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ABSTRACT/REVISED

Objectives: In order to help overcome some of the current challenges for the wide-spread implementation of model based goal oriented dosing of antibiotics, we have launched Individually Designed Optimum Dosing Strategies (ID-ODSTM) on the web in late 2012. The objective of this study was to evaluate the utilization of this on-line dosing tool used to facilitate the optimal dosing of sixteen antibiotics via estimation of patient specific Probabilities of Target Attainment (PTA) and Bayesian adaptive feedback.

Methods: Continuous data collection on individual queries was supported by Rapporater®, a data analysis and reporting application for the use of the R® statistical software environment in the cloud. The number of queries on specific antibiotic templates by geolocalized IP address and anonymised parameters were evaluated for CPU time and for the frequency of successfully generated reports.

Results: The website applications were successfully queried 5678 times during the time of evaluation, 85.9 % of all users connected from North America. The remaining 14.1 % of users joined the site mainly from Europe (47.7%), Asia - Pacific region (25.9%), South America (24.2%) and the rest of the world (2.2%). PTAs for Piperacillin and Tazobactam and estimations of empiric dosing regimens for Vancomycin were the most common reasons for utilization, followed by Bayesian analysis of individual Vancomycin and Aminoglycoside concentration information. They accounted for a combined 54.5% of all data management. Cefepime and Meropenem were the second and third most commonly accessed templates for PTA dose optimization, representing 39.1 % of the entire beta - lactam queries together. CPU times differed substantially for templates running PTAs versus the Bayesian models with a mean + SD of 6.88 + 2.08 seconds and 19.16 + 17.12 seconds, respectively. Generating the reports was aborted early 13.5 % of the time, where the reasons for failure were most commonly linked to inaccurate data entry.

Conclusions: The world-wide web availability of this cross-platform application provides the framework for a point of care clinical decision support tool on mobile and stationary devices for practitioners interested in optimizing antimicrobial therapy. During the first year in live environment, the system was ran successfully over five thousand occasions, providing computational results of high complexity under the average of 20 seconds of time. The utilization information collected during this period will also help us further improve the system to minimize rates of template failure due to inaccurate data entry.

INTRODUCTION

In the past several years, adaptation of the use of on-line applications on mobile devices by health care professionals has become increasingly more common. Tablets, iPad®s and smartphones are relatively new technologies that combine mobile telecommunications and data processing in a devices that can facilitate mobile computing at the point of care. This recently observed increased adoption of mobile devices by health care professionals demonstrates the invaluable opportunity for improved communications at the point of care anywhere at any time^{1,2}. Drug reference resources generally provide information on the pharmacology, dosing, dosage form, drug interactions and the contraindications associated with the use of the agents. The Hopkins Antibiotic Guide and the Sanford Guide both have been available for many years now, with sections focusing on the dosing of antibiotics^{3,4}. Neither of these two popular resources directly provide drug dosing information based on the results of high quality popPK models. They also do not provide the opportunity to evaluate different dosage regimens for probabilities of target attainment based on Monte Carlo simulation. As on-line computing and the use of mobile devices become more and more popular, transition of the free-standing software to a web - based application is likely inevitable. Virtually all available devices have the option to view websites, with some having significantly better aesthetic appearance compared to others⁵. In this experiment, we report on the usage statistics of a multi-platform, web-based clinical application equipped to provide optimum antibiotic dosing information via the use of population pharmacokinetic models and Bayesian adaptive feedback or Monte Carlo simulation for critically ill patients at the point of care.

METHODS

ID – ODSTM Technology Overview^{6,7,8}

- Using any of the popular devices and browsers [1] all parameters passed to Optimum Dosing Strategies (ODS) website [2] are seamlessly transmitted to Rapporater servers over a secure channel for evaluation.
- The channel is backed up by a content delivery network [3] that is also speeding up connection as well as making it possible to provide high availability for ODS users.
- The cluster of webservers [4] process the queries and read the required models and programs to memory from the distributed system of databases [5] to be passed along to the R [6] workers.
- The computations are run in a secured and stateless R environment so that no sensitive information would be stored for future R sessions. The statistical tasks will use any of the numerous, user contributed packages found on CRAN like the FME package as a Bayesian interface.
- The results are returned in Pandoc's markdown format [8] that could be transformed to any popular document format – along with the generated plots in the analysis.

Usage Data Collection

- Continuous data collection on individual queries was supported by Rapporater®, a data analysis and reporting application for the use of the R® statistical software environment in the cloud.
- The number of queries on specific antibiotic templates by geolocalized IP address and anonymised parameters were collected and evaluated for CPU time.
- The frequency of successfully generated reports was also evaluated by comparing the number of queries generated with and without an error message.

