Rapid Analysis of Diagnostic and Antimicrobial Patterns in R (RadaR)

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Rapid Analysis of Diagnostic and Antimicrobial Patterns in R (RadaR): Interactive Open-Source Software App for Infection Management and Antimicrobial Stewardship

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Abstract

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RadaR: An interactive open source software application for infection management and antimicrobial stewardship

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Abstract

Background

Analyzing process and outcome measures for patients suspected of or having an infection in an entire hospital requires processing large datasets and accounting for numerous patient parameters and guidelines. Rapid, reproducible and adaptable analyses usually need substantial technical expertise but can yield valuable insight for infection management and antimicrobial stewardship (AMS) teams.

Objective

We describe a software application (RadaR - Rapid analysis of diagnostic and antimicrobial patterns in R) for infection management allowing user-friendly, intuitive and interactive analyses of large datasets without prior in-depth software or programming knowledge.

Methods

RadaR was built in the open source programming language R using Shiny, an additional package to implement web-application frameworks in R. RadaR was developed in the context of a 1339-bed academic tertiary referral hospital to handle data of more than 180,000 admissions.

Results

RadaR visualizes analytical graphs and statistical summaries in a rapid and interactive manner. Users can filter patient groups by 17 different criteria and investigate antimicrobial use, microbiological diagnostic use and results including antimicrobial resistance, and outcome in length of stay. Results can easily be stratified and grouped to compare defined patient groups based on individual patient features.

Conclusion

AMS teams can use RadaR to identify areas within their institutions that might benefit from increased support and targeted interventions. Diagnostic and therapeutic procedures can be assessed, and analyses can easily be visualized and communicated. RadaR demonstrates the feasibility of developing software tools for infection management and AMS teams in an open source approach making it free to use and adaptable to different settings.

Introduction

In times of rising antimicrobial resistances (AMR), worldwide efforts focus on the preservation of antimicrobials as a precious non-renewable resource. Infection management in the form of antimicrobial stewardship (AMS) programs, defined as "a coherent set of actions which promote using antimicrobials responsibly", is an effective way to tackle this global health problem [1]. Appropriate use of antimicrobials based on appropriate and timely diagnostics are important tools for successful infection management. Stewardship efforts aim at improving quality of care and patient safety as a top priority of any intervention. Thereby, they contribute to efforts in fighting AMR through optimizing the use of antimicrobials. Stewardship interventions and activities are focused both on individual patients (personalized medicine, consulting) and patient groups/clinical syndromes (guidelines, protocols, IT infrastructure/clinical decision support systems, etc.).

AMS setups in hospitals are often heterogeneous but audit and feedback to assess the goals are an essential part of most programs and are included in international guidelines and reviews [2–7]. Important data for AMS programs include for example days of therapy (DOT), daily defined doses (DDD), admission dates, length of stay (LOS) and adherence to local or national diagnostic and therapeutic, or infection management guidelines [1]. Clinical outcomes, quality of care or consumption of hospital resources can be measured, for example using mortality data or surrogate parameters like length of stay. Electronic health records (EHR) and administrative data facilitate collection of such information. Administrative data has also been shown to be a reliable source for assessing clinical outcomes [8].

EHR usually offer quick insights into useful infection management data on the individual patient level. However, easy access to analyze patient groups (e.g. stratified by departments or wards, specific antimicrobials or diagnostic procedures used) is difficult to implement in daily practice. Rapid analysis of larger patient populations (e.g. spread over multiple specialties) is even more

challenging although this information might be available. Yet, this is vital for meaningful analysis, including possible confounders, and pattern recognition across different populations. Even when aggregated data is available it is often not possible to trace back individual patients and analyses lack the ability to be further adjusted or stratified.

AMS teams are multidisciplinary and act beyond the borders of single specialties [9]. They are usually understaffed [10], with limited IT support. They therefore need user-friendly and time-saving IT resources, without the need for profound technical expertise once the system is set up. To aggregate and link data of antimicrobial use, guideline adherence, and clinical outcomes on the institutional level can build the basis for important insights for these teams. These could be used to identify areas within hospitals that might benefit most from supportive AMS interventions (e.g. subspecialties with lower guideline adherence or unusual patterns of antimicrobial use). Feedback from this data could also help physicians to better understand their patient population as a whole and, in addition, administrative departments could allocate resources in a more targeted fashion.

