Universitätsspital Basel

Klinik für Infektiologie und Spitalhygiene

Journal Club 15.11.2021

Narrow-spectrum antibiotics for community-acquired pneumonia in Dutch adults (CAP-PACT): a cross-sectional, stepped-wedge, cluster-randomised, non-inferiority, antimicrobial stewardship intervention trial (VA Schweitzer et al., The Lancet Infectious Diseases, 10/2021)

Tito Bosia

Background

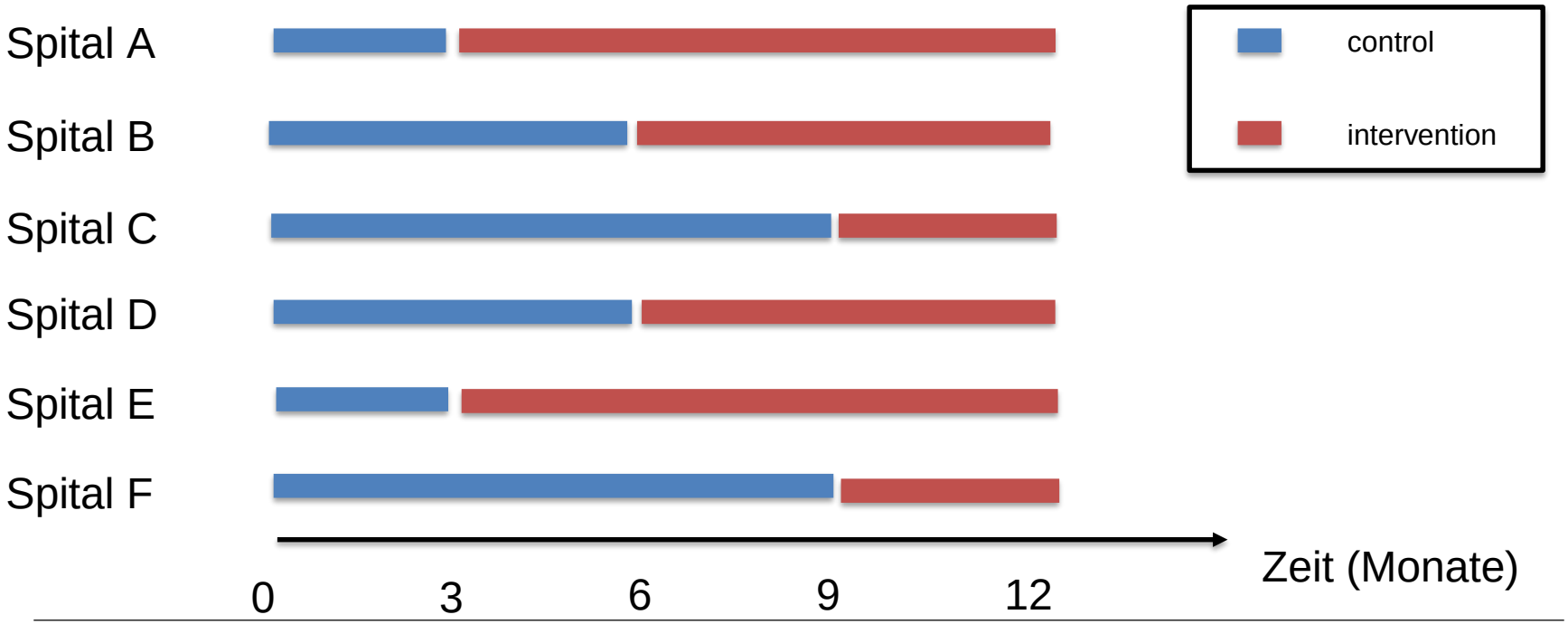
- Antibiotic stewardship: Verbesserung der Antibiotika Einsatz
  - Antibiotikaresistenz minimieren

- Noch unzureichender Evidenz der Gleichwertigkeit von Schmal- und Breitspektrum-Antibiotika in der Behandlung der ambulant-erworbenen Pneumonie

