



# A survey of intravenous tobramycin monitoring and dosage adjustment practice in cystic fibrosis patients in Australia and the United Kingdom

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## Aim

To characterise current intravenous tobramycin monitoring and dosage adjustment practices in cystic fibrosis (CF) patients in Australia and the United Kingdom (UK) and compare practices between the countries

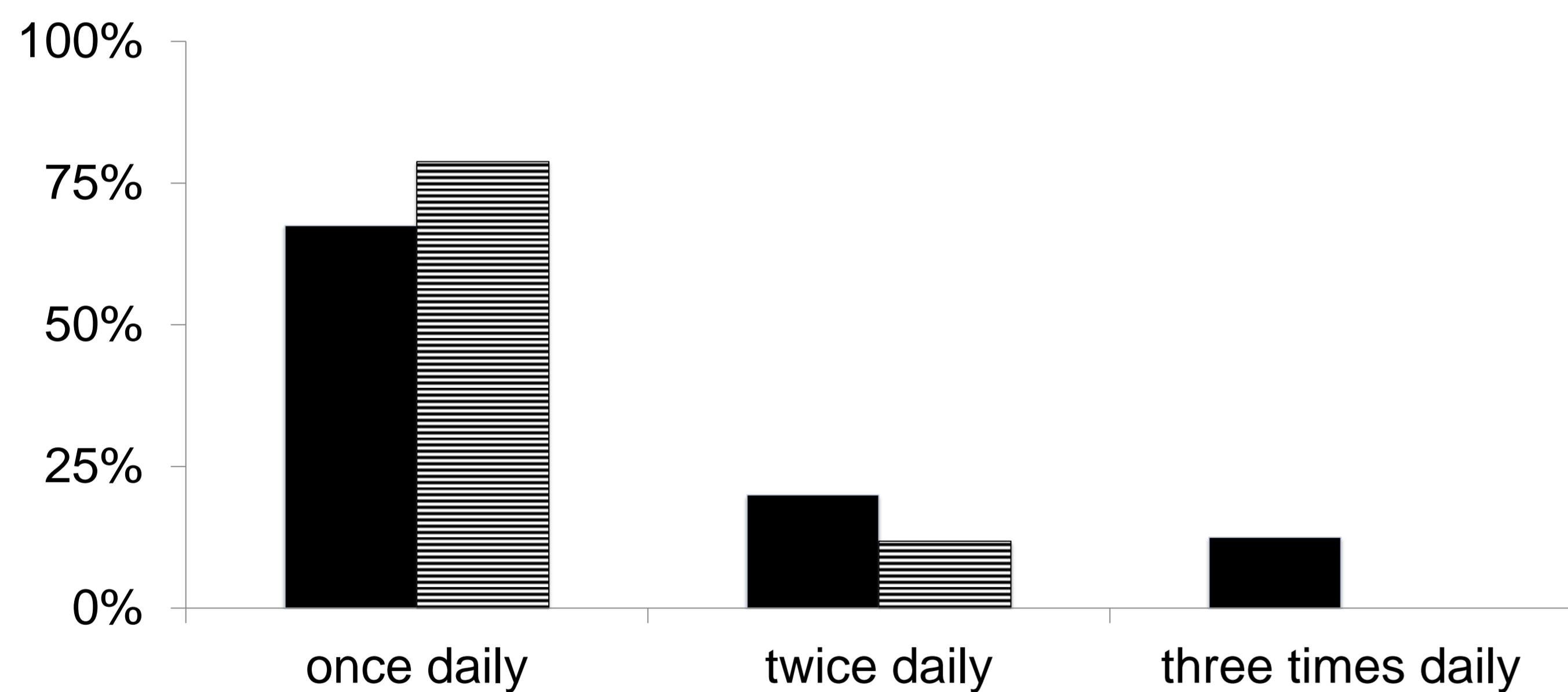
## Methods

- An anonymous, online survey of health professionals caring for CF patients was conducted between November and December 2012
- Survey questions designed to obtain information on tobramycin dosing, therapeutic drug monitoring and toxicity monitoring