Moreover, aggregated data and simultaneous analysis of multiple areas (e.g. use of diagnostics and antimicrobials) present an extensive insight into large patient populations. This also enables comprehensive and multidisciplinary approaches of infection management combining diagnostic and therapeutic perspectives [1,9,11]. Unfortunately, this kind of analyses still requires substantial statistical knowledge and software skills while being time consuming.

Technology, data science, and application development can bring solutions to complex data handling problems like those described above. Application development for medical and epidemiological (research) questions has found many important answers during the last years alone. For example, applications at hospital emergency departments (ED) in form of a software dashboard have been shown to improve efficiency and quality of care for patients requiring emergency admission to hospital [12]. These applications are used to communicate clearly defined clinical problems like

mortality ratio, number of cardiac arrests or re-admission rate to the ED. This led to a decreased length of stay and mortality at the ED. Others used similar approaches to rapidly and interactively display geographical locations of tuberculosis cases without the need of technical expertise improving the understanding of transmission and detection [13]. Furthermore, data driven fields like genomics are front runners in developing new innovative software applications to handle large datasets, in close collaboration with bioinformatics [14]

It is important to note that all of these above-mentioned applications have been created in an open source approach. The underlying source code can be shared, modified and freely distributed through open repositories like GitHub [15], taking open source software license obligations into account. This facilitates collaboration and easy adaptation to many different settings and IT systems and supports the use of advanced data visualization to users with minimal experience in programming and little or no budget for professional database engineers [14].

Different approaches have been described to interactively work with microbiological diagnostics data and EHR: electronic antibiograms, centralized resistance analysis, EHR data mining, and clinical decision support systems for antimicrobial stewardship are great examples for innovation in the field [16–18]. However, a full open source approach for applications working with combined antimicrobials use and diagnostic data of individual patients on the hospital level in the field of infection management is still lacking.

We followed principles of open knowledge [19] to address the need for an interactive, easy-to-use tool that allows users to investigate antimicrobial use, microbiological diagnostic use and patient outcomes at an institutional (hospital) level. We describe an open source software application for infection management and antimicrobial stewardship (RadaR - Rapid analysis of diagnostics and antimicrobial patterns in R). RadaR enables rapid and reproducible data analysis without extensive technical expertise in a graphically appealing way while being adaptable to different settings.

Analyses are based on datasets of individual patients. Therefore, also aggregated results can be stripped down and additional patient features can be investigated. With this application we aim at supporting data-driven hospital insights and decision making for actors in the field of antimicrobial stewardship in a free, transparent, and reproducible way.

Methods

To develop software in an open source environment we used the open source programming language R in conjunction with RStudio [20], an open source integrated desktop environment for R [21]. To build RadaR as a web-browser based application we used the Shiny package for R [22]. Shiny allows R users to build interactive web applications without extensive knowledge in web design and its programming languages. They can be run and hosted online for free [23], on local or cloud-based servers or on personal computers.

The functionality of R can be easily extended by installing additional packages. All packages used for the development of RadaR are listed in Table 1. RadaR is developed in an open source environment and licensed under GNU General Public License v2.0 [24] giving options to change, modify and adapt RadaR to both personal and commercial users' needs while requiring the need to document code changes [24].

Table 1. Required R packages for RadaR

R package	Minimal Version
AMR	0.4.0
data.table	1.11.6
DT	0.4.0

ggridges	0.5.0
lubridate	1.7.4
plotly	4.8.0
qicharts2	0.5.1
rintrojs	0.2.0
shiny	1.1.0
shinyBS	0.61
shinycssloaders	0.2.0
shinydashboard	0.7.0
shinyjs	1.0.0
shinyWidgets	0.4.3
survival	2.42-6
survminer	0.4.3
tidyverse	1.2.1
viridis	0.5.1
zoo	1.8-3

RadaR's calculations and data aggregation are done reactively based on user's selection. Single

observations on the patient level build the basis for any calculation.