- Jährliche Inzidenz der CAP in der Schweiz 1.6-10.8 Fälle/1000 Erwachsenen
  - Davon ca. 1/4 - 1/3 stationär behandelt
  - (Inzidenz des Myokardinfarkts in der Schweiz ca. 30’000 Fälle/Jahr)

Methods

- 12 Spitäler in der Niederlande (jeder mit antibiotic stewardship team)
- Cluster: Spital
- Randomization: Zeitpunkt des Interventionsbeginns



Methods

- Eingeschlossen: erwachsene Patienten (>18J) unter AB-Therapie für ambulant-erworbene Pneumonie auf Normalabteilung (= mittelschwere CAP)
  - *Ausgeschlossen: Immunsupprimierte, stationär vor <14 Tage*

- Interventionsziel: Einsatz von Benzylpenicillin und Amoxicillin für CAP erhöhen

    - Fortbildungsveranstaltungen (jede 6 Monate)

    - Zusammenarbeit mit ärztlicher Leitung der Abteilungen verstärken

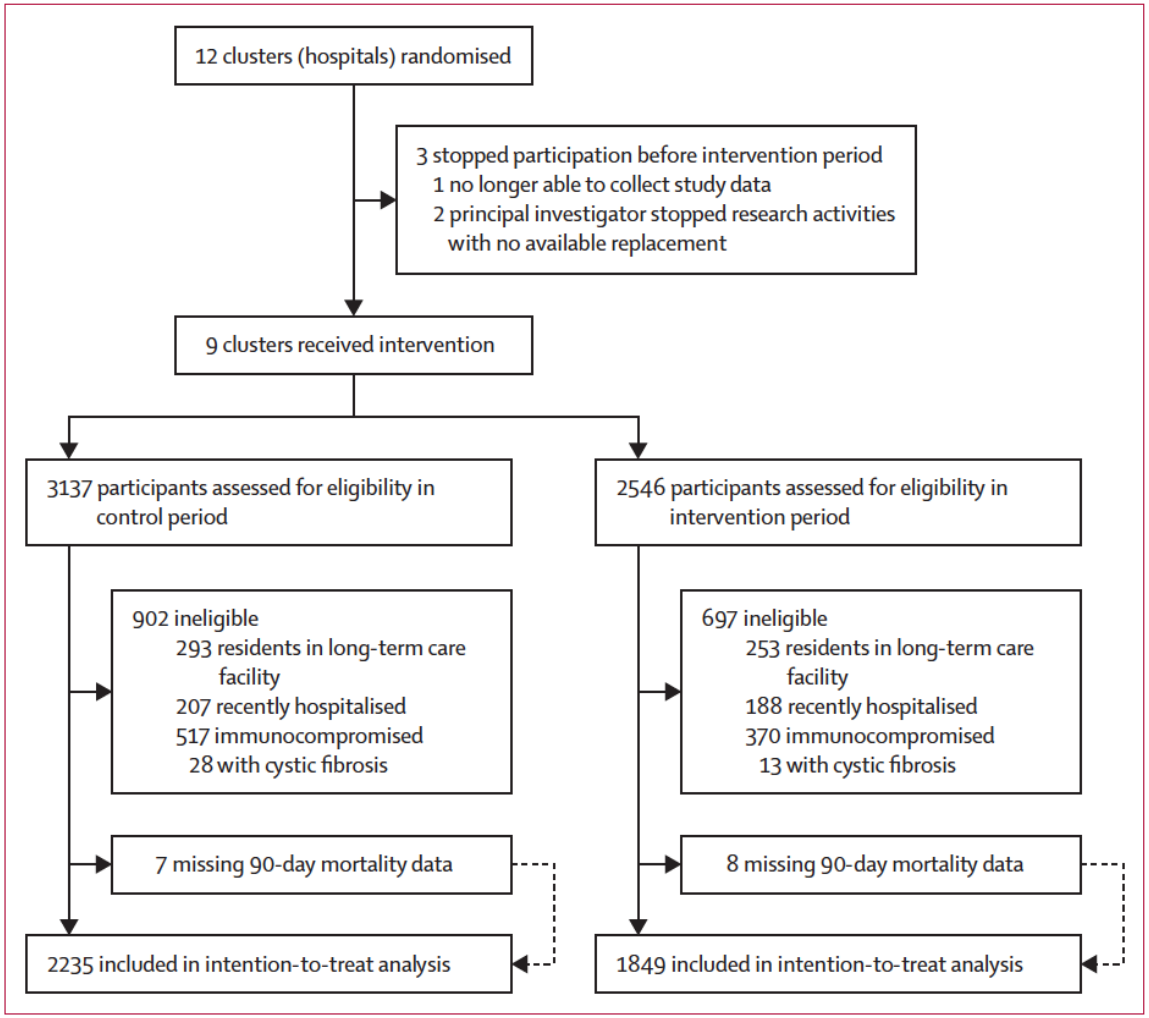
    - Audit/Feedback via antibiotic stewardship team

