UWTASP
tele-antimicrobial stewardship program

5 October 2021

ID Week Highlights

- Alyssa Castillo
- Zahra Kassamali Escobar
- Chloe Bryson-Cahn

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7 vs 14 Days Abx for Febrile UTI in Men:

"Trials That May Change Your Practice"

JAMA | Original Investigation

Effect of 7 vs 14 Days of Antibiotic Therapy on Resolution of Symptoms Among Afebrile Men With Urinary Tract Infection

A Randomized Clinical Trial

Dimitri M. Drekonja, MD, MS; Barbara Trautner, MD, PhD; Carla Amundson, MA; Michael Kuskowski, PhD; James R. Johnson, MD

Drekonja et al. JAMA. 2021 Jul 27;326(4):324-331

- **Controversy:** How long should we treat men with febrile UTI? Are they always truly "complicated" infections?
- **Response:** Shorter may be better!

7 vs 14 Days Abx for Afebrile UTI in Men:

"Trials That May Change Your Practice"

- Randomized controlled, non-inferiority trial
- Double-blind, placebo-controlled
- N = 272 total patients
- Patients randomized to either:
  - 7d abx + 7d placebo
  - 14d abx
- Treated with either:
  - Ciprofloxacin
  - TMP-SMX

Table 1. Baseline Demographics and Comorbid Conditions[a]

Variable	7-Day antimicrobial + 7-day placebo group (n = 136)[b,c]	14-Day antimicrobial group (n = 136)[c]
Age, median (IQR), y	70 (62-73)	70 (62-75)
Race[d,e]	(n = 135)	(n = 135)
White	107 (79)	105 (78)
Black	26 (19)	23 (17)
Native American	1 (1)	5 (4)
Multiple races	1 (1)	2 (1)
Hispanic/Latino ethnicity[d,f]	5/132 (4)	8/134 (6)
Charlson comorbidity index, median (IQR)[g]	1 (0-2)	1 (0-2)
Urinary tract-related comorbidities	(n = 136)	(n = 136)
Any prior UTI	84 (62)	78 (57)
Prostatic hypertrophy	56 (41)	47 (35)
Urinary incontinence	44 (32)	52 (38)
Intermittent catheter use	24 (18)	23 (17)
Prostate cancer	21 (15)	23 (17)
Urethral stricture	17 (13)	16 (12)
Prior prostatitis	16 (12)	18 (13)
Indwelling catheter use	8 (6)	8 (6)
Nonurinary comorbidities	(n = 136)	(n = 136)
Diabetes	46 (34)	60 (44)
Cerebrovascular accident	13 (10)	5 (4)
Chronic kidney disease	8 (6)	14 (10)
Spinal cord injury	5 (4)	6 (4)
HIV	2 (1)	2 (1)
Most common symptoms associated with UTI diagnosis	(n = 136)	(n = 136)
Dysuria	93 (68)	88 (65)
Frequency	80 (59)	70 (51)
Urgency	52 (39)	39 (29)

High rates of BPH and urinary incontinence

High rates of diabetes

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Table 2. Distribution of Organisms Isolated From 145 Urine Cultures With Growth at Greater Than 100 000 Colony-Forming Units/mL[a]

Organism isolated	No. (%)	
	7-Day antimicrobial + 7-day placebo group (n=70)	14-Day antimicrobial group (n-75)
Escherichia coli	30 (43)	29 (39)
Klebsiella species	11 (16)	12 (16)
Enterococcus species	7 (10)	6 (8)
Coagulase-negative staphylococci	6 (9)	8 (11)
Citrobacter species	3 (4)	3 (4)
Morganella morganii	3 (4)	1 (1)
Streptococcus species	3 (4)	2 (3)
Enterobacter species	2 (3)	2 (3)
Proteus mirabilis	2 (3)	2 (3)
Serratia marcescens	2 (3)	1 (1)
Staphylococcus aureus	1 (1)	2 (3)
Aerococcus urinae	1 (1)	1 (1)
Gram-positive bacilli, not further identified	1 (1)	1 (1)
Pseudomonas aeruginosa	0	2 (3)
Salmonella species	0	1 (1)

[a] No culture yielded more than 1 species. All isolated organisms were known (n = 139) or inferred (n = 16) to be susceptible to the prescribed antimicrobial (ciprofloxacin or trimethoprim/sulfamethoxazole). Susceptibility was inferred using facility-specific antimicrobial susceptibility data. Patients with urinary tract infections caused by nonsusceptible organisms were excluded from enrollment.

