Infekce vyvolané Clostridioides difficile

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Clostridium difficile and *Clostridioides difficile*: Oba názvy jsou stále platné

(Oren and Rupnik , 2018)

Why is C. difficile called that?

The species name difficile is a form of the Latin adjective difficilis because when first identified (by Hall and O'Toole in 1935), the organism was difficult to isolate and grew slowly in pure culture.

Na základě analýzy genové sekvence 16S rRNA je pro *Clostridium difficile* nejbližším příbuzným *Clostridium mangenotii* s podobnosti 94,7 % a oba se nacházejí v čeledi *Peptostreptococcaceae*, která je fylogeneticky vzdálená *C. butyricum* a dalším zástupcům *Clostridium* sensu stricto.
Na základě fenotypových, chemotaxonomických a fylogenetických analýz byl nový rod *Clostridioides* gen. nov. je navržen pro *Clostridium difficile*.
Lawson et al., 2016.

Dormant spore vs metabolically active cell

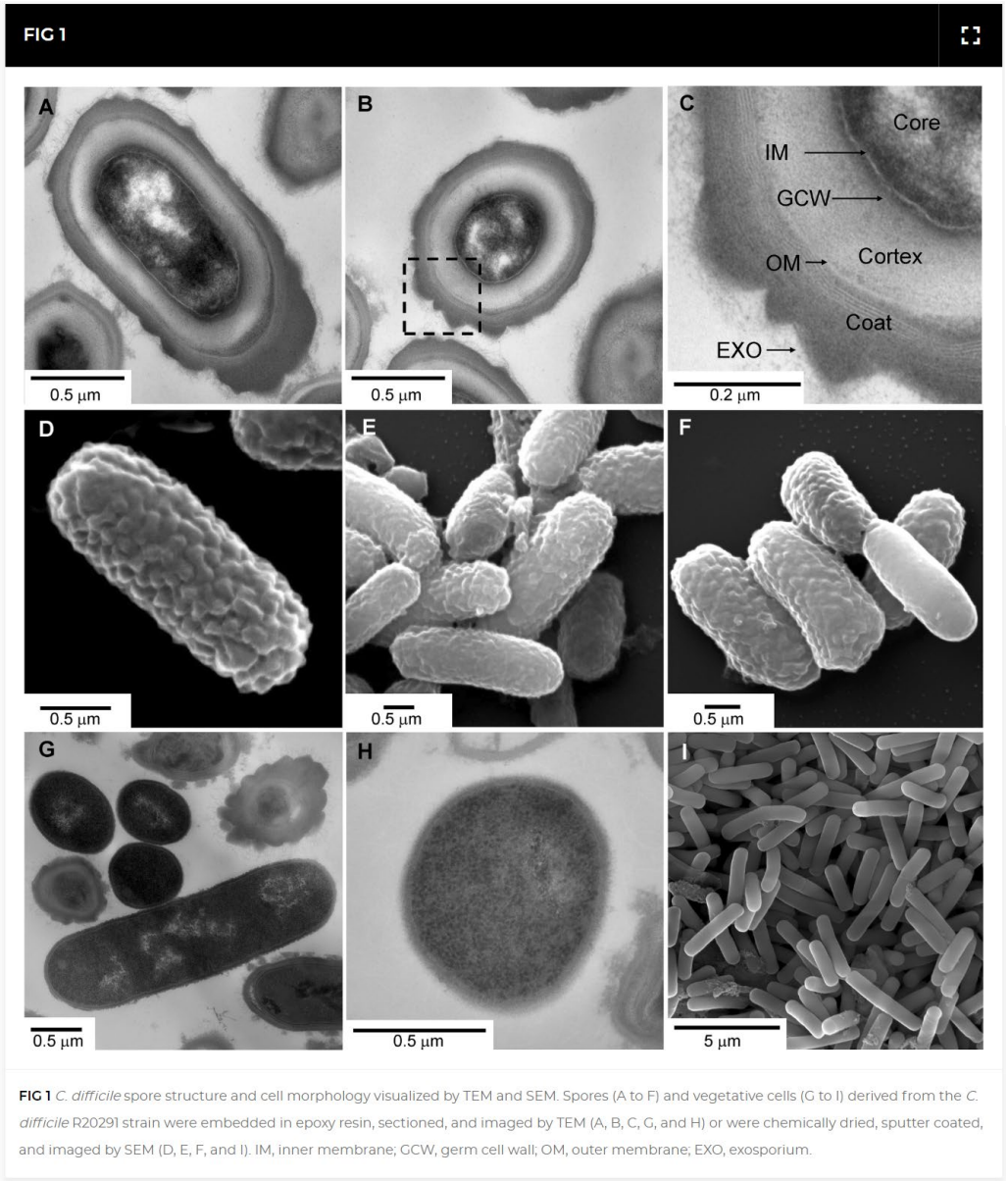
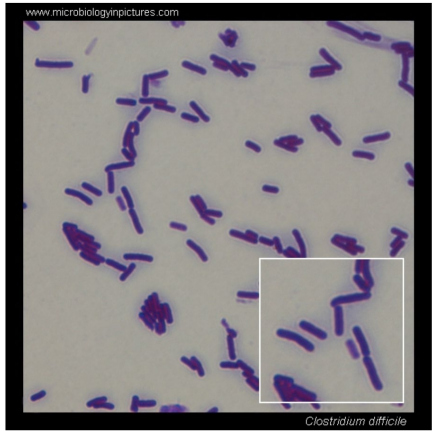
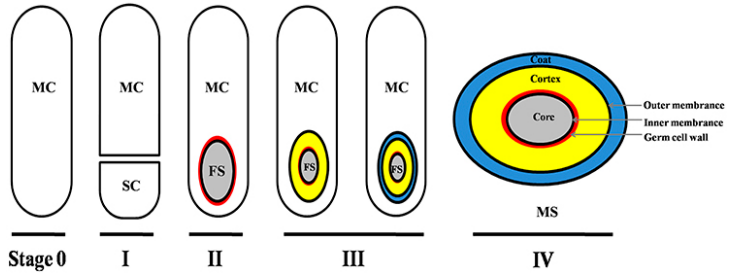


FIG 1 *C. difficile* spore structure and cell morphology visualized by TEM and SEM. Spores (A to F) and vegetative cells (G to I) derived from the *C. difficile* R20291 strain were embedded in epoxy resin, sectioned, and imaged by TEM (A, B, C, G, and H) or were chemically dried, sputter coated, and imaged by SEM (D, E, F, and I). IM, inner membrane; GCW, germ cell wall; OM, outer membrane; EXO, exosporium.



Gram pozitivní
Obligátně anaerobní
Může produkovat toxiny (A, B, některé kmeny, binární)
Tvorba spor

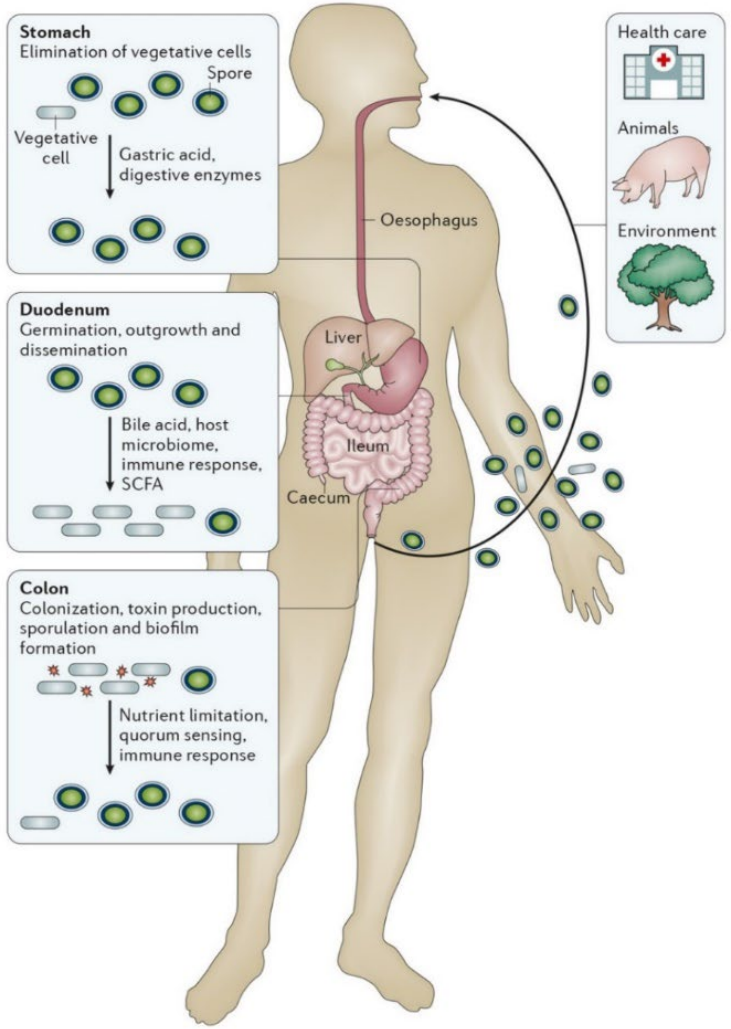


Tvorba spor *C. difficile* je klíčová pro přežití a šíření bakterie v prostředí.

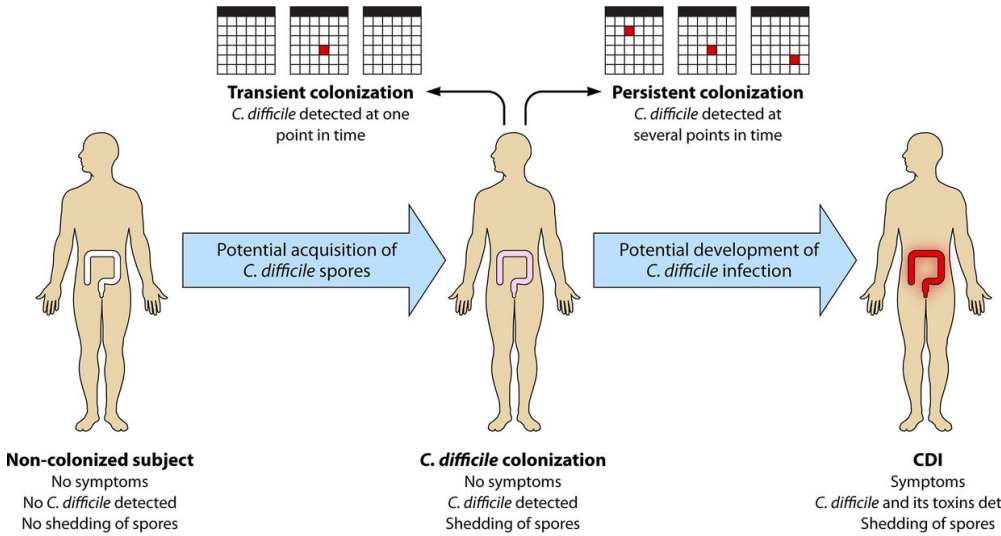
Spící aerotolerantní a vysoce odolné spory usnadňují účinný přenos a perzistenci v hostiteli.

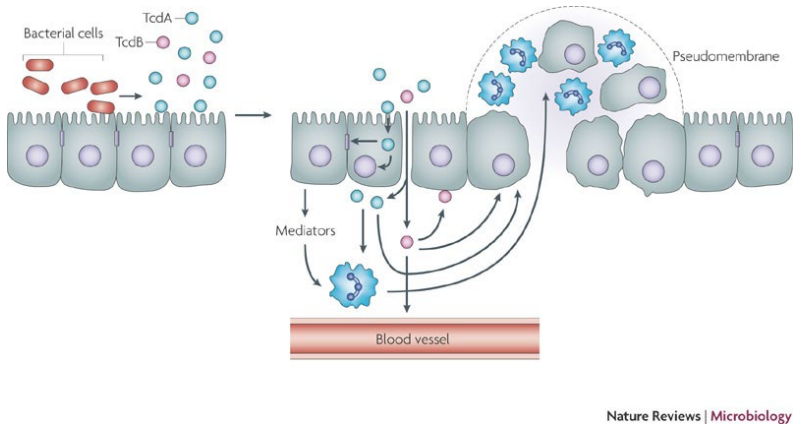
Spory jsou odolné vůči různým podmínkám prostředí, antibiotikům a některým dezinfekčním prostředkům (nutné použití sporicidních).

Infekce vyvolané *Clostridioides difficile* (CDI)



Fekálně-orální cesta přenosu
Asymptomatická kolonizace nebo infekce
Recidiva CDI (25 %, 50 %)
Příznaky: vodnatý průjem, horečka,
ztráta chuti k jídlu, nevolnost,
a bolest/citlivost břicha, pseudomembranózní kolitida,
toxický megakolon.

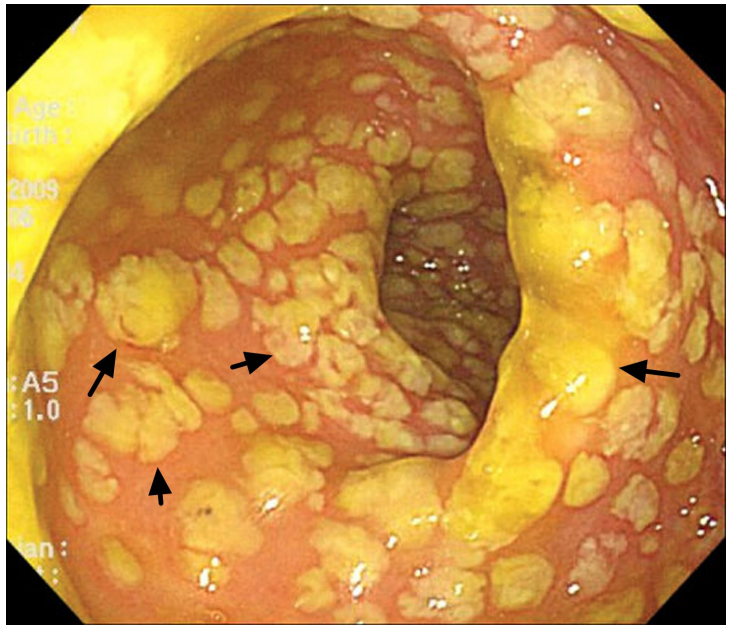




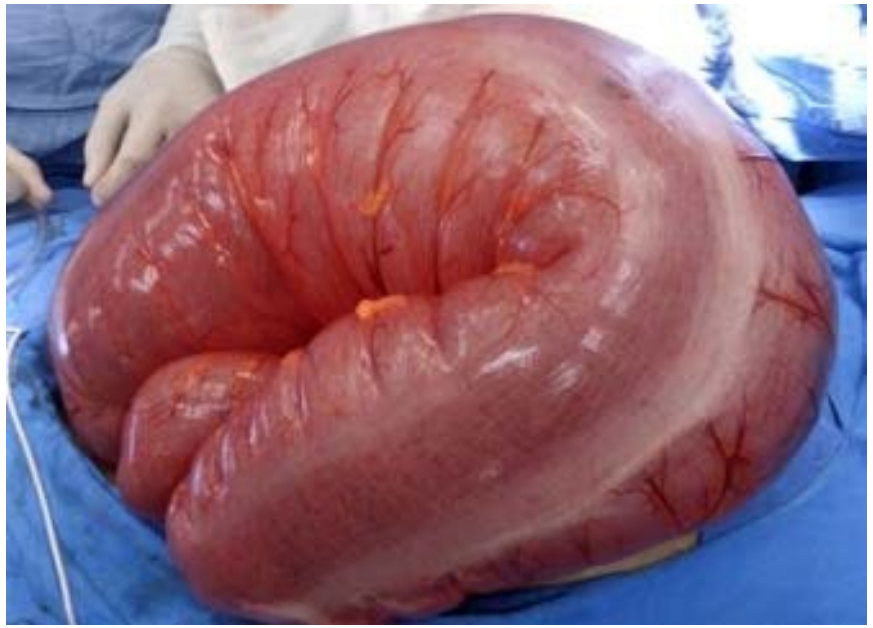
Toxiny = narušení struktury cytoskeletu a těsných spojů s následným zakulacením, oddělením a buněčnou smrtí.

