Software Application Profile

Software Application Profile: Opal and Mica: open-source software solutions for epidemiological data management, harmonization and dissemination

Dany Doiron,1–3*† Yannick Marcon,1† Isabel Fortier,1 Paul Burton4 and Vincent Ferretti5

1Research Institute of the McGill University Health Centre, Montreal, QC, Canada, 2Swiss Tropical and Public Health Institute, Basel, Switzerland, 3University of Basel, Basel, Switzerland, 4University of Bristol, School of Social and Community Medicine, Bristol, UK and 5Ontario Institute for Cancer Research, Toronto, ON, Canada

*Corresponding author. 2155 rue Guy, Office 458, Montreal, QC, Canada H3H 2R9. E-mail: ddoiron@maelstrom-research.org
†Denotes equal contribution.

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Abstract

Motivation: Improving the dissemination of information on existing epidemiological studies and facilitating the interoperability of study databases are essential to maximizing the use of resources and accelerating improvements in health. To address this, Maelstrom Research proposes Opal and Mica, two inter-operable open-source software packages providing out-of-the-box solutions for epidemiological data management, harmonization and dissemination.

Implementation: Opal and Mica are two standalone but inter-operable web applications written in Java, JavaScript and PHP. They provide web services and modern user interfaces to access them.

General features: Opal allows users to import, manage, annotate and harmonize study data. Mica is used to build searchable web portals disseminating study and variable metadata. When used conjointly, Mica users can securely query and retrieve summary statistics on geographically dispersed Opal servers in real-time. Integration with the DataSHIELD approach allows conducting more complex federated analyses involving statistical models.

Availability: Opal and Mica are open-source and freely available at [www.obiba.org] under a General Public License (GPL) version 3, and the metadata models and taxonomies that accompany them are available under a Creative Commons licence.
Introduction

To maximize the use of resources and accelerate improvements in health, significant advances are needed in the discoverability and inter-operability of epidemiological study data. For one, the seemingly simple task of locating pre-existing data available for research is in fact a significant challenge; information on studies and on the data they collect is often either unavailable or difficult to find. Direct contact with study staff is then necessary to enquire about data availability, which results in a time-intensive process for researchers and study managers alike. At the same time, epidemiological research projects are increasingly drawing on co-analysis across multiple studies to enhance statistical power and improve the precision and robustness of results in a cost-effective manner. However, existing studies gather information on individuals using various data collection instruments, data management software and documentation standards, resulting in heterogeneous database systems with disparate formats and models. Large-scale collaborative projects therefore require considerable resource investments to render the information collected by each study compatible and to convert heterogeneous data into compatible formats.

To accelerate the research process while reducing costs associated with it, stakeholders are emphasizing the need for tools that foster the visibility of existing data and enable data compatibility across studies. In recent years, a number of web portals documenting and disseminating research data in the social, environmental and biomedical sciences have emerged. Software applications such as ARK, REDCap and OpenClinica support the collection and management of biomedical research data. Other more generic software solutions for research data dissemination have also been developed. However, little software has been specifically designed to facilitate data harmonization in multi-study projects. Finally, to our knowledge, no integrated solution exists to address the dual aim of disseminating epidemiological metadata to the research community and supporting data inter-operability across studies.

To address this gap, Maelstrom Research proposes the OBiBa (Open Source Software for BioBanks) software suite. In this Software Application Profile we present Opal and Mica, two web-based software products that respectively provide out-of-the-box epidemiological data management/harmonization and metadata dissemination solutions for individual epidemiological studies or study consortia. We also show how the full potential of these applications is harnessed when used conjointly; enabling studies and research networks to easily and securely build a federated database system which allows securely querying and analysing data stored on remote servers. Screenshots showing salient parts of each application are presented in Supplementary materials, available as Supplementary data at IJE online.

Implementation: Opal and Mica design

The Opal and Mica software applications are written in Java, JavaScript and PHP languages. Both applications are built upon a RESTful client-server infrastructure, allowing multiple connections between servers and different software web clients using secure HTTPS protocol. As shown in Figure 1, these clients are designed to ensure a broad range of specialized tasks achieved by different types of users. For example, a study/network coordinator or data manager makes use of the Opal and Mica Admin clients’ point-and-click interfaces, to handle day-to-day operations such as server administration, management of user permissions, connections to other applications, data and metadata upload and content editing. Researchers or statisticians use an R client such as RStudio to conduct statistical analyses of study data stored on Opal, and a Python client allows data managers to handle repeatable tasks such as batch processing or periodic data imports. The Mica Portal client renders study metadata and other non-confidential information hosted on the Mica server and publishes this information on a publicly accessible website. The Mica Portal is designed using Drupal, a popular open-source content management system used by websites worldwide. Importantly, individual-level data always remain managed and stored on a secure Opal server, but communication with the Mica server allows extraction of summary statistics to be presented on Mica Portal.

Client authentication is done through user name and password or by establishing a two-way SSL authentication. Back-end software infrastructure includes Elasticsearch and an R server, which respectively provide a data query engine and an environment to run statistical analyses and reports. MongoDB and/or MySQL are used as database back-end engines for storing study participant data. Opal has no practical limitation related to the number of participants/variables it can store.