7 vs 14 Days Abx for Afebrile UTI in Men:

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Table 3. Primary and Secondary Outcomes

Characteristic	No./total No. (%)		
Resolution of UTI symptoms 14 days after stopping active antimicrobials	7-Day antimicrobial + 7-day placebo group	14-Day antimicrobial group	Absolute difference, % (1-sided 97.5% CI)[a]
As-treated population (primary analysis)	122/131 (93.1)	111/123 (90.2)	2.9 (-5.2 to ∞)
As-randomized population	125/136 (91.9)	123/136 (90.4)	1.5 (-5.8 to ∞)
Recurrence of UTI symptoms within 28 days of stopping study medication (secondary outcome)	7-Day antimicrobial + 7-day placebo group	14-Day antimicrobial group	Absolute difference, % (2-sided 95% CI)[b]
As-treated population	13/131 (9.9)	15/123 (12.9)	-3.0 (-10.8 to 6.2)
As-randomized population	14/136 (10.3)	23/136 (16.9)	-6.6 (-15.5 to 2.2)

Abbreviation: UTI, urinary tract infection.

[a] The primary analysis used a 1-sided 97.5% CI for noninferiority, which was established if the lower bound of the 1-sided 97.5% CI did not cross the noninferiority margin of −10% difference in symptom resolution.

[b] The secondary outcome was analyzed using a 2-tailed superiority hypothesis test of differences in proportions (2-sample test for equality of proportions with continuity correction) with α = .05 and with 2-sided 95% CIs.

- Adverse events similar (19.8% in 7d group vs 23.6% in 14d group)

Conclusions:

- 7d abx is non-inferior to 14d for afebrile UTI in men
- Unclear if this finding applies to other abx not tested

3 Days Beta-Lactams for CAP:
"Trials That May Change Your Practice"

THE LANCET

Discontinuing β-lactam treatment after 3 days for patients with community-acquired pneumonia in non-critical care wards (PTC): a double-blind, randomised, placebo-controlled, non-inferiority trial

Aurélien Dinh, Jacques Ropers, Clara Duran, Benjamin Davido, Laurène Deconinck, Morgan Matt, Olivia Senard, Aurore Lagrange, Sabrina Makhloufi, Guillaume Mellon, Victoire de Lastours, Frédérique Bouchand, Emmanuel Mathieu, Jean-Emmanuel Kahn, Elisabeth Rouveix, Julie Grenet, Jennifer Dumoulin, Thierry Chinet, Marion Pépin, Véronique Delcey, Sylvain Diamantis, Daniel Benhamou, Virginie Vitrat, Marie-Christine Dombret, Bertrand Renaud, Christian Perronne, Yann-Erick Claessens, José Labarère, Jean-Pierre Bedos, Philippe Aegerter, Anne-Claude Crémieux, for the Pneumonia Short Treatment (PTC) Study Group

- **Controversy:** For patients with CAP who are clinically stable at 3d of beta-lactam therapy, are additional abx days required?
- **Response:** Once again, shorter may be better!

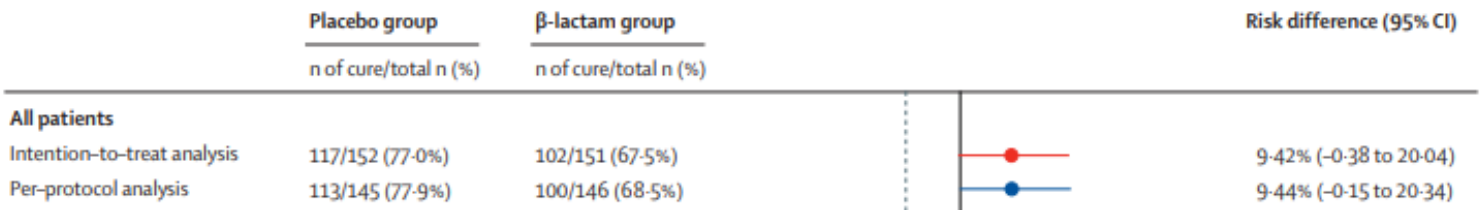
3 Days Beta-Lactams for CAP:

"Trials That May Change Your Practice"