Smits et al., 2016; Crobach et al., 2018; Chilton et al., 2018

Těžké formy CDI

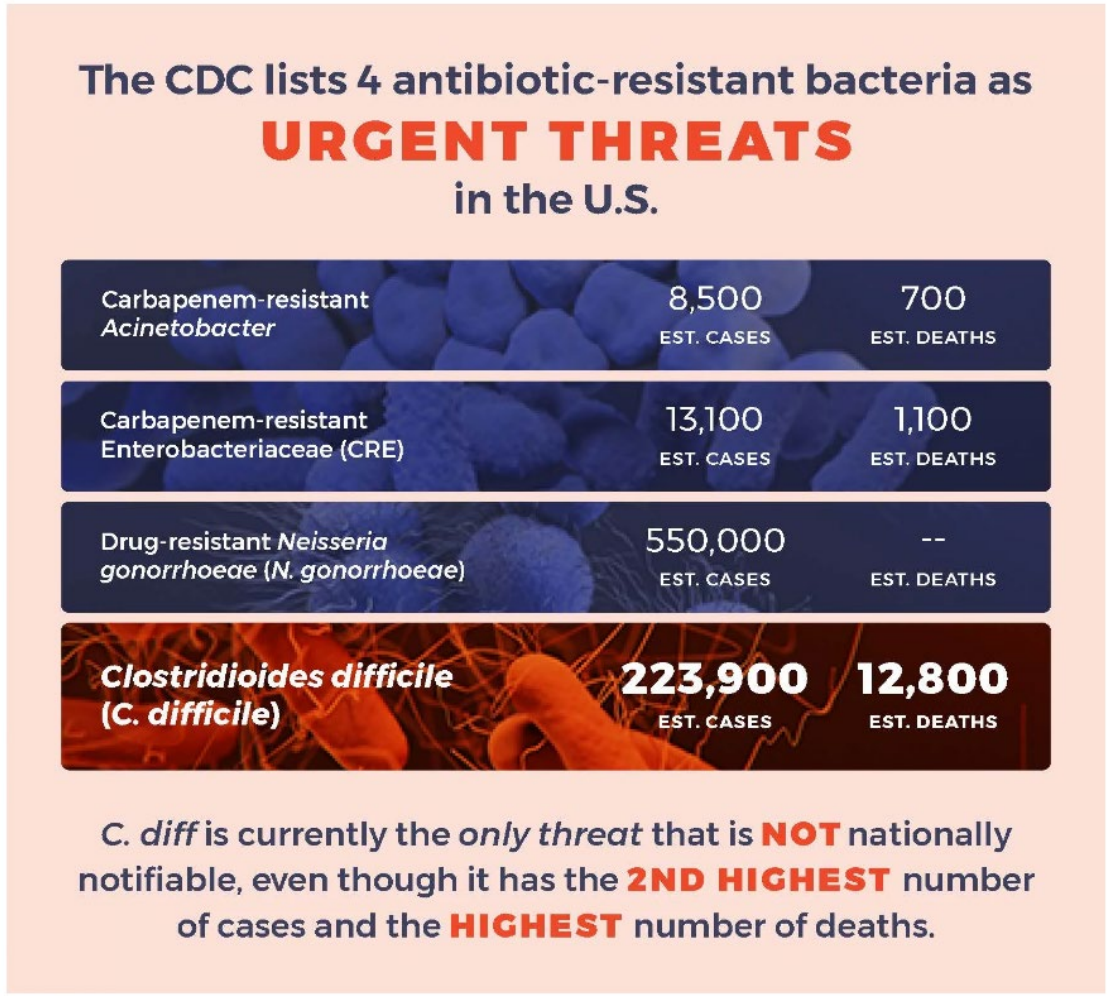


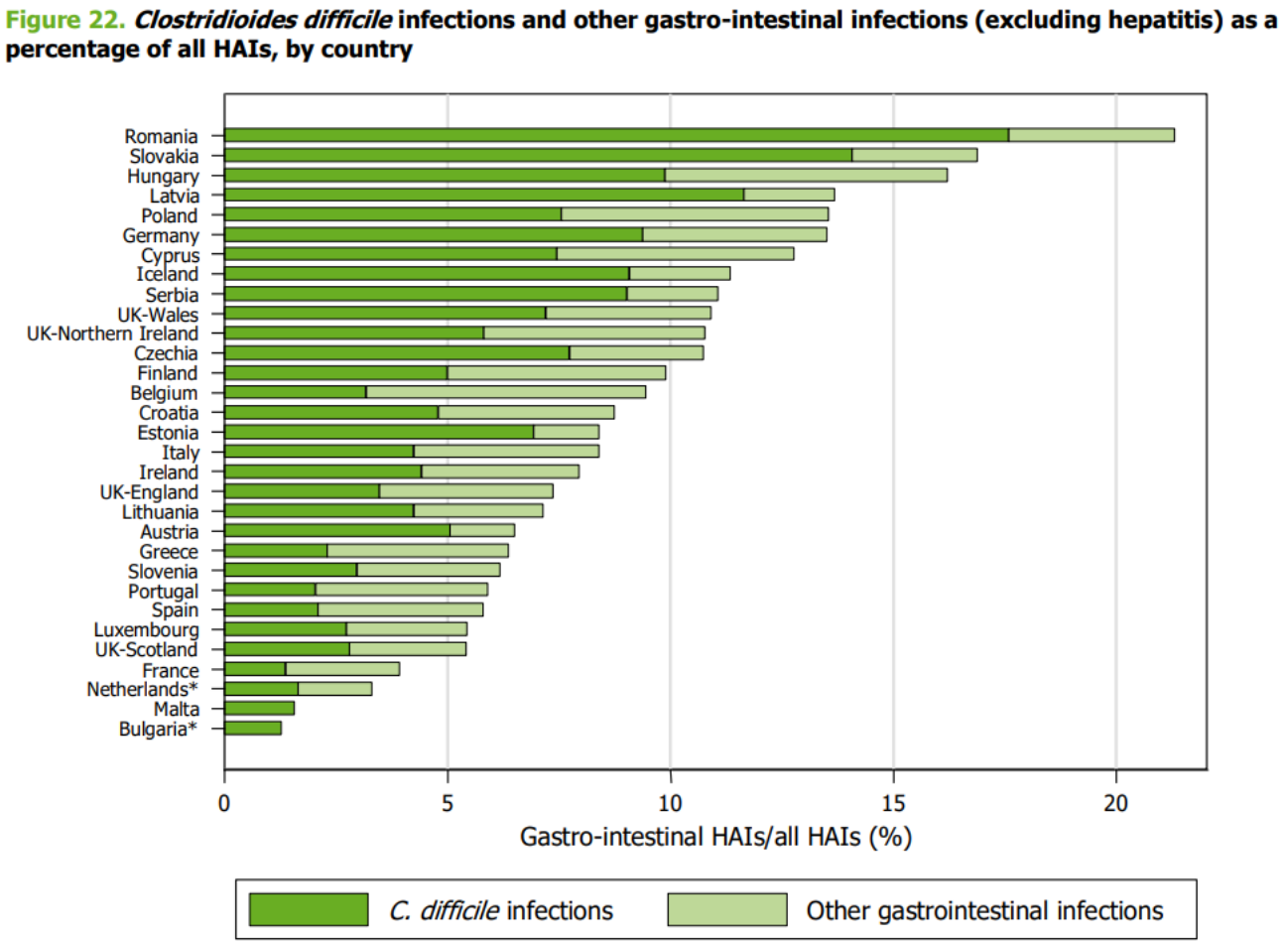
Pseudomembranózní kolitida



Paralytický ileus = toxický megakolon, chirurgický intervence, vysoká úmrtnost

Jak častá je CDI?

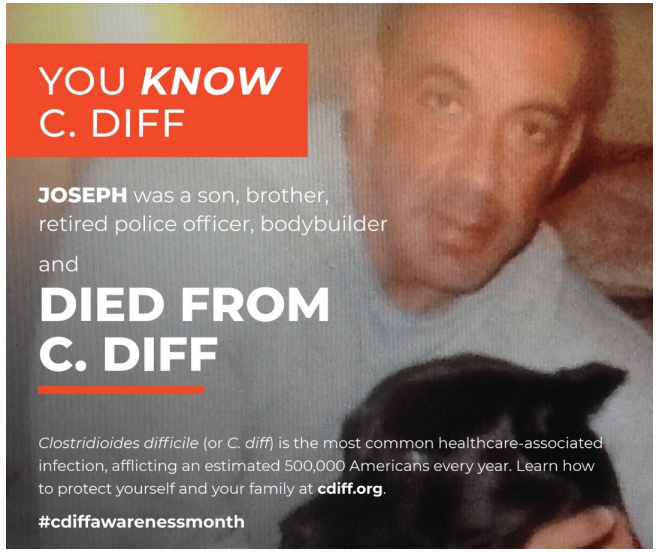


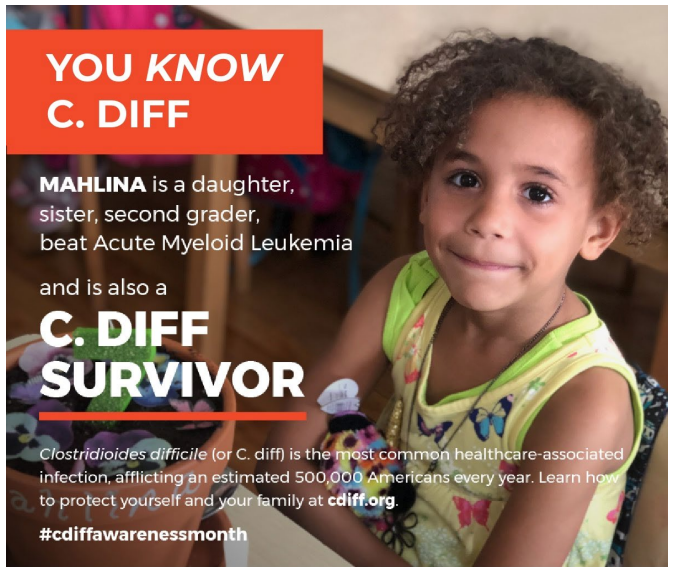


124 000 případů CDI ročně
Přibližně 17 % zemře. 4 % ve vztahu k CDI

Evropský průměr: 5 případů na 10 000 lůžkodnů

Jak vypadá pacient s rizikem CDI?





RIZIKOVÉ FAKTORY pro CDI

Vyšší věk ≥ 65 let
Komorbidity
Užívání inhibitorů protonové pumpy
Antibiotická léčba
Předchozí hospitalizace
Imunosuprese(rakovina, chemoterapie, transplantace orgánů, HIV)
Manipulace s trávicím traktem (vyživovací sondy, chirurgie)

VŠE, CO OVLIVŇUJE MIKROBIOTU

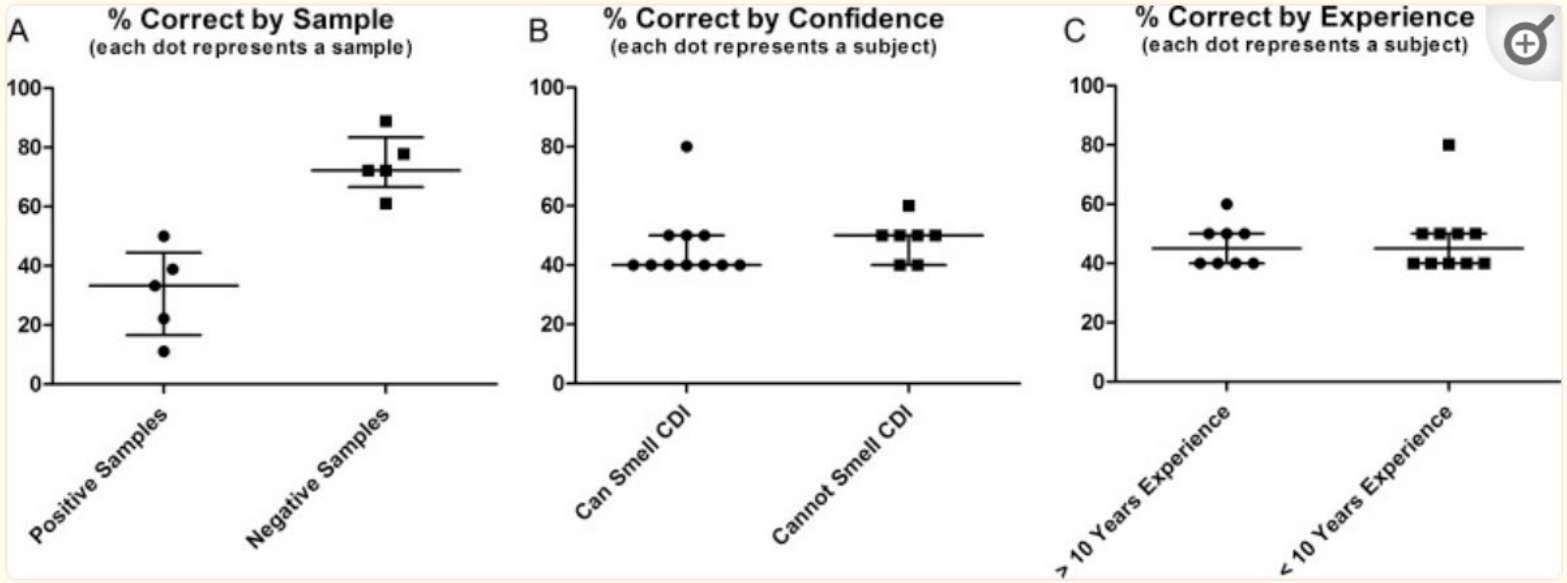
Laboratorní diagnostika – podle zápachu?

Clin Infect Dis. 2013 Feb 15; 56(4): 615–616.
doi: 10.1093/cid/cis974

PMCID: PMC3571629
PMID: 23166192

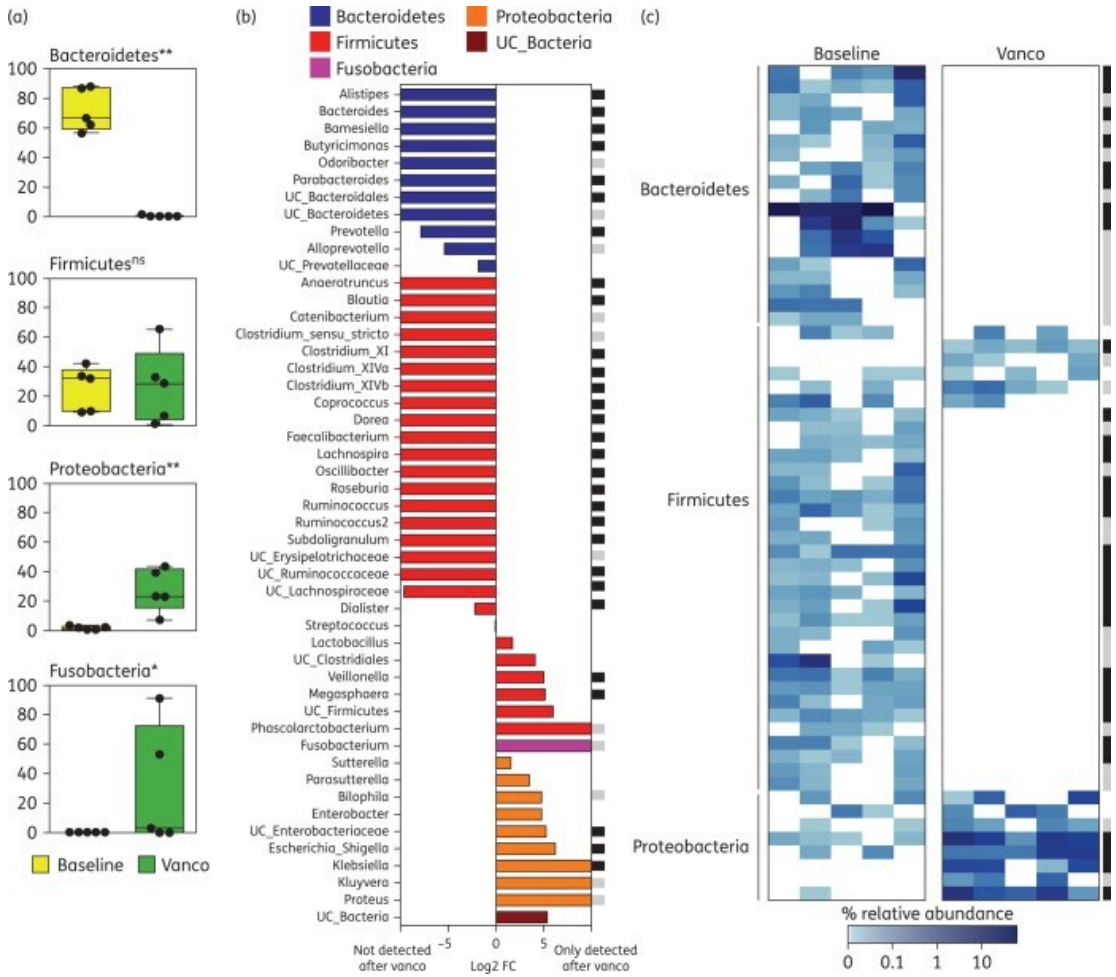
The Nose Knows Not: Poor Predictive Value of Stool Sample Odor for Detection of *Clostridium difficile*

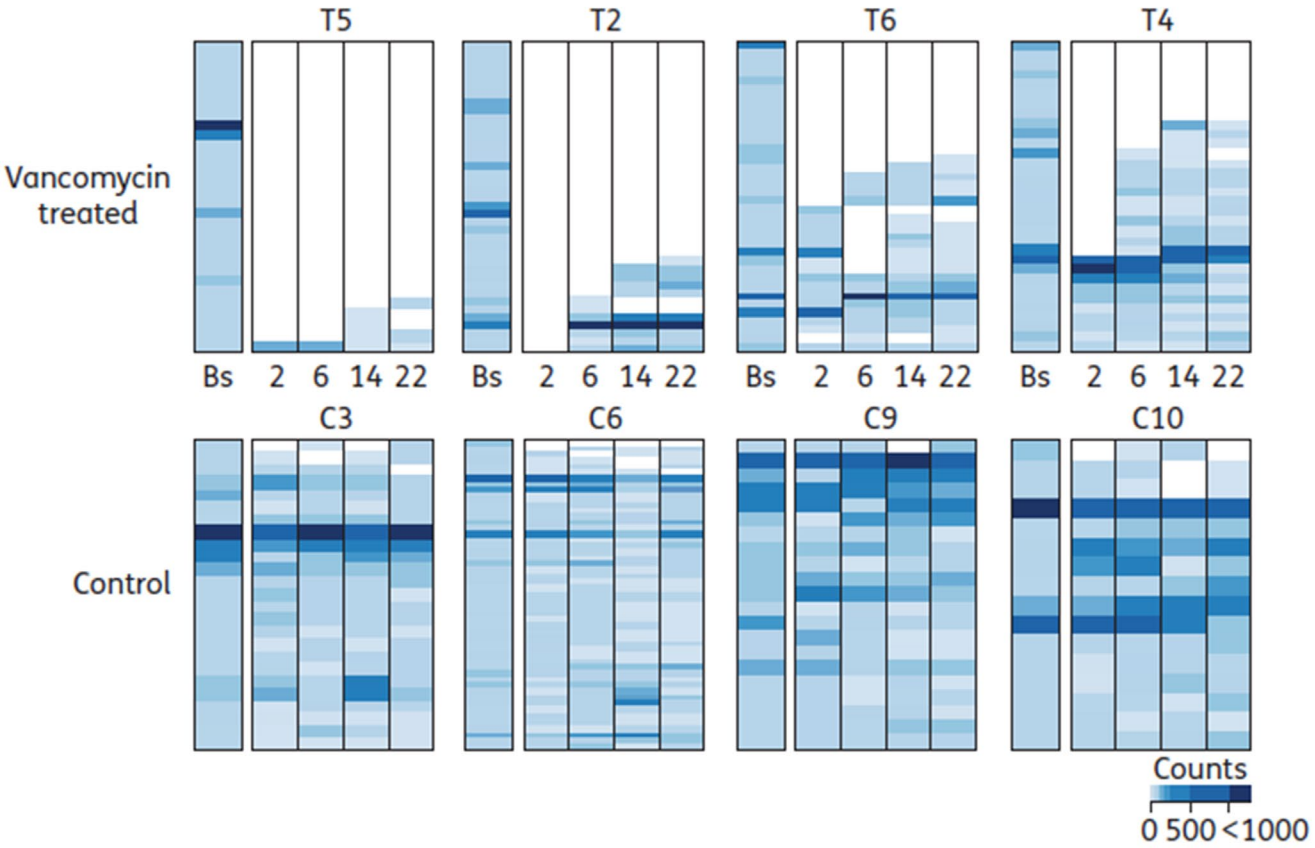
Krishna Rao,[1,2] Daniel Berland,[1,3] Carol Young,[4,5] Seth T. Walk,[1,2,6] and Duane W. Newton[4,5]



Pes správně identifikoval 25 z 30 případů (senzitivita 83 %, 65 % až 94 %) a 265 z 270 kontrol (specificita 98 %, 95 % až 99 %).

