



Supplement of

Early switch to oral antibiotic therapy for the treatment of patients with bacterial native vertebral osteomyelitis: a quaternary center experience, systematic review, and meta-analysis

Matteo Passerini et al.

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Supplement

Fig.1S Assessment of certainty of evidence according to GRADE criteria

Certainty assessment							No of patients		Effect		Certainty	Importance
No of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Early switch to oral therapy	Non-early switch	Relative (95% CI)	Absolute (95% CI)		
Failure or relapse (Obs studies)												
7	observational studies	serious	not serious	not serious	very serious ^a	none	3/69 (4.3%)	88/734 (12.0%)	OR 1.073 (0.370 to 3.115)	8 more per 1,000 (from 72 fewer to 178 more)	⊕○○○ Very low	
Failure or relapse (RCT)												
1	randomised trials	not serious	N/A	not serious	very serious ^a	none	0/18 (0.0%)	3/18 (16.7%)	OR 0.120 (0.006 to 2.500)	143 fewer per 1,000 (from 165 fewer to 167 more)	⊕⊕○○ Low	

CI: confidence interval; **OR:** odds ratio

Explanations

a. The Optimal Information Size Criteria was not met. The CI was very wide

Fig.2S Search strategy for the literature research

OVID

Database(s): **Ovid MEDLINE(R) 1946 to Present and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) Daily, EBM Reviews - Cochrane Central Register of Controlled Trials** November 2021, **EBM Reviews - Cochrane Database of Systematic Reviews** 2005 to December 02, 2021, **Embase** 1974 to 2022 February 02

#	Searches
1	Osteomyelitis/
2	*Spondylitis/
3	*Osteitis/
4	*Bone Diseases, Infectious/
5	osteomyelitis.mp. or osteitis.ti,ab.
6	(spondylitis or spondylodiscitis or spondylodiskitis or diskitis or discitis).ti,ab.
7	((osteoarticul* or bone or musculoskelet* or skelet* or vertebra*) adj2 (infect* or abscess* or empyema*)).ti,ab,kw,kf.
8	or/1-7
9	exp Anti-Bacterial Agents/
10	Anti-Infective Agents/
11	(antibiotic* or antiinfective or "anti-infective" or antimicrobial* or "anti-microbial*" or antibacterial* or "anti-bacterial*").mp. or (Aminoglycosides or Amoxicillin or Ampicillin or Arbekacin or Astromicin or Azlocillin or Azithromycin or Amikacin or Bacitracin or Balofloxacin or Besifloxacin or Bacampicillin or Bekanamycin or Biapenem or Cadazolid or Cefacetrile or Ceftezole or Cefotaxime or Carbapenems or Carbenicillin or Cefalosporin* or Cephalosporins or Cephroxadine or Cefodizime or Ciprofloxacin or Cephacetrile or Cefaclor or Cephotaxime or CefadroxilCe or Cefadroxil or Cephacolor or Cefovecin or Cefovecin or Cefaloglycin or Cefuroxime or Ceftibuten or Cephaloglycin or Cephuroxime or Ceftiofur or Cefalonium or Cefuzonam or Ceftiolene or Cephadoxil or Cefonicid or Cefpimizole or Cloxacillin or Cefalexin or Cephonicid or Cefpodoxime or Cephalexin or Cefprozil or Ceferam or Cephalonium or Cefmetazole or Ceftizoxime or Cefaloridine or Cephmetazole or Cephtizoxime or Cephaloridine or Cefotetan or Ceftriaxone or