Methods

- Outcomes:
    - Anzahl an Therapietage mit Breit-Spektrum Antibiotika
    - 90-days mortality (all cause)
    - Sekundäre outcomes: 30-days mortality, 30-days-hospital-readmission, IPS-Verlegung
- Statistische Analysen:
    - superiority analysis für Einsatz der Breit-Spektrum Antibiotika
    - non-inferiority analysis (margin 3%) for 90-days mortality

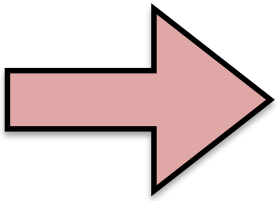
Results

- Trial profile



Results

- Baseline characteristics

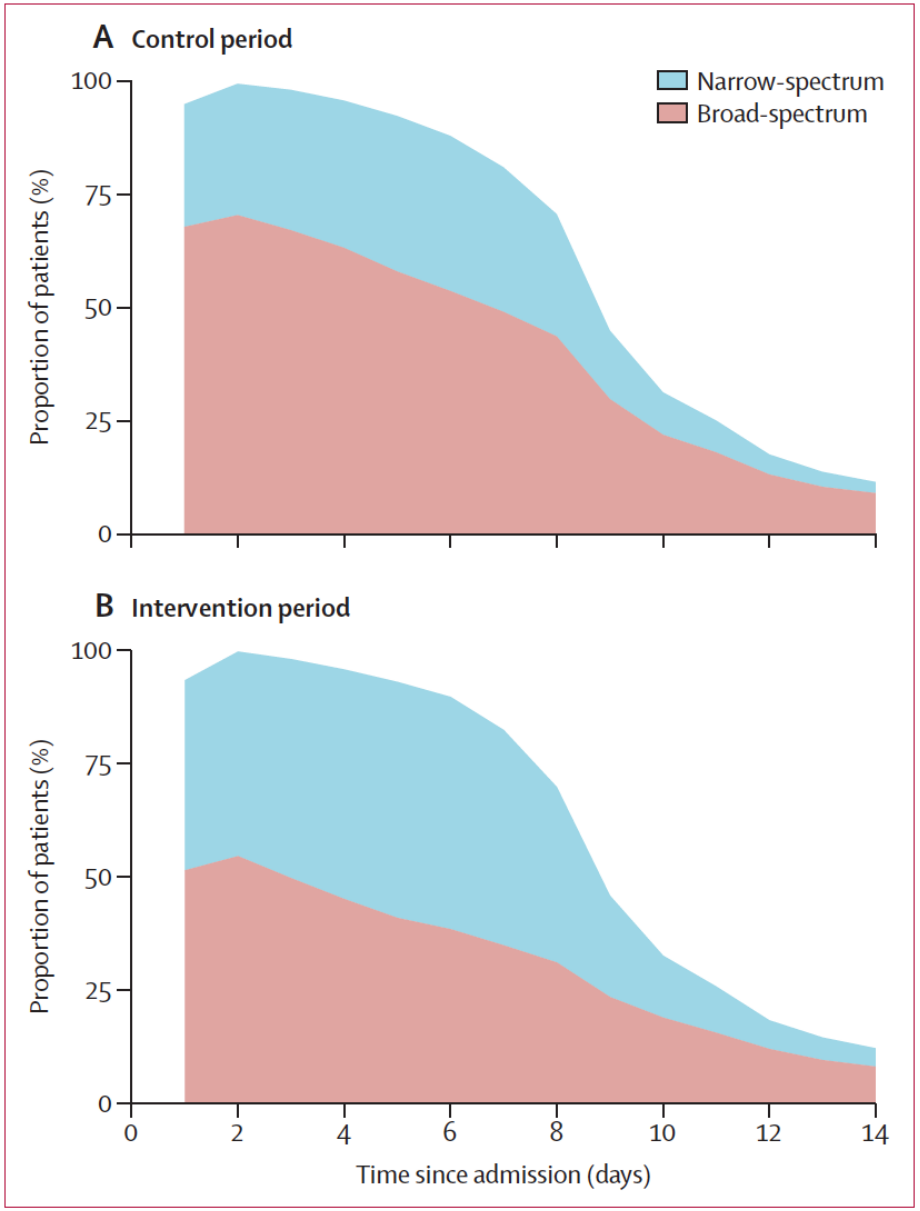


	Hospitalised in control period (n=2235)	Hospitalised in intervention period (n=1849)
Age, years	73 (63–81)	74 (64–82)
Sex		
Female	1047 (46·8%)	874 (47·3%)
Male	1188 (53·2%)	975 (52·7%)
Antibiotic use 2 weeks before admission	742 (33·2%)	569 (30·8%)
Smoking status		
Current smoker	512/1881 (27·2%)	412/1494 (27·6%)
Past smoker	725/1881 (38·5%)	626/1494 (41·9%)
Never smoker	396/1881 (21·1%)	264/1494 (17·7%)
Not currently smoking but history unknown	248/1881 (13·2%)	192/1494 (12·9%)
Medical speciality admitted to		
Internal medicine	416 (18·6%)	349 (18·9%)
Pulmonology	1731 (77·4%)	1426 (77·1%)
Other	88 (3·9%)	74 (4·0%)
Comorbidities		
COPD or asthma	962 (43·0%)	880 (47·6%)
Cardiovascular disease	300 (13·4%)	259 (14·0%)
Diabetes	389 (17·4%)	315 (17·0%)
Malignancy	239 (10·7%)	185 (10·0%)
