

# IDCRP



Uniformed  
Services  
University



## Enteric Disease

Major Dan Burns

Infectious Diseases Registrar

UK PI PREVENT TD Trial



# The Problem

## HERRICK data

- 40% attack rate over 6 months
- 2.7 days off and 4 days underperforming per episode
- Total – 45000 man days lost on HERRICK 10 (or 2 companies at any one time)
- Risk to self while underperforming

## Kenya data

- ASKARI STORM 15% rate
- ASKARI SERPENT 13 % rate

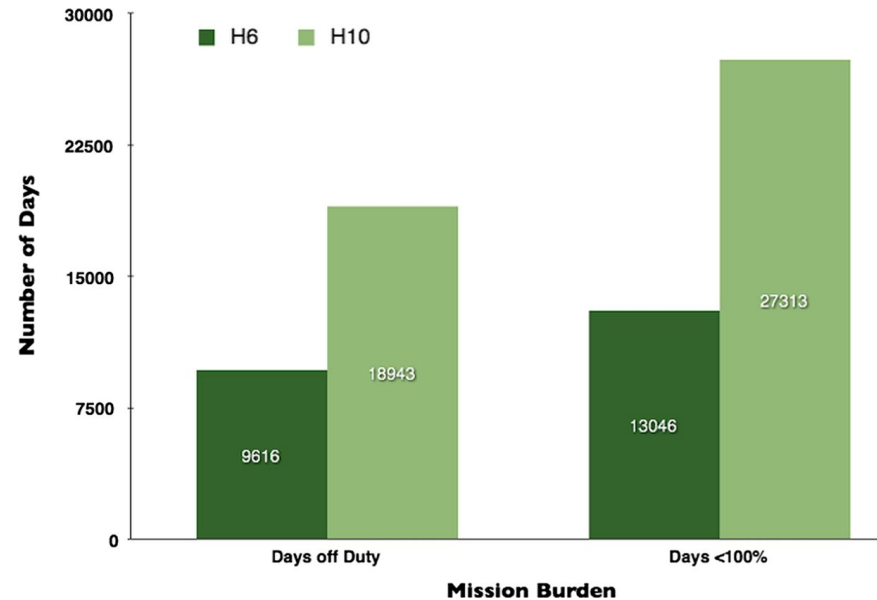
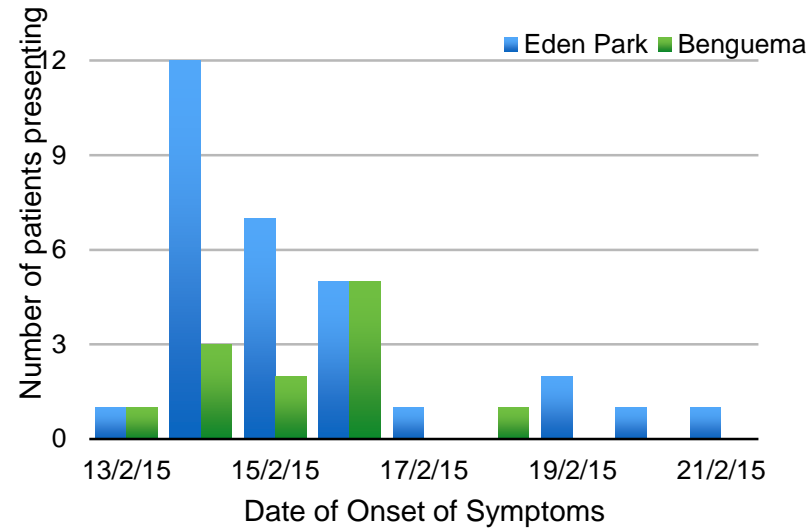
## Op TRENTON data

127 diarrhoeal episodes over 4months

6-7 times risk of IBS

Risk to self while underperforming

Diarrhoeal Outbreak Op GRITROCK 13-21 Feb 2015: All patients with diarrhoea



Connor P, Hutley E et al. Enteric disease on Operation HERRICK. *J* 2013;159:229–236. doi:10.1136/jramc-2013-000084.

An outbreak inside an epidemic: managing an infectious disease outbreak while treating Ebola. Horne S, Forbes K, Burns D, et al. *JRAMC* 2017;163:7-12.