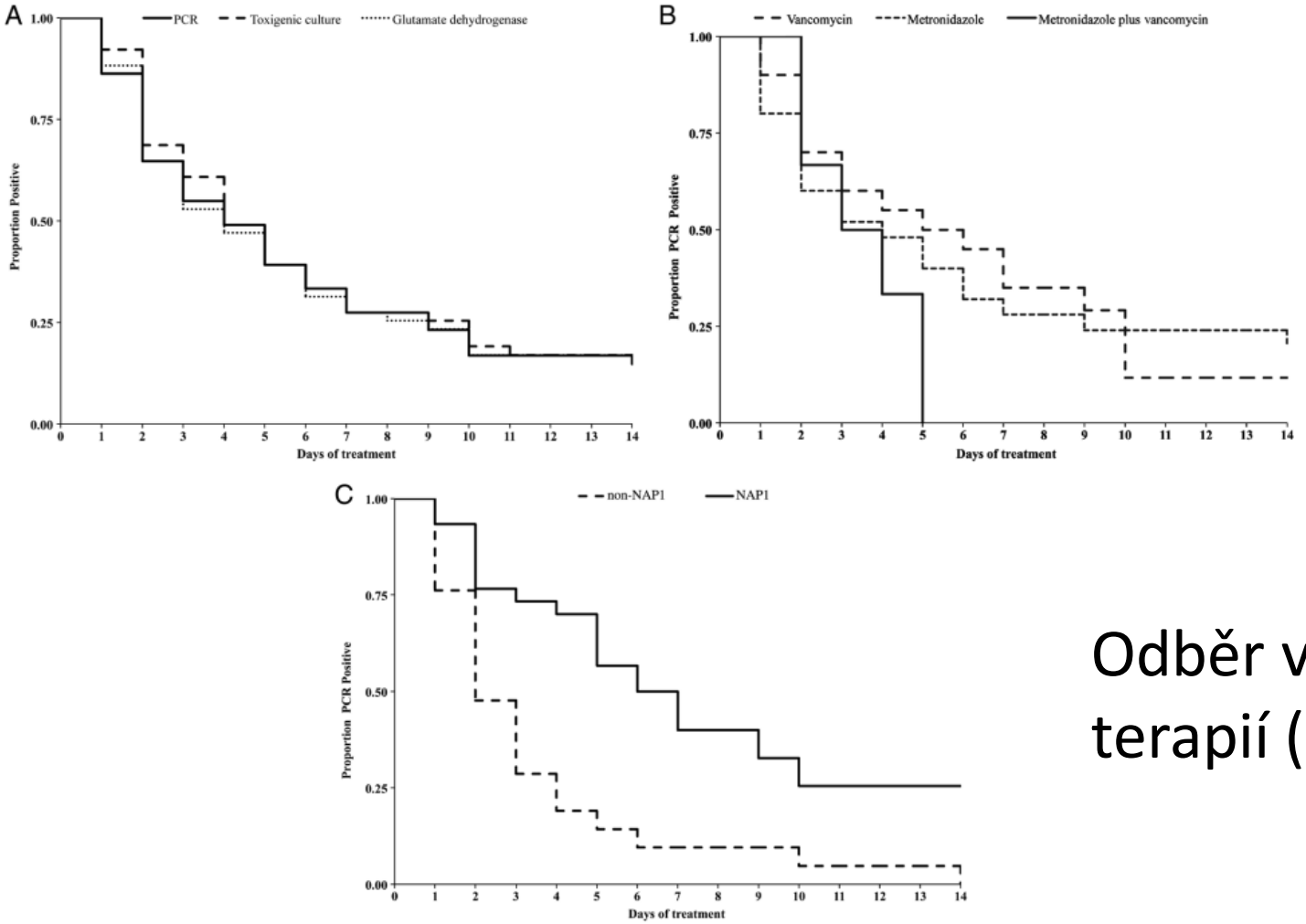
Vankomycin a jeho vliv na střevní mikroflóru





Isaac, JAC, 2017

Empirická terapie CDI vede k falešně negativním výsledkům diagnostických testů



Odběr vzorků před ATB terapií (pokud je to možné)!

Sunkesula et al., 2013

Kdo by měl být testován?

Všichni hospitalizovaní pacienti ve věku ≥2 roky, kteří měli tři nebo více neformovaných stolic do 24 hodin
*40 000 hospitalizovaných pacientů ročně není diagnostikováno, protože se na CDI nemyslelo

Děti do 2 let by měly být testovány případ od případu po konzultaci s pediatrem a klinickým mikrobiologem.
(V Motole není věkové omezení, děti z různými diagnózami)

U dětí, pokud je indikováno laboratorní vyšetření CDI, by měla být zvážena pravděpodobnost kolonizace *C. difficile* a koinfekce jinými střevními patogeny.

Crobach et al., 2016; Krutova et al., 2022, Davies et al., 2014)

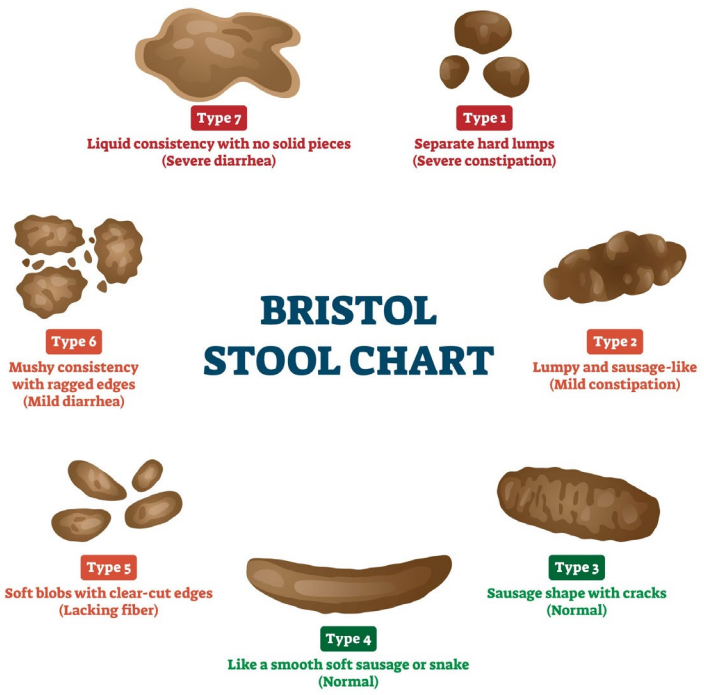
Kdo by měl být testován?

V primární péči by se měli testovat pacienti, kteří nereagují na perorální rehydrataci a kde se zvažuje specifická léčba 
(hospitalizace)

U dětí, pokud je indikováno laboratorní vyšetření CDI, by měla být zvážena pravděpodobnost kolonizace *C. difficile* a koinfekce jinými střevními patogeny.

Krutova et al., CMI, 2022

Odběr vzorků pro vyšetření CDI



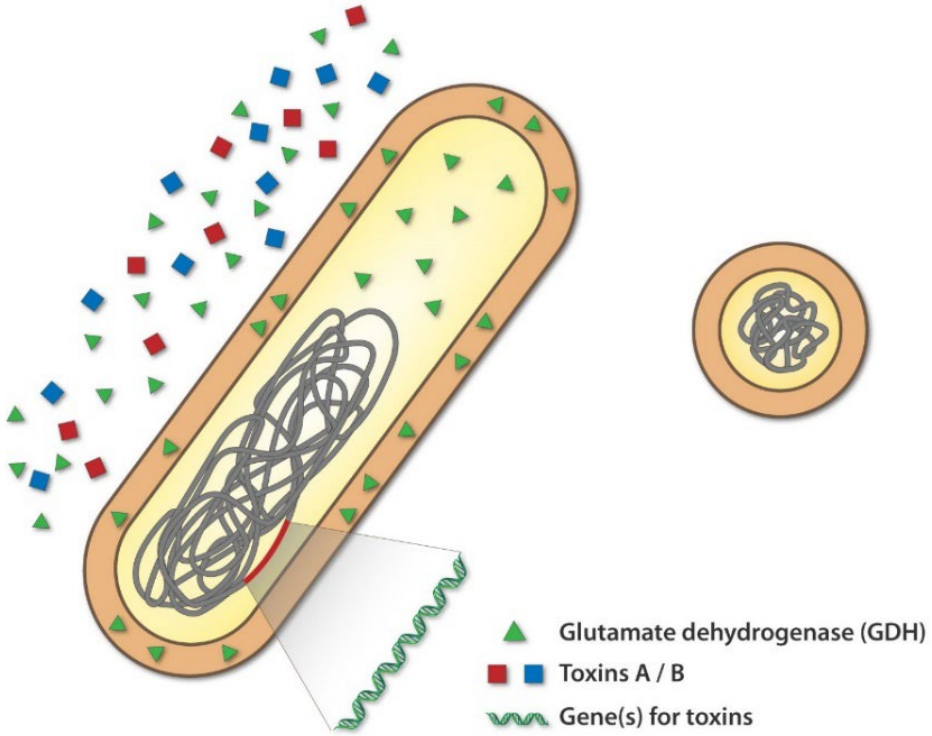
Vzorek neformované stolice (kopírující tvaru kontejneru)

Rektální výtěr:

Pouze paralytický ileus

Kultivace: stolice není k dispozici

Co můžeme testovat?



Glutamátdehydrogenáza (GDH)
(enzym produkovaný všemi kmeny *C. difficile*),EIA

Toxiny A/B
(faktor(y) virulence), EIA

Fragment(y) genu (fragmentů) pro toxiny, PCR
(Nenahlašujte toxiny!)

Kultivace *C. difficile*
(spory)

Jaké testy by měly být použity?

PPV and NPV for different categories of index tests at hypothetical CDI prevalences of 5, 10, 20 and 50%

Test type	CDI prevalence 5%		CDI prevalence 10%		CDI prevalence 20%		CDI prevalence 50%	
	PPV	NPV	PPV	NPV	PPV	NPV	PPV	NPV
Well-type EIA GDH	38	100	54	99	72	98	91	94
Membrane-type EIA GDH	34	100	52	100	71	99	91	98
Well-type EIA toxins A/B	69	99	83	98	91	96	98	87
Membrane-type EIA toxins A/B	81	99	90	98	95	95	99	83
NAAT	46	100	64	100	80	99	94	96

Pooled estimates of sensitivity and specificity compared to cell cytotoxicity neutralization assay were used to calculate the predictive values.
CDI, *Clostridium difficile* infection; EIA, enzyme immunoassay; GDH, glutamate dehydrogenase; NAAT, nucleic acid amplification test; NPV, negative predictive value; PPV, positive predictive value.

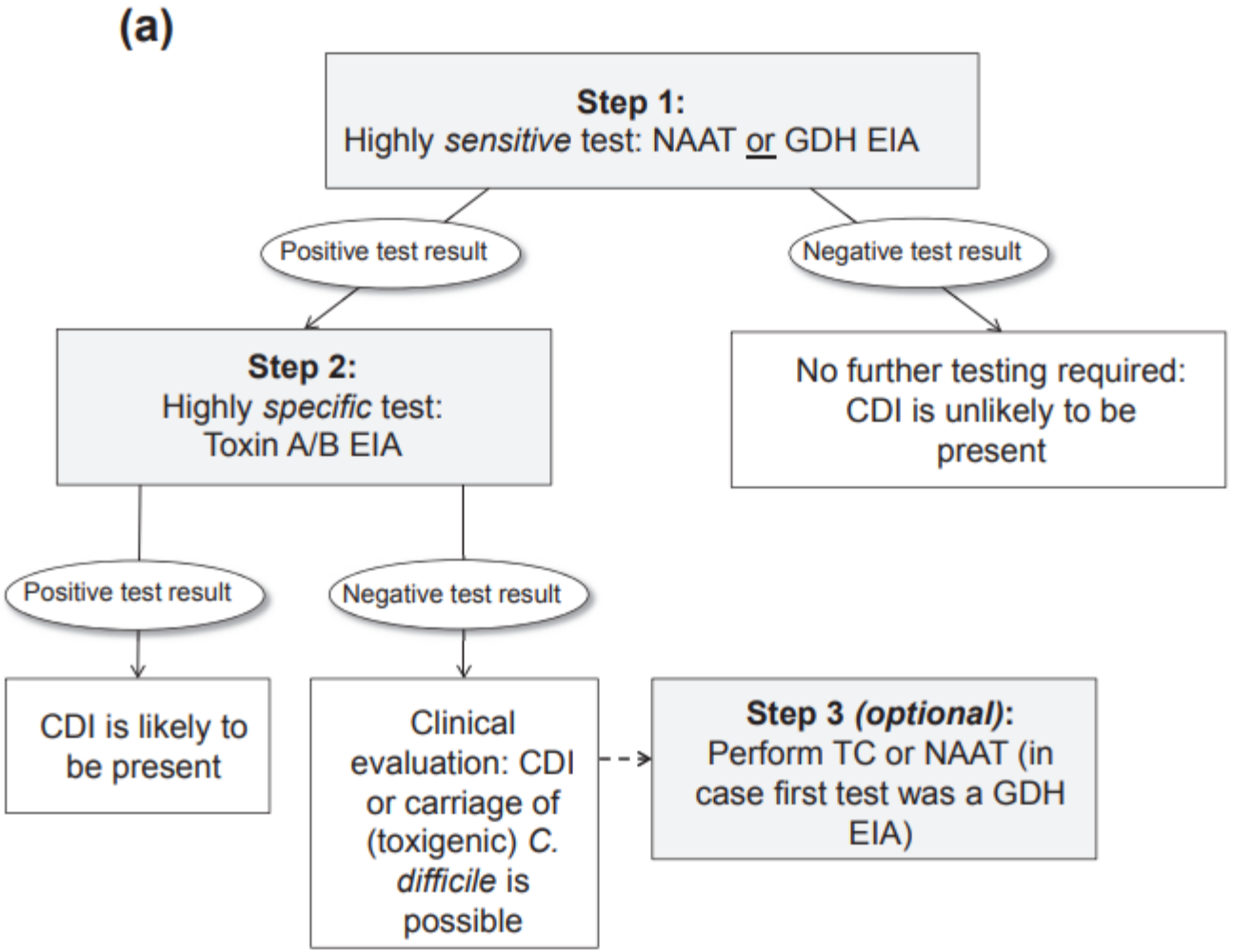
Žádný jednotlivý komerční test nelze použít jako samostatný test pro diagnostiku CDI v důsledku neadekvátních pozitivních prediktivních hodnot při nízké prevalenci CDI.

✓ **Proto se doporučuje použít dvoustupňový algoritmus**

Crobach et al., CMI, 2016

Laboratorní diagnostika CDI

M.J.T. Crobach et al. / Clinical Microbiology and Infection 22 (2016) S63–S81



Crobach et al., CMI, 2016

Děti – koinfekce

U dětí by CDI test neměl být jediným testem v případě průjmu!

de Graaf et al., 2015

Table 2 Number of reported gastrointestinal co-infections in *C. difficile*-positive patients by pathogen

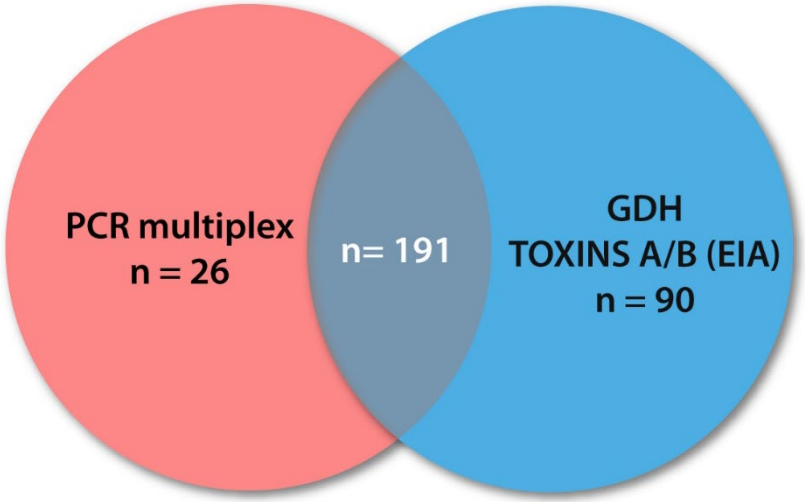
Pathogen	Number of co-infection reports (%)
Viruses	164 (73.9)
Rotavirus	97 (43.7)
Adenovirus	32 (14.4)
Norovirus	17 (7.7)
Astrovirus	9 (4.1)
Sapovirus	5 (2.3)
Others[a]	4 (1.8)
Bacteria	53 (23.9)
E. coli	17 (7.7)
Enteropathogenic	8 (47.1)
Enterotoxigenic	3 (17.6)
Verocytotoxin-producing	4 (23.5)
O18	1 (5.9)
Not specified	1 (5.9)
Salmonella spp.	11 (5.0)
Campylobacter spp.	11 (5.0)
Yersinia spp.	6 (2.7)
Others[b]	8 (3.6)
Parasites	5 (2.3)
Blastocystis hominis	1 (0.45)
Entamoeba histolytica	2 (0.9)
Giardia spp.	2 (0.9)

[a] Calicivirus (n=2), coxsackievirus (n=1), enterovirus (n=1)

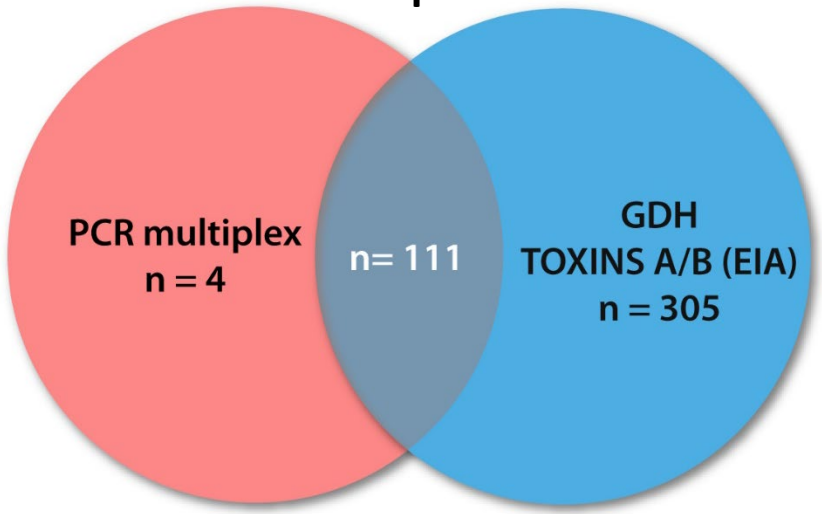
[b] *Bacillus cereus* (n=3), *Aeromonas* spp. (n=2), *Shigella* spp. (n=2), *Vibrio cholerae* (n=1)

