

# Research During Active War in Ukraine
# Experiences From the PACT-ARROW Study


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Anschutz

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NIH PRAGMATIC TRIALS COLLABORATORY
Rethinking Clinical Trials®

# Disclaimer, disclosures, conflicts

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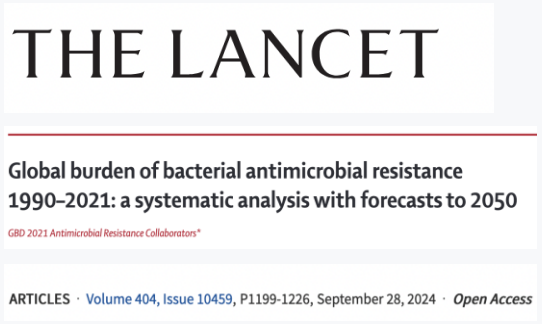
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# Overview

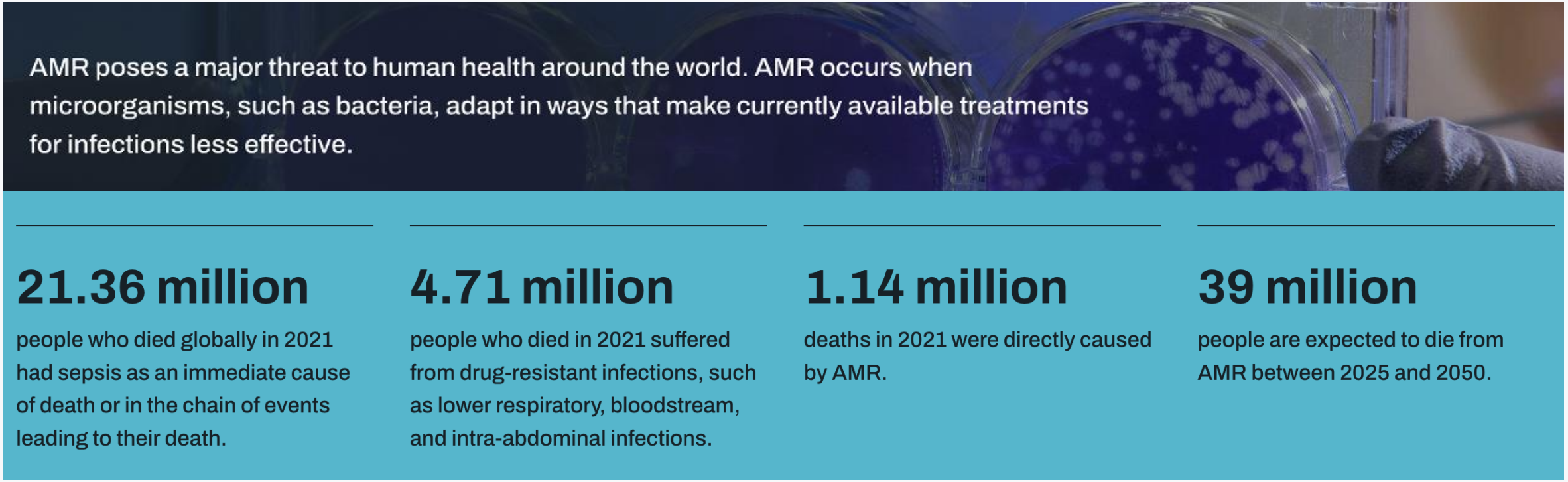
1. The context: war, injury, infection
2. The problem: evidence gap
3. Possible solution: master protocol
4. PACT-ARROW: applying a platform model to traumatic wounds in Ukraine
5. Discussion

PART 1

# The context: war, injury, infection




# Antimicrobial resistance (AMR) an emerging threat




**21.36 million**

people who died globally in 2021 had sepsis as an immediate cause of death or in the chain of events leading to their death.

**4.71 million**

people who died in 2021 suffered from drug-resistant infections, such as lower respiratory, bloodstream, and intra-abdominal infections.

**1.14 million**

deaths in 2021 were directly caused by AMR.

**39 million**

people are expected to die from AMR between 2025 and 2050.

GBD 2021 Antimicrobial Resistance Collaborators. Global burden of bacterial antimicrobial resistance 1990-2021: a systematic analysis with forecasts to 2050. Lancet. 2024 Sep 28;404(10459):1199-1226. doi: 10.1016/S0140-6736(24)01867-1. Epub 2024 Sep 16. PMID: 39299261; PMCID: PMC11718157.

# Armed conflicts, health systems, and AMR

United Nations

**General Assembly**

**Seventy-ninth session**
Agenda item 127
**Global health and foreign policy**




United Nations. UNGA. 79th Session. Agenda item 127. Glboal Health and Foreign Policy, 2024.
Silori R, Shrivastava V, Mazumder P, Kumar M. Antimicrobial resistance surge in the context of pollution, war, and pandemic. Current Opinion in Environmental Science & Health. 34 2024.

WORLD

Select: ESPAÑA

# Superbugs pose 'huge challe treating Ukraine war wounds



EL PAÍS

ernational

RUSSIAN WAR IN UKRAINE >

# Superbugs gain a foothold in the trenche Ukraine war

am of German physicians treating war-wounded soldiers and civ ed about the high number of antibiotic-resistant pathogens they ied



# Challenges of care in Ukraine

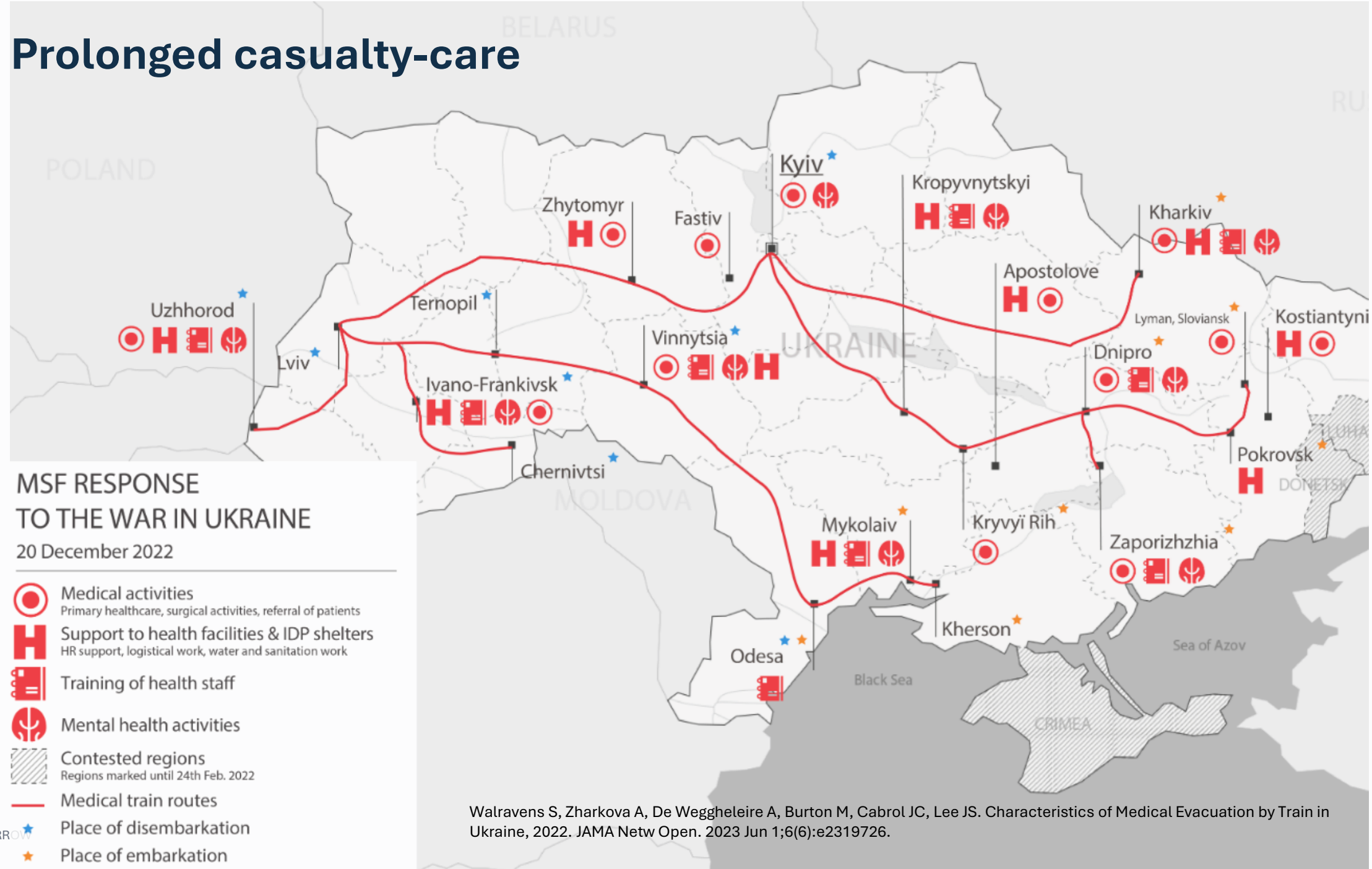
- Drone warfare
- Resource scarcity
- Available personnel
- Logistical challenges
- Psychological stress
- Prolonged evacuation