Epidemiology and etiology of diarrhea in UK military personnel serving on the United Nations Mission in South Sudan in 2017: A prospective cohort study. [Biswas JS](#), et al. *TMID*. 2019 Mar - Apr;28:34-40. doi: 10.1016/j.tmaid.2018.12.004. Epub 2018 Dec 12.

# Current solutions



# Solutions 1: Early treatment

Clinical

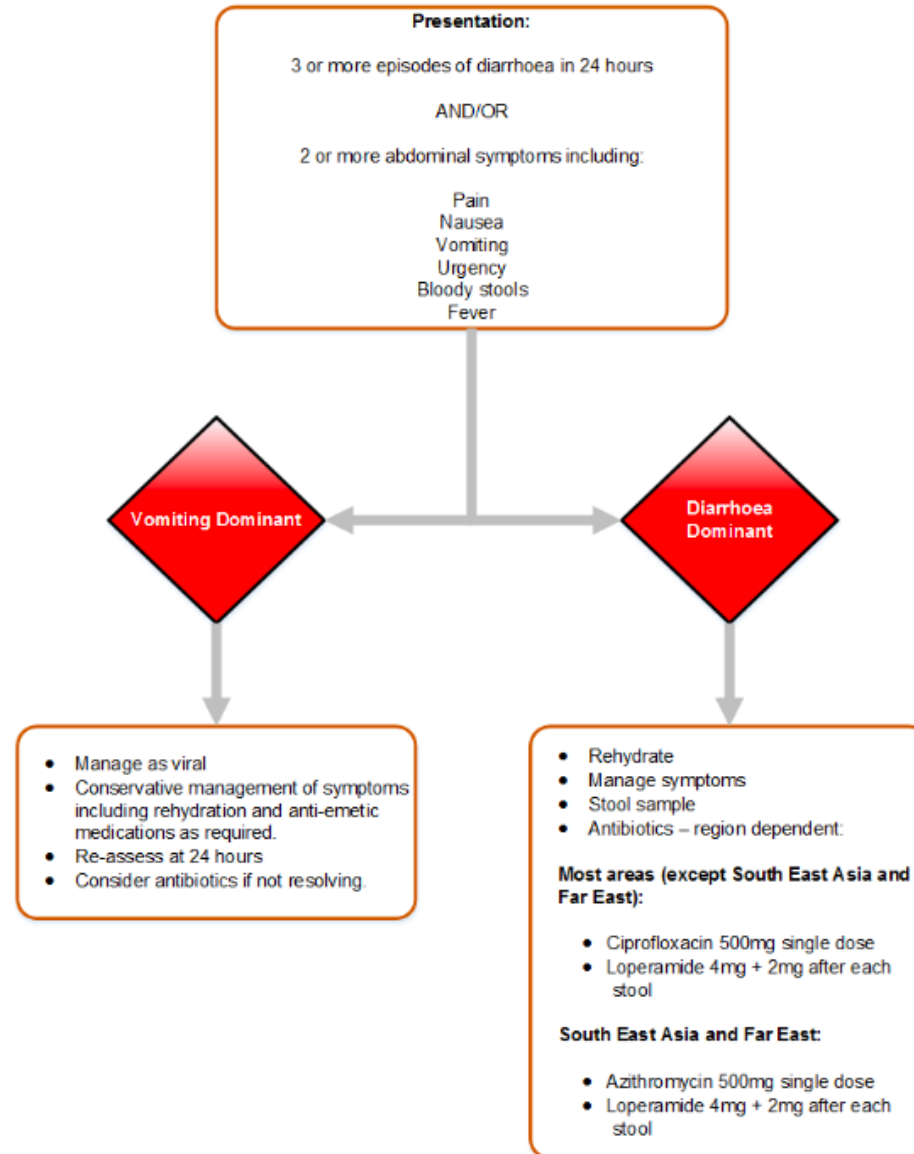
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# Early treatment in practice

## ASKARI STORM 2PARA 2018

- Post CALFEX phase
- 35 cases over 12 hours within a FOB
- Severe stomach cramps, diarrhoea
- Crowded camp (approx 1000), sub-optimal latrines and intermittent water
- Single dose abx
- Loperamide



	Length of Symptoms	Time Bedded Down	Time from Tx to clinical cure
Average	12hrs	36hrs	28hrs
Range	1 – 36 hrs	24 – 58hrs	17 – 49hrs

- 2987 man hours lost
- **? 1680 man hours saved (2 days/man)**

Demographics?	?
Age?	24.5 (19-35)?
Gender?	33 Male, 2 Female?
Trade?	31 Inf, 3 CMT, 1 Log?
Nationality?	32 British, 3 US?