Testování stolice: ÚLM FNM

Děti



Dospělí



květen-srpen 2022

- **Multiplex PCR** (denně)
- bakterie, viry, paraziti
- AusDiagnostics (panel M)
- 20 cílů (také *C. difficile*)

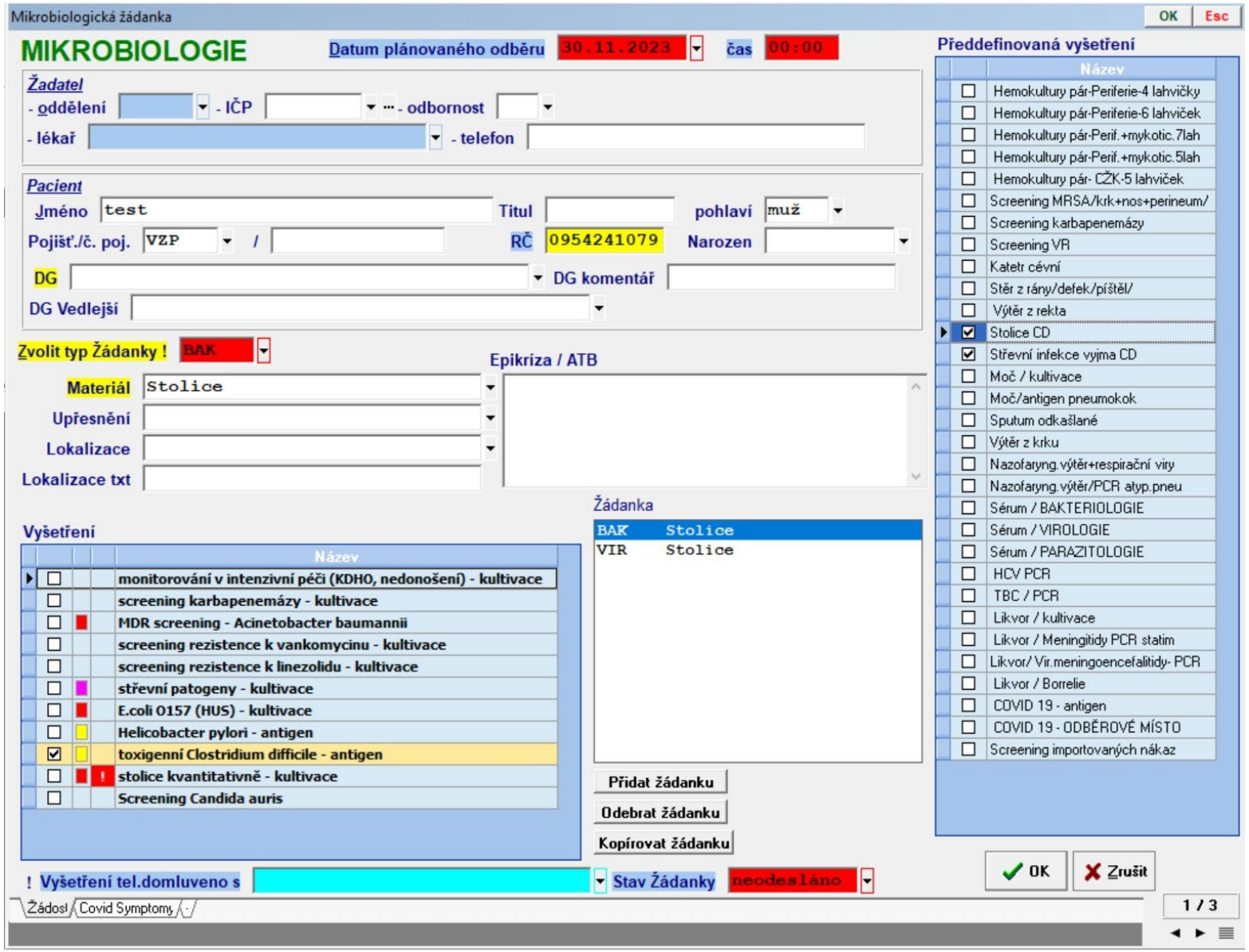
CDI (2 hod) - EIA

ArcDia - mariPOC CDI

- Glutamátdehydrogenáza(GDH)
- *C. difficile* toxiny A/B

Interní evaluace: Krutova et al., JCM, 2019

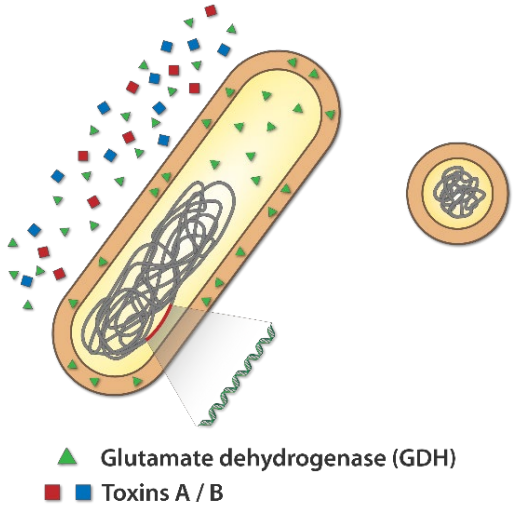
Testování stolice: ÚLM FNM-elektronická žádanka



Testování stolice: ÚLM FNM

Telefonické hlášení

- ✓ Aktuální klinický stav pacienta (časová prodleva)
- ✓ Počet a konzistence stolice!
- ✓ Vysvětlení jednotlivých laboratorních nálezů
- ✓ GDH pozitivita bez toxinů
- ✓ **Terapie s antibiotickým centrem**
- ✓ **Izolace pacienta s epidemiology**



C. difficile (PCR positive)

n=21/115 (18.3%)

GDH negative
toxin A/B negative

n=2/21 (9.5 %)

Shigella (n=1)
Adenovirus (n=1)

n=2/2 (100%)

No patient was treated

C. difficile (PCR positive)

n=65/191 (34.0%)

GDH negative
toxin A/B negative

n=6/65 (9.2 %)

mNAAT negative

n=6/6 (100%)

No patient was treated

C. difficile (PCR positive)

n=21/115 (18.3%)

GDH positive
toxin A/B positive

n=14/21 (66.7%)

Aeromonas (n=2)
Rotavirus + Adenovirus (n=1)

n=3/14 (21.4%)

All patients were treated for CDI

Rotavirus a Norovirus co-infecti-on – 96 years old patient

C. difficile (PCR positive)

n=65/191 (34.0%)

GDH positive
toxin A/B positive

n=29/65 (44.6%)

Aeromonas (n=2)
Rotavirus (n=4)
Adenovirus (n=3)
Norovirus + Adenovirus (n=1)

n=10/29 (34.5%)

Four patients (40%) were treated from co-infection group.
Nine patients (47.4%) were treated from *C. difficile* „only" group.
Frequent diarrhea significant dehydration, weight loss

C. difficile (PCR positive)

n=21/115 (18.3%)

GDH positive
toxin A/B negative

n=5/21 (23.8%)

Campylobacter (n=1)
Rotavirus (n=1)
Norovirus GII (n=1)

n=3/5 (60.0%)

One adult patient– abdomen pain, diarrhoea, palliative care, treated by vancomycin, RT012

C. difficile (PCR positive)

n=65/191 (34.0%)

GDH positive
toxin A/B negative

n=30/65 (46.2%)

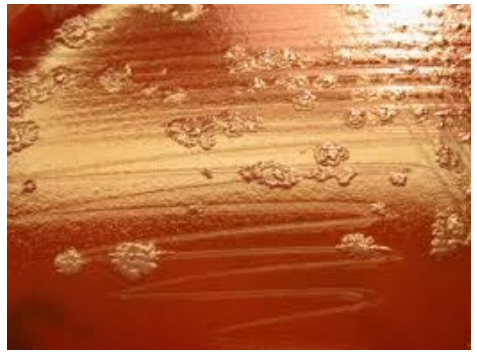
Sapovirus (n=1)
Rotavirus (n=3)
Norovirus GII (n=3)
Adenovirus (n=2)
Astrovirus (n=2)
Rotavirus a Norovirus (n=1)
Norovirus a Adenovirus (n=1)

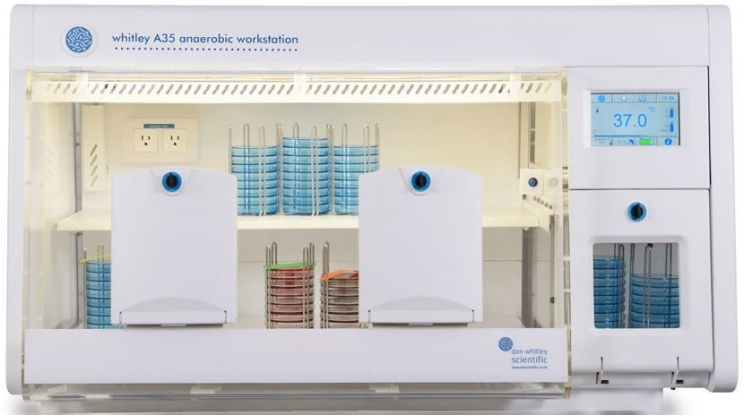
n=6/6 (100%)

One patient treated (after 2nd cycle of chemotherapy, diarrhoea, increasing CRP, 9 month)

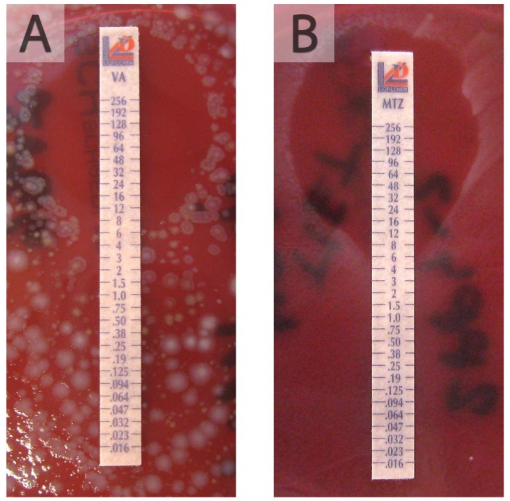
RT033 (del *tcdA* gene, *tcdB* gene – not present, binary toxin genes)

Kultivace *C. difficile*-proč?

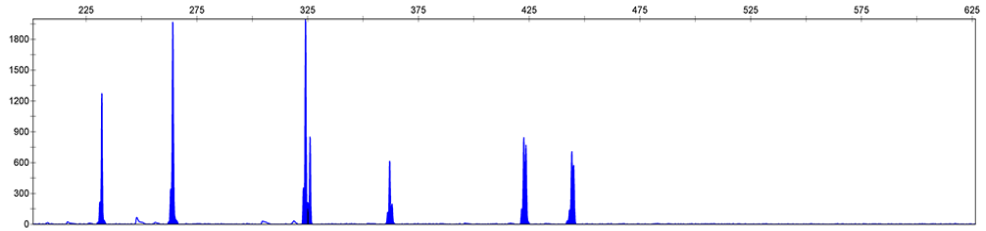




Vzorek stolice a alkoholu 1:1, 30 minut. Potlačení růstu ostatních bakterií ve vzorku, povzbuzení klíčení spor. Kultivace na selektivních médiích, anaerobní atmosféra 24-48 hod.



Testování antimikrobiální citlivosti a charakterizace kmene pro epidemiologické účely



Doporučené postupy USA/Evropa

Clin Infect Dis. 2018 Mar 19;66(7):987-994. doi: 10.1093/cid/ciy149.

Clinical Practice Guidelines for Clostridium difficile Infection in Adults and Children: 2017 Update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA)

L Clifford McDonald [1], Dale N Gerding [2], Stuart Johnson [2 3], Johan S Bakken [4], Karen C Carroll [5], Susan E Coffin [6], Erik R Dubberke [7], Kevin W Garey [8], Carolyn V Gould [1], Ciaran Kelly [9], Vivian Loo [10], Julia Shaklee Sammons [6], Thomas J Sandora [11], Mark H Wilcox [12]

Practice Guideline Clin Infect Dis. 2021 Sep 7;73(5):755-757. doi: 10.1093/cid/ciab718.

Clinical Practice Guideline by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA): 2021 Focused Update Guidelines on Management of Clostridioides difficile Infection in Adults

Stuart Johnson [1 2], Valéry Lavergne [3 4], Andrew M Skinner [1 2], Anne J Gonzales-Luna [5], Kevin W Garey [5], Ciaran P Kelly [6], Mark H Wilcox [7]

Clin Microbiol Infect. 2021 Dec;27 Suppl 2:S1-S21. doi: 10.1016/j.cmi.2021.09.038. Epub 2021 Oct 20.

European Society of Clinical Microbiology and Infectious Diseases: 2021 update on the treatment guidance document for Clostridioides difficile infection in adults

Joffrey van Prehn [1], Elena Reigadas [2], Erik H Vogelzang [3], Emilio Bouza [2], Adriana Hristea [4], Benoit Guery [5], Marcela Krutova [6], Torbjorn Norén [7], Franz Allerberger [8], John E Coia [9], Abraham Goorhuis [10], Tessel M van Rossen [3], Rogier E Ooijevaar [11], Karen Burns [12], Bente R Scharvik Olesen [13], Sarah Tschudin-Sutter [14], Mark H Wilcox [15], Maria J G T Vehreschild [16], Fidelma Fitzpatrick [17], Ed J Kuijper [18];
Guideline Committee of the European Study Group on Clostridioides difficile

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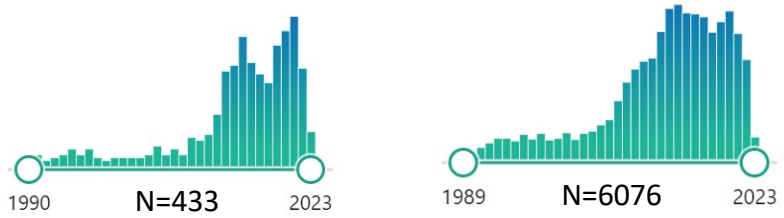
journal homepage: www.clinicalmicrobiologyandinfection.com

Narrative review

How to: *Clostridioides difficile* infection in children

Marcela Krutova [1, 7, 8, *], Tim G.J. de Meij [2], Fidelma Fitzpatrick [3, 7, 8], Richard J. Drew [4, 7], Mark H. Wilcox [5, 7], Ed J. Kuijper [6, 7, 8]



Evropské pokyny nezahrnují děti, samostatný dokument (názor expertů).

České doporučené postupy (léčba CDI a FMT)

infektologie.cz

Updated Czech guidelines for the treatment of *Clostridioides difficile* infection

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Content

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Full text (pdf)

Abstract

The updated Czech guidelines differ in some aspects from the 2021 guidelines issued by the ESCMID Study Group for *Clostridium difficile*. The key points of these Czech recommendations may be summarized as follows:

● The drug of choice for hospitalized patients is orally administered fidaxomicin or vancomycin. In outpatients with a mild first episode of *C. difficile* infection, metronidazole can also be used.

● If the patient´s response to treatment is good and there are no complications, the duration of antibiotic treatment can be reduced (e.g., to 5 days in case of fidaxomicin or to 6-7 days in case of vancomycin).

● If oral therapy is impossible, the drug of choice is tigecycline, 100 mg i.v., b.i.d., with initial shortening of the interval between the first and second doses for faster saturation. If the severity of the disease progresses during this antibiotic treatment, it is necessary to access the ileum or cecum, i.e. to perform double ileostomy or percutaneous endoscopic cecostomy, and to instill vancomycin or fidaxomicin lavages.

● Fulminant *C. difficile* colitis should be treated with oral fidaxomicin ± tigecycline i.v. If peristalsis ceases, fidaxomicin should be administered into the ileum or cecum as described above. If sepsis develops, a broad-spectrum beta-lactam antibiotic (piperacillin/tazobactam, carbapenem) i.v. is added to topically administered fidaxomicin instead of tigecycline i.v.; at the same time, colectomy should be considered as the last resort.

● To treat first recurrence, fidaxomicin or vancomycin is administered with a subsequent fecal microbiota transplant (FMT) from a healthy donor. For second or subsequent recurrence, administration of fidaxomicin is of little benefit; the therapy of choice is oral vancomycin and subsequent FMT. Prolonged vancomycin or fidaxomicin taper and pulse treatment is appropriate only when FMT cannot be performed. The guidelines were reported and defended at the Annual Meeting of Heads of Infectious Disease Departments in the Czech Republic.

Keywords

Clostridioides difficile infection, vancomycin, fidaxomicin, metronidazole, fecal microbiota transplant

Doporučený postup fekální bakterioterapie pro léčbu rekurentní klostridiové kolitidy

Doporučený postup Společnosti infekčního lékařství České lékařské společnosti J. E. Purkyně

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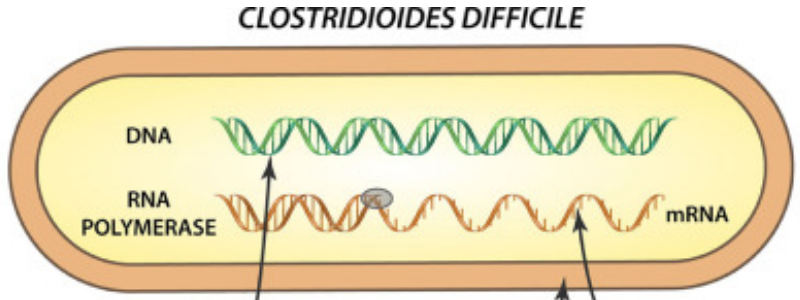
Schváleno

- výborem Společnosti infekčního lékařství (SIL) ČLS JEP

Datum vydání

- 9. dubna 2018

Antimikrobiální látky schválené pro léčbu CDI



	METRONIDAZOLE	VANCOMYCIN	FIDAXOMICIN
SYSTEMIC ABSORPTION	HIGH	LOW	LOW
STOOL CONCENTRATION	LOW	HIGH	HIGH
REDUCTION OF BIOACTIVITY BY FAECES	HIGHEST	LOWER	LOWER
EFFECT ON DIVERSITY OF MICROBIOTA	REDUCTION	REDUCTION	PRESERVATION
STOOL SHEDDING DECLINE	SLOW	RAPID	RAPID
ENVIRONMENTAL CONTAMINATION	HIGHEST	LOWER	LOWER (STEEPER)
SPOROCIDAL EFFECT	—	NO	YES
INHIBITION OF SPORULATION	NO	NO	YES

SUPPORTIVE · LESS-SUPPORTIVE · NON-SUPPORTIVE · — NO DATA

Overview of pharmacodynamic, pharmacokinetic and microbiological properties for oral administration of metronidazole, vancomycin and fidaxomicin.

Farmakokinetické rozdíly metronidazolu, vankomycinu a fidaxomicinu.