Palyvoda R, Olexandr K, Yan V et al (2024) Maxillofacial Surgery in Ukraine During a War: Challenges and Perspectives-A National Survey. Mil Med 189(9-10): 1968–75

International Rescue Committee (2024) State of Health Workforce. Mental Health in Ukraine: October 2024. Available at: https://www.rescue.org/sites/default/files/2024-11/IRC_October%202024_Mental%20Health_Health%20Workforce. pdf

# Prolonged casualty-care




Walravens S, Zharkova A, De Weggheleire A, Burton M, Cabrol JC, Lee JS. Characteristics of Medical Evacuation by Train in Ukraine, 2022. JAMA Netw Open. 2023 Jun 1;6(6):e2319726.

# Prolonged casualty-care

**1**

## Point of injury

Blast trauma; soil-contaminated wounds

**2**

## Stabilization point

Minimal capacity for infection prevention and control

**3**

## Regional hospital

Early surgery; often the first admission

**4**

## Referral center

Polytrauma, burns, rehabilitation

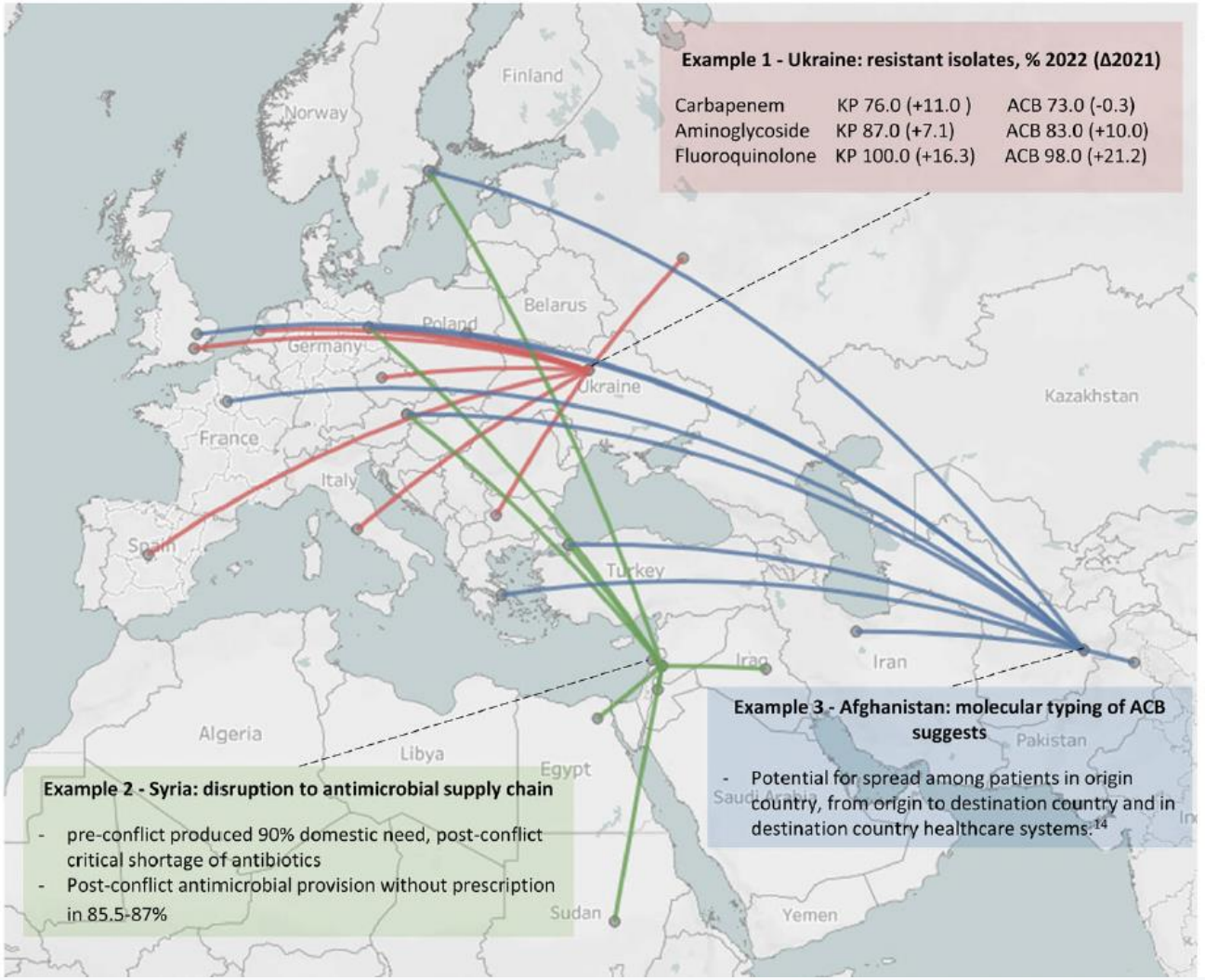
**Patients typically pass through at least two facilities before final admission.** Facilities with high circulation of resistant organisms, weak stewardship, and limited infection control increase risk of infection

Kovalchuk V, Kondratiuk V, McGann P, et al. Temporal evolution of bacterial species and antimicrobial resistance in war-related wound infections in Ukraine, 2014–2023. J Hosp Infect. 2024;152:99–104.
Holubnycha V, Kholodylo I. War impact on antimicrobial resistance and bacteriological profile of wound infections in Ukraine. Commun Med 2025.

communications medicine

# The contribution of human conflict to the development of antimicrobial resistance

Scott J. C. Pallett[1✉], Sara E. Boyd[2], Matthew K. O'Shea[1], Jessica Martin[3], David R. Jenkins[4] & Emma J. Hutley[1]




| From | Population | Displaced to |
|---|---|---|
| Ukraine | 6411343 | Ukraine |
| | 1275925 | Russia |
| | 1004382 | Germany |
| | 958519 | Poland |
| | 433638 | Czechia |
| | 183399 | UK |
| | 162672 | Spain |
| | 151750 | Italy |
| | 149231 | Bulgaria |
| | 103647 | Netherlands |
| Syria | 3535898 | Turkey |
| | 2224580 | Syria |
| | 817047 | Lebanon |
| | 660892 | Jordan |
| | 576793 | Germany |
| | 257439 | Iraq |
| | 145658 | Egypt |
| | 112432 | Sweden |
| | 93478 | Sudan |
| | 91167 | Austria |
| Afghanistan | 4457522 | Afghanistan |
| | 3413249 | Iran |
| | 1781419 | Pakistan |
| | 215677 | Germany |
| | 139394 | Turkey |
| | 74636 | France |
| | 52701 | Austria |
| | 38246 | Greece |
| | 28249 | Sweden |



