USC University of Southern California

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ESCMID Postgraduate Technical Workshop Population Modeling and Dose Optimization with Pmetrics and BestDose: Antimicrobial Applications

Using BestDose Stand-Alone

BestDose features

- Windows Program
- Model-based dosing
- Bayesian estimation of **individual PK parameters**
- Calculation of an **optimal dosage regimen** to achieve a concentration target

BestDose features

- Population models are **nonparametric**
- Existing models: aminoglycosides, vancomycin, digoxin, anti-epileptic drugs – all for adults
- **New models** built with Pmetrics can be added with some limitations
  - 1 or 2 compartments
  - Covariates : weight, creatinine clearance or any substitutes written the patient file
  - Linear relationships between covariates and parameters

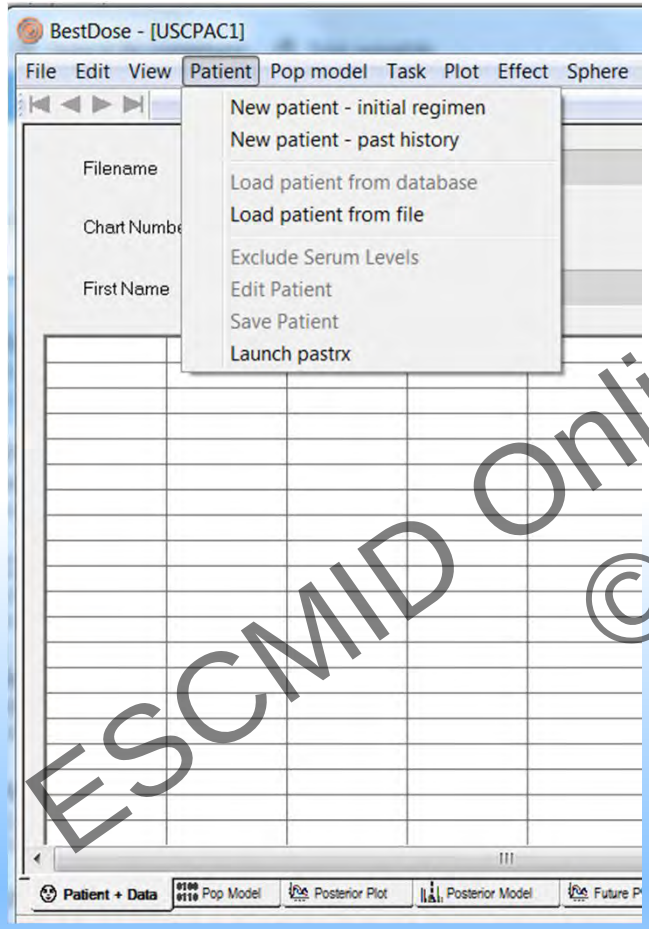
BestDose strenghs

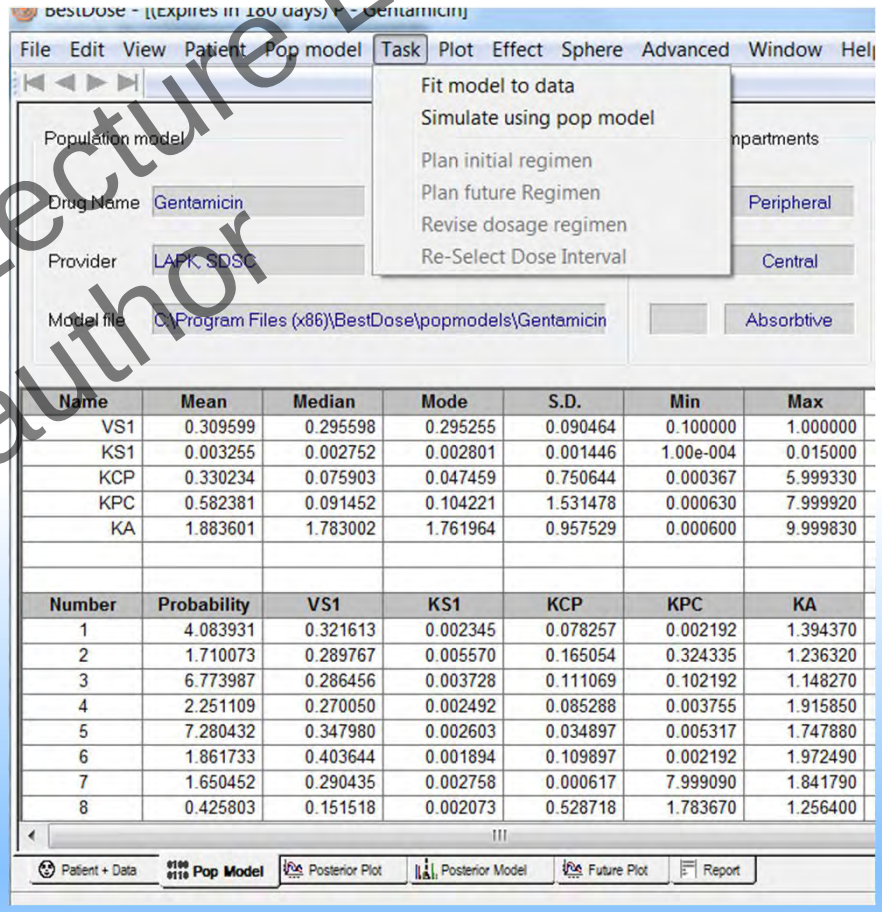
- The only dosing software based on NP, multiple-model priors
- The only dosing software with **optimisation criterion** in dosage design (minimization of MWSE)
- User friendly interface and plotting
- **Advanced fitting** options
  - Interactive Multiple-Model
  - Hybrid fit