Krůtová et al., 2022

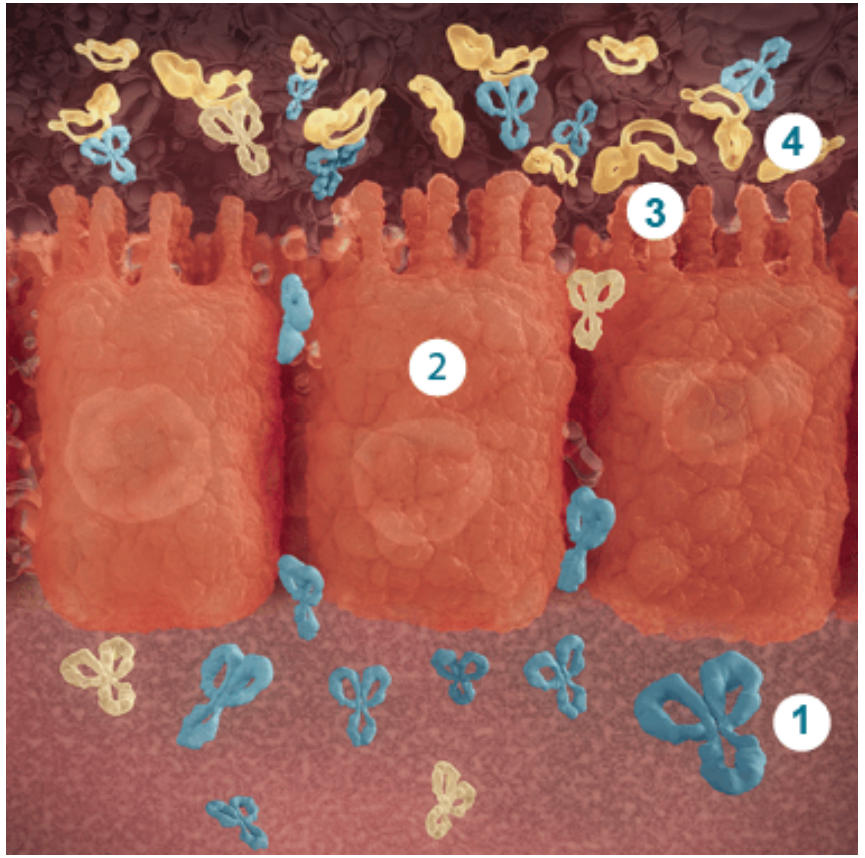
Pasivní imunizace

Bezlotoxumab (ZINPLAVATM) je lidská monoklonální protilátka, která se váže na toxin B *Clostridioides difficile* a je indikovaný k prevenci recidivy CDI.

Měl by být používán pouze v kombinaci s antibakteriální léčbou CDI!

Clinical Trial › N Engl J Med. 2017 Jan 26;376(4):305-317. doi: 10.1056/NEJMoa1602615.

The rate of recurrent *C. difficile* infection was significantly lower with bezlotoxumab alone than with placebo (MODIFY I: 17% [67 of 386] vs. 28% [109 of 395]; adjusted difference, **-10.1** percentage points; 95% confidence interval [CI], -15.9 to -4.3; P<0.001; MODIFY II: 16% [62 of 395] vs. 26% [97 of 378]; adjusted difference, -**9.9** percentage points; 95% CI, -15.5 to -4.3; P<0.001)



1. ZINPLAVA
2.Poškozené střevní epiteliální buňky, toxin B
3.ZINPLAVA se váže na toxin B

FMT: Transplantace fekální mikrobioty

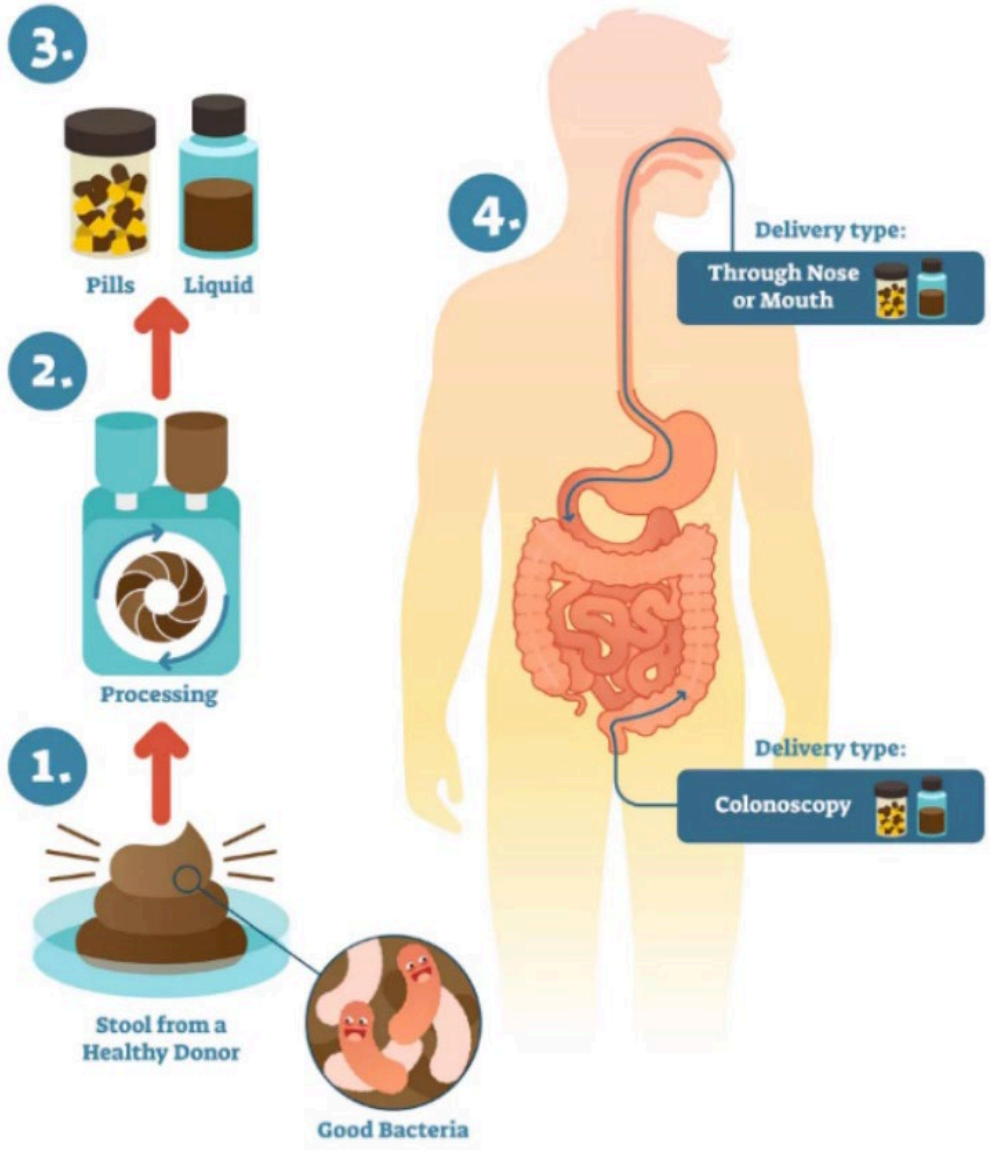


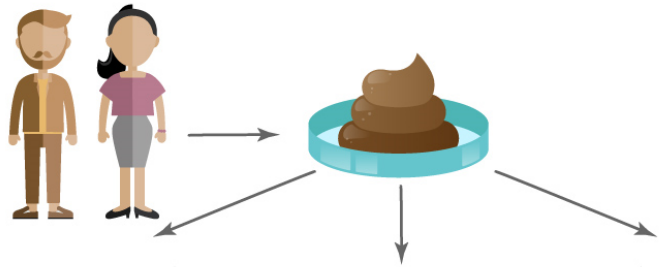
Table 2
Donor screening by laboratory screening of faeces and serum

Laboratory screening serum	Laboratory screening faeces
• Hepatitis A (IgM + IgG) • Hepatitis B (HBsAg + anti-Hbcore) • Hepatitis C (anti-HCV) • Hepatitis E (IgM + IgG) • HIV (anti-HIV, type 1 and 2) • Lues; *Treponema pallidum* (Ig) • Cytomegalovirus (IgM + IgG) • Epstein Barr Virus (IgM + IgG) • *Strongyloïdes* (IgG1/IgG4)[a]	• *Clostridium difficile* (PCR) • *Helicobacter pylori* (antigen test) • Bacterial gastroenteritis: (PCR, followed by culture) *Salmonella* spp. *Campylobacter* spp., *Campylobacter jejuni*, *C. coli*, *Shigella* spp., *Yersinia enterocolitica* and *Y. pseudotuberculosis*, *Aeromonas* spp., *Plesiomonas shigelloides*, and Shiga Toxin-producing *E. coli* • Antibiotic-resistant bacteria (culture); ESBL and/or carbapenemase-producing bacteria, vancomycin-resistant enterococci, and methicillin-resistant *Staphylococcus aureus* • Viral pathogens (PCR): Norovirus serotype I+II, Astrovirus, Sapovirus, Rotavirus, Adenovirus 40/41, Adenovirus non-40/41, Enterovirus, Parechovirus, Hepatitis E • Parasites (PCR): *Giardia lamblia*, *Entamoeba histolytica*, *Cryptosporidium parvum* and *C. hominis*, *Microsporidium* spp, *Strongyloïdes*[a] • Microscopy for ova, cysts, and larvae [69]: e.g. *Blastocystis hominis*

Questionnaire: 1 day before donation of faeces
Stool frequency/pattern, general health, use of antibiotics, travel history, sexual behaviour

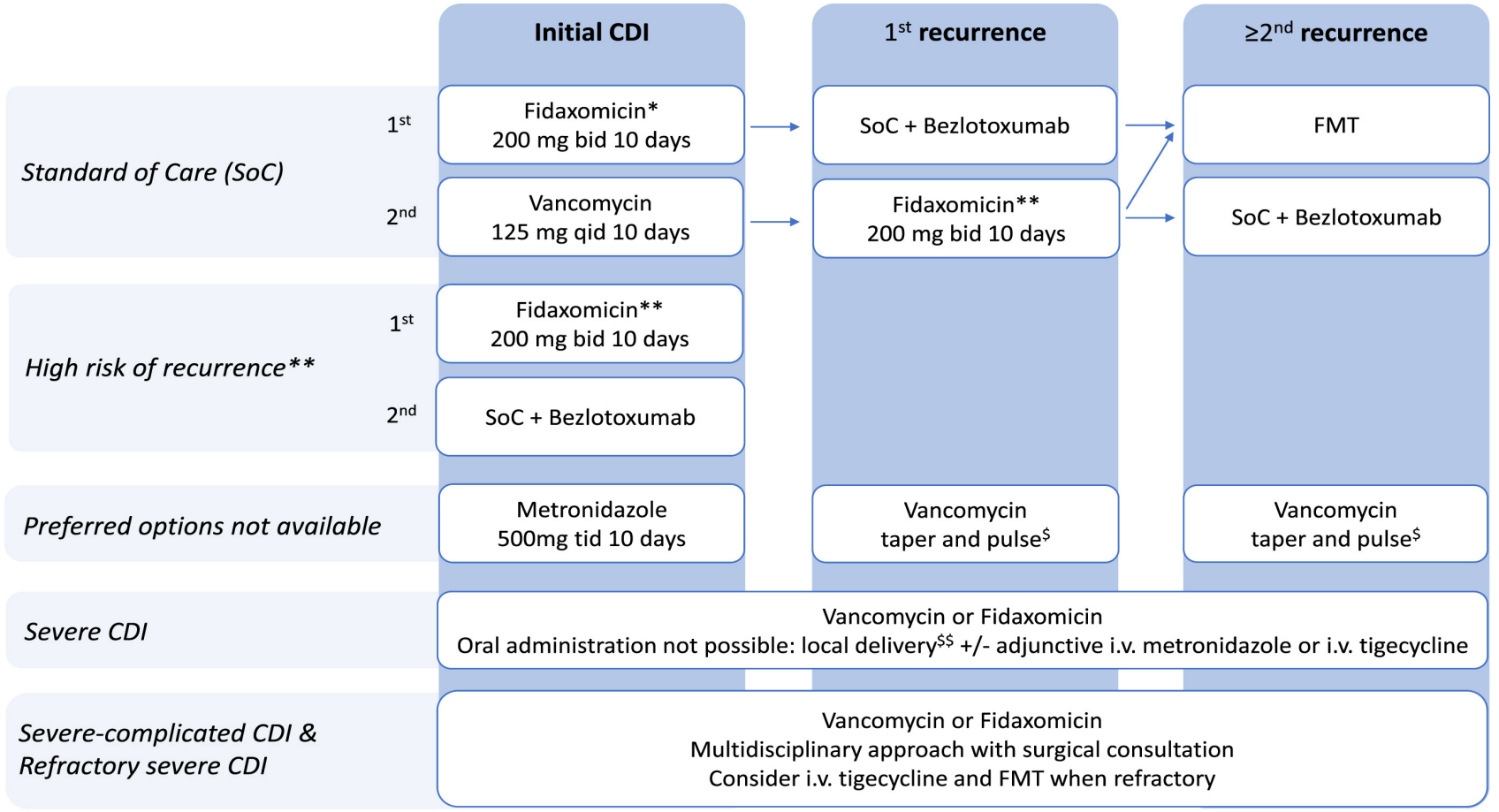
Terveer et al., 2017

Budoucí FMT? Živá bioterapeutika



PRODUCT NAME	RBX2660	SER-109	VE303
PRODUCT TYPE	FMT-DERIVED		BACTERIAL CONSORTIA
STOOL PROCESSING	Dilution (0.9% saline/polyethylene glycol)	Spore enrichment (50 – 70% v/v EtOH 2-hrs treatment)	Bacterial culture (8 strains of Clostridiales)
FORM OF DELIVERY	Liquid enema	4x Oral capsules	2x / 10x Oral capsules Low dose / High dose
REDUCTION OF rCDI	13.1%	28.0%	8.5% / 31.7%
BATCH-TO-BATCH VARIATION	YES	YES	NO
CHARACTERIZATION OF COMPOSITION	NO	NO	YES
RISK OF PATHOGEN (AMR) TRANSMISSION	POSSIBLE	POSSIBLE	LIMITED

Aktuálně platné pokyny pro léčbu CDI



* Risk stratification for risk of recurrence may be applied for selective use of fidaxomicin in case of limited access or resources.

** Consider extended fidaxomicin: 200 mg bid on day 1-5, 200 mg q48h on day 7-25. Most important risk factor for recurrence is age >65-70 years. Additional risk factor(s) to consider are healthcare-associated CDI, prior hospitalization ≤ 3 months, prior CDI episode, continued non-CDI antibiotic use, and PPI therapy started during/after CDI diagnosis. The risk of recurrence is assumed higher with more risk factors present.

$ Vancomycin taper and pulse: 2 weeks 125 mg qid, followed by 1 week 125 mg bid, then 1 week 125 mg qd, then 1 week 125 mg q48h, and finally 125 mg q72h for 1 week.

$$ Rectal or nasoduodenal delivery

van Prehn et al., 2021

Prevence šíření *C. difficile*

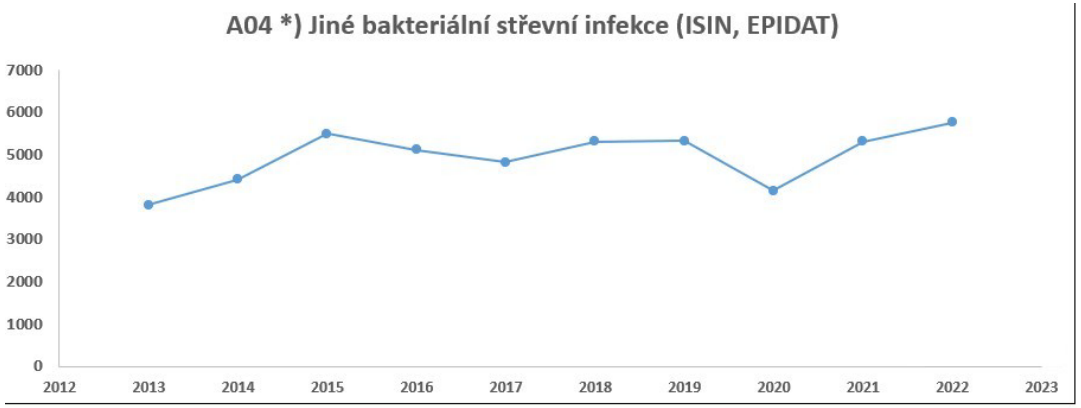
Review > Clin Microbiol Infect. 2018 Oct;24(10):1051-1054. doi: 10.1016/j.cmi.2018.02.020. Epub 2018 Mar 2.

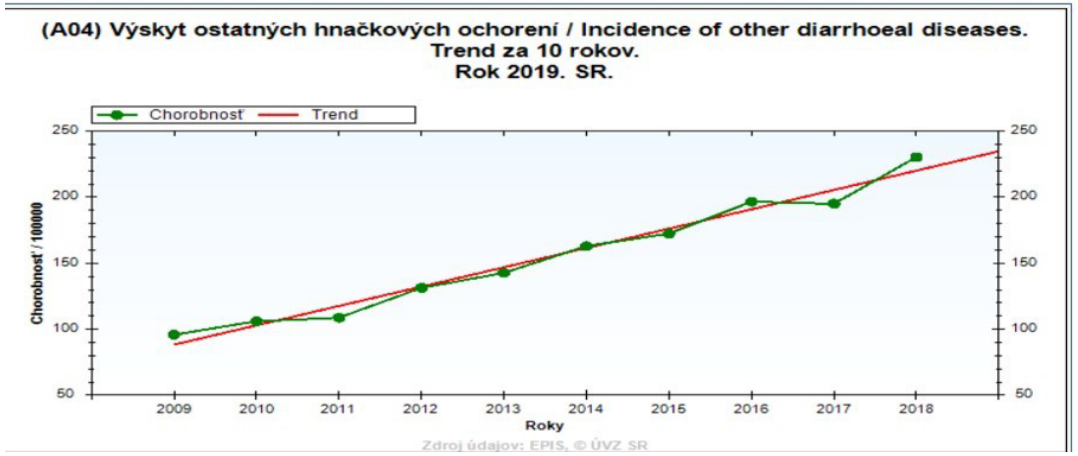
Guidance document for prevention of Clostridium difficile infection in acute healthcare settings

- ✓ Hygiena rukou – voda a mýdlo (místo alkoholu), a co kombinace?
- ✓ Používání osobních ochranných prostředků: rukavice a pláště/jednorázové zástěry
- ✓ Kontaktní opatření
- ✓ Zavést každodenní sporicidní dezinfekci a terminální dezinfekci pokojů pacientů s CDI
- ✓ Omezení používání určitých skupin antibiotik je účinné
- ✓ Zkrácení doby antibiotické terapie (léčba přidružených infekcí)
- ✓ Vzdělávat zdravotnické pracovníky v oblasti prevence CDI s cílem rozšířit jejich znalosti a dovednosti
- ✓ Poučit pacienty a návštěvníky CDI o preventivních opatřeních pro CDI

Surveillance CDI!