Pallett SJC, Boyd SE, O'Shea MK, Martin J, Jenkins DR, Hutley EJ. The contribution of human conflict to the development of antimicrobial resistance. Commun Med (Lond). 2023 Oct 25;3(1):153. doi: 10.1038/s43856-023-00386-7. PMID: 37880348

# Microbial flora in war wounds from the Ukrainian front line

## EARLY SAMPLING

**127** Ukrainian soldiers

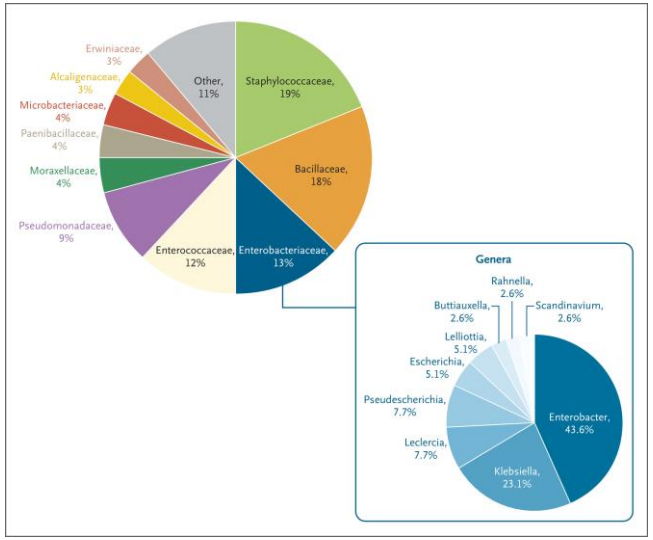
**90%** blast injuries

**7 h** median injury → swab

**100 of 127 cultures yielded bacteria**

## GROWTH

**324** nonduplicative isolates




**Dominated by common commensal and environmental organisms**

## HIGH-RISK AMR WAS UNCOMMON

**1** K. pneumoniae ST147 with notable AMR genes

**1** A. baumannii ST2 with blaOXA-23 carbapenemase

**Lack of highly resistant pathogens often reported in later care**



Dumchev K, Mc Gann P, Danyliuk O, et al. Microbial flora in war wounds from the Ukrainian front line. N Engl J Med. 2026;394:926–28.

# Microbial flora in war wounds from Ukrainian hospitals

## LONGTIDUNAL SAMPLING

**350** Ukrainian patients

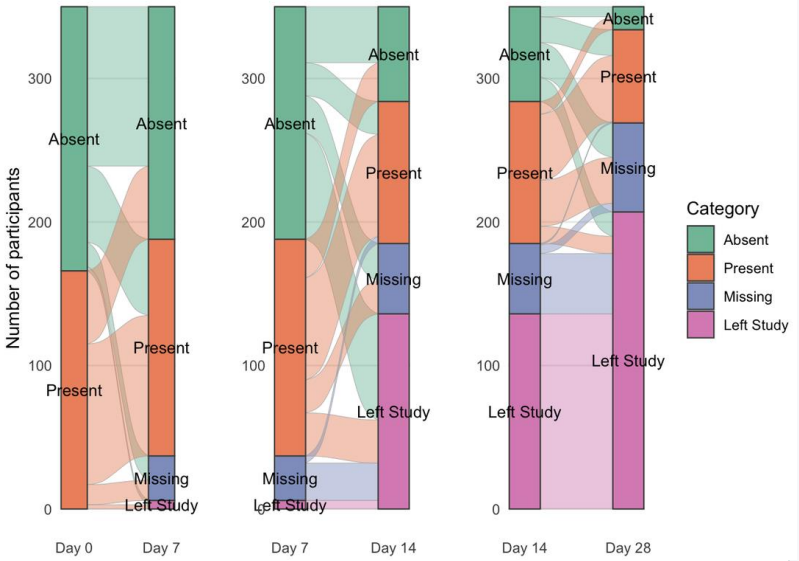
**80%** blast injuries

**6 d** median injury → swab

**547 of 1001 cultures yielded bacteria**

## GROWTH

**701** nonduplicative isolates




**61% patients with bacteria were ESKAPEE**

## HIGH-RISK AMR WAS COMMON

**86** ***K. pneumoniae*** isolates (88%) carried an extended-spectrum β-lactamase (ESBL) gene

**33** ***Acinetobacter spp.*** *Isolates* 63% carried a carbapenemase gene including blaOXA-23 (n=19)

**Many highly resistant pathogens often reported in later care**

Bills CB, et al. Bacterial profiles and trends of traumatic wounds in the Ukrainian war MHSRS. Orlando, FL. August 2026.

PART 2

# The problem:  evidence gap

# Scoping review: 76 studies across conflict and disasters

| 74% | 80% | 63% | 13% |
| --- | --- | --- | --- |
| studies were war/conflict/combat | retrospective + case series | delivered care in high-income countries | prehospital + field-hospital studies |
| **Studies are broad** | **Practice is guided by observational experience** | **Despite 90% of injury-related deaths globally occurring in LMICs** | **Evidence is limited to high-resource settings** |

Molina KC, Bills C, Bebarta VS, Fishchuk R, Mueller SW, Peers JL, Simon S, Trent SA, Ginde AA. The Evolving Frontline of Antimicrobial Resistance: Adapting Testing and Treatment for Austere and Combat Settings. Mil Med. 2026 Mar 12:usag024.
Bills CB, et al.. Care of patients with trauma related wounds: A scoping review of interventions for the care of patients injured during conflict and disasters. BMJ Open. In submission.