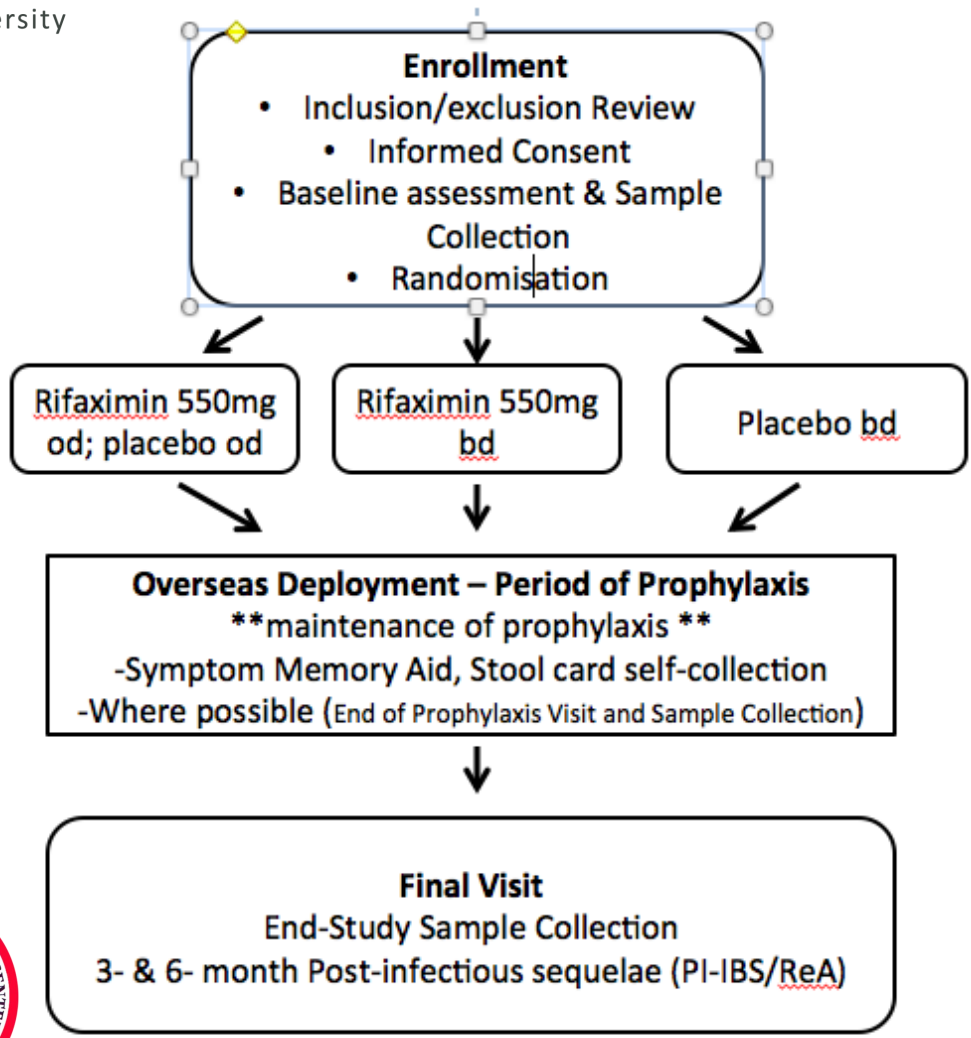
Captain John Colvin  
 Captain Emily Reilly  
 Major Paddy Wilkinson

# Solution 2: Antimicrobial prophylaxis

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## Prevent TD Trial





# Research in practice



	<b>US Subjects</b>	<b>UK Subjects</b>	<b>Total</b>	<b>p-value</b>
<b>Total N (%)</b>	144(42)	195(58)	339	
<b>Age</b>				
Median (IQR)	28(23-35)	26(23-30)	27(23-32)	0.0336
<b>18-24</b>	54(38)	71(36)	125(37)	0.0035
<b>25-35</b>	57(40)	104(53)	161(47)	
<b>35-50</b>	32(22)	20(10)	52(15)	
<b>&gt; 50</b>	1(<1)	0(0)	1(<1)	
<b>Gender</b>				
Male	120(83)	189(97)	309(91)	<0.0001
Female	24(17)	6(3)	30(9)	
<b>Travel Duration (days)</b>				
Median (IQR)	48(22-104)	44(40-48)	44(37-49)	0.3447
<b>Duration of Prophylaxis (days)</b>				
Median (IQR)	31(18-42)	35(32-37)	35(27-41)	0.4909



