

Ethical considerations of antibiotic treatment in the elderly

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Why should I care?

- TREAT is a decision support system for antibiotic treatment.
- It uses a causal probabilistic network to predict with a high precision the probabilities of site of infection, pathogen distribution and susceptibilities to antibiotics.
- It then uses a cost benefit model to advise on the antibiotic drug/s with the best cost benefit difference.

Cost-benefit model

- **Benefit**
 - Appropriate antibiotic reduces mortality risk by ~1.6
 - Reduces hospital stay by ~2 days
- **Cost**
 - Direct costs, administration and monitoring costs
 - Adverse events costs
 - Costs of future resistance

Costs of future resistance:

- Costs to the individual model the patient's next infection
- Costs to future patients assume a policy of using the specific antibiotic for all similar patients.
- Rise in the use of this antibiotic will cause a rise in resistance to the same and other antibiotics.
- This translates into a higher chance for inappropriate treatment for future patients, and a higher chance for death or disability.

Leibovici et al, Int J Antimicrob Agents 2007

Driving the model:

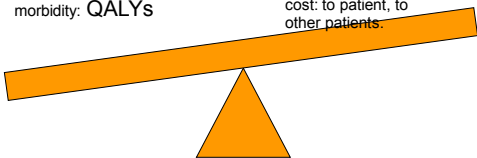
- The model balances a benefit to a present patient vs harm to future patients.
- Is this ethically acceptable?
- Is this a 1:1 ratio?

Utilitarian theories: The most benefit for all people:

Cost-effectiveness or cost-utility or cost benefit analysis

Benefits: better survival; less morbidity: QALYs

Costs: direct, side-effects, ecological cost: to patient, to other patients.



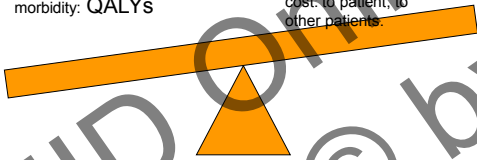
Should we balance a benefit to future, unknown patients with the harm to the present patient?

- The Georgetown mantra of bioethics: beneficence, non-maleficence, autonomy, and justice.
- 'Justice between generations' (Rawls J. A Theory of Justice. Cambridge, MA, USA: Belknap Press of Harvard University Press, 1971.)
- '...when a person takes something from nature and makes it his own property, one is allowed to do so only where there is enough, and as good left in common for others' (John Locke's Second Treatise of Government)
- Medical professionalism: The fair distribution of healthcare resources is one of the principles of professionalism, and commitment to just distribution of finite resources is one of its commitments. (ABIM Foundation, ACP-ASIM Foundation, European Federation of Internal Medicine. Medical professionalism in the new millennium: a physician charter. Ann Intern Med 2002; 136: 243-6.)

42 years old patient with severe infection

Benefits: better survival; less morbidity: QALYs

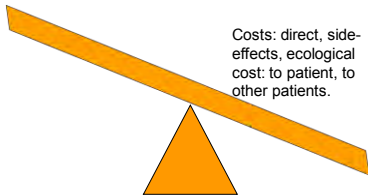
Costs: direct, side-effects, ecological cost: to patient, to other patients.



80 years old healthy patient with severe infection:

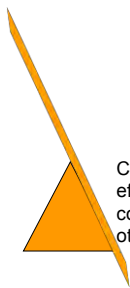
Few QALYs

Costs: direct, side-effects, ecological cost: to patient, to other patients.



80 years patient with severe dementia for years, pressure sores, urinary catheter and severe contractures, severe infection :


No QALYs



Costs: direct, side-effects, ecological cost: to patient, to other patients.

80 years patient with refractory AML: severe infection

No QALYs



Costs: direct, side-effects, ecological cost: to patient, to other patients.

Immanuel Kant:

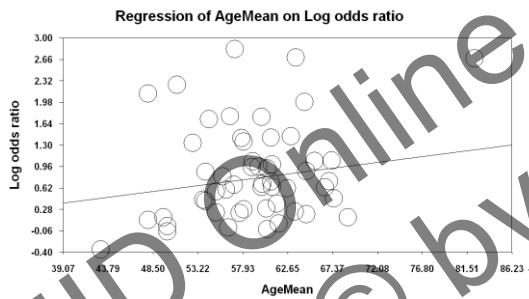
“Act in such a way that you treat humanity, whether in your own person or in the person of any other, never merely as a means to an end, but always at the same time as an end.”