# Why context-specific trials matter

## Älgå et al. 2020

Pragmatic multisite RCT
Iraq + Jordan
Acute conflict-related extremity wounds

**Negative pressure wound therapy vs standard treatment**

## Result

**No clear advantage for wound closure by day 5 or net clinical benefit.**

Widely used ≠ proven effective in conflict settings

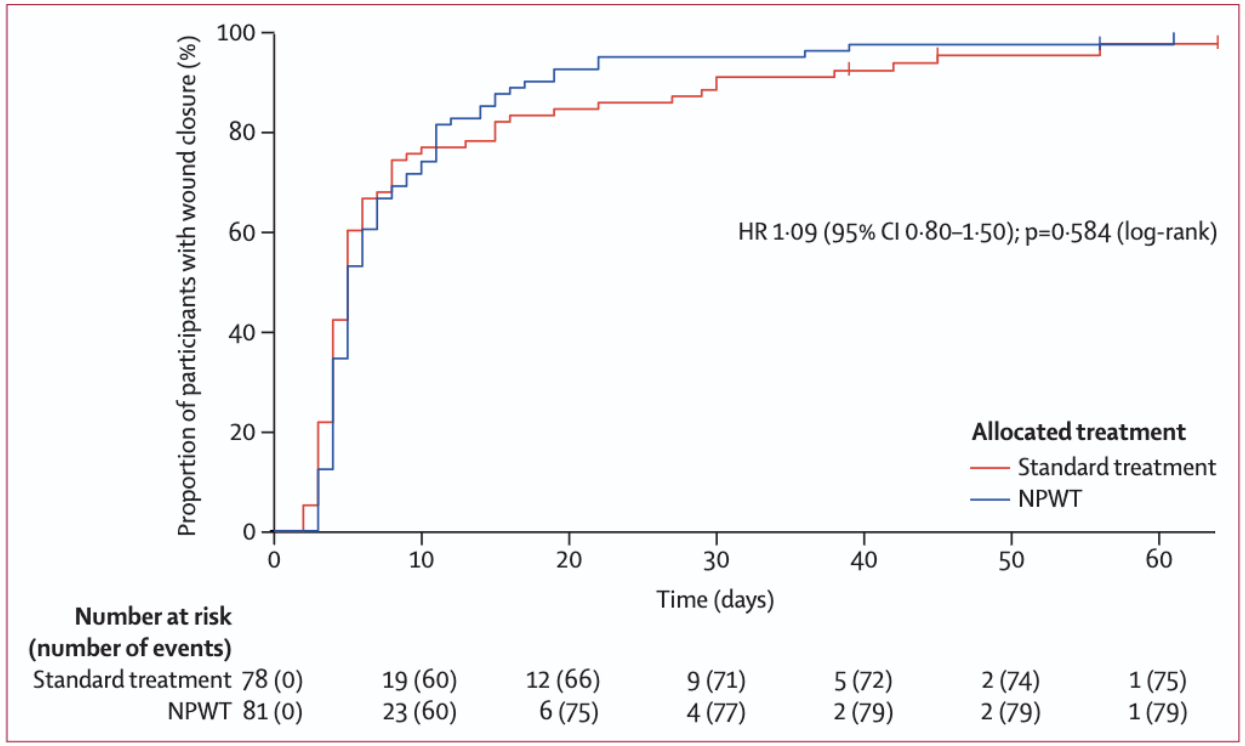



***Figure 2:*** **Probability of wound closure (Kaplan-Meier estimate) over time from randomisation**
Standard treatment is reference. HR=hazard ratio. NPWT=negative pressure wound therapy.

Älgå A, Haweizy R, Bashaireh K, et al. Negative pressure wound therapy versus standard treatment in acute conflict-related extremity wounds. Lancet Glob Health. 2020;8:e423–29.

# Why trials are hard to run during an active war

### 1 Data completeness

Attacks on energy and power make continuous data collection challenging.

### 2 Clinical priorities

Research must never overwhelm clinical care; staff time is scarce.

### 3 Logistics

Shipping samples and investigational products in and out of the country is difficult.

### 4 Layered approvals

Local ethics, national regulators, and US IRBs each add time.

### 5 Unstable enrollment

Patient flow varies with local and national threats.

### 6 Attacks on health care

Thousands of documented attacks on facilities disrupt operations (WHO).

Bills CB, et al. Lessons Learned from Implementation of Antimicrobial Resistance Research to Improve Outcomes of Traumatic Wounds in Ukraine MHSRS. Orlando, FL. August 2026.

# Without trials, treatment relies on extrapolation and caution

1. **Empiric practice is cautious and broad**
   JTS, WHO, ICRC all have recommendations

2. **Studies cannot be compared**
   Wide variation in primary outcomes limits comparison of effectiveness

3. **One-size protocols may fail**
   Resistance patterns differ by hospital and department

4. **Ongoing surveillance is thin**
   Few in-country data exist, especially early sampling near the point of injury

International Committee of the Red Cross. War wounds: basic surgical management—the principles and practice of the surgical management of wounds produced by missiles or explosions. Geneva: International Committee of the Red Cross, 2015.

PART 3

# Possible solution: Master protocol

# What is a master protocol?

## A single overarching protocol

**Shared infrastructure**
Sites • governance • data systems

**Shared standards**
Eligibility • outcomes • safety

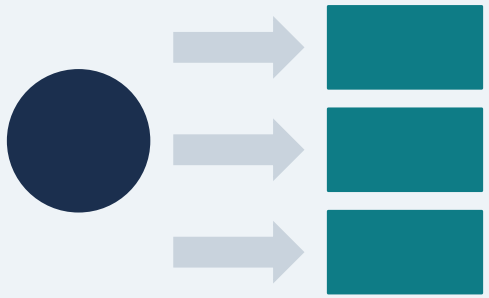
**Multiple questions**
Several interventions • populations

**Adaptability**
Arms can enter or leave over time

*Source: FDA. Master Protocols for Drug and Biological Product Development, draft guidance, June 2026.*

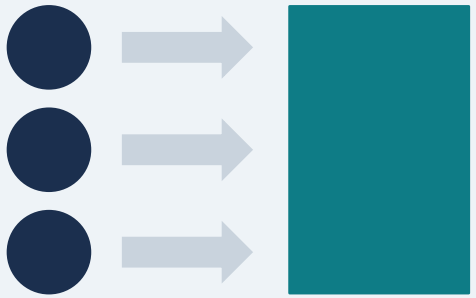
# Three master protocol designs: basket, umbrella, and platform

## Basket



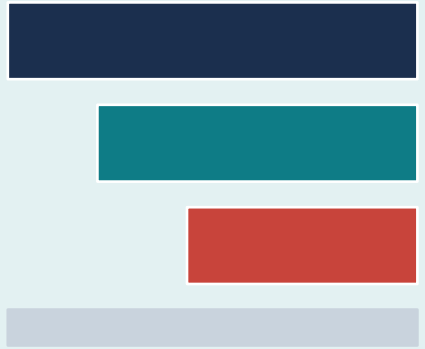
**One therapy, many diseases or subtypes**

## Umbrella



**Many therapies, one disease, often by biomarker**

## Platform



**Many therapies, one disease; arms enter and leave over time**

*e.g., PACT-ARROW*

Woodcock J, LaVange LM. Master protocols to study multiple therapies, multiple diseases, or both. N Engl J Med 2017;377:62-70. doi:10.1056/NEJMra1510062

# Master protocols trade upfront complexity for speed and efficiency

## Advantages

- Faster
- Shared control and infrastructure reduce duplication
- Standardized eligibility, outcomes, and data
- Flexible: arms can be added, dropped, or combined
- Pre-positioned capacity for rapid response

## Challenges

- Heavier upfront design, approval, and governance work
- Statistical complexity: multiplicity, shared or changing controls
- Need an expert body to decide which arms enter
- Wide scope can dilute focus if outcomes are not standardized
- Sustained funding is required to keep the platform alive

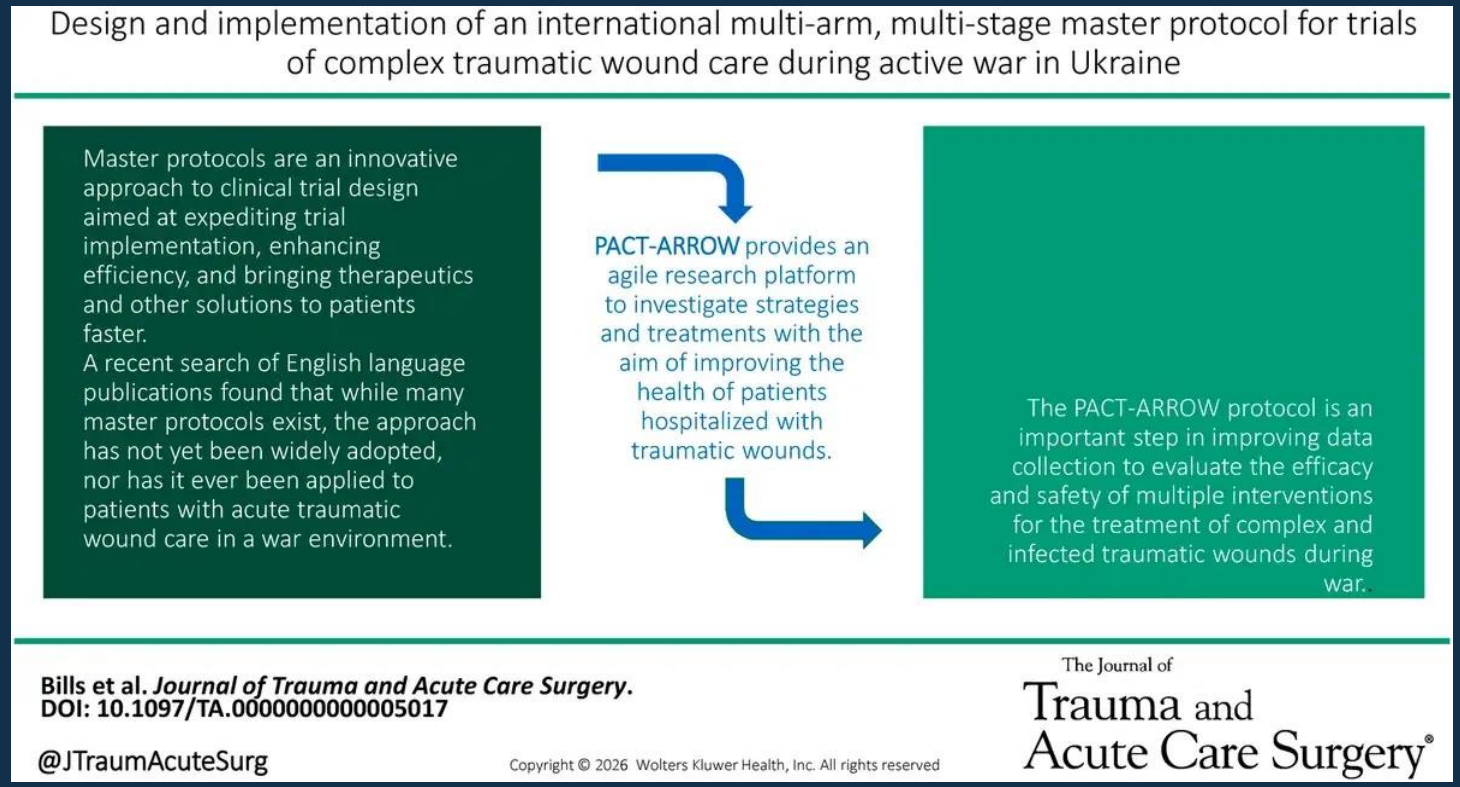
Woodcock J, LaVange LM. Master protocols to study multiple therapies, multiple diseases, or both. N Engl J Med 2017;377:62-70.
Bills CB, et al. Design and implementation of an international multiarm, multistage master protocol for trials of complex traumatic wound care during active war in Ukraine (PACT-ARROW). J Trauma Acute Care Surg 2026;101:S58-S65