RadaR uses common csv-files (comma-separated values) as input. Three different data sources are

read in RadaR for admission, antimicrobial, and microbiological data which are merged and transformed upon start. A patient number or study number is used as an unique identifier. All antimicrobial and microbiological data is checked for falling in the interval of admission dates.

The data should be structured in a dataset format where each variable is one column and each observation is one row. This follows the concept of 'tidy data' as defined by Hadley Wickham [25]. Table 2 displays the set of variables underlying RadaR's functionality. Additional variables are calculated and transformed using the package lubridate and zoo for time points and intervals and AMR for antimicrobial (group) names, microbial isolate names, first isolate identification and resistance analysis [26–28]. Microbiological resistance is calculated per antimicrobial substance or as co-resistance if more than one substance is selected.

Table 2. Input variables for RadaR

Variable	Detail
Admission data	
adm_end_date	Discharge date (YYYY-MM-DD)
adm_id	Admission ID
adm_route	Origin
adm_start_date	Admission date (YYYY-MM-DD)
birth_date	Birth date (YYYY-MM-DD)
death_during_adm	In-hospital death (TRUE/FALSE)
gender	Gender
id	Patient ID or study ID
specialty	General specialty (internal medicine, surgery, other)
sub_specialty	Sub-specialty

Antimicrobial data

ab_route	Administration route
ab_start_date	Start of antimicrobial (YYYY-MM-DD)
ab_stop_date	Stop of antimicrobial (YYYY-MM-DD)
atc_code	5th level of the WHO ATC classification system[a]
ddd_per_day	Defined daily dose of antimicrobial according to WHO ATC classification system per day[a]
id	Patient ID or study ID

Microbiological data

antimicrobial susceptibility testing	Several columns of tested antimicrobial agents (e.g. amoxicillin, ciprofloxacin etc.) with resistance results (R / I / S)
id	Patient ID or study ID
material	Test material
mo	Microbial ID (if test = positive)[b]
specialty	Ordering specialty
test_date	Test date (YYYY-MM-DD)

a) [29]
b) as defined by the AMR package for R [28]

RadaR can be used for graphical exploratory data analysis. Differences in length of stay are displayed by a Kaplan-Meier curve in conjunction with a log-rank test using the survminer package [30]. Time trends for number of admissions, antimicrobial consumption, and resistance counts per year, quarter, or month are visualized in run charts using the qicharts2 package [31]. Non-random variation in these run charts is tested using Anhøj's rules [32].

RadaR has been developed in macOS High Sierra (1.4 GHz, 4 GB RAM) and it was successfully tested in Windows 7 and Linux (Ubuntu 16.04.4 LTS). A running example version has been deployed

to shinyapps.io, a publicly available web-hosting service for R Shiny applications [33].

The entire source code of RadaR is freely accessible on GitHub [34]. We intend to integrate suggestions and feedback coming from its users and the R community.

RadaR was developed using data of patients admitted to the University Medical Center Groningen, Groningen, The Netherlands. Data was collected retrospectively, and permission was granted by the ethical committee (METc 2014/530). RadaR can be used locally in protected environments or hosted online provided appropriate measures have been taken to guarantee data protection depending on national regulations.

Results

We have developed RadaR, a dashboard application providing an intuitive platform for rapid analysis of large datasets containing information about patients' admission, antimicrobial use, and results of microbiological diagnostic tests. This application can help users (i.e. professionals involved in antimicrobial stewardship programs) to find answers to questions like: "What are the most commonly used antimicrobials at an institution/specialty/department and have they changed over time?", "Were adequate microbiological diagnostics performed at the start of antimicrobial treatments?", "What are the most frequent microorganisms found and their resistance patterns in different departments?", "Can we identify priority areas within a hospital where antimicrobial or microbiological diagnostic use has the largest room for improvement?"

