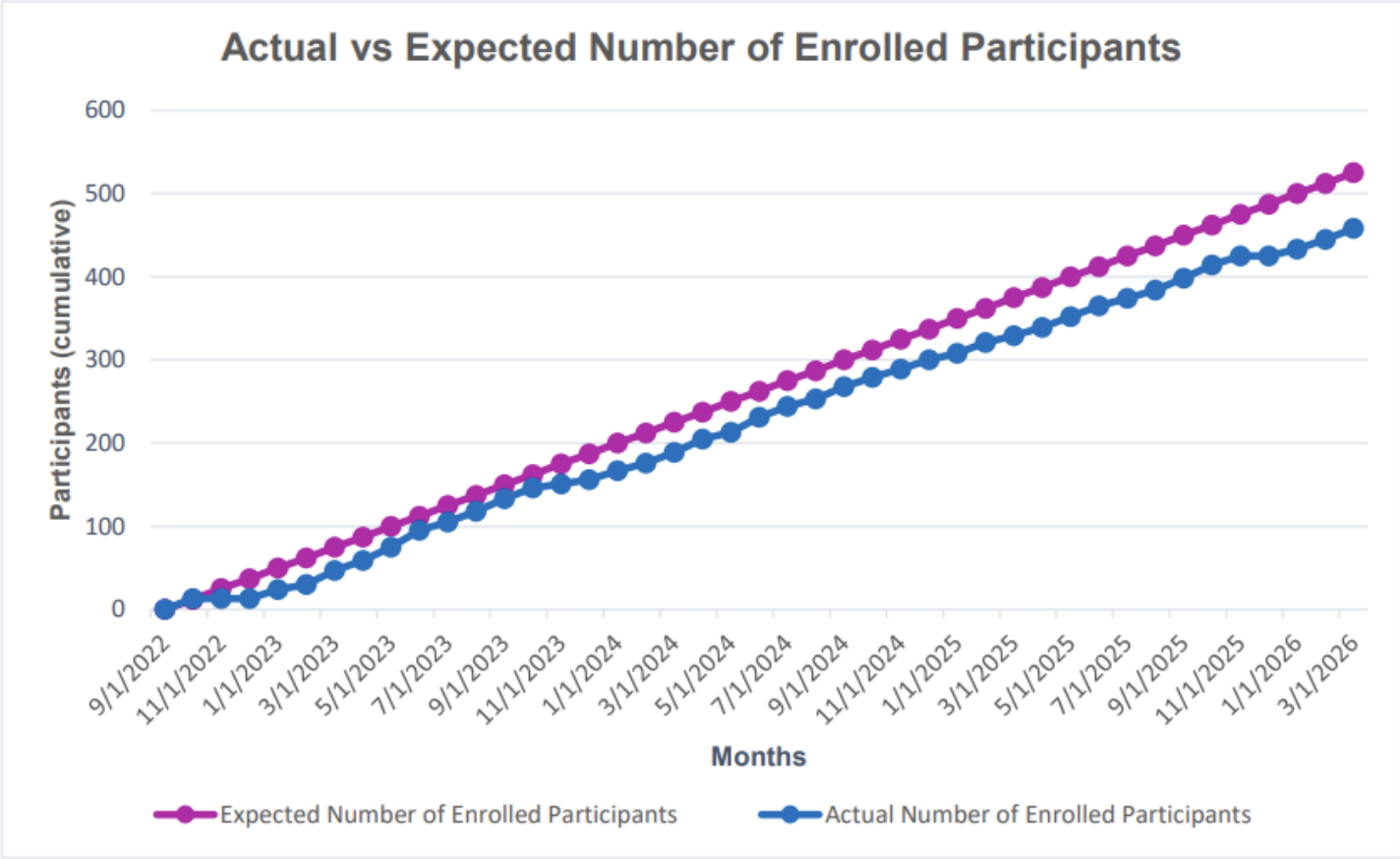
Gentamicin Open (GO) Tibia trial

Definitive trial

- Same protocol
- Higher concentration of gentamicin (80mg in 5mL vs 40mL)
- Enrollment target: 445 / arm = 890 total

Gentamicin Open (GO) Tibia trial

Definitive trial



Current enrollment: 470 of 890

A win-win?