# Why a master protocol suits acute wound care in war

| War challenge | Master protocol response |
| --- | --- |
| **Approvals take months** | Ethics and regulatory frameworks approved once, then extended through trial-specific appendices |
| **Data burden is high** | Minimal standardized dataset; follow-up limited to hospital discharge or day 28 |
| **Outcomes are inconsistent** | A preset menu of primary outcomes enables comparison across trials |
| **Needs change quickly** | Trials can start and stop independently as the epidemiology changes |

PART 4

# PACT-ARROW: applying a platform model to traumatic wounds in Ukraine



# ARROW

## ANTIMICROBIAL RESISTANCE RESEARCH TO IMPROVE OUTCOMES OF TRAUMATIC WOUNDS

**PACT-ARROW master protocol**

Shared eligibility, outcomes, randomization approach, data systems, oversight

**ARROW**

Observational cohort

**HERO**

Electroceutical dressing trial; n=150

**Future trials**

Prevention, topical, antimicrobial, surgical, critical illness

*Steering committee screens which interventions enter the platform*

Bills CB, et al. Design and implementation of an international multiarm, multistage master protocol for trials of complex traumatic wound care during active war in Ukraine (PACT-ARROW). J Trauma Acute Care Surg 2026;101:S58-S65

# PACT-ARROW Overview

| | |
|---|---|
| **Collaborator** | National CCC in Ukraine (IF), Ukraine CRO, CU |
| **Purpose** | To test safety, efficacy, and or effectiveness of wound care interventions |
| **Design** | Multiarm, multistage (MAMS) platform master protocol |
| **Population** | Hospitalized adults with acute traumatic wounds in Ukraine |
| **Comparator** | Intervention + standard of care vs standard of care |
| **Follow-up** | Through hospital discharge or day 28 |

# Eligibility

## Include

- Age 18 or older
- Admitted at a participating Ukrainian site
- At least one traumatic wound
- Less than 60 days from injury
- Informed consent

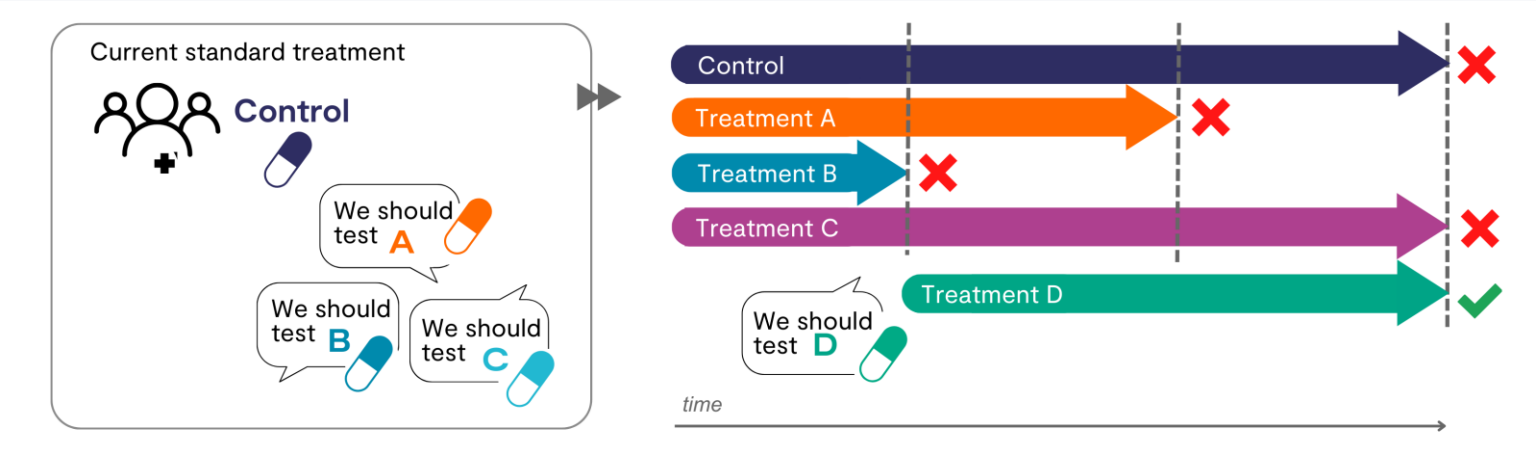
## Exclude

- Prisoner or prisoner of war
- Discharge or transfer expected within 24 h
- Moribund (life expectancy under 48 h)
- Comfort care only
- Unable or unwilling to follow procedures

## Set per trial

- Pathogen or syndrome
- Wound severity
- Time since injury
- Contraindications and prior therapies

