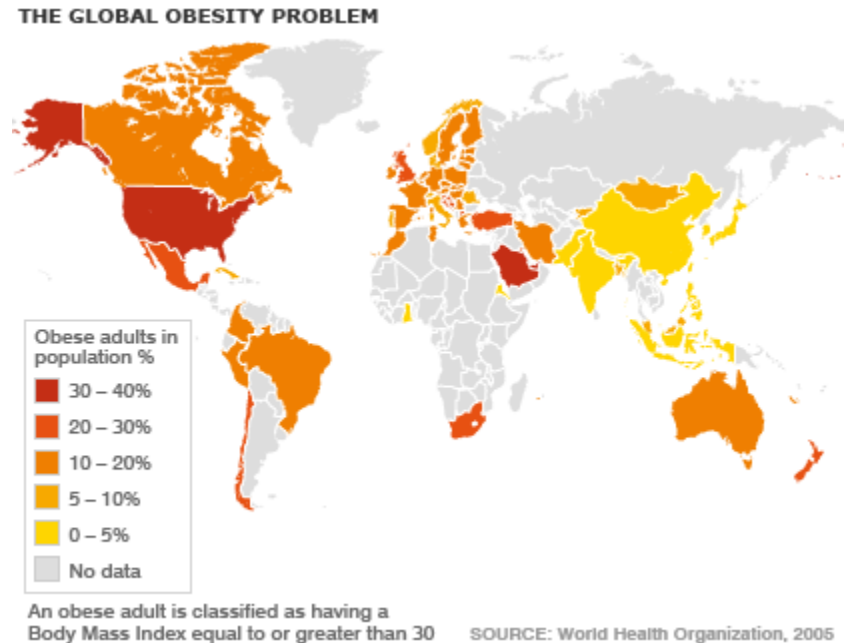


Obesity complicates antimicrobial therapy: a multicentre cross-sectional study

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International statistics on obesity and infection

- Global weighted average 14%
- £3.7 billion in health and economic costs in UK alone
- Known to increase risk of infection in specific specialties
- Independent risk factor for surgical site infections
 - 5 fold increase in risk