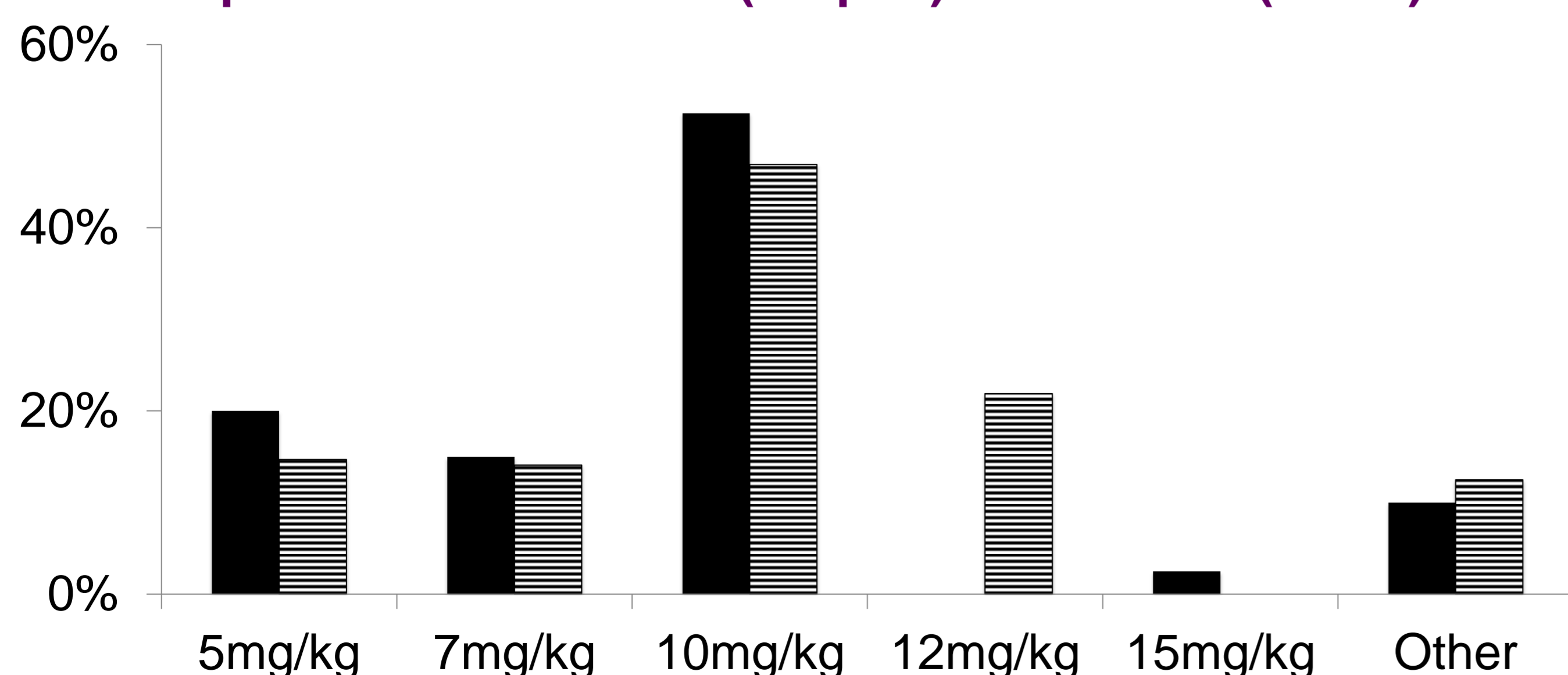
## Results

- Survey sent to 232 CF health professionals. A response rate of 29.4% and 33.3% achieved from Australian and UK recipients respectively.
- Once daily dosing of tobramycin was the preferred administration regimen for 93.8% of Australian and 67.5% of UK participants (Figure 1)
- 68.8% of Australian and 55% of UK participants initiated tobramycin therapy at a dose of 10mg/kg/day or greater (Figure 2)
- Only 9.4% of Australian and 2.5% of UK participants used Bayesian forecasting to guide tobramycin dosage adjustment (Table 1)
- The main reason participants did not use computerised methods (Bayesian forecasting or linear regression analysis) for dosage adjustment was lack of programme availability and access (Table 2)
- The main challenge participants faced when using computerised methods was timely access to tobramycin levels (Table 3)
- Targets aimed for during use of computerised methods varied (Table 4)
- Nephrotoxicity monitoring, through measurement of serum creatinine several times during admission, was undertaken by 62.5% of Australian and 77.5% of UK participants.
- Ototoxicity monitoring was not routinely undertaken by 34.4% of Australian and 35% of UK participants