Pneumonia severity index score	89 (70–112)	91 (72–113)
Risk class I	101 (4·5%)	73 (3·9%)
Risk class II	473 (21·2%)	357 (19·3%)
Risk class III	581 (26·0%)	493 (26·7%)
Risk class IV	823 (36·8%)	722 (39·0%)
Risk class V	257 (11·5%)	204 (11·0%)
CURB-65 score	2 (1–2)	2 (1–2)
Radiologically confirmed disease	1689 (75·6%)	1377 (74·5%)
Blood culture	1602 (71·7%)	1387 (75·0%)
Sputum culture	888 (39·7%)	784 (42·4%)
Pneumococcal urinary antigen test	965 (43·2%)	1173 (63·4%)
Legionella spp urinary antigen test	1297 (58·0%)	1255 (67·9%)

Results

- primary outcome:
  - adjusted rel. reduction: 26.6%
  - entspricht eine Reduktion von 6.5 (control) auf 4.8 Tage (intervention) mit Breit-spektrum Antibiotika

- 90-days mortality:
  - control group 10.9%
  - intervention group 10.8%
  - adjusted risk difference 0.4%



Results

- Keine relevante Unterschiede zwischen control und intervention bezüglich secondary outcomes

- Bei mehr Patienten in der Interventionsgruppe wurde die Therapie deeskaliert in Vergleich zur Kontrollgruppe
  - Grunde für fehlende Umstellung:
    - COPD
    - klinische Verschlechterung
    - V.a. resistenten Keim

- Grosse Variabilität zwischen Spitäler bezüglich Teilnahme an der Fortbildungsveranstaltungen (e-learning: 2% bis 72%; klinische Vorlesung: 10.5 bis 52.5%)