National *C. difficile* surveillance





FN MOTOL

ISIN (Informační systém infekčních nemocí)
-dříve EPIDAT

EPIS (Epidemiologický informační systém)

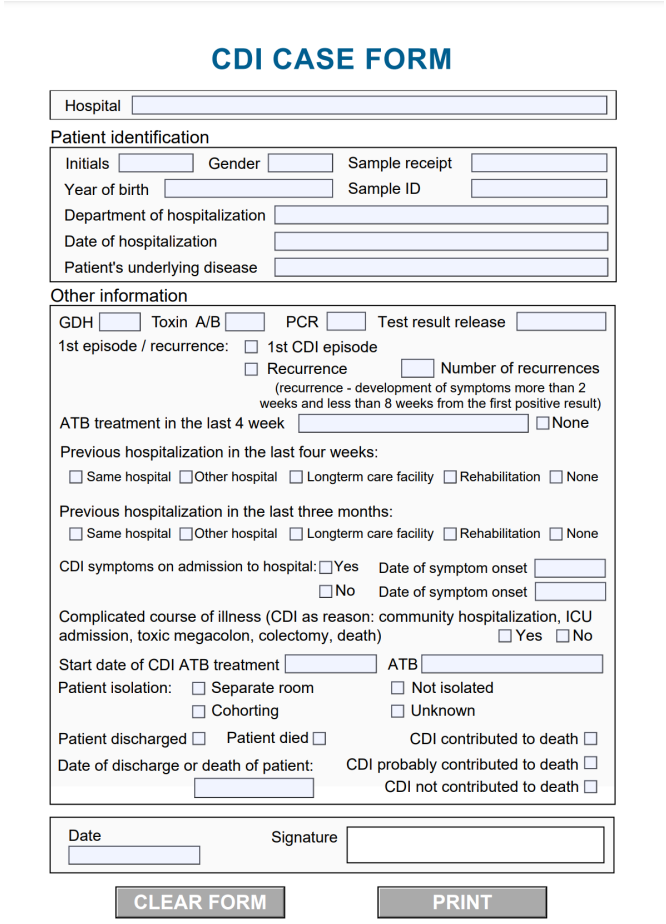
Český a slovenský systém pro hlášení infekčních nemocí.
Kód A04: Jiné bakteriální střevní infekce

C. difficile surveillance

Table 1. Information collected for different CDI surveillance options

	Minimal surveillance	Light surveillance	Enhanced surveillance	Form
Collected information	• **Minimum CDI surveillance for each hospital** (aggregated numerator data) • **Hospital data for each hospital** (aggregated denominator data)	• **Minimum CDI surveillance for each hospital** (aggregated numerator data) • **Hospital data for each hospital** (aggregated denominator data)	• **Minimum CDI surveillance for each hospital** (aggregated numerator data) • **Hospital data for each hospital** (aggregated denominator data)	• **Form H** (aggregated numerator and denominator data)
		• **Information on each CDI case** (case-based numerator data)	• **Information on each CDI case** (case-based numerator data)	• **Form C** (case-based numerator data)
			• **Microbiological data** (for the first 5 consecutively detected cases in each participating healthcare facility: characterisation, susceptibility testing and typing of each *C. difficile* isolate)	• **Form M** (one form for each *C. difficile* isolate)
Surveillance period	**Recommended:** continuous surveillance for 12 months, starting on the first* day of the month. The **recommended minimum** surveillance period is three consecutive months, preferably from 1 October to 31 December, or from 1 January to 31 March. The absolute minimum surveillance period is one month, starting on the first day of the month. *The pilot study demonstrated that completion of Form H is made much easier by starting surveillance on the first day of a month.			

ECDC, CDI surveillance protocol v2.4, 32 pages



CDI CASE FORM

Hospital

Patient identification

Initials | Gender | Sample receipt

Year of birth | Sample ID

Department of hospitalization

Date of hospitalization

Patient's underlying disease

Other information

GDH | Toxin A/B | PCR | Test result release

1st episode / recurrence: ☐ 1st CDI episode

☐ Recurrence ☐ Number of recurrences

(recurrence - development of symptoms more than 2 weeks and less than 8 weeks from the first positive result)

ATB treatment in the last 4 week ☐ None

Previous hospitalization in the last four weeks:

☐ Same hospital ☐ Other hospital ☐ Longterm care facility ☐ Rehabilitation ☐ None

Previous hospitalization in the last three months:

☐ Same hospital ☐ Other hospital ☐ Longterm care facility ☐ Rehabilitation ☐ None

CDI symptoms on admission to hospital: ☐ Yes Date of symptom onset

☐ No Date of symptom onset

Complicated course of illness (CDI as reason: community hospitalization, ICU admission, toxic megacolon, colectomy, death) ☐ Yes ☐ No

Start date of CDI ATB treatment | ATB

Patient isolation: ☐ Separate room ☐ Not isolated ☐ Cohorting ☐ Unknown

Patient discharged ☐ Patient died ☐ CDI contributed to death ☐

Date of discharge or death of patient: CDI probably contributed to death ☐

CDI not contributed to death ☐

Date | Signature

CLEAR FORM PRINT

Krutova M. - Faculty Hospital Motol

C. difficile surveillance-Evropa

Surveillance Atlas of Infectious Diseases

Healthcare-associated infections: Clostridium difficile infections | Clostridium difficile infections | - Subpopulation - | - Indicator - | 2017

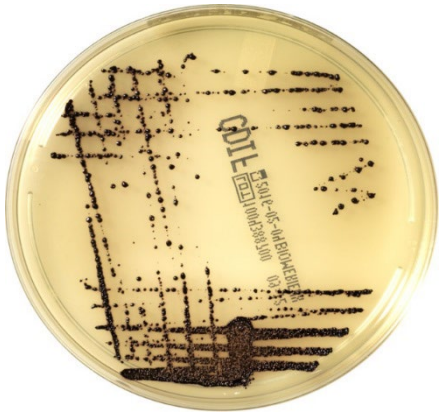
Region	CDI, all cases (N/10 000 patient-days)
EU/EEA	3.51
Austria	.
Belgium	2.58
Croatia	.
Estonia	7.83
Finland	4.88
France	3.10
Germany	.
Hungary	2.93
Ireland	3.56
Latvia	.
Lithuania	8.82
Malta	1.62
Netherlands	2.91
Poland	.
Portugal	.
Slovakia	3.32
Spain	.
United Kingdom - England	3.97
United Kingdom - Scotland	1.60
United Kingdom - Wales	1.24

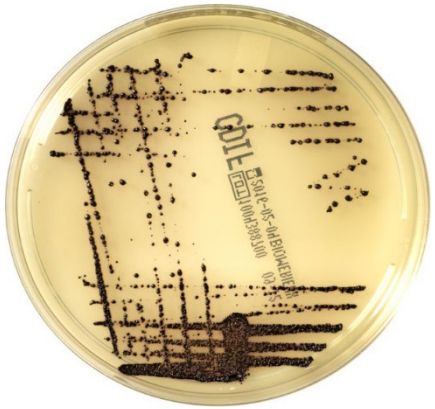
CDI, all cases (N/10 000 patient-days)

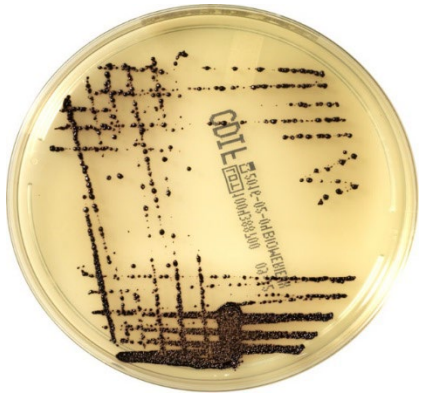
- 0.00 - 2.04
- 2.05 - 5.39
- 5.40 - 7.83
- 7.84 - 8.82
- 8.83 - 16.94

Proč bychom měli charakterizovat izoláty *C. difficile* (případy CDI)? Pojmenujte případ CDI!



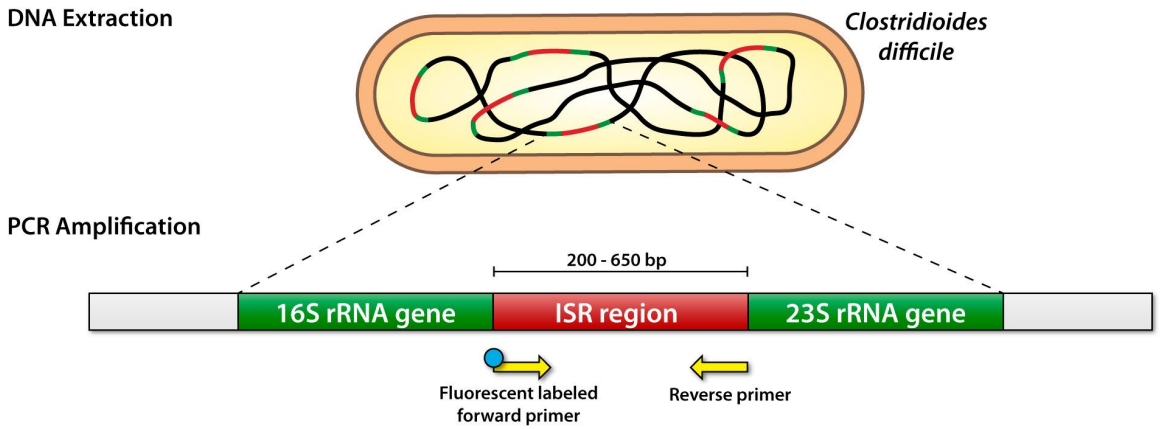


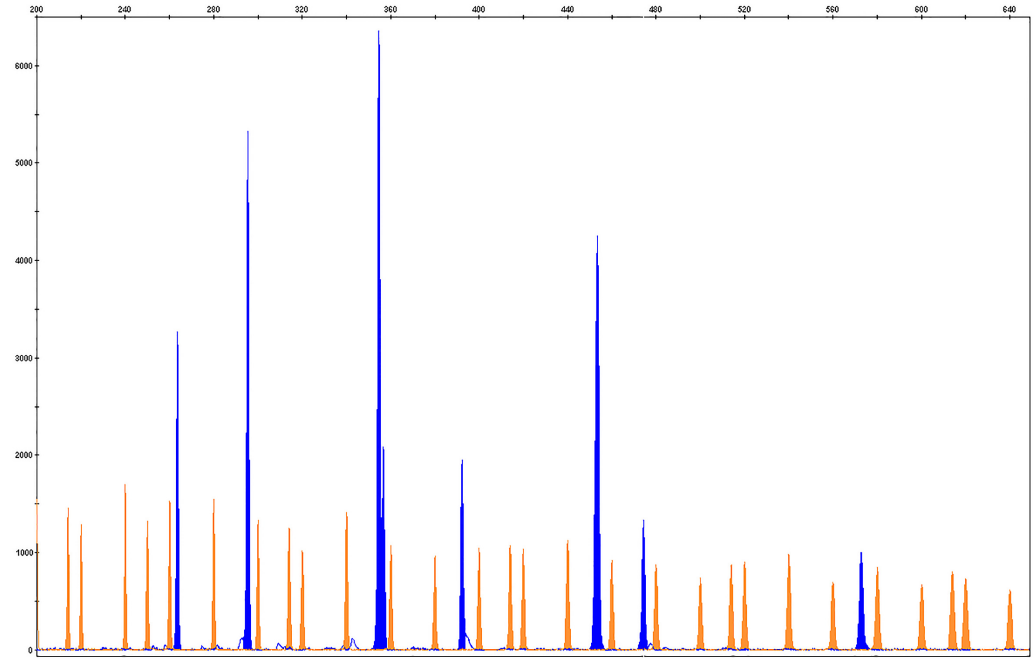




Sledování výskytu a šíření ve zdravotnickém zařízení

C. difficile PCR ribotypizace





AGES
Österreichische Agentur für Gesundheit und Ernährungssicherheit GmbH

WEBRIBO

Implementace typizačních dat do rutinní mikrobiologie

Makroskopie

Kultura

Charakterizace izolátu

Testování stolice

Kult	Dat		Operace	
			Makroskopický vzhled	
	11.03-10:57		Makroskopický vzhled:	~~barva zelená; konzistence tekutá; hlen ne; krev ne; poznámka~~
			Kultivace cílená na Clostridium difficile	
1	11.03-13:23		půda pro Cl.difficile	Clostridium difficile
	14.03-07:35		Identifikace Maldi - anaerobi	~~Clostridioides difficile~~
	14.03-07:35		E-test Clostridium difficile	VAN+ MET+
			PCR průkaz toxinu Cl.difficile	
	14.03-09:00		Gen pro produkci toxinu A:	POZITIVNÍ
	14.03-09:00		Gen pro produkci toxinu B:	POZITIVNÍ
	14.03-09:00		Gen pro produkci binárního toxinu:	negativní
	14.03-09:00		Ribotyp:	001
			Gastropanel (FIA)	
	11.03-10:57		C. difficile - GDH:	32,2 - POZITIVNÍ
	11.03-10:57		C. difficile - toxiny A/B:	246,1 - POZITIVNÍ
	11.03-10:57		Norovirus GII.4:	~~negativní~~
	11.03-10:57		Norovirus GI:	~~negativní~~
	11.03-10:57		Rotavirus:	~~negativní~~
	11.03-10:57		Adenovirus:	~~negativní~~
	11.03-10:57		Campylobacter spp.:	~~negativní~~

445 E-test (CLDI) Uzavřít

ATB	Mez	Výsl		Hodn	T	*
vanko	2-2	0.38	C	C	☑	☐
metro	2-2	0.75	C	C	☑	☐

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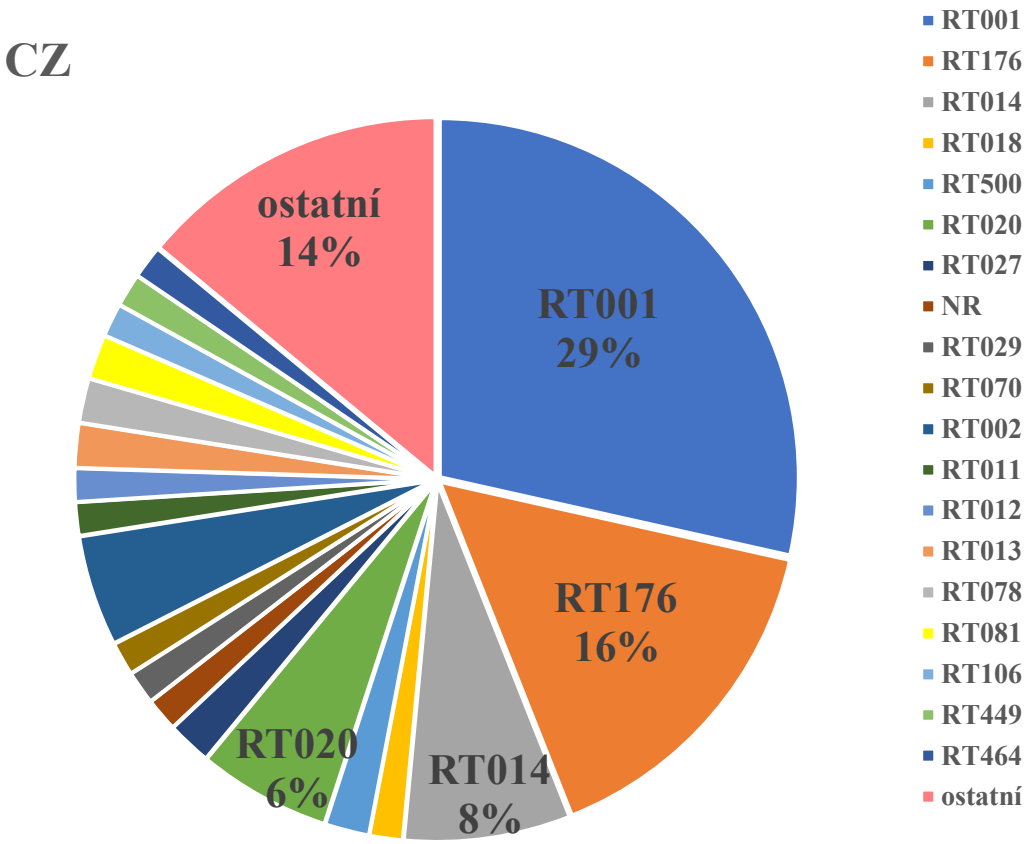
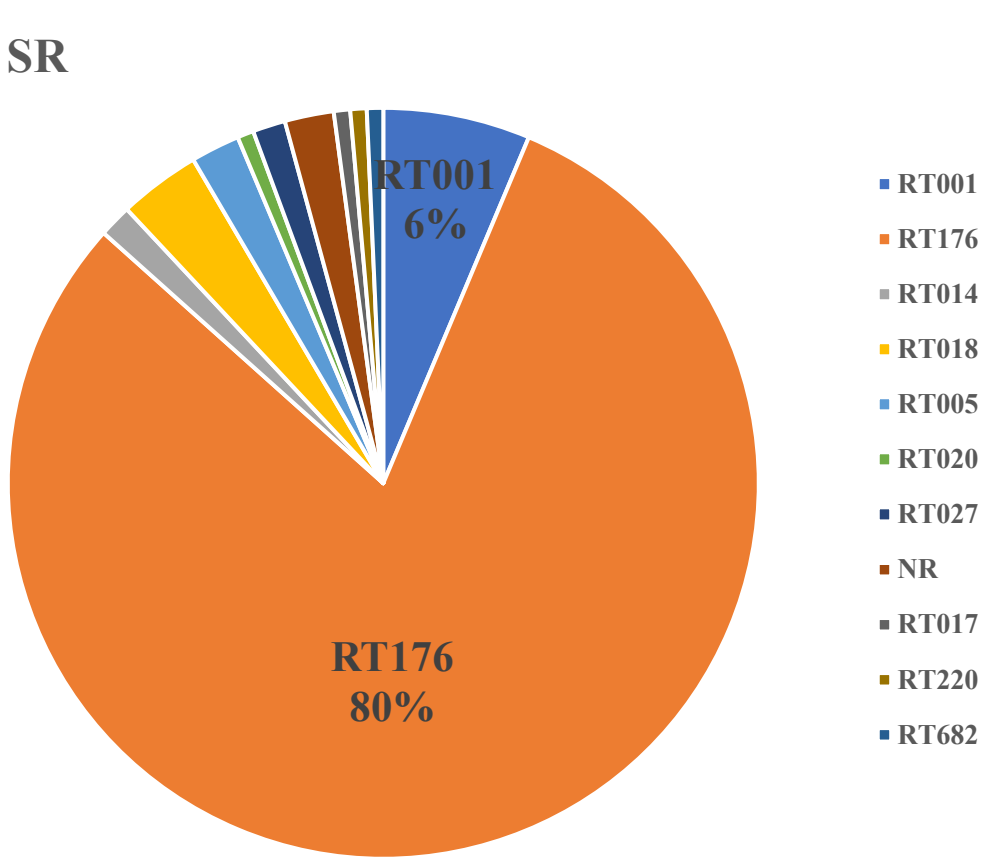
Mikrobiologický laboratorní informační systém