	CefalotinCephotetan or Cephtriaxone or Cefalothin or Cefoxitin or Cefoperazone or Cephalotin or Cephoxitin or Cephoperazone or Cefapirin or Cefbuperazone or Cephtazidime or Cephapirin or Cefminox or Cephalothin or Cefatrizine or Cefotiam or Cefpiramide or Cephatrizine or Cefamandole or Cefaclidine or Cefazaflur or Cephmandole or Cefepime or Cefazedone or Ceforanide or Cephepime or Cefazolin or Cefcapene or Cefluprenam or Ceftazidime or Ciprofloxacin or Clarithromycin or Clindamycin or Clinafloxacin or Doxycycline or Dalfopristin or Daptomycin or Dalbavancin or Dibekacin or Doripenem or Dicloxacillin or Enoxacin or Eperezolid or Eperezolid or Ertapenem or Erythromycin or Faropenem or Fidaxomicin* or Fleroxacin or Floxacillin or Flucloxacillin or Fluoroquinolone* or Fortimicin or "Fusidic acid" or Gemifloxacin or Gatifloxacin or Gentamicin or Grepafloxacin or Imipenem or Isepamicin or Kanamycin or Latamoxef or Levofloxacin or Levaquin or Linezolid or Lipiarmycin* or Lomefloxacin or Loracarbef or Macrolide* or Meropenem or Methicillin or Meticillin or Metronidazole or Mezlocillin or Moxifloxacin or Nadifloxacin or Nafcillin or Netilmicin or Norfloxacin or Nitazoxanide or Nitrofurantoin or Ofloxacin or Ornidazole or Oritavancin or Oxacillin or Oxazolidione* or Panipenem or Pazufloxacin or Pefloxacin or penicillin* or Piperacillin or Pivampicillin or Pivmecillinam or Prulifloxacin or Quinolone* or Quinupristin or Ribostamycin or Rifaximin or Rifampicin or Roxithromycin or Rufloxacin or Spectinomycin or Sisomicin or Sitafloxacin or Sparfloxacin or Streptomycin or Tedizolid or Teicoplanin or Telavancin or Tobramycin or Temafloxacinor Temocillin or Tetracycline or Tiacumicin or Tolevamer or Tosufloxacin or Ticarcillin or Trimethoprim or Trovafloxacin or Vancomycin* or Vanocin* or Vancomycin or Verdamicin).ti,ab,nm.
12	or/9-11
13	Administration, Oral/
14	oral*.mp.
15	13 or 14
16	Administration, Intravenous/
17	(parenteral* or intravenous* or IV or peripheral* or catheter*).ti,ab,kw,kf.
18	(switch* or transition* or course* or long or prolong* or short* or early or delay* or continu* or extend* or duration* or step* or route* or method* or manag* or therap* or treat* or versus or vs or compare* or compari* or timing or efficac* or effectiv*).ti,ab,kw,kf.
19	or/16-18
20	8 and 12 and 15 and 19