Application design

RadaR is designed in form of a browser-based dashboard that most users are familiar with from typical websites and online tools (Fig. 1). The basis of RadaR's functionality is filtering datasets and producing analytical graphs according to selection criteria defined by the user. Any calculations and

data aggregation are based on single observations of individual patients. To identify and analyze

groups of patients, 17 different selection criteria can be found in the sidebar (Table 3). The output of

RadaR is grouped into four panels (patient, antimicrobials, diagnostics, and outcome) that each

consist of three to four output boxes displaying the results.
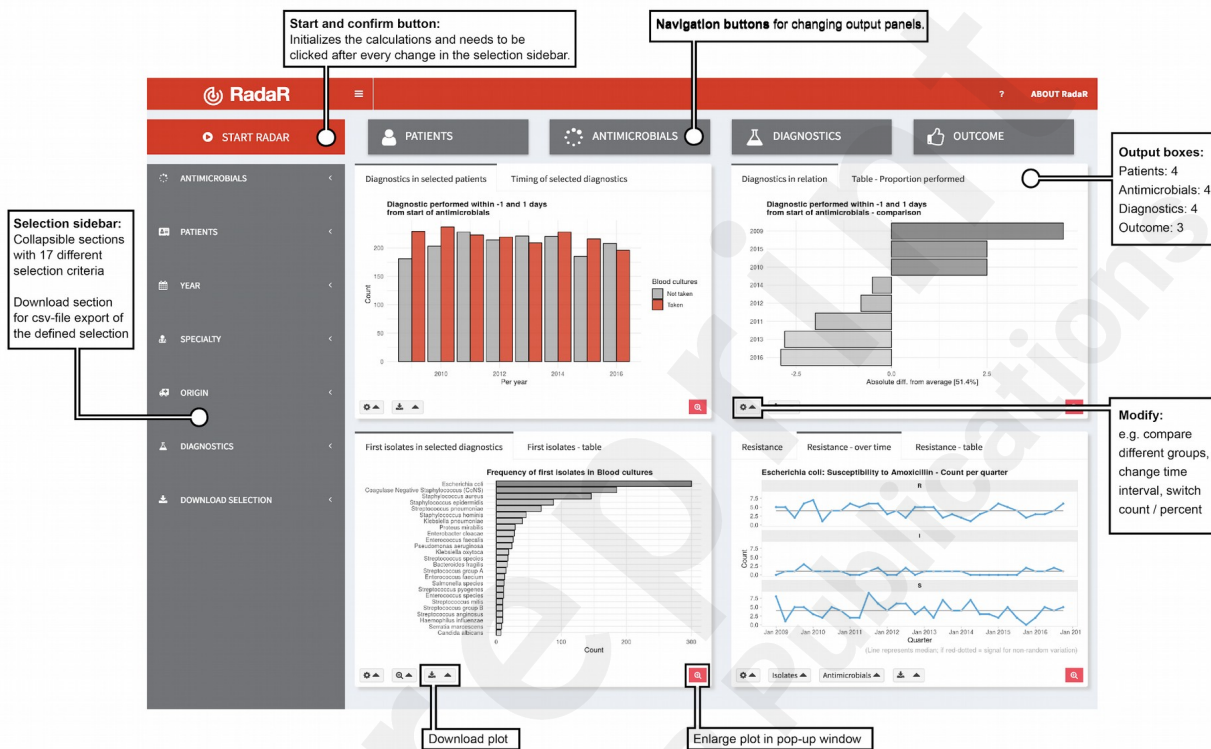
Figure 1. Application design

Table 3. Selection criteria in sidebar

Tab name	Criteria	Functionality
Antimicrobials	Start of antimicrobials (in relation to start of admission)	Select patients starting treatment in a defined time period
	Minimum duration of treatment (days) - all antimicrobials	Select patients with a minimum treatment duration