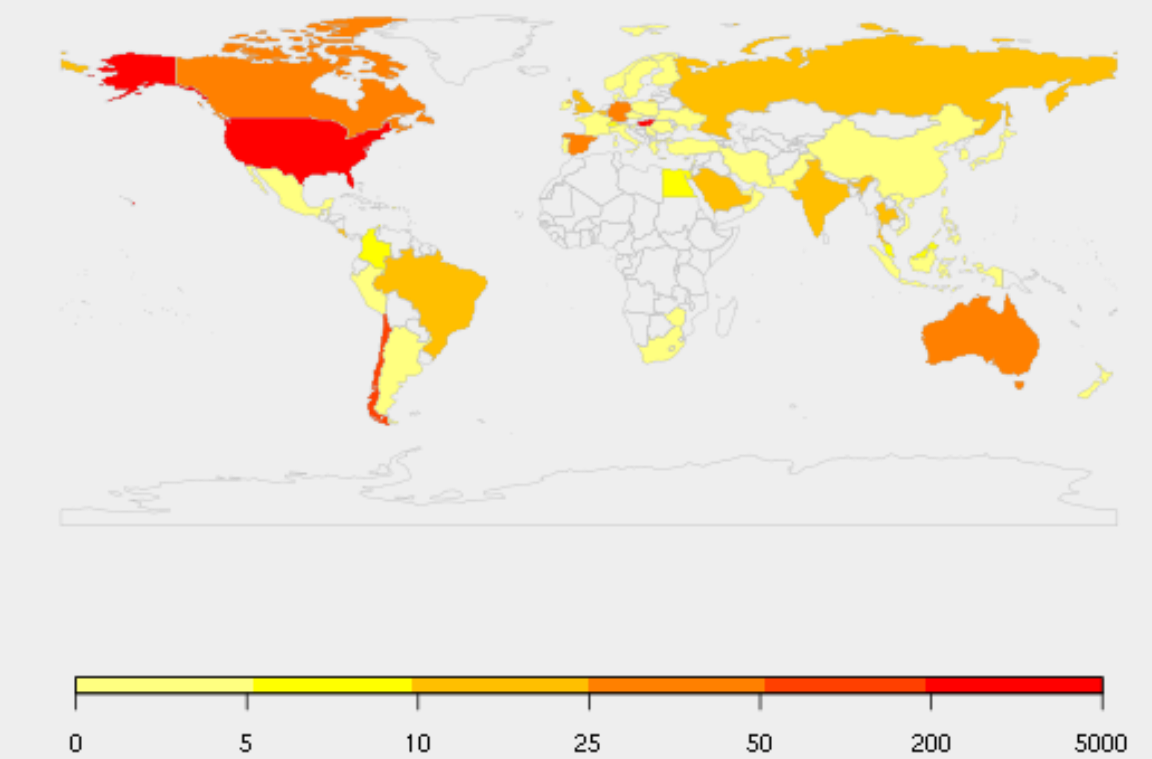
Data Analysis and Graphics

- The R® software environment for statistical computing and graphics was used to generate the plots and calculate summary statistics of the data.

Figure 1. Graphical overview of the technology of ID - ODSTM

RESULTS

IDODS visitors (n = 5678) all around the world

Figure 2. Cluster map of ID – ODSTM visitors from around the world

Template	% of all Utilization	Mean ± SD CPU Time (sec)	% Aborted
Piperacillin and Tacobactam PTA	15.90	5.40 ± 1.34	2.82
Empiric Vancomycin Dosing	15.10	4.90 ± 1.05	3.73
Bayes Aminoglycosides Optimization	15.50	9.00 ± 64.42	37.14
Bayes Vancomycin Optimization	7.90	18.30 ± 6.85	41.65
Cefepime PTA	14.10	8.50 ± 3.32	4.23
Meropenem PTA	8.70	10.70 ± 3.05	1.87
Other	22.80	6.00 ± 1.18	11.91

Table 1. Summary statistics of select ID – ODSTM template utilization

CONCLUSION

- The availability of this cross-platform application provides the foundations for a multi-model based, point of care clinical decision support tool on desktops and mobile devices for clinicians interested in optimizing anti-infective therapy.
- This system has been used to improve antibiotic dosing practices at the bedside via the utilization of modern principles of antimicrobial pharmacodynamics, popPK model based approach and Monte Carlo simulation over 5000 times since implementation.
- Subsequent development will focus on improving the user interface in order to attempt to minimize the rate of inaccurate data entry into ID - ODSTM, the web - based clinical decision support tool used to individualize antimicrobial therapy.

REFERENCES

1. Garritty et al. J Med Internet Res. 2006, 8(2):e7.
2. Mosa et al. BMC Med Inform Decis Mak. 2012, 12:67
3. <http://hopkins-abxguide.org>
4. <http://www.sanfordguide.com>
5. Burdette et al. CID 2008, 47: 117-122
6. <http://www.R-project.org>
7. <http://rapporater.net>
8. www.optimum-dosing-strategies.org