21	(exp animals/ or exp nonhuman/ or models, animal/ or Disease models, animal/) not Humans/
22	((("animal stud*" or "animal research" or alpaca or alpacas or algae* or amphibian or amphibians or animal or animals or antelope or armadillo or armadillos or avian or baboon or baboons or bats or beagle or beagles or bee or bees or bird or birds or bison or bovine or buffalo or buffaloes or buffalos or "c elegans" or "Caenorhabditis elegans" or camel or camels or canine or canines or canis or carp or cats or catfish or cattle or chamaeleo* or chameleon* or chick or chicken or chickens or chicks or chimp or chimpanze or chimpanzees or chimps or cow or cows or "D melanogaster" or "dairy calf" or "dairy calves" or deer or dog or dogs or donkey or donkeys or drosophila or "Drosophila melanogaster" or duck or duckling or ducklings or ducks or equid or equids or equine or equines or feline or felines or ferret or ferrets or finch or finches or fish or flatworm or flatworms or fox or foxes or frog or frogs or "fruit flies" or "fruit fly" or "G mellonella" or "Galleria mellonella" or geese or gerbil or gerbils or goat or goats or goose or gorilla or gorillas or groundhog or groundhogs or hamster or hamsters or hare or hares or heifer or heifers or horse or horses or iguana or iguanas or insect or insects or jellyfish or kangaroo or kangaroos or kitten or kittens or "laboratory animal*" or lagomorph or lagomorphs or lamb or lambs or lemur or lemurs or lemuridae or llama or llamas or macaque or macaques or macaw or macaws or marmoset or marmosets or mice or minipig or minipigs or mink or minks or monkey or monkeys or mouse or mule or mules or muskrat or muskrats or nematode or nematodes or newt or newts or octopus or octopuses or orangutan or "orang-utan" or orangutans or "orang-utans" or oxen or parrot or parrots or pig or pigeon or pigeons or piglet or piglets or pigs or porcine or primate or primates or poultry or quail or rabbit or rabbits or rat or rats or reptile or reptiles or rodent or rodents or ruminant or ruminants or salmon or sheep or shrimp or slug or slugs or swine or tamarin or tamarins or tilapia or tilapias or toad or toads or trout or urchin or urchins or vole or voles or waxworm or waxworms or weasel or weasels or wolf or wolves or worm or worms or wrass* or xenopus or "zebra fish" or zebrafish or zoonotic) not (human or humans or patient or patients)).ti,ab,hw,kw.
23	(rat or rats or mice or mouse or murine or pig or pigs or porcine or swine or dog or dogs or zoonotic).ti.
24	((animal or animals or canine* or cat or cats or dog or dogs or feline or hamster* or lamb or lambs or mice or monkey or monkeys or mouse or murine or pig or pigs or piglet* or porcine or primate* or rabbit* or rats or rat or rodent* or sheep* or veterinar*) not (human* or patient*)).ti,ab,kw.
25	or/21-24
26	20 not 25

27	(conference abstract or conference review or editorial or erratum or note or addresses or autobiography or bibliography or biography or blogs or comment or dictionary or directory or interactive tutorial or interview or lectures or legal cases or legislation or news or newspaper article or patient education handout or periodical index or portraits or published erratum or video-audio media or webcasts).mp. or conference abstract.st.
28	26 not 27
29	limit 28 to english language [Limit not valid in CDSR; records were retained]
30	limit 28 to no language specified [Limit not valid in CDSR; records were retained]
31	29 or 30
32	limit 31 to yr="1985 -Current"
33	remove duplicates from 32

SCOPUS via Elsevier 1788 +

1	TITLE-ABS-KEY (osteomyelitis) OR TITLE (spondylitis OR spondylodiscitis OR spondylodiskitis OR diskitis OR discitis) OR TITLE ((osteoarticul* OR bone OR musculoskelet* OR skelet* OR vertebra*) W/2 (infect* OR abscess* OR empyema*))
2	TITLE-ABS-KEY (antibiotic* or antiinfective or "anti-infective" or antimicrobial* or "anti-microbial*" or antibacterial* or "anti-bacterial*")
3	TITLE (aminoglycosides OR amoxicillin OR ampicillin OR arbekacin OR astromicin OR azlocillin OR azithromycin OR amikacin OR bacitracin OR balofloxacin OR besifloxacin OR bacampicillin OR bekanamycin OR biapenem OR cadazolid OR cefacetrile OR ceftazidime OR cefotaxime OR carbapenems OR carbamicillin OR cefalosporin* OR cephalosporins OR cephroxadine OR cefodizime OR ciprofloxacin OR cephacetrile OR cefaclor OR cephotaxime OR cefadroxil OR cefadroxil OR cephaclor OR cefovecin OR cefovecin OR cefaloglycin OR cefuroxime OR ceftibuten OR cephaloglycin OR cephiroxime OR ceftiofur OR cefalonium OR cefuzonam OR ceftiofene OR cephadroxil OR cefonicid OR cefpimizole OR cloxacillin OR cefalexin OR cephalonicid OR cefpodoxime OR cephalixin OR cefprozil OR cefteram OR cephalonium OR cefmetazole OR ceftizoxime OR cefaloridine OR cephametazole OR cephtizoxi