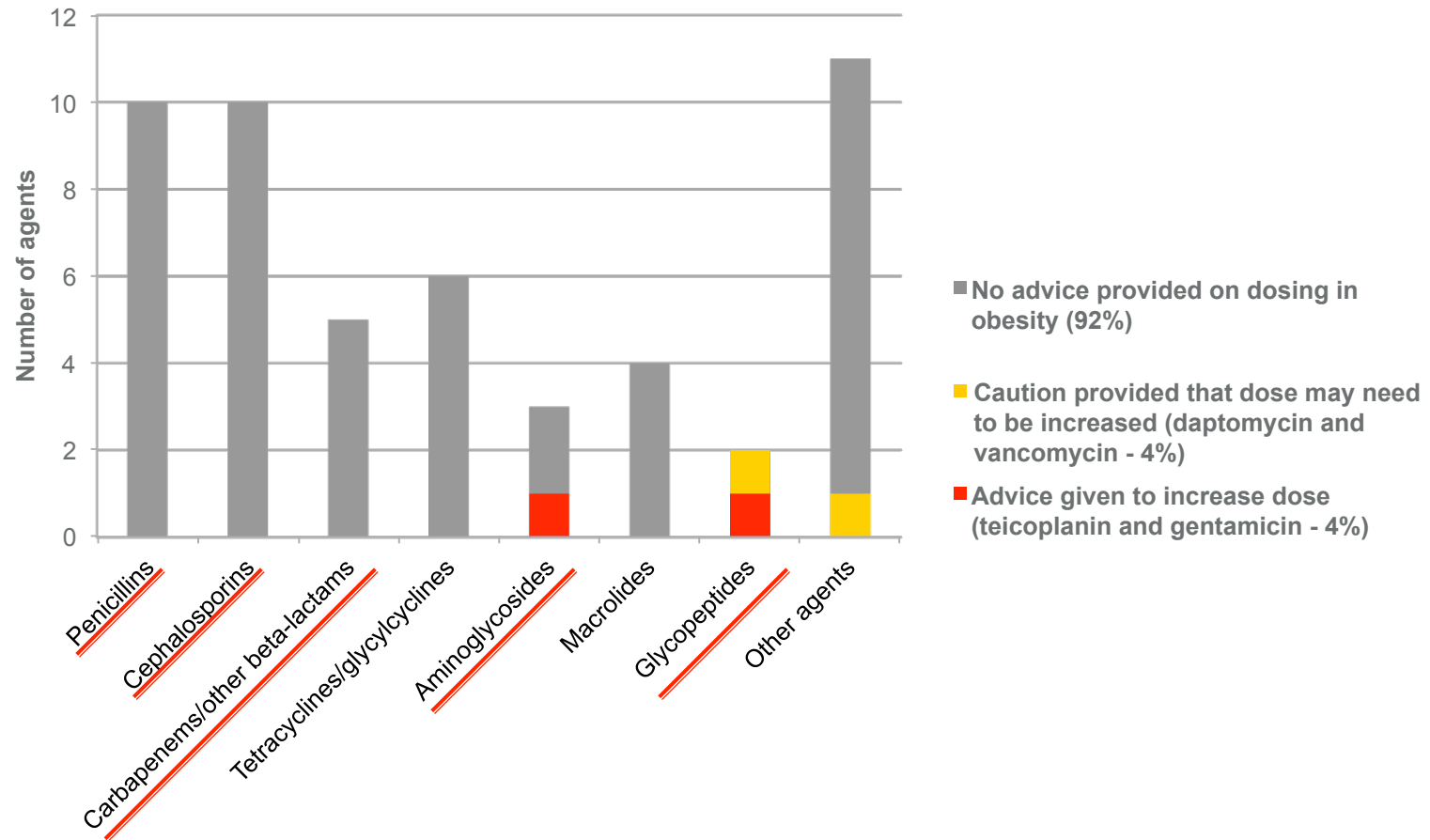


Figures from the OECD/WHO (2009)

The relationship between obesity and infection

- Increasing evidence of an association between obesity and infection
- Obesity associated with
 - Poorer infection outcomes
 - ↑ healthcare associated infections
- Contributing factors:
 - Physiological changes
 - Metabolic syndrome
 - **There is a gap in data from pharmacokinetic pharmacodynamic trials on antimicrobial dosing in obesity**

Analysis of dosing advice in obesity for UK licensed antimicrobials n=52



Key Questions

- What is the prevalence of obesity amongst hospitalised patients in the NHS?
- What is the current practice for antimicrobial dosing in our hospital setting?
- Are there any differences in infection related outcomes based on BMI and what are the implications of this?

Study Design: cross-sectional

- ❑ Inclusion/exclusion criteria
 - ❑ Three tertiary National Health Service Hospitals
 - ❑ Adult medical and surgical wards
 - ❑ excluding maternity and Obs and Gynecology
 - ❑ Data collected in two episodes 2011 & 2012
 - ❑ Weight and height data
 - ❑ Figure rating scale used
 - ❑ Harris et al Intern J of Obes 2008;32:336-342

Antimicrobial therapy was defined as 'complicated' if patients' therapy met two or more for the following criteria :

- 1) second or third line therapy according to local policy;
- 2) intravenous therapy, where an alternative oral therapy was appropriate;
- 3) longer than the recommended duration of therapy as per local policy recommendations;
- 4) repeated courses of therapy to treat the same infection; and/or
- 5) specialist advice into antimicrobial therapy provided by the medical microbiology or infectious diseases teams.

- What is the prevalence of obesity amongst hospitalised patients in the NHS?