**Figure 1: Preferred administration regimen for iv tobramycin in CF patients in Australia (striped) and the UK (black)**



**Figure 2: Standard initial daily dosing of (iv) tobramycin in CF patients in Australia (striped) and the UK (black)**



Other: remainder of participants used a fixed dosing, dosing based on a patient's body surface area, dosing based on a previous admission or did not answer this question

**Table 1: Dosage adjustment methods used for iv tobramycin in CF patients in Australia and the UK**

Method	Australia	UK
Linear regression analysis	40.6%	0%
Bayesian forecasting	9.4%	2.5%
Trough measurement	28.1%	55%
Peak and trough measurement	6.3%	37.5%
Nomogram	3.1%	5%
Unsure	12.5%	

**Table 2: Main reasons why survey participant's did not use computerised methods for dosage adjustment**

- 23.7% Programme availability and access
- 17.3% Insufficient professional skills and expertise
- 15.7% Local protocols and policies
- 14.7% Belief that computerised methods are not superior
- 11.2% Timely access to plasma concentrations
- 7.1% Lack of awareness of such methods

**Table 3: Main challenges survey participant's faced when using computerised methods for dosage adjustment**

- 29.2% Timely access to plasma concentrations
- 22.5% Insufficient professional skills and expertise
- 16.9% User-friendliness of the programme
- 14.6% Uncertainty with interpretation of results

**Table 4: Targets aimed for during use of computerised methods for dosage adjustment**

Dosing	Targets	Values <sup>a</sup>	Sampling time post-dose
<b>Linear Regression Analysis</b>			
OD	AUC	100	1h, 6-14h
OD	AUC	NS	1h, 6-14h
OD	AUC	70-100	1h, 4h
OD	AUC	100 <sup>b</sup>	2h, 6h
OD	AUC	100	2h, 6h
OD	AUC & C <sub>max</sub>	<100, 20-25	1h, 4-6h
OD	AUC & C <sub>max</sub>	100, 20-25	2h, 6-14h
OD	AUC & C <sub>max</sub>	<100, 25 <sup>c</sup>	30min, 4-6h
OD	AUC & C <sub>min</sub>	NS, <1	1h, 12h
OD	AUC & C <sub>min</sub>	NS	End of infusion, 6-8h
OD	AUC, C <sub>max</sub> & C <sub>min</sub>	85-100, 22-30, <0.5	1h, 4-6h
OD	AUC, C <sub>max</sub> & C <sub>max</sub> :MIC	100, 25-30, NS	2h, 6h
OD	AUC, C <sub>max</sub> & C <sub>max</sub> :MIC	100, >20, 10:1	2h, 6-14h
<b>Bayesian Forecasting</b>			
OD	AUC	100	30min-1.5h, 6-14h
OD	AUC	NS	4-6h
OD	AUC, C <sub>max</sub>	80-100, 30-35 1 <sup>st</sup> week, 25-30 2 <sup>nd</sup> week	1h, 6-14h
BD	C <sub>max</sub> and C <sub>min</sub>	8-12, <2	1h, 12h

AUC= area under the concentration-time curve, BD= twice daily dosing, C<sub>min</sub>= trough concentrations, C<sub>max</sub>= peak concentrations, OD= once daily dosing, <sup>a</sup>AUC units: mg.h/L, C<sub>max</sub>, C<sub>min</sub> units: mg/L, <sup>b</sup>range: 90-110 mg.h/L, <sup>c</sup>up to 30 mg/L with increasing severity

## Conclusions

- Survey participants in Australia were more likely to dose tobramycin once daily, use a higher initial dose and adjust tobramycin dosage according to an AUC estimate than those in the UK.
- Only 9.4% of Australian and 2.5% of UK survey participants used Bayesian forecasting to guide tobramycin dosage adjustment. The three main reasons for not using such methods were problems with programme availability and access, insufficient professional skills and expertise and local protocols and policies