	<b>US Subjects</b>	<b>UK Subjects</b>	<b>Total</b>
<b>Number of Subjects who met criteria for TD only</b>	24	11	35
Duration of TD Hours: Median (IQR)	24.0(8.0-36.0)	16.0(8.0-64.0)	24.0(8.0-48.0)
Number of subjects unable to work due to incapacitation from TD	15(62)	8(72)	23(66)
Decreased level of activity	9(60)	6(75)	15(65)
Unable to participate	6(40)	2(25)	8(35)
Total number of unformed stools in a TD episode: Median (IQR)	6.0(3.5-12.5)	9.0(3.0-14.0)	6.0(3.0-13.0)
Max number of Unformed stools in 24-hour period: Median (IQR)	4.0(3.0-7.0)	6.0(4.0-9.0)	4.0(3.0-7.0)
<b>Moderate-Severe TD</b>	15(62)	8(72)	23(66)
AWD	12(80)	5(62)	17(74)
Febrile	1(6)	2(25)	3(13)
Dysentery	2(13)	1(13)	3(13)

**Results end of 2019**

**Applications: short term, high risk overseas deployments on risk assessed basis**

# Research resilience

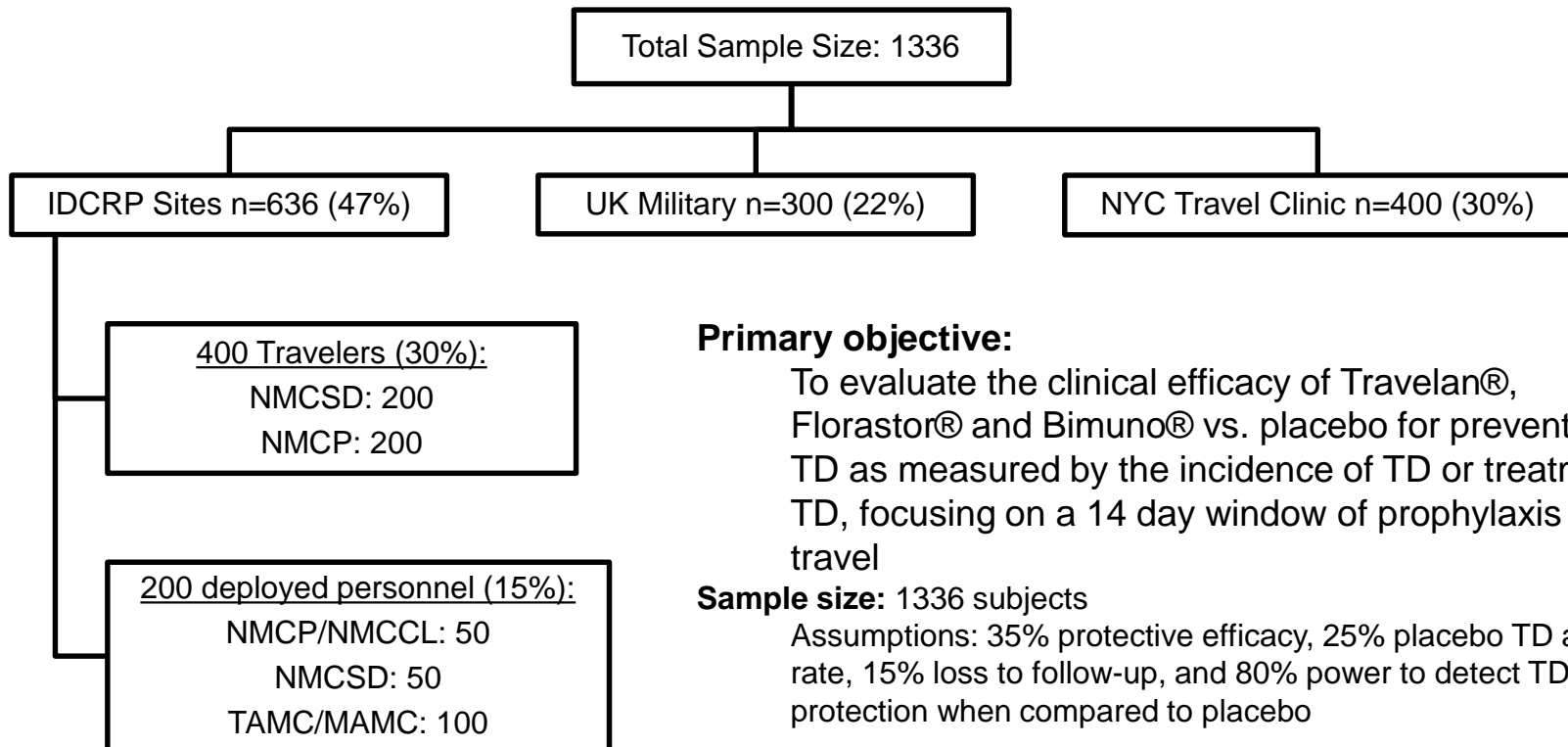
- 12 Investigators trained
  - 4 GDMOs
  - 4 nurse investigators
  - 4 medicine trainees
- Defence pathology
  - 4 BMS deployed
  - Research laboratory set up
  - -80 freezer funded
- Research monitor trained
- Drug delivery & storage
- Pharmacist & pharmacy tech
- Existing Caldicott compliant record storage