- Randomized, controlled trial
- Double-blind, placebo-controlled
- Inclusion criteria:
  - Adults admitted to hospital with moderately-severe CAP
  - Stable on abx day 3 (no ICU)
- Randomized to either:
  - 3 days beta lactam (3rd gen CEPH or amox-clav) +
    - 5 days placebo, OR
    - 5 additional days amox-clav

	Placebo group (n=152)	β-lactam group (n=151)
Age, years	72·5 (54·0–85·3)	74·0 (58·0–83·0)
Sex		
Female	66 (43%)	57 (38%)
Male	86 (57%)	94 (62%)
Temperature, °C	38·8 (38·3–39·3)	38·7 (38·3–39·3)
Oxygen therapy	60 (39%)	59 (39%)
Comorbidities*	34 (22%)	39 (26%)
Liver disease	5 (3%)	2 (1%)
Heart failure	30 (20%)	33 (22%)
Cerebrovascular disease	13 (9%)	10 (7%)
Renal disease	13 (9%)	11 (7%)
Coronary insufficiency	24 (16%)	20 (13%)
Diabetes	24 (16%)	32 (21%)
Chronic obstructive pulmonary disease	31 (20%)	40 (26%)
At least two comorbidities	34 (22%)	39 (26%)
Active smoking	30 (20%)	25 (17%)
PSI score	80·5 (57·0–103)	83·0 (58·0–104)
Risk class 2 (<70)	56 (37%)	55 (36%)
Risk class 3 (71–90)	39 (26%)	34 (23%)
Risk class 4 (91–130)	45 (30%)	56 (37%)
Risk class 5 (≥131)	12 (8%)	6 (4%)

3 Days Beta-Lactams for CAP:
"Trials That May Change Your Practice"



	Placebo group	β-lactam group	Risk difference (95% CI)
	n of cure/total n (%)	n of cure/total n (%)	
All patients			
Intention-to-treat analysis	117/152 (77·0%)	102/151 (67·5%)	9·42% (–0·38 to 20·04)
Per-protocol analysis	113/145 (77·9%)	100/146 (68·5%)	9·44% (–0·15 to 20·34)

- **Primary Outcome: Cure** (Apyrexia, "respiratory improvement")
  - 77% vs 68% (non-inferior)
- **Secondary Outcomes:**
  - Adverse events: 14% vs 19% (non-significant)
  - Mortality at 30 days: 2% vs 1% (non-significant)

Conclusions:

- For moderately severe CAP, 3d beta lactam is likely okay!
- Caution in extrapolating to people with aspiration, intracellular bacteria, and immunocompromised hosts
- Did not address non-beta lactam antibacterial agents

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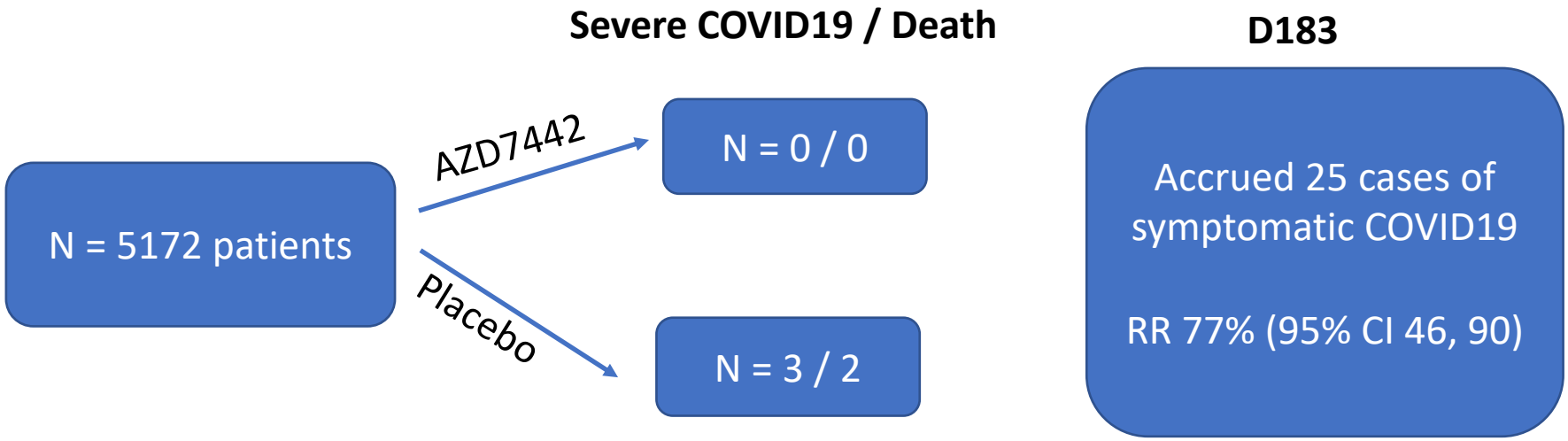
Clinical Trials that will Change Practice:

"Viral Infections"

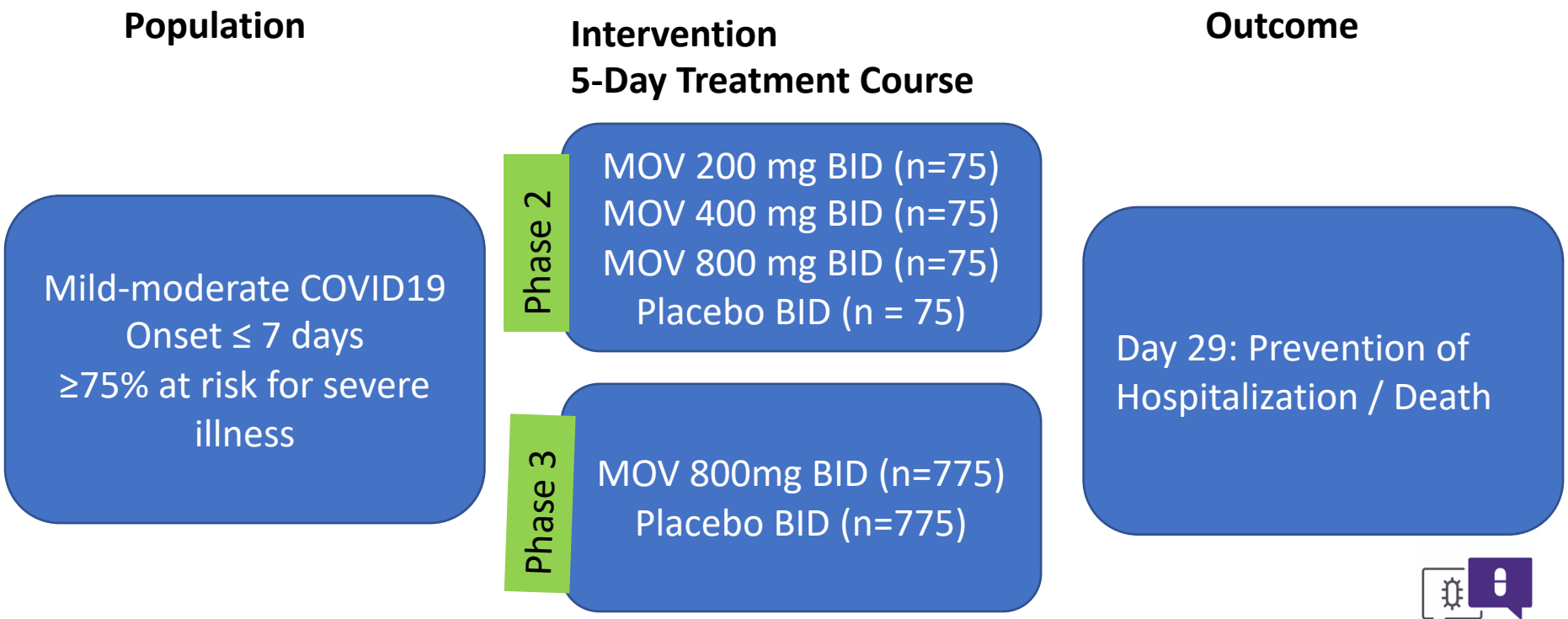
- **New Long-Acting MAb for Pre-exposure Prophylaxis:**
- AZD7442 – combo of tixageivmab + cilgavimab
- Single dose (2 IM injections)



IDWeek 2021: Genovefa Papanicolaou, MD
Data from Astra Zeneca Press Releases

Clinical trials that may change practice:
"Viral Infections"

- **Molnupiravir** PO Antiviral
- RNA prodrug – incorporates into viral genome and inhibits viral replication