# Interventions




## Prevention

IPC, prophylactic antibiotics

## Topical

Dressings, ointments, non-surgical debridement

## Antimicrobials

Approved or repurposed older agents

## Surgery

Novel or established surgical strategies

## Complications

Treatments for sepsis or other wound-associated complications

## Strategies

Risk prediction, diagnostics

# A standardized outcome framework

## Survival

All-cause mortality

## Recovery

Wound healing
Hospital discharge

## Progression

Clinical signs of infection
Culture and colonization
Major complications

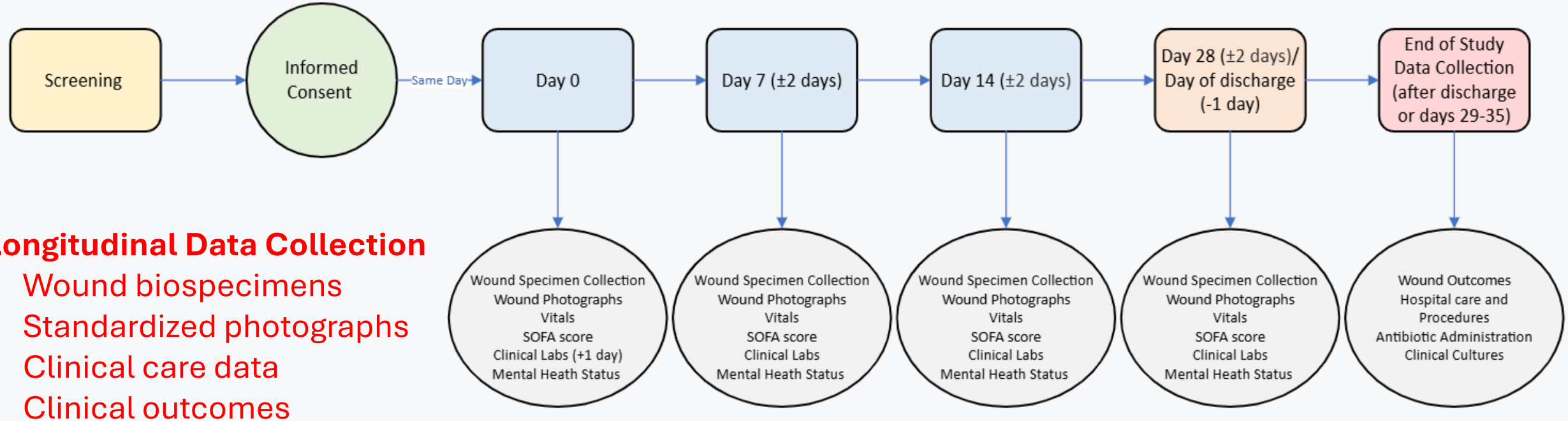
**Follow-up through hospital discharge or day 28**

Secondary: organ failure, secondary infections, wound photography, procedures, microbiology, patient-reported outcomes

*Primary outcome examples (one chosen per trial)*

ARROW

- Prospective longitudinal cohort study
- 5 civilian hospitals in Ukraine (mainly military casualties)
- 2 front-line and 3 referral centers
- Hospitalized adult patients with acute traumatic wounds
- Sample size: Up to 1000 patients total
- Duration: 1.5 years of data collection
- Participants followed up to 28 days (in-hospital)



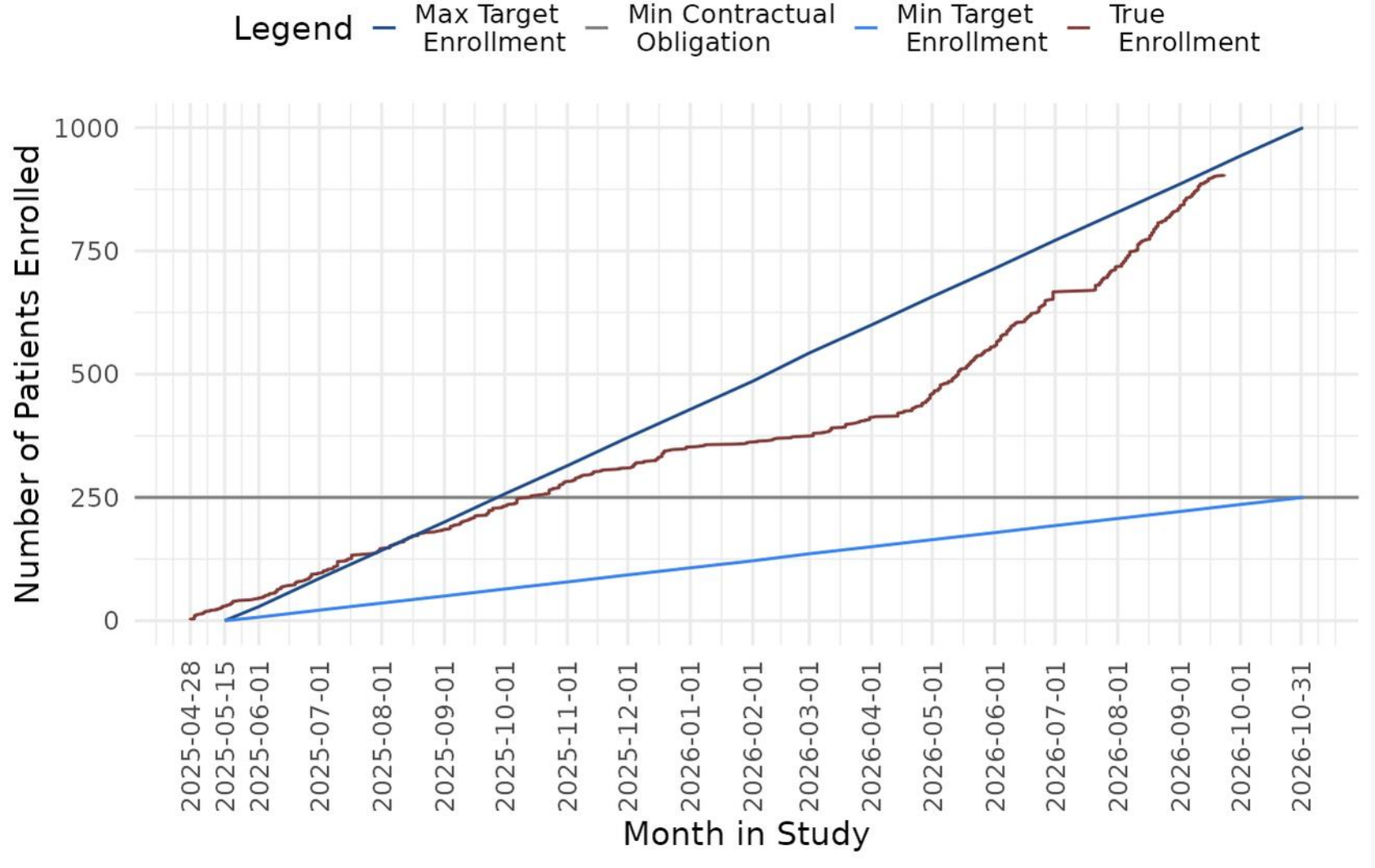

**Longitudinal Data Collection**

- Wound biospecimens
- Standardized photographs
- Clinical care data
- Clinical outcomes