	Minimum duration of prescription (days) - single antimicrobial	Define the minimum duration of a prescription for any selected antimicrobial
	Administration route	Intravenous or oral
	First antimicrobial only	Filter patients for first prescribed antimicrobial only or any (based on all other selection criteria)
	Groups of antimicrobials	4th level of the WHO ATC classification system[a]
	Antimicrobials	5th level of the WHO ATC classification system[a]
Patients	Gender	Female or male
	Age	As available in the data
Year	Year	Years available in the data
Specialty	Specialty	Internal medicine, surgery or other
	Minimum number of patients per subspecialty	0, 10, 100, 1 000 or 10 000
	Include only this subspecialty	All other subspecialties will be excluded
	Exclude subspecialty	Define single subspecialties to be excluded
Origin	Origin at admission	As available in the data
Diagnostics	Type of diagnostics	Blood culture or urine culture test
	Days to first test (in relation to start of antimicrobials	Define time period for tests to be performed in

a) [29]

All output is based on the selection criteria defined by the user in the sidebar. Each new selection and any change needs to be confirmed by clicking the confirm selection button (Fig. 1). Users can

navigate between the different analysis panels through clicking the respective button.

Results are shown in bar charts, density plots, run charts, a bubble plot and a Kaplan-Meier curve for length of stay in hospital. Each panel further displays a table summarizing the respective data analyses. All output boxes and their content are described in Table 4. Most output boxes include modification options that can be identified by small gear icons (Fig. 1). These clickable icons allow for further specification of the generated plots and tables. Users can compare different groups (e.g. antimicrobial use by antimicrobial agent, resistance patterns per isolate, or length of stay by specialty) or modify the plots (e.g. switch from count to proportion, change the chart type, or show or hide the legend). Plots and tables can be download through download buttons as png-files (portable network graphics) for plots and csv-, excel- or pdf-files (portable document format) for tables.

Table 4. Output boxes for analysis results

Output panel	Output box	Output type	Content	Modification options
Patients	Subspecialties in selection	Bubble chart[a]	Number of patients per subspecialty	• Show top ten by number of patients
	Subspecialties - table	Table	Total number of patients and per subspecialty	
	Patient age	Density plot (distribution)	Age distribution in selection	• Group by gender
	Number of admissions	Run chart	Count of admissions per time period	• Per year, per quarter, or per month
Antimicrobials	Antimicrobials	Bar chart	(Group of) antimicrobials sorted by prescription, DDD or DOT	• Single antimicrobials or groups • Select prescription count, DDD or DOT per 100 bed days

	Defined daily doses (DDD)	Run chart	DDD per 100 bed days per group and per time period	• Group by: none, specialty, subspecialty, origin • Per year, per quarter, per month
	Days of therapy (DOT)	Run chart	DOT per 100 bed days per group and per time period	• Group by: none, specialty, subspecialty, origin • Per year, per quarter, per month
	DDD/DOT table	Table	Summary of DDD/ DOT per 100 bed days per group	• DDD or DOT per 100 bed days • Group by: antimicrobial (group), year, specialty, subspecialty, origin
Diagnostics	Diagnostics in selected patients	Bar chart	Diagnostics taken vs. not taken in specified timespan	• Count or proportion • Per year, quarter or month
	Timing of selected diagnostics	Bar chart	Time of diagnostics performed in days after treatment start	
	Diagnostics in relation	Bar chart	Absolute difference from average proportion of selected diagnostics performed	• Group by: antimicrobial (group), year, specialty, subspecialty, origin
	Table - Proportion performed	Table	Summary of proportion of diagnostics performed	• Group by: antimicrobial (group), year, specialty, subspecialty, origin
	First isolates in selected diagnostics	Bar chart	First isolates of microorganisms sorted by frequency	• Group by: antimicrobial (group), year, specialty, subspecialty, origin