IDWeek 2021: Genovefa Papanicolaou, MD

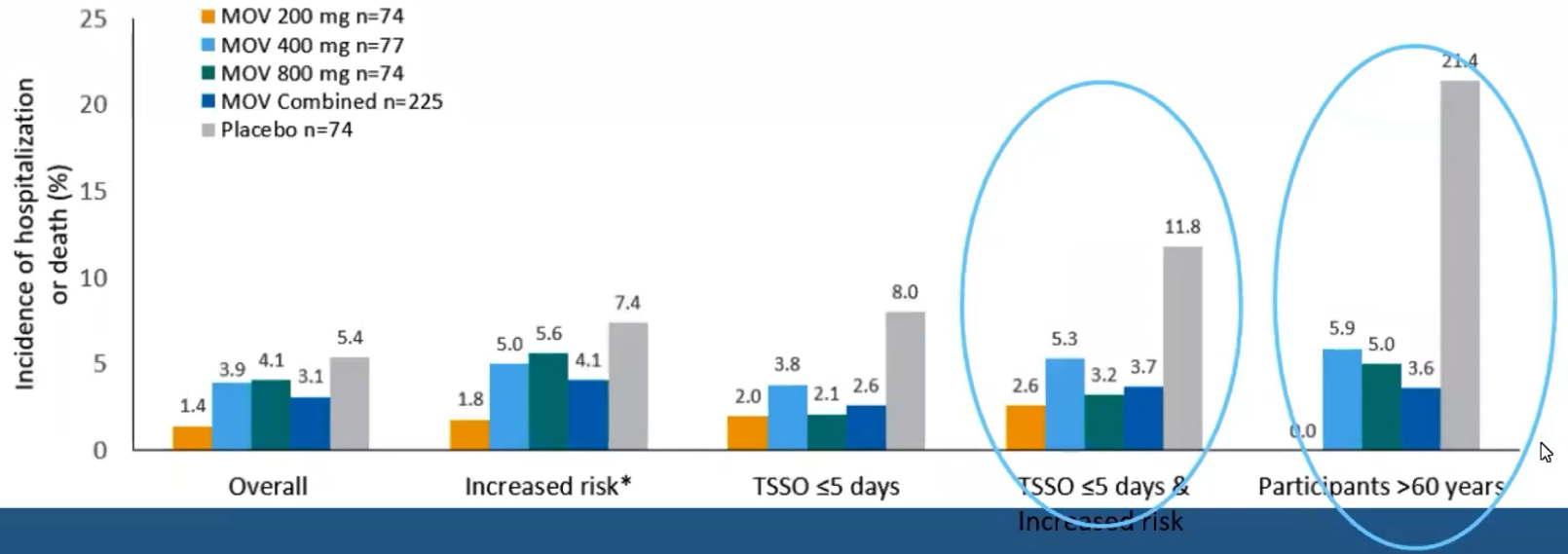
Clinical Trials that will Change Practice:

"Viral Infections"

Molnupiravir for treatment of COVID19

- All doses well tolerated during the 5-day treatment period and follow up with AEs comparable to placebo.

- MOV reduced the incidence of hospitalization or death through Day 29, particularly in subgroups with risk factors



Caraco MK-4482 P002 Phase 2 ECCMID 2021

IDWeek 2021 Genovefa Papanicolaou

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CODE Blue: Resuscitating AMS and Healthcare Epi Post-COVID

Moving Forward and Back to "Normal"

Arjun Srinivasan, MD

"The future is already here, it's just not evenly distributed"
-William Gibson

Remembering the Before Times

- In 2015, hospitals meeting 7 CDC Core Elements of Stewardship
  - 26% of CAHs
  - 66.1% of 200+ bed hospitals
- Disparities in AR pathogens by socioeconomic factors, gender, race
- Healthcare was already understaffed, especially nursing and nurse assistants
- Really limited data reporting (HAI, AU, capacity/resources)

The Current Times

- Infection preventionists spending 80% of their time on COVID-19 related response
- AMS programs ~95% report somewhat decreased or strongly decreased traditional AMS work

BUT

- 16K CMS funded SNFs are now reporting COVID data to NHSN

What Should our New "Normal" Look Like

- Strive for uniformity
- Understand and address health disparities (including facility level disparities)
  - 2020: CAH meeting CDC Core Elements 26% -> 83%
- More staffing – more people in general & all HCPs better trained at baseline
  - CDC Project Firstline
- More data with less work
  - Electronic case reporting (eCR)
- Better innovations that cause change without us