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4	2 or 3
5	1 and 4
6	TITLE-ABS-KEY (parenteral* OR intravenous* OR iv OR peripheral* OR catheter*) OR TITLE (switch* OR transition* OR course* OR long OR prolong* OR short* OR early OR delay* OR continu* OR extend* OR duration* OR step* OR route* OR method* OR manag* OR therap* OR treat* OR versus OR vs OR compare* OR compari* OR timing OR efficac* OR effectiv*)
7	5 and 6

8	INDEX(embase) OR INDEX(medline) OR PMID(0* OR 1* OR 2* OR 3* OR 4* OR 5* OR 6* OR 7* OR 8* OR 9*)
9	7 not 8
10	PUBYEAR AFT 1984
11	9 and 10
12	(TITLE-ABS-KEY ((alpaca OR alpacas OR amphibian OR amphibians OR animal OR animals OR antelope OR armadillo OR armadillos OR avian OR baboon OR baboons OR beagle OR beagles OR bee OR bees OR bird OR birds OR bison OR bovine OR buffalo OR buffaloes OR buffalos OR "c elegans" OR "Caenorhabditis elegans" OR camel OR camels OR canine OR canines OR carp OR cats OR cattle OR chick OR chicken OR chickens OR chicks OR chimp OR chimpanze OR chimpanzees OR chimps OR cow OR cows OR "D melanogaster" OR "dairy calf" OR "dairy calves" OR deer OR dog OR dogs OR donkey OR donkeys OR drosophila OR "Drosophila melanogaster" OR duck OR duckling OR ducklings OR ducks OR equid OR equids OR equine OR equines OR feline OR felines OR ferret OR ferrets OR finch OR finches OR fish OR flatworm OR flatworms OR fox OR foxes OR frog OR frogs OR "fruit flies" OR "fruit fly" OR "G mellonella" OR "Galleria mellonella" OR geese OR gerbil OR gerbils OR goat OR goats OR goose OR gorilla OR gorillas OR hamster OR hamsters OR hare OR hares OR heifer OR heifers OR horse OR horses OR insect OR insects OR jellyfish OR kangaroo OR kangaroos OR kitten OR kittens OR lagomorph OR lagomorphs OR lamb OR lambs OR llama OR llamas OR macaque OR macaques OR macaw OR macaws OR marmoset OR marmosets OR mice OR minipig OR minipigs OR mink OR minks OR monkey OR monkeys OR mouse OR mule OR mules OR nematode OR nematodes OR octopus OR octopuses OR orangutan OR "orang-utan" OR orangutans OR "orang-utans" OR oxen OR parrot OR parrots OR pig OR pigeon OR pigeons OR piglet OR piglets OR pigs OR porcine OR primate OR primates OR quail OR rabbit OR rabbits OR rat OR rats OR reptile OR reptiles OR rodent OR rodents OR ruminant OR ruminants OR salmon OR sheep OR shrimp OR slug OR slugs OR swine OR tamarin OR tamarins OR toad OR toads OR trout OR urchin OR urc

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2	PMID=(0* or 1* or 2* or 3* or 4* or 5* or 6* or 7* or 8* or 9*)
3	1 not 2
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5	TS=((alpaca OR alpacas OR amphibian OR amphibians OR animal OR animals OR antelope OR armadillo OR armadillos OR avian OR baboon OR baboons OR beagle OR beagles OR bee OR bees OR bird OR birds OR bison OR bovine OR buffalo OR buffaloes OR buffalos OR "c elegans" OR "Caenorhabditis elegans" OR camel OR camels OR canine OR canines OR carp OR cats OR cattle OR chick OR chicken OR chickens OR chicks OR chimp OR chimpanze OR chimpanzees OR chimps OR cow OR cows OR "D melanogaster" OR "dairy calf" OR "dairy calves" OR deer OR dog OR dogs OR donkey OR donkeys OR drosophila OR "Drosophila melanogaster" OR duck OR duckling OR ducklings OR ducks OR equid OR equids OR equine OR equines OR feline OR felines OR ferret OR ferrets OR finch OR finches OR fish OR flatworm OR