Limitations

- Kein blinding möglich
- Welche Intervention war am Hilfreichsten?
- Generalisability? Resistenz von *S. pneumoniae* für Penicillin in der Niederlande ca. 6%

Conclusions

- Eine antibiotic stewardship Intervention für mittelschwere ambulant-erworbene Pneumonie ist möglich und Effektiv in der Reduktion des Einsatzes von Breit-spektrum Antibiotika

- Umso wichtiger sind solche Interventionen bei Krankheitsbilder mit grosser Prävalenz/Inzidenz in der Bevölkerung (“big fishes”)

- Anhaltender Effekt?

Vielen Dank
für Ihre Aufmerksamkeit

Supplementary material - Antibiotikatherapie

- Schmal-spektrum Antibiotika:
  - Benzylpenicillin, Amoxicillin, *Doxycyclin*
- Breit-spektrum Antibiotika:

Broad-spectrum		
Beta-lactams		
Amoxicillin – clavulanic acid	426 (19.0%)	244 (13.2%)
Ceftriaxone	114 (5.1%)	111 (6.0%)
Cefuroxime	149 (6.7%)	91 (4.9%)
Cefotaxime	-	-
Ceftazidime	12 (0.5%)	6 (0.3%)
Cefazolin	1 (0.0%)	-
Piperacillin/tazobactam	10 (0.4%)	2 (0.1%)
Macrolides		
Azithromycin	9 (0.4%)	3 (0.2%)
Clarithromycin	10 (0.4%)	-
Erythromycin	-	1 (0.1%)
Fluoroquinolones		
Moxifloxacin	62 (2.8%)	22 (1.2%)
Levofloxacin	4 (0.2%)	-
Ciprofloxacin	20 (0.9%)	13 (0.7%)
Other		
Co-trimoxazole	10 (0.4%)	12 (0.6%)
Clindamycin	2 (0.1%)	-
Combination therapy		
Amoxicillin + ciprofloxacin	153 (6.8%)	122 (6.6%)
Penicillin + ciprofloxacin	211 (9.4%)	159 (8.6%)
Amoxicillin– clavulanic acid + ciprofloxacin	99 (4.4%)	60 (3.2%)
Ceftriaxone + ciprofloxacin	40 (1.8%)	20 (1.1%)
Cefuroxime + ciprofloxacin	33 (1.5%)	11 (0.6%)
Cefuroxime + erythromycin	25 (1.1%)	5 (0.3%)
Cefuroxime + clarithromycin	23 (1.0%)	1 (0.1%)
Amoxicillin + cefuroxime	14 (0.6%)	14 (0.8%)
Amoxicillin + penicillin + ciprofloxacin	12 (0.5%)	9 (0.5%)
Amoxicillin– clavulanic acid + penicillin + ciprofloxacin	13 (0.6%)	12 (0.6%)
Other*		103 (5.6%)

Supplementary material - sensitivity analysis

Table S6: Sensitivity analyses for patients with radiologically confirmed CAP.

Radiologically confirmed CAP	Fully adjusted* analysis
90-day mortality	RD: 1.8% (90% CI: -1.3% to 4.3%)
Broad-spectrum DOT	AR: -1.9 (95% CI: -2.6 to -1.1) RR: 26.8% (95% CI: 17.8% to 36.7%)
Doxycyclin classified as broad-spectrum antibiotic	
90-day mortality	RD: -0.2% (90% CI: -2.1% - 1.5%)
Broad-spectrum DOT	AR: -1.7 (95% CI: -2.4 to -1.1) RR: 26.6% (95% CI: 18.1% to 35.3%)