Record of Height and Weight N= 1014

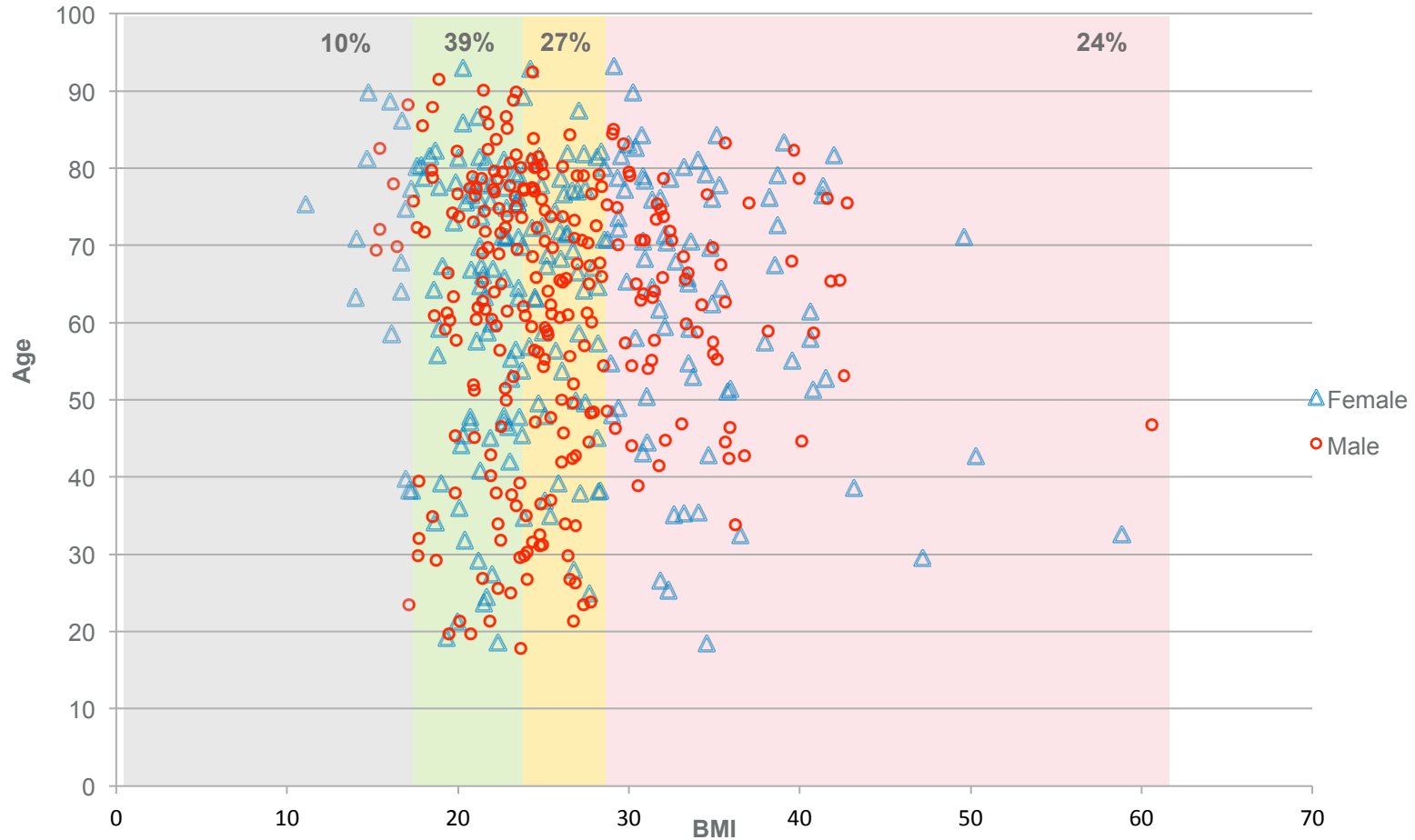
Charani et al *BMJ Open*, In Press

- **50%** of patients admitted to hospital do not have their weight measured.
- **4 in every 10** of patients receiving narrow therapeutic index antibiotics **did not have a weight recorded.**

Antimicrobials (n)	% of episodes of each drug prescribed in class with no weight recorded (n)
Vancomycin (61)	44 (27)
Amikacin (10)	30 (3)
Gentamicin (12)	25 (3)
Teicoplanin (6)	33 (2)
Total = 89	39 (35)

- Part of this gap in practice is due to systems and pathways which need to be simplified and streamlined to minimise workflow disruptions.