- HICs struggle with sample size and high cost
- LICs lack research capacity and produce < 0.1% of literature

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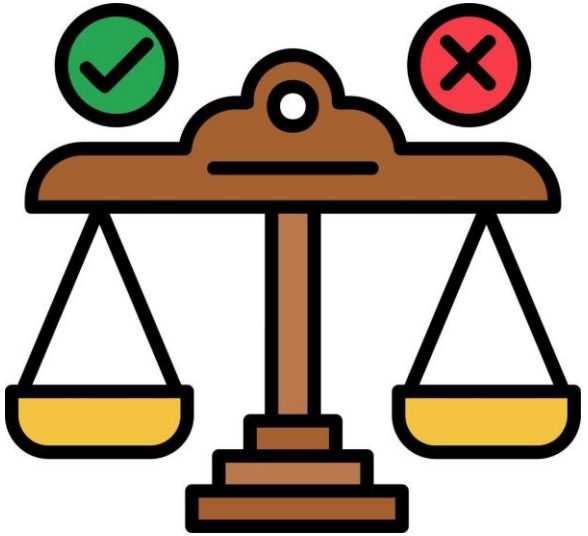
Table 1: Published clinical trials reporting outcomes of open tibial shaft fractures

Studies	Total Sample	**Open tibia sample**	Number centers	Duration (yrs)	Enrolled/ Center	Enrolled/ Center/Year	Follow up rate
FLOW Trial (23)	2447	912	41	4	22	6	90%
SPRINT Trial (24)	1226	392	29	5	13	3	93%
MOI IMN v. Ex-fix (22)	**240**	**240**	**1**	**1.3**	**240**	**180**	**92.1%**
TRUST Trial (26)	501	114	43	4.5	3	<1	96%
LEAP Study (27)	569	173	8	3	22	7	96%
Alberta Cohort (29)	791	140	3	8	47	6	94%

Ethical considerations



1. Research of mutual benefit
2. Locally affordable and safe treatments
3. Plan for training and integration of local leaders to establish capacity and ownership
4. Ensuring local impact of results

SIGN Fracture Care

- NGO
- Manufactures and donates IM nails
- Requires no C-arm, power instruments
- Sites must report all cases in a database