Using BestDose

- The steps
  - Create a **patient's file** using the PastRx program (dosing history, drug levels, covariates)
  - Load the patient's file
  - Select and load a **population model**
  - **Fit** model to data
  - **Plan** future regimen

Using BestDose





Name	Mean	Median	Mode	S.D.	Min	Max
VS1	0.309599	0.295598	0.295255	0.090464	0.100000	1.000000
KS1	0.003255	0.002752	0.002801	0.001446	1.00e-004	0.015000
KCP	0.330234	0.075903	0.047459	0.750644	0.000367	5.999330
KPC	0.582381	0.091452	0.104221	1.531478	0.000630	7.999920
KA	1.883601	1.783002	1.761964	0.957529	0.000600	9.999830

Number	Probability	VS1	KS1	KCP	KPC	KA
1	4.083931	0.321613	0.002345	0.078257	0.002192	1.394370
2	1.710073	0.289767	0.005570	0.165054	0.324335	1.236320
3	6.773987	0.286456	0.003728	0.111069	0.102192	1.148270
4	2.251109	0.270050	0.002492	0.085288	0.003755	1.915850
5	7.280432	0.347980	0.002603	0.034897	0.005317	1.747880
6	1.861733	0.403644	0.001894	0.109897	0.002192	1.972490
7	1.650452	0.290435	0.002758	0.000617	7.999090	1.841790
8	0.425803	0.151518	0.002073	0.528718	1.783670	1.256400

Using BestDose
Clinical Example #1: initial dosing

- A female patient with severe acute pyelonephritis has to receive IV ceftriaxone 1g/day and amikacin

- Patient's characteristics
  - 77 years
  - 48 kg, 158 cm
  - CCr = 36 ml/min/1.73m^2

- Which initial dose amount and dosing interval would be appropriate for IV amikacin ?

Using BestDose
Clinical Example #2: dose adjustment

- A 87 years old man presented a *Staphylococcus epidermidis* disco-vertebral infection

- Initial prescription: rifampicin 900 mg/day + vancomycin 1g/12h

- Characteristics: 65 kg, SCr = 44 µmol/L, CCr = 98 ml/min
- Vancomycin trough target = 20 mg/L

- How to monitor his vanco therapy ?

Using BestDose
Clinical Example #2: dose adjustment

- Vancomycin concentrations available on the second day of therapy

  Cmin = 6 mg/L just before dose 2

  Cmax = 20 mg/L 30 min after dose 2

- Which dosage regimen should be prescribed to achieved the target Cmin as soon as possible ?

Using BestDose
Clinical Example #2: dose adjustment

- The initial dosage regimen of 1g/12h would lead to a suboptimal trough ≈ 15 mg/L at the steady-sate

- Optimal regimen
  - Reloading dose: 1500 mg q12 during one day
  - Then 1250 mg/12h
  - Trough ≈ 19-20 mg/L by day 4-5

Using BestDose
Clinical Example #2: dose adjustment

- Vancomycin trough measured on day 4 in agreement with model prediction: 19.5 mg/L
- Advanced fitting options can provide a better fit for this patient