Spread of BMI by Age n= 491 Charani et al, 2015



Univariate analysis

	Normal/overweight (n=696) n (%) mean (sd)	Obese (n=225) n (%) mean (sd)	Underweight (n=93) n (%) mean (sd)	Total (n=1014)** n (%) mean (sd)	Pvalue*
Non-infection related univariate analysis					
Demographic data:					
Gender Male (vs Female)	386 (55.46)	101 (44.89)	33 (35.48)	520 (51.28)	P<0.001
Age (n=1012) mean (sd)	65.57 (18.74)	65.25(15.65)	70.97(18.20)	65.99 (18.10)	P=0.0036
17-34	60 (8.63)	11 (4.91)	4 (4.30)	75 (7.41)	
35-64	228 (32.81)	79 (35.27)	23 (24.73)	330 (32.61)	
65-79	236 (33.96)	95 (42.41)	31 (33.33)	362 (35.77)	
80-100	171 (24.60)	39 (17.41)	35 (37.63)	245 (24.21)	P<0.001
Ethnicity (n=1003)					
White British	380 (55.15)	117(52.70)	49 (53.26)	546 (54.44)	
White Other	73 (10.60)	29 (13.06)	12 (13.04)	114 (11.37)	
Black Other/ Black Caribbean	58 (8.42)	21 (9.46)	4 (4.35)	83 (8.28)	
Black African	39 (5.66)	11 (4.95)	6 (6.52)	56 (5.58)	
Indian/ Pakistani/ Bangladeshi	58 (8.42)	18 (8.11)	6 (6.52)	82 (8.18)	
Other Asian	31 (4.50)	9 (4.05)	8 (8.70)	48 (4.79)	
Other	50 (7.26)	17 (7.66)	7 (7.61)	74 (7.38)	P=0.824
Site					
Hospital 1	250 (35.92)	65 (28.89)	27 (29.03)	342 (33.73)	
Hospital 2	211 (30.32)	86 (38.22)	24 (25.81)	321 (31.66)	
Hospital 3	235 (33.76)	74 (32.89)	42 (45.16)	351 (34.62)	P=0.027

*Statistical differences are by Chi2 Test

	Normal/overweight (n=696) n (%) mean (sd)	Obese (n=225) n (%) mean (sd)	Underweight (n=93) n (%) mean (sd)	Total (n=1014)** n (%) mean (sd)	Pvalue*
Patients who had an Infection as reason for admission or who acquired subsequent infection in hospital n=492					
Infection by category:					
Infection other	175 (52.87)	45 (39.13)	18 (39.13)	238 (48.37)	
Hepatobiliary	23 (6.95)	9 (7.83)	0	32 (6.50)	
Pneumonia	62 (18.73)	21 (18.26)	15 (32.61)	98 (19.92)	
Surgical Site Infection	10 (3.02)	8 (6.96)	0	18 (3.66)	
Skin and soft tissue	25 (7.55)	21 (18.26)	3 (6.52)	49 (9.96)	
Urinary tract infection (UTI)	36 (10.88)	11 (9.57)	10 (21.74)	57 (11.59)	P<0.001

- What is the current practice for antimicrobial dosing in our hospital setting?
- Are there any differences in infection related outcomes based on BMI and what are the implications of this?

Antimicrobial dosing *Charani et al 2015, manuscript under review*

- ❑ No dose adjustment made for antimicrobial therapy in the obese
- ❑ 'Complex antimicrobial therapy':
 - ❑ Obese significantly more likely to be on 'complex antimicrobial therapy' (**36% vs 19% and 23%, respectively , p=0.002**)
- ❑ After adjustment for hospital, age group, comorbidities (i.e. diabetes and hypertension), and the type of infection, obese patients remained at significantly increased odds of receiving 'complicated' antimicrobial therapy compared with normal/overweight patients (OR=2.01, 95% confidence interval [CI], 1.75 to 3.45).

Analysis of therapeutic monitoring: vancomycin

- Therapeutic range 10-15 mg/L
- For 45 Patients on intravenous vancomycin we have data on the TDM
- 50% of obese (n=18) spent 50% of the course time in sub-therapeutic levels**
- 13% of non-obese (n=30) spent 50% of course time in sub-therapeutic levels**
- Could this be contributing to:
 - Therapy failure?
 - Emergence of resistance?

Conclusions

- ❑ One in 5 hospitalised patients are obese
- ❑ Obesity predisposes individuals to requiring more complicated antimicrobial therapy
- ❑ Future studies needed to investigate impact of obesity on PK/PD profile of individual antimicrobials

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