**Triservice, multiple cadres (nursing, MOs, pharmacy, BMS)  
Used existing research infrastructure & created new**

# Solution 3: Microbiome based prophylaxis

## A Randomized, Double-Blind, Placebo-Controlled Trial Evaluating the Efficacy of Non-Antibiotic OTC Products for Travellers' Diarrhoea (TD) Prevention (P4TD)





	<b>Travelan®</b> Immuron Ltd  (passive immunoprophylaxis)	<b>Florastor®</b> Biocodex Inc  (probiotic)	<b>Bimuno®</b> Clasado  (prebiotic)
<b>Active ingredient:</b>	anti-ETEC HBC	<i>Saccharomyces boulardii</i>	β-Galacto-Oligosaccharide [B-GOS]
<b>Dose used in prior studies showing efficacy:</b>	400 mg tid with ETEC challenge 200 mg tid with ETEC challenge	500 mg/d and 1000 mg/d starting 5 days before travel	2.76g B-GOS once daily
<b>Commercially available formulation</b>	200 mg caplet	250 mg capsule 500 mg sachet	3.65g sachet 2.76g pastille
<b>Manufacturers recommended dose</b>	1 caplet tid with meals	2 capsules 1-2 times daily 1 sachet 1-2 times daily	Travelaid: 2.76g/pastille 3 pastilles once daily starting 7 days before travel.
<b>Available Form</b>	<b>Pack - 30 caplets</b>	<b>Bottle – 100 capsules</b>	<b>Packet – 30 sachets</b>
<b>Cost:</b>	\$25.57 (0.85/pill) £19.77 (0.66/pill)	\$55.09 (0.55/pill) £42.50 (0.43/pill)	\$12.15 (0.41/sachet) £9.36 (0.31/sachet)
<b>API Dose selected for P4TD: (start 3 days before and continue for 14 days during travel)</b>	<b>AM DOSE:</b> 400 mg <b>PM DOSE:</b> 400 mg	<b>AM DOSE:</b> 500 mg <b>PM DOSE:</b> 500 mg	<b>Option 1:AM DOSE:</b> 2.76 g <b>PM DOSE:</b> Placebo

**Cheap, safe, physiological  
?dosed in rations**

# Summary

- Military diarrhoea remains a threat
- Degrades individual & collective performance and combat power
- Limitations of existing tools require innovative solutions
- Early treatment reduces burden
- Rifaximin prophylaxis may be a new tool
- Microbiome focused solutions likely to be cheaper and easier to dose
- Successful enteric research programme develops research capacity and resilience across cadres and build US-UK relationship



# IDCRP

# Thanks



- Lt Cols Fitchett & Hutley
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- 2PARA
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  - Sgt Young
  - Cpl Haffenden & Mills
  - Majors O’Sullivan & Tom Troth
  - Sqn Leaders Nevin & Eveson
  - Capt Reilly, Colvin, Geddes & Matthews
- Research monitor – Sqn Leader Mulvanney
- Pharmacy team
  
- Cols Woods, Connor & Wilson & Gp Captain Lamb