	<p>flatworms OR fox OR foxes OR frog OR frogs OR "fruit flies" OR "fruit fly" OR "G mellonella" OR "Galleria mellonella" OR geese OR gerbil OR gerbils OR goat OR goats OR goose OR gorilla OR gorillas OR hamster OR hamsters OR hare OR hares OR heifer OR heifers OR horse OR horses OR insect OR insects OR jellyfish OR kangaroo OR kangaroos OR kitten OR kittens OR lagomorph OR lagomorphs OR lamb OR lambs OR llama OR llamas OR macaque OR macaques OR macaw OR macaws OR marmoset OR marmosets OR mice OR minipig OR minipigs OR mink OR minks OR monkey OR monkeys OR mouse OR mule OR mules OR nematode OR nematodes OR octopus OR octopuses OR orangutan OR "orangutan" OR orangutans OR "orang-utans" OR oxen OR parrot OR parrots OR pig OR pigeon OR pigeons OR piglet OR piglets OR pigs OR porcine OR primate OR primates OR quail OR rabbit OR rabbits OR rat OR rats OR reptile OR reptiles OR rodent OR rodents OR ruminant OR ruminants OR salmon OR sheep OR shrimp OR slug OR slugs OR swine OR tamarin OR tamarins OR toad OR toads OR trout OR urchin OR urchins OR vole OR voles OR waxworm OR waxworms OR worm OR worms OR xenopus OR "zebra fish" OR zebrafish) NOT (human OR humans))</p>
6	4 not 5
7	6 Refined By:Document Types: Articles or Meeting Abstracts or Proceedings Papers or Review Article

Table 1S. Assessment of risk of bias of the included studies

Randomized controlled trial								
Study	Randomization	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Other (funding, conflict of interest)		
Li, 2019	Low risk	Low risk	Low risk	Low risk	Some concerns	Low risk		
Observational comparative studies								
Study	Selection of cohort 1	Selection of cohort 2	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability	Ascertainment of outcome	Follow-up long enough for outcomes to occur	Adequacy of follow-up
Flury, 2014	Low risk	High risk	Low risk	Low risk	Unclear	Low risk	Low risk	Low risk
Lestin-Bernstein, 2018	Low risk	Low risk	Low risk	Low risk	Unclear	Low risk	Low risk	Low risk
Locke, 2013	High risk	High risk	Low risk	Low risk	High risk	Low risk	Low risk	Low risk
Oh, 2007	High risk	High risk	Low risk	High risk	High risk	Low risk	Low risk	Low risk

Kim, 2019	Unclear	Unclear	Low risk	Low risk	High risk	Low risk	Low risk	Low risk
Russo, 2020	Unclear	Unclear	Low risk	Low risk	High risk	Low risk	Low risk	Low risk
Mayo cohort	High risk	Low risk	Low risk	Low risk	Unclear	Low risk	Low risk	Low risk
Observational non-comparative studies								
Study	Representativeness of the cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Ascertainment of outcome	Follow-up long enough for outcomes to occur	Adequacy of follow-up	Description with sufficient details to be replicated?	
Bettini, 2009	High risk	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear	
Del Pozo, 2018	Low risk	Low risk	Low risk	Low risk	Unclear	Unclear	Unclear	
Guo, 2021	High risk	Low risk	Low risk	Low risk	Low risk	Low risk	High risk	
Livorsi, 2008	High risk	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear	
Azamgarhi, 2021	Unclear	Low risk	Low risk	Low risk	Low risk	Low risk	High risk	
Sakeni, 2008	Unclear	Low risk	Low risk	Low risk	Unclear	Unclear	High risk	