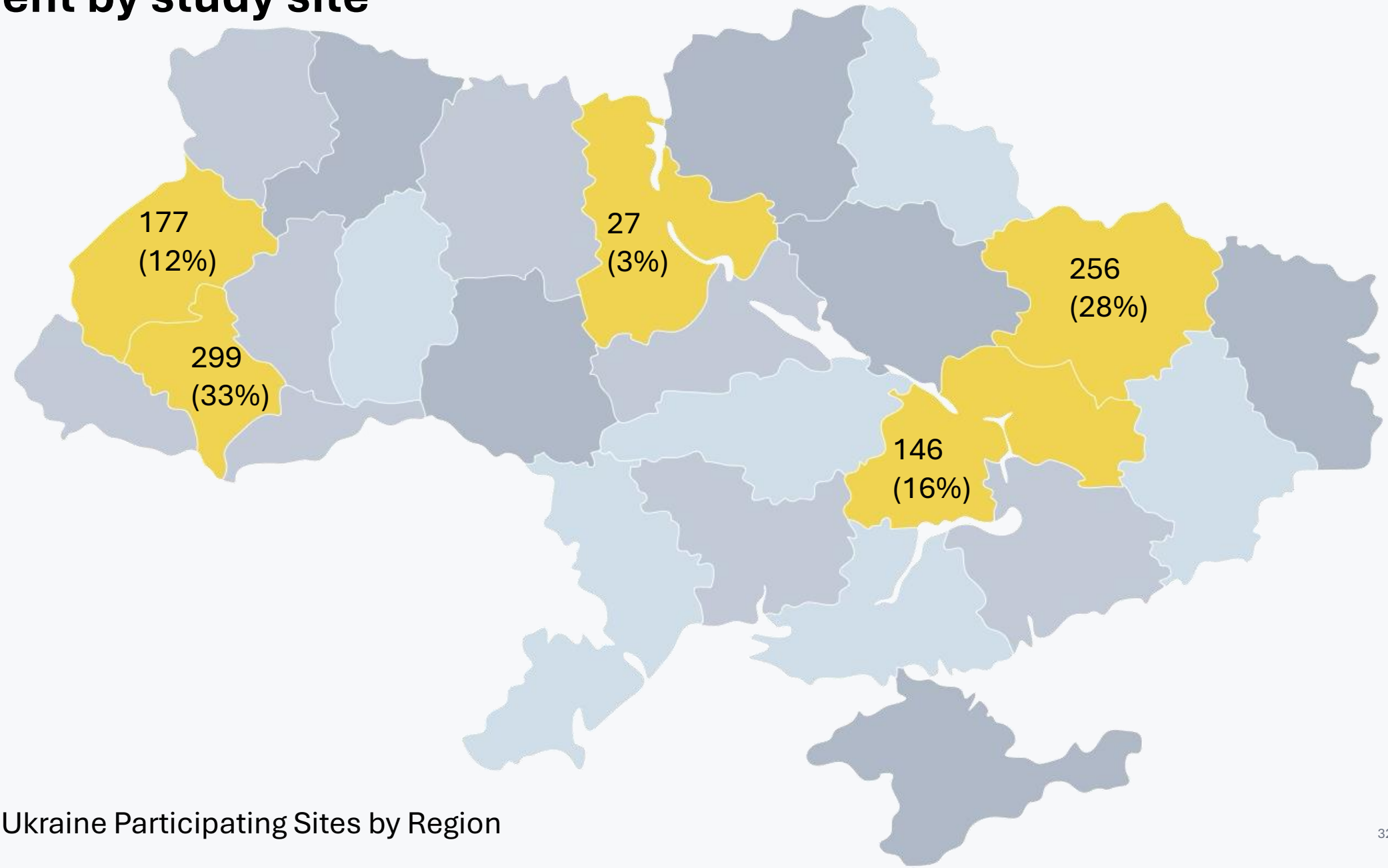
# Enrollment by month

ARROW Enrollment

N=905



# Enrollment by study site

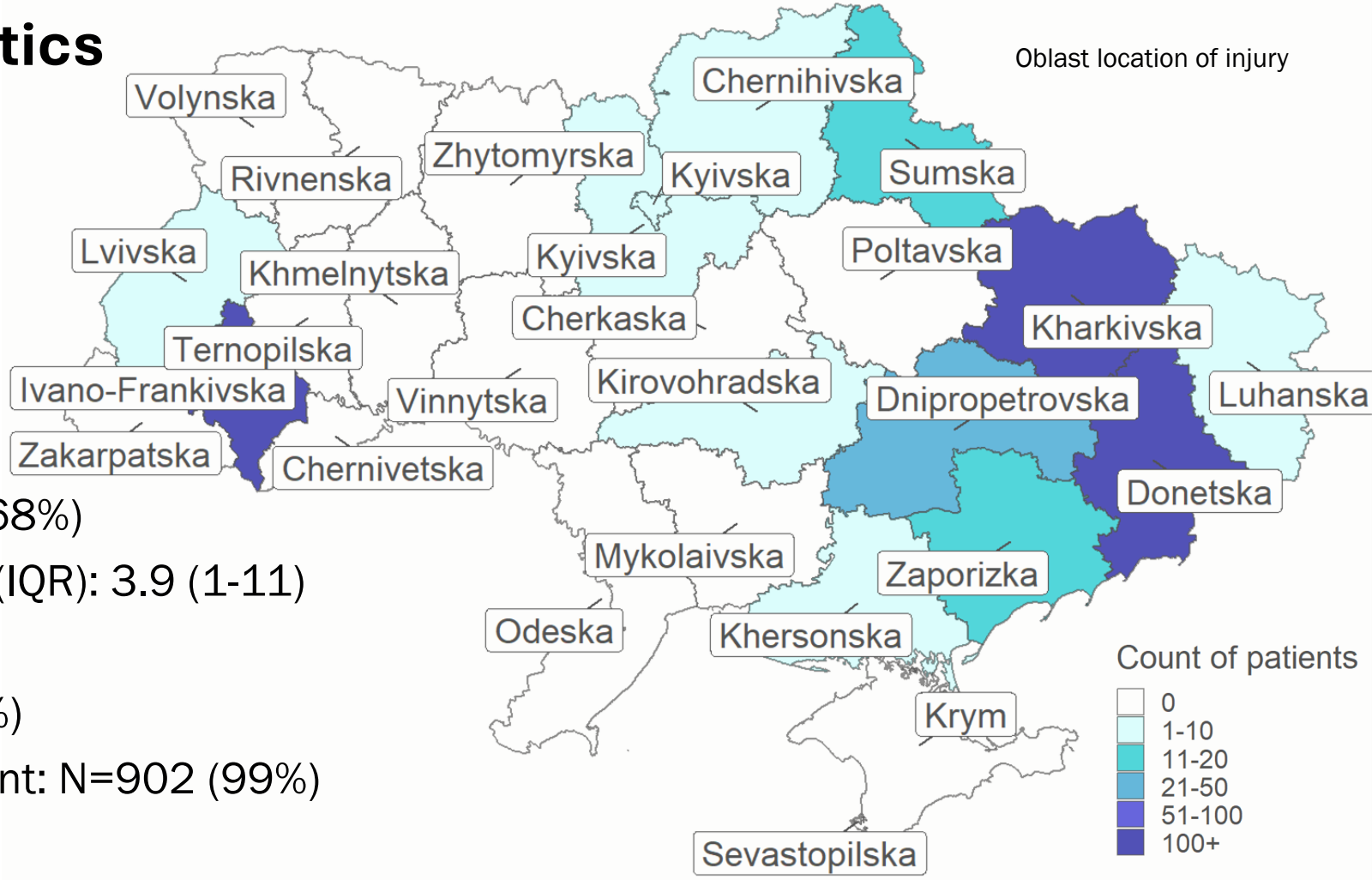



Ukraine Participating Sites by Region

# Patient injury characteristics

**Total Patients Enrolled: 905**

- Male: N=758 (84%)
- Median age (range): 42 (18-87)
- Transported by ambulance: N=614 (68%)
- Days from injury to hospital, median (IQR): 3.9 (1-11)
- **Penetrating** Injury: N=820 (91%)
- **Blast** Injury Mechanism: N=510 (56%)
- Clinical signs of infection at enrollment: N=902 (99%)
- Amputation: N=82 (9%)