				• Zoom to select more or less isolates shown in graph
First isolates - table	Table	Frequency table of first isolates	• Group by: year, specialty, subspecialty, origin
Resistance analysis	Bar chart	Count or proportion of (co-)resistance to selected antimicrobials in selected isolates in "R", "S", and "I" categories	• Select isolates • Select antimicrobials • Group by: year, specialty, subspecialty, origin • Select count or proportion
Resistance - over time	Run chart	Count of (co-)resistance to selected antimicrobials in selected isolates in "R", "S", and "I" categories over time	• Select isolates • Select antimicrobials • Per year, per quarter or per month
Table	Table	Count or proportion of (co-)resistance to selected antimicrobials in selected isolates in "R", "S", and "I" categories	• Group by: year, month, quarter, specialty, subspecialty, origin • Select isolates • Select antimicrobials • Select count or proportion
Outcome	Length of stay	Density plot or histogram	Distribution of length of stay per group	• Group by: all, gender, year, antimicrobial (group), diagnostics performed, specialty, subspecialty, origin • Show histogram • Show legend

			• Spread out to remove overlaps
Length of stay - Kaplan-Meier	Kaplan-Meier curve	Kaplan-Meier curve per group	• (Groups shown as selected in Length-of-stay-box)
Length of stay - table	Table	Summary of length of stay per group	• Group by: gender, year, antimicrobial (group), diagnostics performed, specialty, subspecialty, origin

a) Interactive plot showing additional information when hovering over plot

DDD: Defined daily doses

DOT: Days of therapy

Finally, two datasets (antimicrobial/admission data and microbiological data) of the user-defined selection can be downloaded from the sidebar menu in a csv-file format for further analysis (e.g. retrieving a list of patient numbers of the selected patient group).

Development process

RadaR has been developed in close contact with infection management team at the University Medical Center Groningen, Groningen, the Netherlands, to meet the needs and requirements of this user group. Subsequently, all members of the European Society of Clinical Microbiology and Infectious Diseases Study Group for Antimicrobial stewardshiP (ESGAP) were asked to evaluate and test the application through a running online example of RadaR and by filling out an online survey. The ESGAP comprises around 200 members coming from more than 30 countries worldwide. Twelve members took part in the evaluation. This yielded important information on user experiences with the application and led to further improvements that are reflected in the version we present in this report. In a next phase, RadaR will be tested in different settings of ESGAP members and other

interested partners using locally available data.

Workflow

RadaR was developed and tested with a dataset of all patients admitted to our institution, a 1339-bed academic tertiary referral hospital, within the years of 2009 to 2016 comprising over 180,000 admissions. For simulation purposes and online user testing we have created a test dataset of 60,000 simulated patients that do not represent real patients. This dataset cannot be used for any meaningful results but allows testing of RadaR's functionality.

A typical example workflow with RadaR comprises six steps (with examples from the test dataset):

1. Define the selection: For example, patients receiving intravenous second- or third-generation cephalosporins as first treatment for at least two days starting within the first two days of hospital admission from any specialty in all years in the dataset.

2. Patients panel: Identify the total number of patients and the subspecialties with the highest number of included patients (example: 537 patients selected in total with 97 patients from internal medicine). Investigate patients' gender and age distribution.

3. Antimicrobials panel: Identify the total use of the initial cefuroxime treatment in DDD and DOT per 100 bed days (example: 4.51 and 1.5 respectively). Stratify the results by subspecialty and identify the highest number of DDD and DOT per 100 bed days (example: highest use by DDD and DOT in internal medicine).

4. Diagnostics panel: Check if the selected microbiological diagnostic test (e.g. blood culture test) has been performed on the same day as start of treatment (defined in the sidebar). Investigate the proportion of performed tests over the years and which subspecialty performs best compared to others (example: Pediatrics). Check which microorganisms (as first isolates) were found in the selected diagnostic specimens (most common: *Escherichia coli*). Investigate the proportion of isolates resistant to cefuroxime (8.9%) and analyze the trend

over time.

5. Outcome panel: Check for patterns of differences in LOS in the defined patient group by subspecialties or performed diagnostics (example: highest mean LOS of 7.8 days in Surgery).

6. Refine the selection: Investigate a subgroup of the original selection. For example, select only the top three subspecialties by number of patients and repeat step two to five.