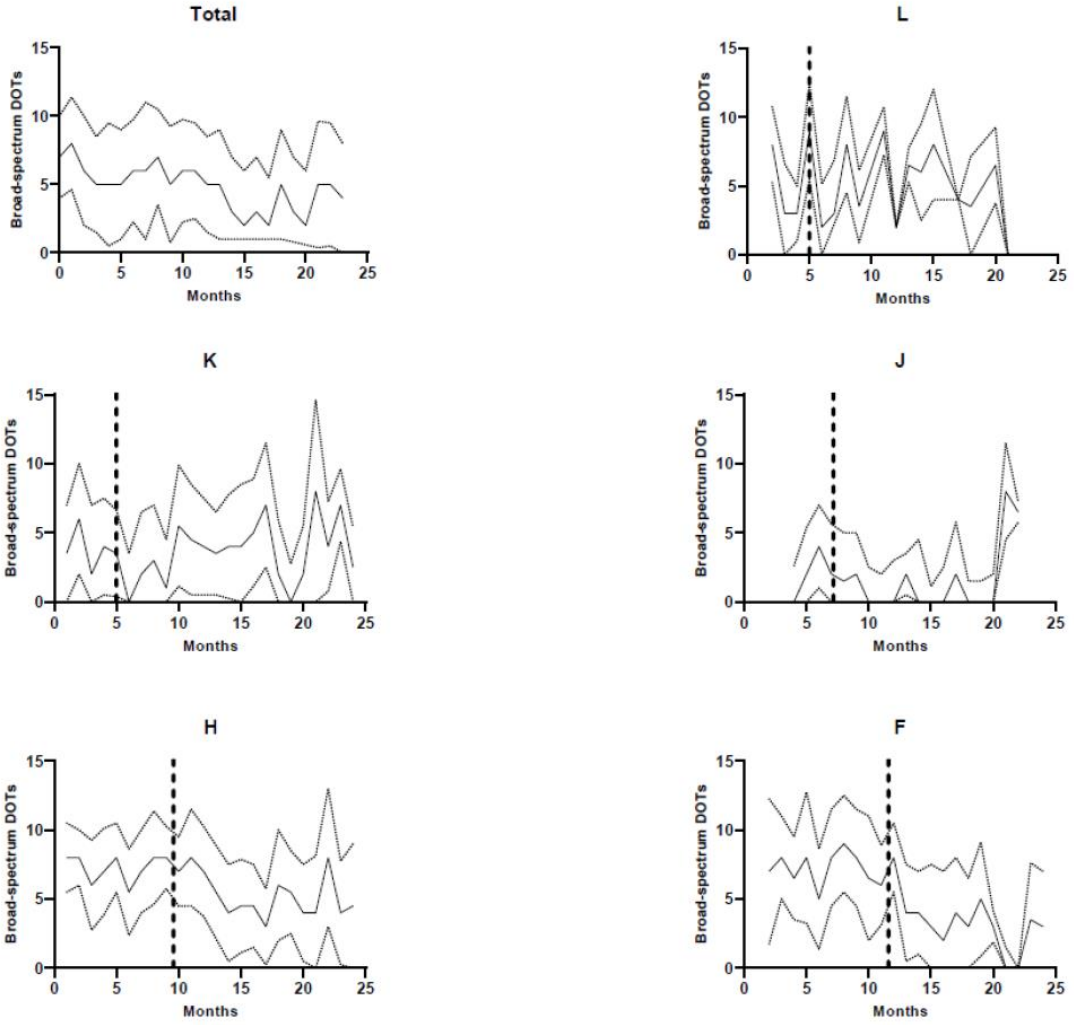
* Adjusted for design, time and for possible confounders.

Supplementary material - complications

Table S8. Complications of patients with CAP hospitalised to a non-ICU ward in the control compared to the intervention period

	Control (n=2,235)	Intervention (n=1,849)
Pleural effusion	398 (17.8%)	326 (17.6%)
Organ failure	78 (3.5%)	87 (4.7%)
Clostridioides difficile associated disease	56 (2.5%)	45 (2.4%)
Empyema	22 (1.0%)	23 (1.2%)
Septic shock	12 (0.5%)	4 (0.2%)
Acute respiratory distress syndrome	10 (0.5%)	7 (0.4%)
Pneumothorax	9 (0.4%)	3 (0.2%)
Lung abscess	9 (0.4%)	1 (0.1%)
Other	244 (10.9%)	205 (11.1%)

Supplementary material - DOT Broadspectrum trend



Universitätsspital Basel