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Factual questions:

- Does appropriate empirical antibiotic treatment confer the same benefit in the elderly? **Yes for LY; It depends for QALY**
- Is there a subgroup of patients where there is no survival benefit? **Probably yes.**
- Is there a subgroup of patients that would have opted for no treatment? **Yes.**

Meta-analysis, unadjusted

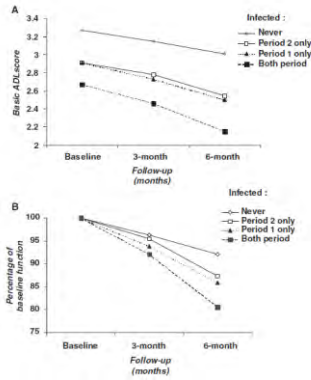


Paul et al. AAC

- Combined data from 2 prospective cohort studies
- The Netherlands and USA 1995-1998
- 932 nursing home residents with dementia and lower respiratory infections who received antibiotics
- ADL decline: at least 1 point in a 6-point scale raking from complete independence to full dependence with regard to eating, walking and dressing
- At 3 months, 33% died and 39% of residents remaining alive had ADL decline

Van der Steen et al. Int J Geriatr Psychiatry 2007

- Prospective study, Switzerland
- 1,324 residents aged 65 and older from 39 nursing homes
- Functional status every 3 months; infections monitored continually
- At 3 months, adjusted OR for cognitive decline or death 1.61. 95% CI 1.19–2.19

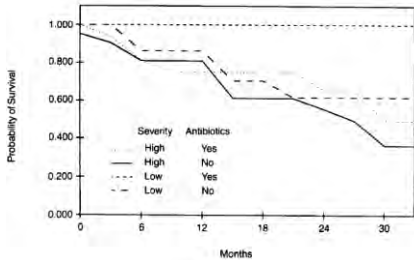


Bula et al. J Am Geriatr Soc 2004

Subgroup analysis, Israeli studies

	Retrospective	Prospective
Patients with dementia and decubitus ulcers	62	87
Mortality	59.7%	53.3%
inappropriate antibiotic treatment vs. mortality, adjusted	OR 0.37 95% CI 0.11-1.28	OR 1.36 95% CI 0.50-3.76
	Chowers M et al.	Leibowici et al.

Alzheimer dementia



USA, aggressive care vs. palliative care without antibiotics for management of fever in institutionalized patients with Alzheimer's disease dementia

Fabiszewski et al. JAMA 1990

Patients' opinions on treatment

	Location	N	Scenario	CPR	Mechanical ventilation	NG feeding	Antibiotics
Bosshard 2003	Switzerland	50	severe pneumonia				55%
Gjerdingen 1999	USA	84	severe acute illness	69%	55%	51%	96%
Ainslie 1994	USA	116	early AD/pneumonia		17%		32%
Ainslie 1994	USA	116	advanced AD/pneumonia		13%		23%
Gjerdingen 1999	USA	84	severe dementia	7%	8%	11%	39%
Low 2003	Australia	52	severe dementia		47%	26%	74%
Gjerdingen 1999	USA	84	complete dementia	4%	5%	4%	33%
Matsushita 1999	Japan	562	near vegetative state		11%	8.7%	38%

	OR (95% CI)	P-value		OR (95% CI)
Age 50-80 >80	1.5 (1.1-2.1) 2.5 (1.7-3.7)	0.0116 <0.0001	Age	6.1 (1.6-61)
Haemodialysis	1.5 (1.1-2.0)	0.0227	Horn index severe or fulminant	9.6 (1.2-76.7)
Non-surgical admission	2.2 (1.9-2.2)	<0.0001	Additional antibiotic use	10 (1.5-68.3)
ICU stay (weeks)	2.1 (1.7-2.9)	<0.001	Antitoxin A IgG	52.5 (1.5-1000)

Independent risk factors for recurrent CDAD

- Summing up:**
- Prescription of antibiotics entails balancing benefit to the present patients vs harm to future patients.
 - This can be supported by common ethical models in use; but only a utilitarian model (e.g. cost benefit) will allow a quantitative balance.
 - The old fare bad in a 'stupid' cost benefit model; this has to be addressed.
 - However there are patients in which no benefit can be demonstrated.

Factual solutions:

- Encourage living wills; with detailed lists of interventions; that allow discussion with patients or care-takers; if the local laws and mores allow it.
- Define (to a fine resolution) groups that do not benefit from antibiotic treatment:
 - From empirical antibiotic treatment

Decision on the collective

- Can we decide that in a given situation patients have such a limited life expectancy that antibiotic treatment can be given up?
- Can we decide that in a given situation patients have such a low quality of life that antibiotic treatment can be given up?
- Can we decide that in patients with



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