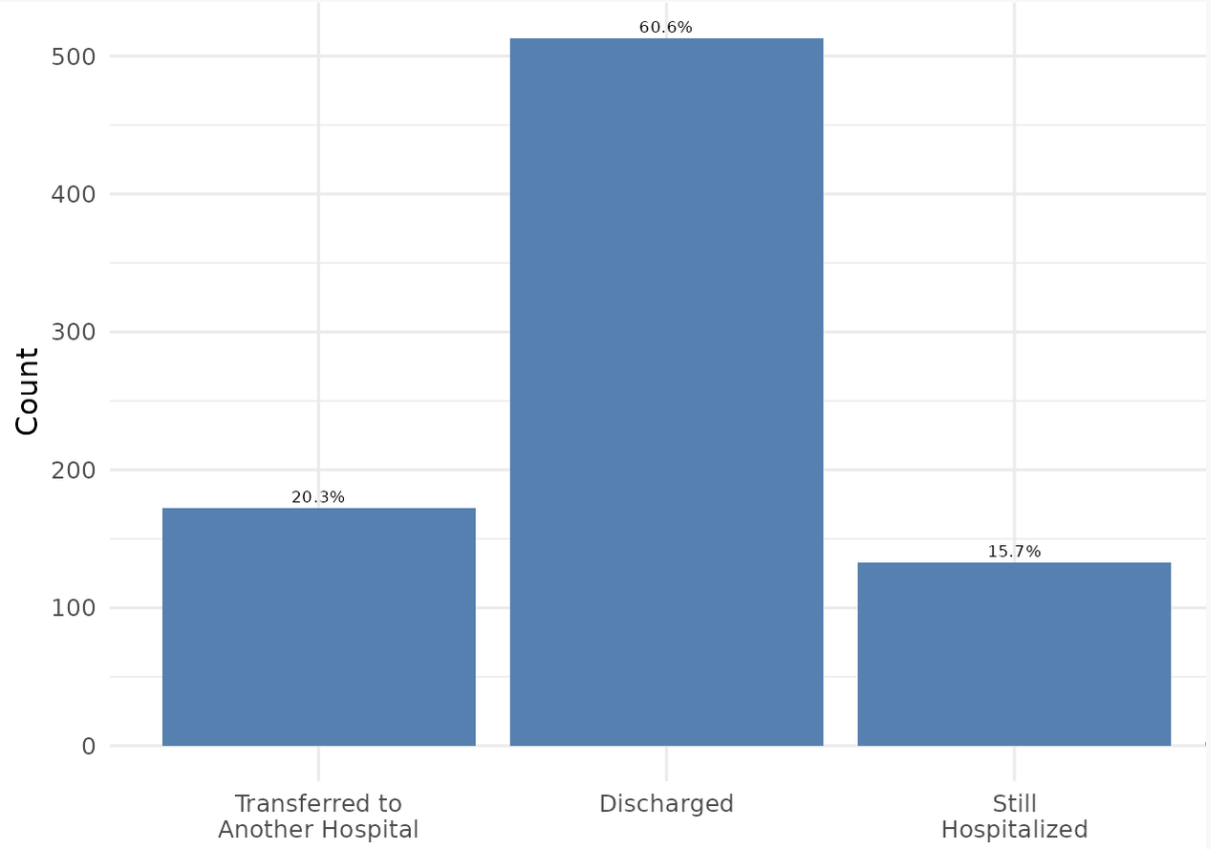



- Prolonged time to hospitalization with high rates of penetrating blast injuries and clinical signs of infection
- More than 50% of study participants injured in 2 Oblasts

# Clinical severity and disposition

- 36% of study patients were transferred or are still hospitalized at Day 28
- Substantial site-specific variation

| Characteristic | N = 846[1] |
|---|---|
| Amputation | 82 (9.7%) |
| Admitted to ICU | 22 (2.6%) |
| Mechanical ventilation | 10 (1.2%) |
| Vasopressor administered | 2 (0.2%) |
| Blood product administered | 47 (5.6%) |
| Central line | 31 (3.7%) |
| Thoracostomy | 4 (0.5%) |
| Fasciotomy | 13 (1.5%) |
| Infection (excluding wound infection) | 32 (3.8%) |



# Bacteria type and AMR

***Data in collaboration with the Multidrug-Resistant Organism Repository and Surveillance Network (MRSN)***

Many ESKAPEE bacteria isolated from wounds in Ukraine had at least one concerning resistance gene to known commonly used antibiotics

| Species | Total Bacteria N=701 (%) |
|---|---|
| Enterococcus spp. | 150 (21.4%) |
| Klebsiella spp. | 115 (16.4%) |
| Acinetobacter spp. | 64 (9.1%) |
| Enterobacter spp. | 54 (7.7%) |
| Pseudomonas aeruginosa | 47 (6.7%) |
| Staphylococcus spp. | 39 (5.6%) |
| Escherichia coli | 28 (4.0%) |
| Other species | 204 (29.1%) |

- **Klebsiella species**
  - 86 (88%) isolates had extended-spectrum β-lactamase (ESBL)
  - 81 (83%) of isolates had resistance to carbapenemases
- **Acinetobacter species**
  - 33 (64%) had at least one carbapenemase resistance gene
  - 28 (54%) of isolates carried an ESBL resistance gene
- **P. aeruginosa**
  - 8 (17%) isolates had at least one resistance gene

# HERO

Healing Electroceutical Dressing for the Recovery of Open Wounds

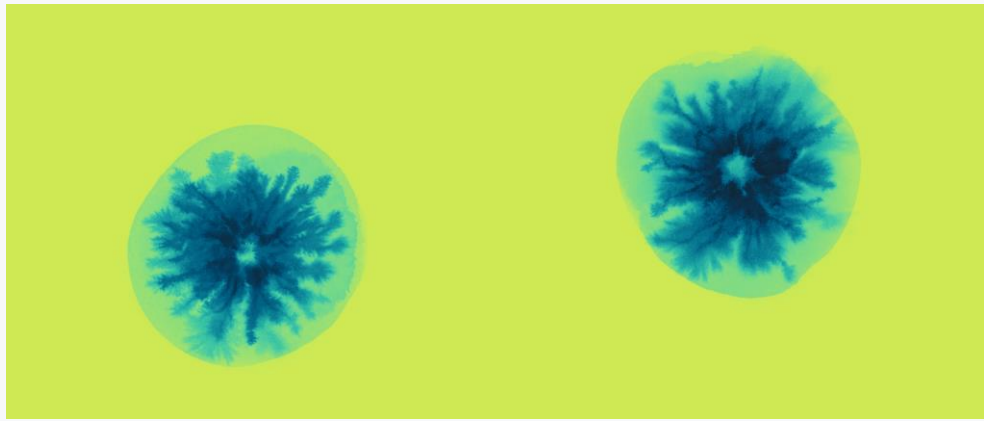
BIOLOGY

## Bacteria Use Brainlike Bursts of Electricity to Communicate

With electrical signals, cells can organize themselves into complex societies and negotiate with other colonies

By Gabriel Popkin, Quanta Magazine on September 9, 2017





University of Pittsburgh




| | |
|---|---|
| Methods: RCT | Ethics approved as Appendix to PACT ARROW |
| Objective: Efficacy of Wireless Electroceutical dressing (WED) | 4 of 5 sites actively enrolling |
| Intervention: PowerHeal Dressing | 73 patients enrolled |
| Comparator: SOC | 150 total (1:1) |
| Decreased clinical signs of infection & improved healing | Anticipated end 11/30/2025 |

# PACT-ARROW proposed interventions

## POC molecular or Rapid AST

- **Gap:** Clinicians interpret wounds as infected >99%, there is a lack of frontline culture data, and the positivity rate of cultures is 50%, leads to potential discordance in antibiotic use
- **Question:** Can POC testing at frontline sites lead to ***decreased or tailored antibiotic use*** or earlier in a patients care?

## Topical enzymatic dressing

- **Gap:** Prolonged time to definitive care coupled with scarcity of surgical resources leads to ***delays in debridement and surgical care***
- **Question:** Can non-surgical debridement be performed earlier to the time of injury and does it lead to decreased infection and promote earlier wound healing?

## Serial AI-assisted wound photographs

- **Gap:** Wound assessment for infection is subjective, provider dependent and often related to experience leading variability in wound treatment
- **Question:** Can AI-assisted models be used to support both ***earlier diagnosis*** of wound infection and support ***more objective measures*** of wound outcomes?

# Lessons from implementation in an active war zone

1. **Start with an observational cohort**
   ARROW showed which data are feasible before any intervention was tested

2. **Keep the data burden small**
   Minimum necessary dataset; limit follow-up

3. **Solve logistics locally**
   A Ukrainian carrier ships samples in country; an in-country CRO brokers international shipping

4. **Partner for regulatory speed**
   A national coordinating center; local CRO guide multi-level approvals

# Discussion

1. Infected traumatic wounds and antimicrobial resistance are a growing threat in Ukraine
2. There is little trial evidence for wound care in active conflict
3. Master protocols pre-position ethics approvals, infrastructure, and standard outcomes
4. PACT-ARROW applies a MAMS platform to acute wound care in Ukraine

RESOLUTE
Research to Improve Outcomes in Ukraine

# ARROW

**A**NTIMICROBIAL **R**ESISTANCE **R**ESEARCH TO IMPROVE **O**UTCOMES OF TRAUMATIC **W**OUNDS


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