PCR ribotypizace národní data



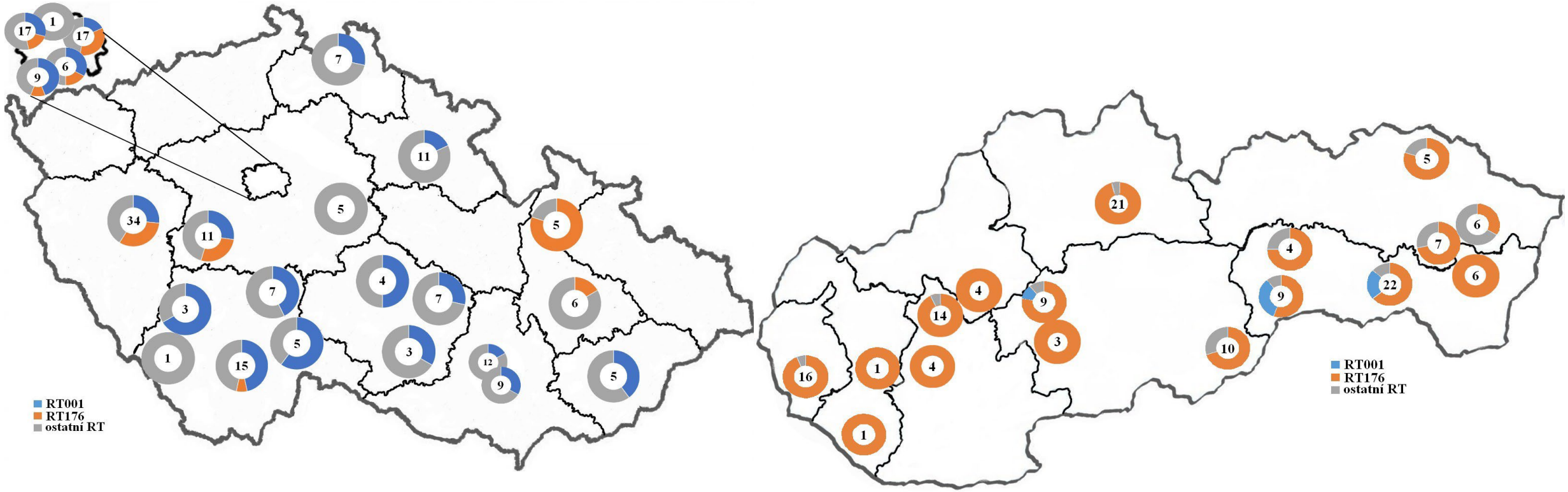


52 ribotypizačních profilů

Zíková J., diploma thesis

RT=ribotype, NR=new ribotype

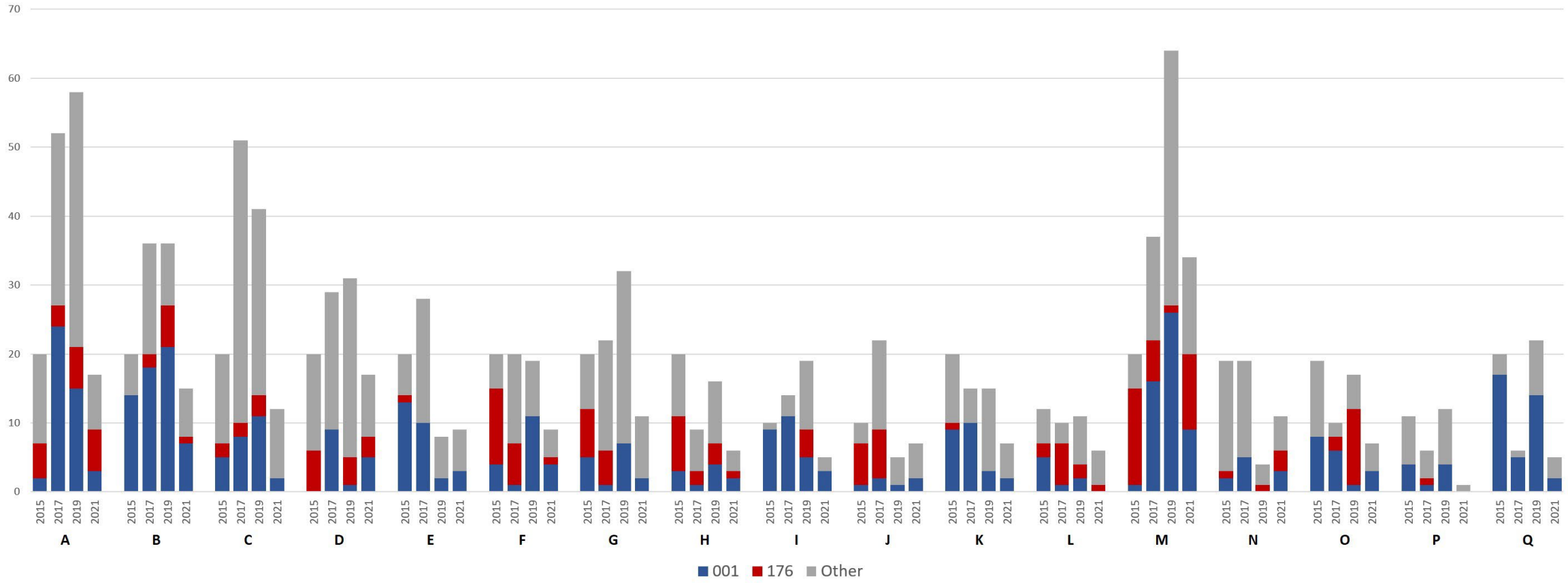
Geografické rozložení zúčastněných nemocnic



Zíková J., diplomová práce

Zíková J., diploma thesis

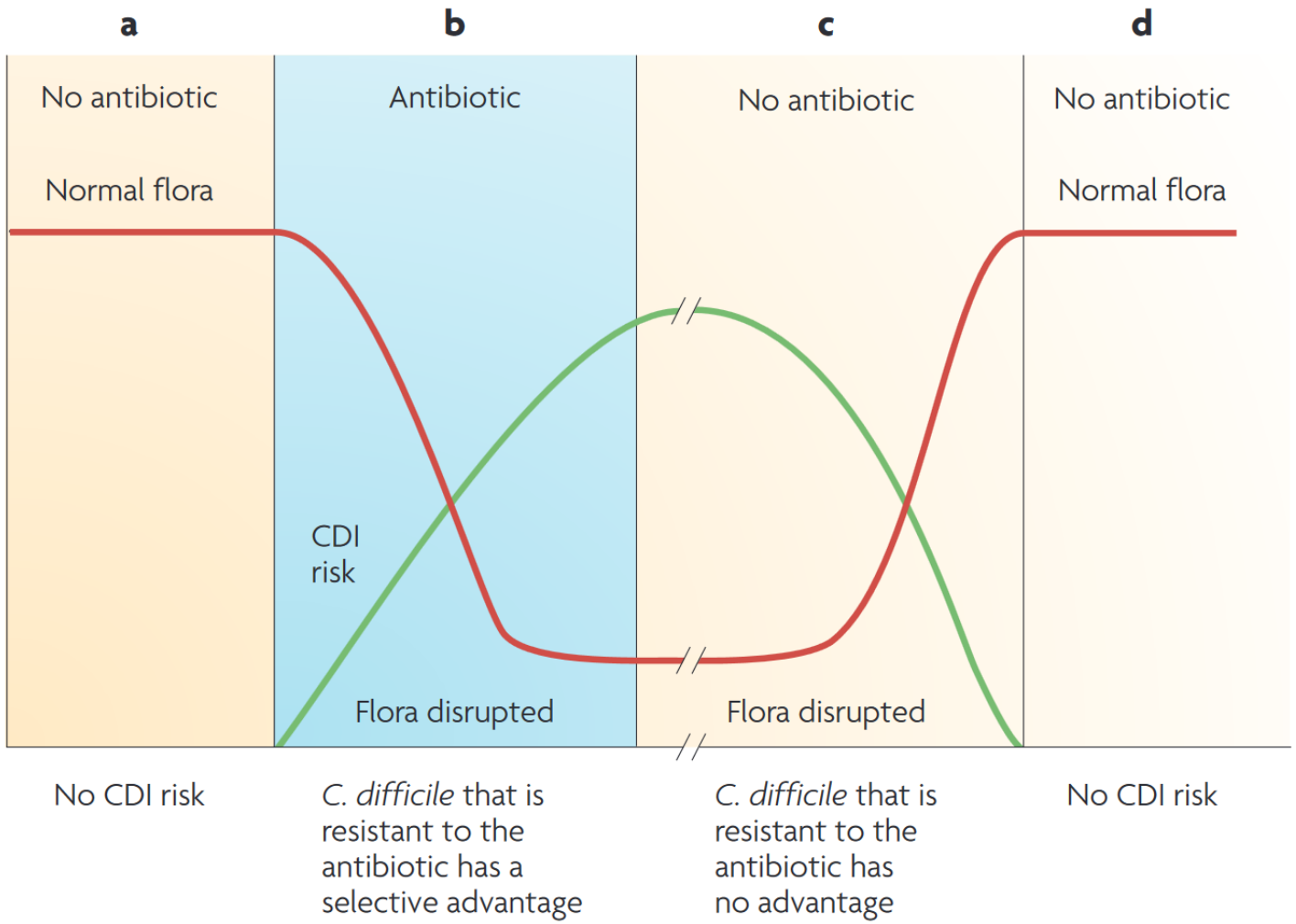
Česká republika2015-2021



2015 - RT001 33% RT176 25%
2017- RT001 33% RT176 11%

2019 – RT001 33% RT176 10%
2021 - RT001 29% RT176 16%

Bezpečná antibiotika pro pacienty s rizikem CDI – Kolonizace *C. difficile*

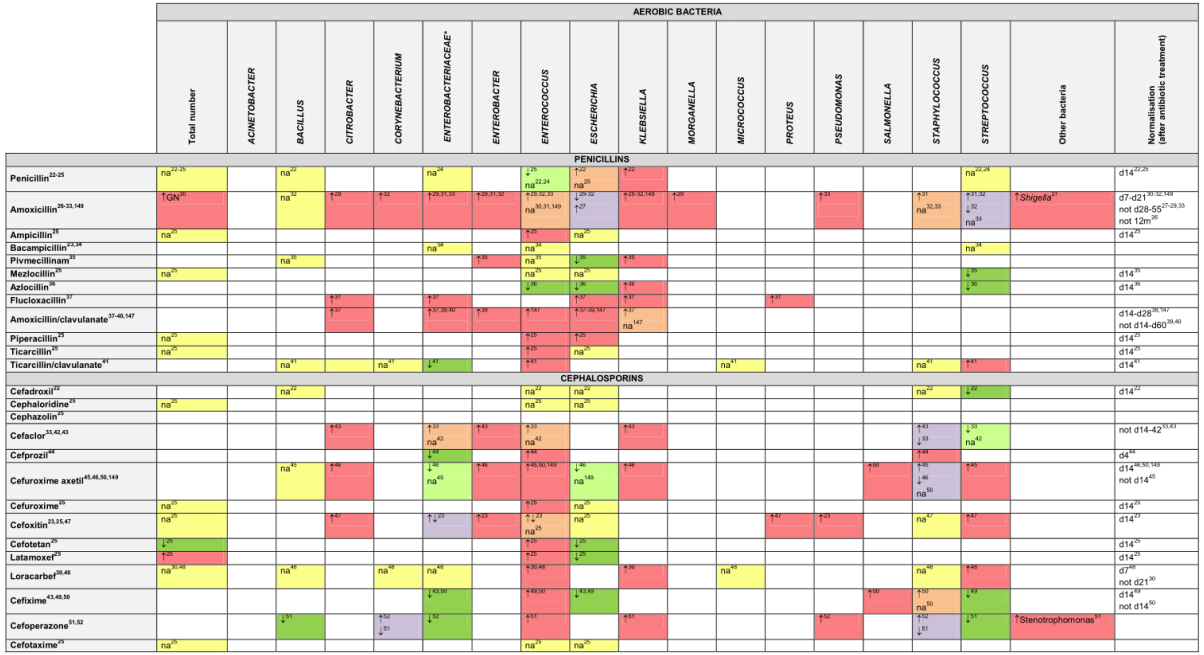


Rupnik et al., 2009

Bezpečná antibiotika pro pacienty s rizikem CDI?
Vliv antibiotik na složení střevní mikroflóry

Table 1a
Changes in the abundance of aerobic bacteria in the intestinal microbiota associated with adminstration of antibiotics (reported on genus level).

Increased abundance | Decreased abundance | Inconsisted findings
Increased abuandance or no change | Decreased abundance or no change | No change in aubundance
White boxes depict that no finfings were reported for the respective bacteria



(*continued on next page*)

P. Zimmermann and N. Curtis / Journal of Infection 79 (2019) 471–489

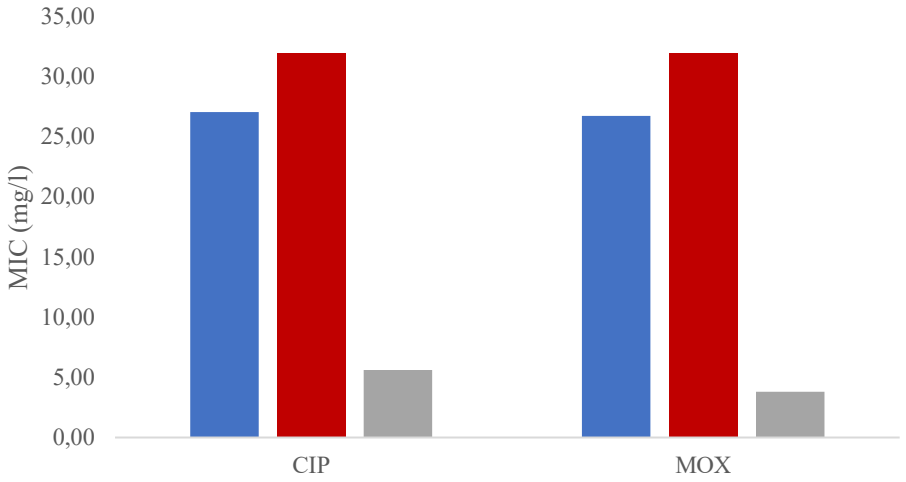
- ✓ Antibiotika způsobují významné změny ve střevní mikroflóře.
- ✓ Mezi tyto změny patří snížení bakteriální diverzity, změny v množství některých bakterií a zvýšení rezistence na antibiotika.
- ✓ Nejdelší trvání změn bylo pozorováno po léčbě ciprofloxacinem (jeden rok), klindamycinem (dva roky) a klarithromycinem metronidazolem (čtyři roky). Tato zjištění jsou však omezena dobou sledování.

(Zimmermann and Curtis, JI, 2019)

Rizikové ATB
fluorochinolony a klindamycin

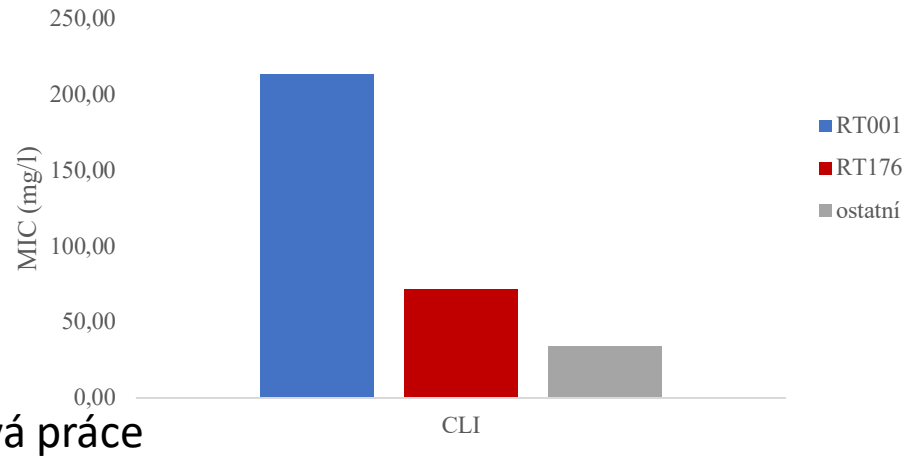
- CZ

AK substituceT82I v GyrA

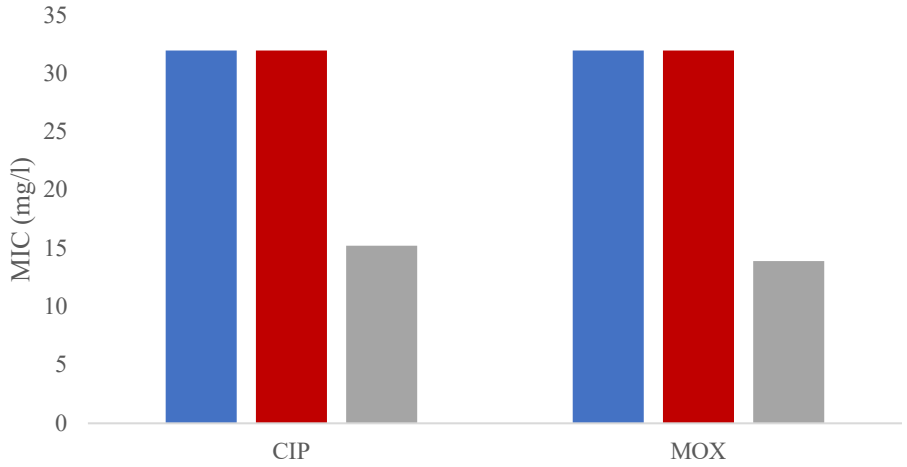


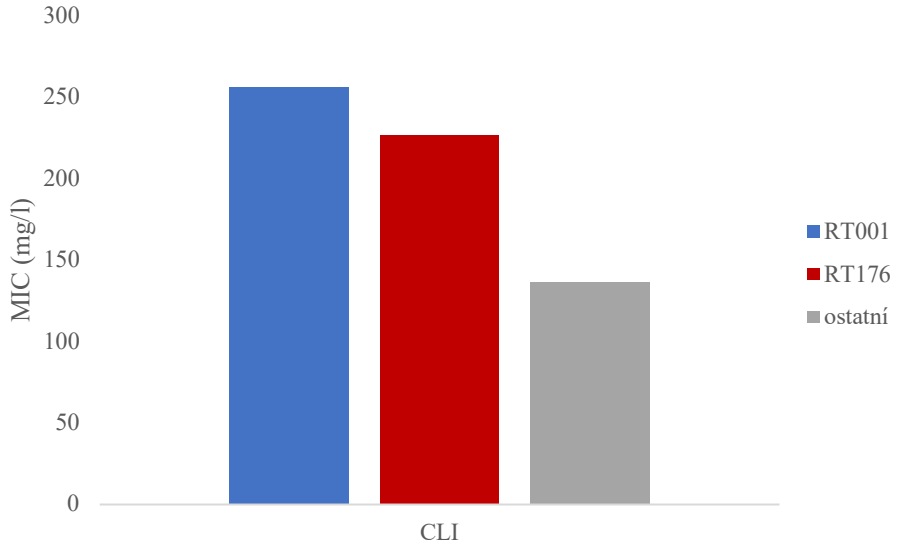
*erm*B, *cfr*B

Přenositelnost!