Customization

For setting up RadaR in a new environment after data preparation, users only need to perform the following four steps:

1. Downloading R and RStudio [20,21], which are free to use and open source software.

2. Download or copy and paste RadaR's source code [34] into three files in RStudio: global.R, server.R, and ui.R.

3. In global.R manually edit the paths for the prepared datasets to be imported into RadaR.

4. Run the application in RStudio with the calling the function runApp() in the console or by clicking the green run app button. This will download and install the required R packages needed for the application if they have not been installed previously and create the final dataset for analysis. The RadaR interface will open in the RStudio viewer pane or in a new window of the standard browser of the user's operating system.

RadaR's appearance has been customized with using a CSS (Cascading Style Sheets) script [35] that is loaded into the application upon its start. This script needs to be saved into a subdirectory of the directory of the three main files (global.R, server.R, ui.R) called "www". We recommend RStudio's project function to create a single project for RadaR and to store all information in this project directory. Users with experience in using CSS can fully alter RadaR's design by changing the

underlying CSS script.

Discussion

We have developed a web-browser based application for rapid analysis of diagnostic and antimicrobial patterns that can support AMS teams to tailor their interventions. It has been designed to enhance communication of relevant findings while being easily accessible also for users without prior extensive software skills. In our experience this system can be adapted to new settings within one day when the required data (table 2) is available.

Commercial software for infection management is available (e.g. Epic® antimicrobial stewardship module, TREAT Steward™). They offer extensive options for filtering, analyzing, and visualizing EHR with real-time connections to hospital data infrastructures and have been shown useful in clinical practice [36]. Yet, it is difficult to compare functionalities of these tools due to their non-open source nature. This fact, together with the required budget to purchase the software, drastically limits their use. We believe that transparent software development can support the adoption of data-driven developments while enhancing optimal quality of care and patient safety which is crucial in the light of new data-driven developments of using EHR [37,38].

The global nature of infections further call to make software tools applicable also in resource-limited settings [39]. open source approaches for data analysis, like RadaR, have advantages over traditional methods like Excel or SPSS. Hughes et al. described those in their report of an application for RNA-sequencing data analysis [14]. They highlight aspects that were also fundamental for the development of RadaR. Firstly, R allows transparent, reproducible and sustainable data analysis through scripts that can easily be shared and changed. This can build the basis for collaboration and enforces the spirit of open science (also through the strong collaborative R community online). Secondly, R is open source and free to use, therefore, enabling use in resource-limited settings, too. Finally, Shiny empowers users to interact with the data making even very large datasets quickly

interpretable.

Innovative approaches in supporting infection management by leveraging EHR are being researched [16–18]. Reporting on antimicrobial resistances, antimicrobial use, and hospital infections (e.g. for quality assurance) is well established but it is important to integrate these data sources in one approach that allows detailed filtering options on all input. Merely looking at antimicrobial use alone or comparing aggregated results (e.g. total amount of a specific antimicrobial substance per hospital correlated with the total count of a resistant isolate) will result in a loss of information. Detailed data and calculation based on each individual patient is crucial to draw informed conclusions. Unfortunately, the above-mentioned infection management approaches [16–18] depend on additional commercial software for data visualization or the source code is not openly available. We want to encourage others to turn towards available open source software solutions, like R, for an increased potential of collaboration and transparency. Their strength, however, is the connection to real-time data flows. This enables the prospective use and increases their usability for daily clinical practice. RadaR is currently still limited to retrospective data analysis due a changing hospital data infrastructure in our setting. Technically it is feasible to connect R based applications like RadaR to hospital data infrastructures running with clinical data standards [40]. For a start, access to static data extraction is often easier and faster to achieve. RadaR can be used to advocate the use of data visualization tools and improved accessibility of hospital data sources. Until then it can support users as a stand-alone option for retrospective data analysis in infection management. Next steps will involve testing in multiple settings and forming a user and research group to continue and expand the use of open source technology and open science principles in infection management.

RadaR demonstrates the feasibility of developing software tools for infection management and AMS team in an open source approach making it free to use, share or modify according to various needs in different settings.

Acknowledgments

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Conflicts of Interest

None.

Multimedia appendix

1: Screenshot of RadaR.