Countries with SIGN Programs

Countries with low income: **$1,135 or less per year***

Countries with lower-middle income: **$1,136 to $4,495 per year***

Countries with upper-middle income: **$4,496 to $13,935 per year***

Country with high income: **$13,935 more per year***

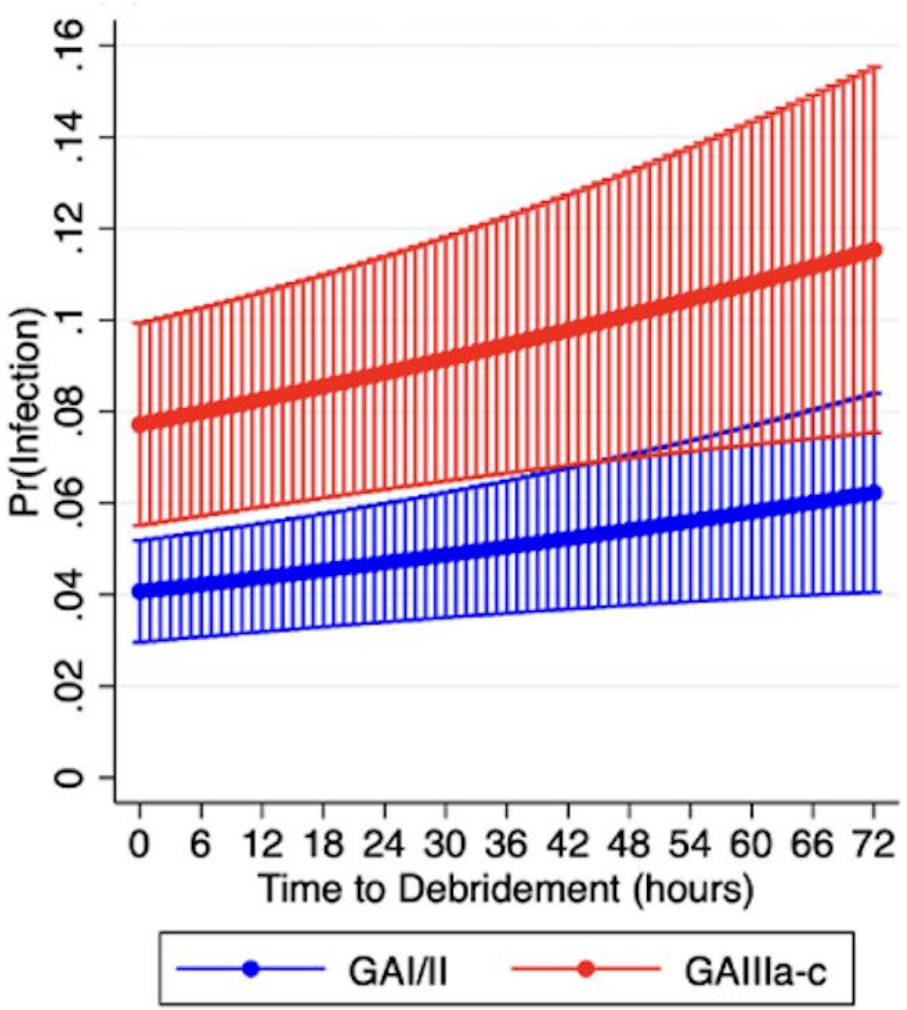
**Income data from World Bank, Gross National Income per capita, 7/2025.*

***Current data unavailable. Not categorized.*

What is the optimal timing for open fracture debridement?

6 hours? 24 hours?

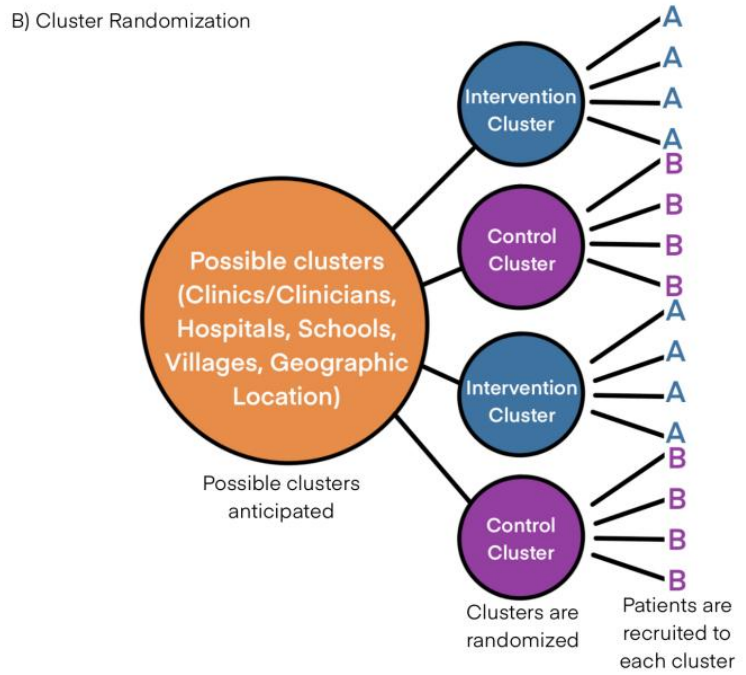
Impact of Debridement Timing on Infection



Data from >10,000 open fractures in the SIGN Database

What is the future?

- Continued capacity building and collaboration
- Expansion to multicenter trials, pragmatic designs
- Platform clinical trials



Take-home messages

- Research has an important role in creating global health equity
- Patients in HICs can benefit from ethically appropriate research in LMICs
- High-quality trials for carefully selected interventions may be a win-win

IGOT

Thank you!

- Muhimbili Research Team
  - Billy Haonga
  - Joshua Ngyahoma
  - Justin Kessy
  - Ibrahim Sasillo

SIGN Fracture Care

IGOT