- SR





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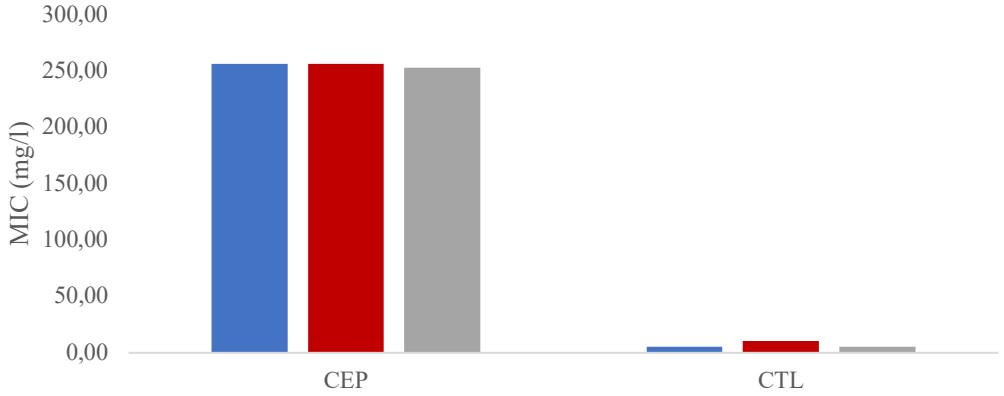
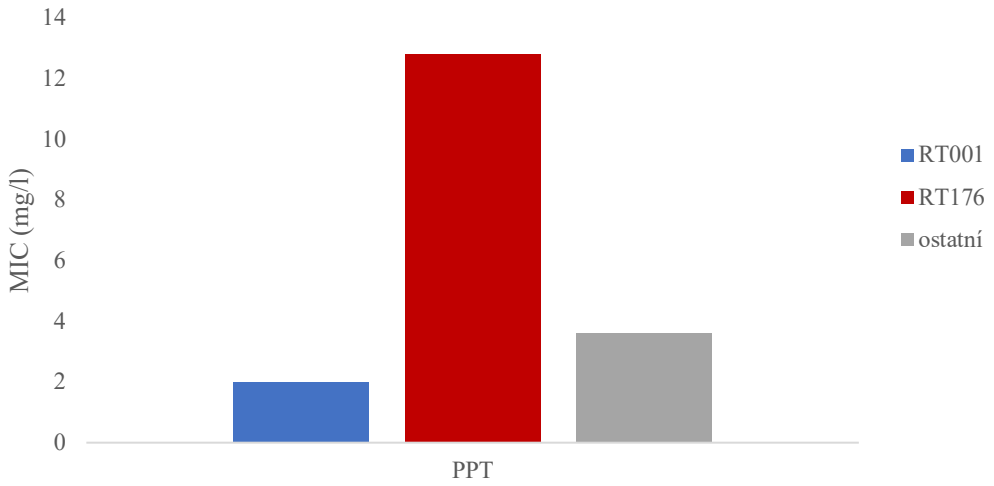
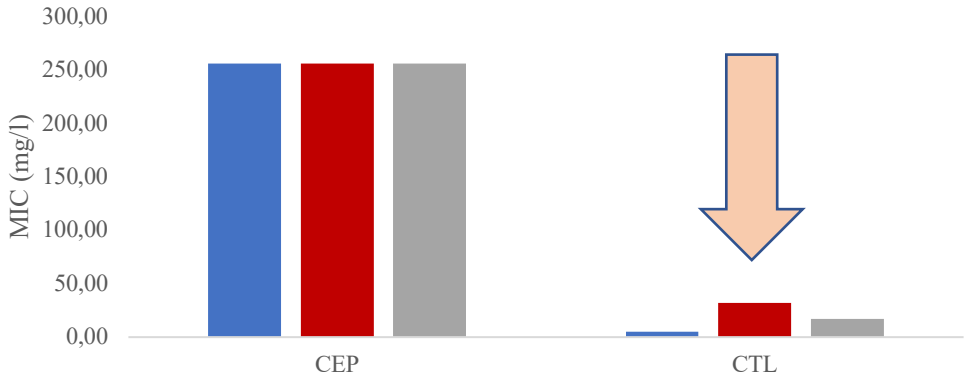
Často používané ATB
Cefalosporiny nebo piperacilin tazobaktam?

- ČR





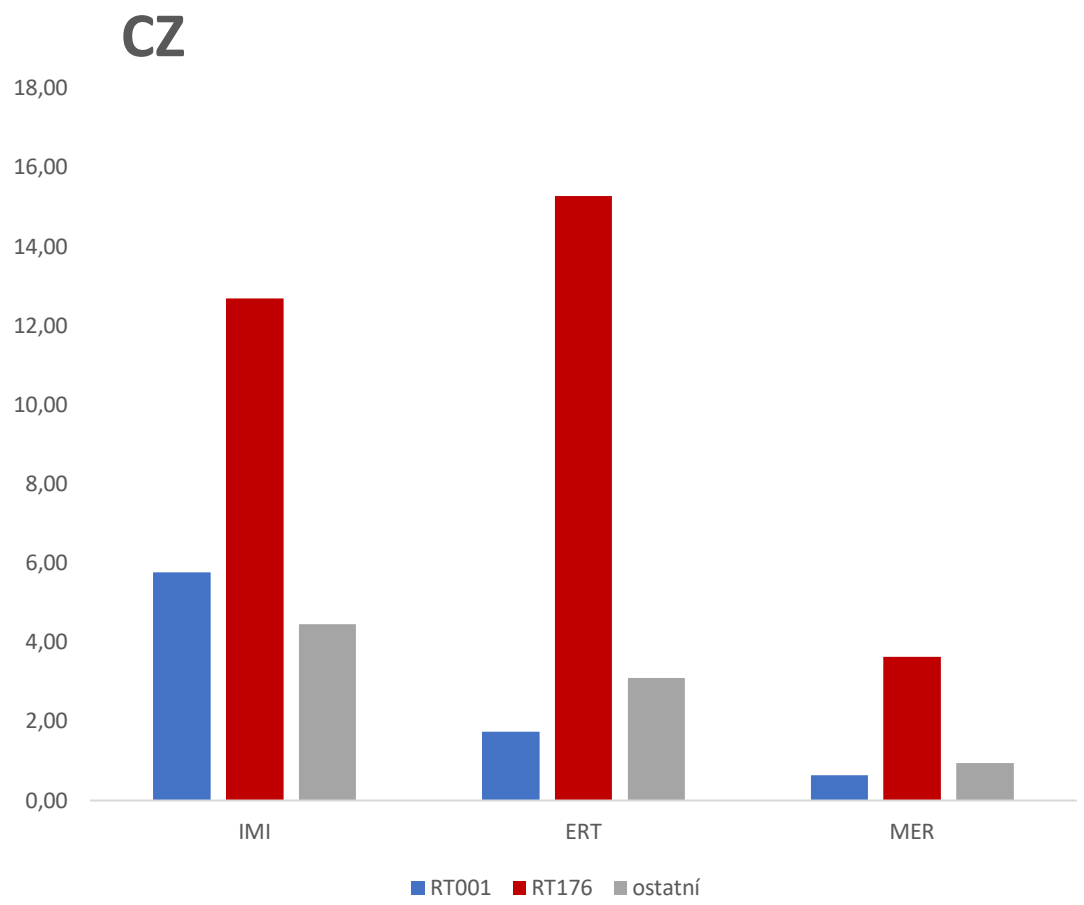
- SR

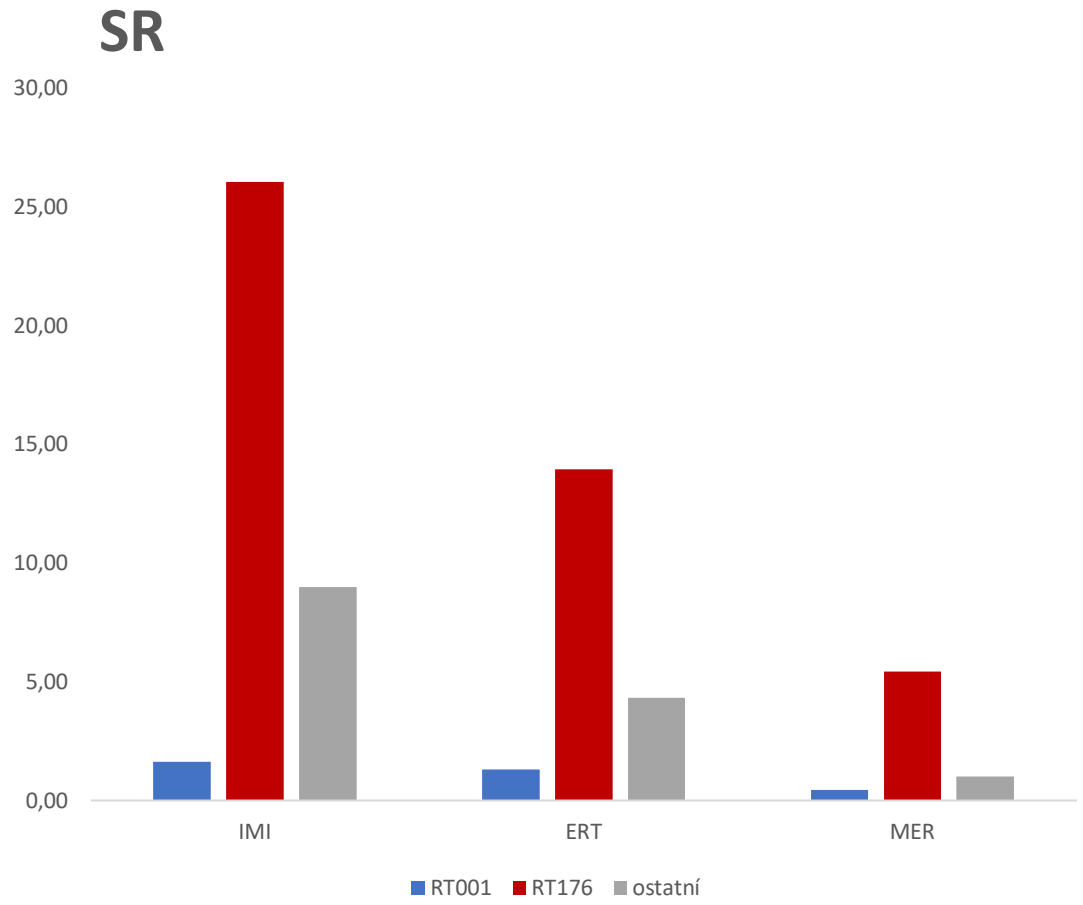


Mechanismy zatím neznáme

Zíková J., diploma thesis

Carbapenems

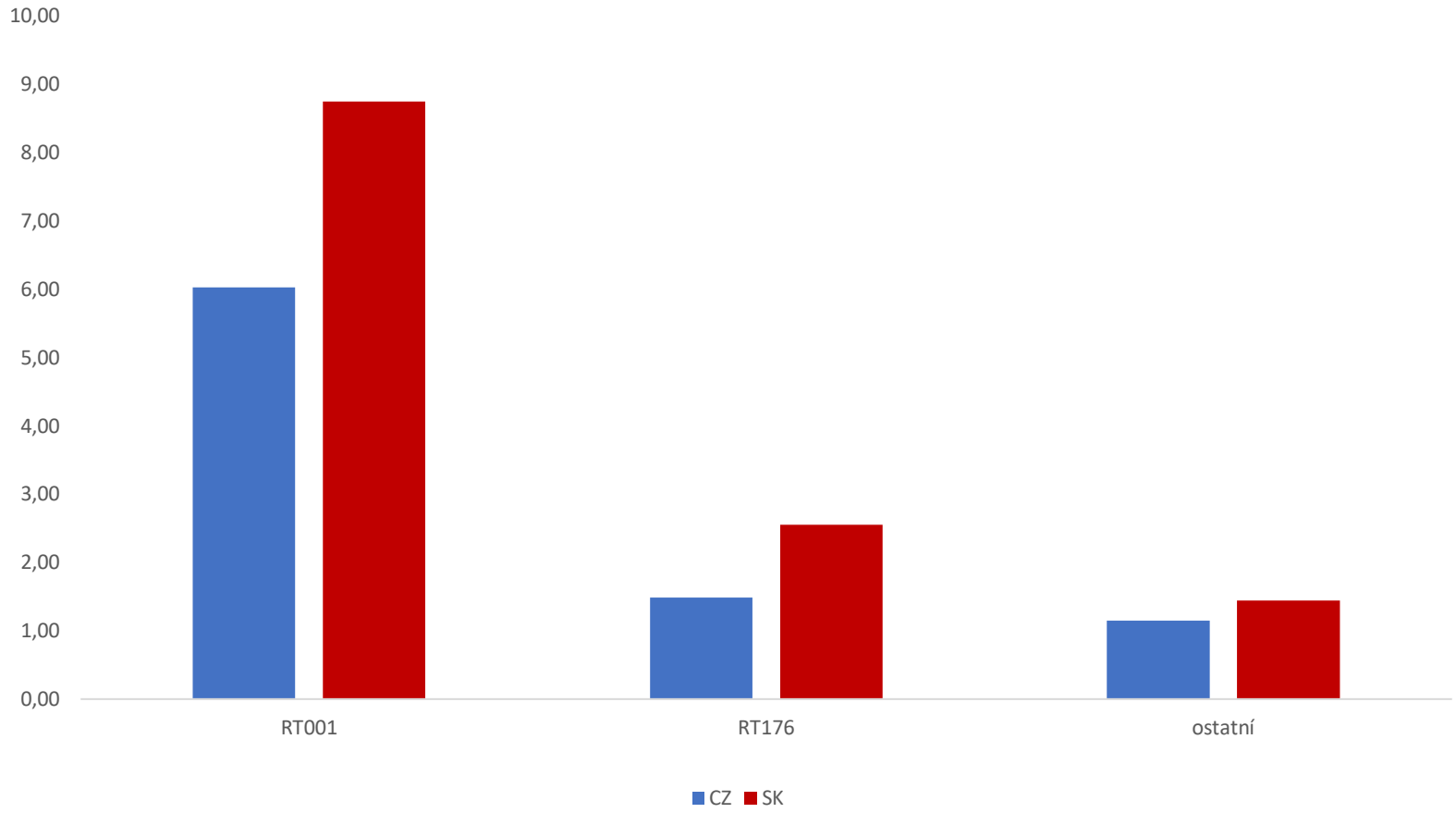




Zíková J., diploma thesis

We don't know the mechanism yet

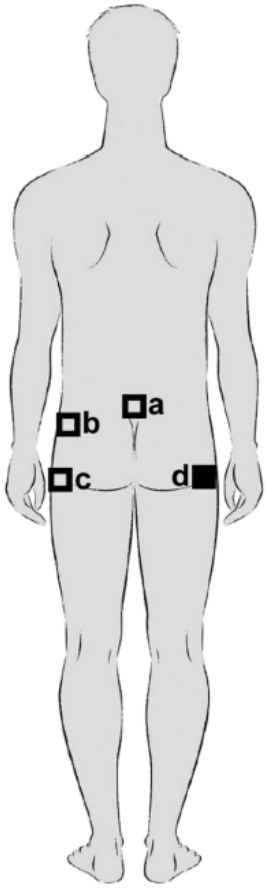
Linezolid v ohrožení!!



Přítomnost genu *cfrB*, který také způsobuje rezistenci na klindamycin a erythromycin!

Zíková J., Diplomová práce

Extraintestinální *C. difficile* infekce



MICROBIOLOGICAL FINDINGS AND TREATMENT

2nd day

Decubitus ***a-d***: polymicrobial findings: MRSA, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Enterococcus faecalis*, and *Alcaligenes faecalis*.

14th day

Decubitus ulcers ***a, b*** – plastic surgery

Antibiotic coverage: vancomycin and piperacillin/tazobactam

26th day

Change to cotrimoxazol

37th day

Decubitus ***d***: *Pseudomonas aeruginosa*, decubitus ***a-c***: normal microflora

Urine: *Klebsiella pneumoniae* (ESBL positive)

Change to piperacillin/tazobactam

41st day

Drain decubitus ***b***: ESBL-positive *E. coli*

Change to imipenem/cilastatin

43th day

Decubitus ulcers ***c, d*** – surgical intervention

Antibiotic coverage: imipenem/cilastatin was supplemented by vancomycin

54th day

Decubitus ***d***: *Pseudomonas aeruginosa* resistant to imipenem/cilastatin

Change to: cefoperazone/sulbactam and amikacin

71st day

Decubitus ***d***: *Clostridium difficile*

Change to: metronidazole (the first six days intravenously and then orally for the next eight days)

81st day

Decubitus ***d:*** surgical revision

Antibiotic coverage: piperacillin/tazobactam (20 days) and vancomycin (16 days)

Fig. 1 Localization of decubitus ulcers (a–d) and timeline of microbiological findings and antibiotic treatment

Nyč et al., 2015

Extraintestinální infekce způsobené *C. difficile* jsou vzácné.

-
- **Příklady**:
- Bakteriémie
- Nitrobřišní infekce, abscesy (slezina, mozek)
- Reaktivní artritida
- Osteomyelitida
- infekce protetických náhrad ramenního a kolenního kloubu

- Nehojící se rány
- V prostředí kontaminovaném sporami
- *C. difficile* je jediným patogenem

Přemýšlejte o ANAEROBECH

Děkuji vám za pozornost!

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