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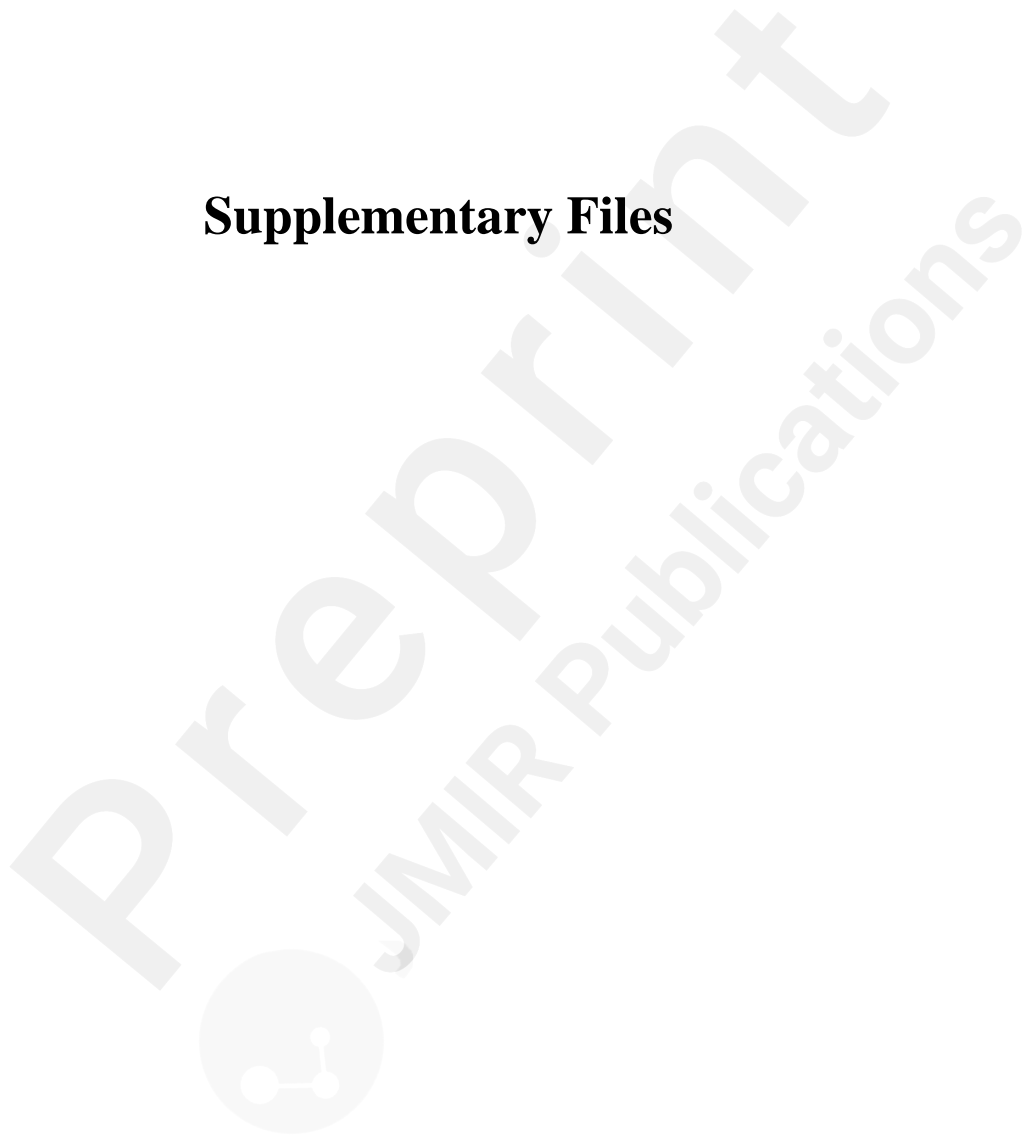
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Supplementary Files

Multimedia Appendixes

Screenshot of RadaR.
URL: https://asset.jmir.pub/assets/5d37c7d7bd612c12cff71eda7ee51c7f.mov