Opal: a data management and harmonization tool

Opal provides a centralized web-based data management system allowing study coordinators and data managers to securely import/export a variety of data types (e.g. text, numerical, geolocation, images, videos) and formats (e.g. SPSS, CSV) using a point-and-click interface. Opal then converts, stores and displays these data under a standardized model. Opal can also read data directly from other
data source engines such as LimeSurvey or SQL databases. Once data have been imported, the Opal web application facilitates data curation and quality control procedures and allows automated descriptive statistics computation with graphical displays such as bar charts and scatter plots. The application also allows annotating variables with metadata to create rich, searchable data dictionaries. For example, using a variable classification taxonomy developed by Maelstrom Research, each data item collected by a study can be annotated with a standard list of domains of information. This then facilitates metadata browsing and data discoverability using the Mica web portal. Thanks to its integration with the R software and R markdown, statistical analyses and reports on data stored in Opal can also be performed. To ensure privacy, Opal stores participant identifiers in a distinct and secure database and provides administrators with tools to manage them. For example, to de-identify data disseminated to researchers, Opal can create new sets of unique participant identifiers (UIDs) when exporting datasets. Since mapping of UIDs remains in Opal, disseminated UIDs can be re-linked to internal UIDs at import.

When used across multiple studies, Opal is a powerful tool to harmonize epidemiological study data. Opal supports all steps of the Maelstrom Research retrospective data harmonization process. As such, Opal includes functionalities to: define variables targeted for harmonization, develop and implement processing algorithms used to derive common-format data, and efficiently document data harmonization decision making. To facilitate algorithm development, Opal also includes a comprehensive JavaScript library of functions commonly used to create harmonized variables. Establishing a secure connection with an R client also allows use of the R programming language to derive common format variables.

**Mica: a metadata catalogue and data discovery tool**

Mica is used to create websites and metadata portals for individual epidemiological studies or multi-study consortia, with a specific focus on supporting observational cohort studies. The Mica application helps data custodians and study or network coordinators to efficiently organize and disseminate information about their studies and networks without significant technical effort. Mica is made up of a number of different modules developed to add and edit descriptive information pertaining to epidemiological research networks, studies and datasets. The network description module allows Mica users to disseminate information such as network description and the number, design and geographical coverage of participating studies. A study description module is used to assemble and publish information on epidemiological studies such as participant selection criteria, sample size and data collection timelines. A dataset module supports the display and dynamic search of study data dictionaries (i.e. codebooks). For a consortium of studies, a special dataset module also allows
documenting and presenting variables targeted for harmonization and harmonization results. A data access module provides customizable web forms and workflows to facilitate online submission and management of data access requests. All Mica modules are customizable, i.e. information fields can be added or modified to meet the specific needs of a study or research network. Further, although the software is preconfigured for English or French, its user interfaces can be translated in any International Organization for Standardization (ISO) language without the need to modify the code. Mica also supports the creation of multilingual websites. A number of other Drupal-based extensions such as events calendars, discussion forums and dissemination tools can be used by studies or research networks to enhance the Mica portal as needed.

Once populated with study and variable metadata, Mica includes a powerful search engine which allows investigators to quickly find the information they need for their research projects. For example, in a Mica instance with only one study, users may use the metadata search features to easily browse the variables it collects. In a Mica instance with multiple studies, users can quickly identify a list of studies with a given profile (e.g. cohorts recruiting middle aged participants), which collect data on a specific health outcome (e.g. depression), risk factors of interest (e.g. physical activity) and confounding factors (e.g. age, sex, income, education, work status). As shown in the subsequent section, connecting Mica to one or more Opal database(s) allows users to search beyond the metadata by securely querying the actual study data hosted on remote servers.

**Connecting Opal and Mica: a federated database infrastructure for collaborative epidemiology**

Opal and Mica were developed in parallel as interoperable and complementary applications. When used conjointly, they allow study networks to create a federated database infrastructure via secure web services. Under such a framework, individual-level data are securely stored in study-specific Opal instances, but can be remotely queried using a Mica-powered web portal. This then gives the research community the ability to retrieve descriptive statistics (e.g. minimum, maximum, mean, standard deviation, counts) and produce contingency tables in real-time across multiple geographically dispersed study databases. Since all potentially disclosive data remain behind the originating institution’s firewall, and only aggregate descriptive statistics are sent to the Mica web portal, the privacy and confidentiality of study participants are ensured. More complex analyses involving statistical models or specialized disclosure controls (e.g. for scatter plots) can be applied to harmonized datasets thanks to Opal’s integration with the DataSHIELD statistical analysis approach. Under DataSHIELD, analysis requests are sent from a central analysis computer to the harmonized data held on several Opal instances. Computation is done simultaneously but in parallel on each Opal server linked by non-disclosive summary statistics. As in the federated Opal-Mica configuration, individual-level data thereby stay at source, under the governance structure and control of the originating study/institution. Figure 2 outlines the steps of a federated data analysis using Opal, Mica and DataSHIELD. Use of these software applications as a federated database infrastructure was first piloted in the BioSHaRE consortium. Below are some of the key epidemiological research initiatives that have made use of Opal and Mica.

**Usage case 1: Canadian Longitudinal Study on Aging (CLSA)**

The CLSA is a cohort study which is following 50,000 men and women between the ages of 45 and 85 for at least 20 years. To support its data platform, the Opal and Mica software respectively serve as CLSA’s data management system and data dissemination portal [https://datapreview.clsa-elcv.ca/datasets]. To date, 10 terabytes of data including questionnaires, magnetic resonance images (MRI), videos and sound tracks collected from 11 assessment centres across Canada are stored, curated and analysed with Opal. Users of the Mica-powered CLSA portal can search variables by domains of information or standardized scales/ questionnaires and securely interrogate the data-holding Opal server to retrieve variable distributions in real-time.

**Usage case 2: Canadian Partnership for Tomorrow Project (CPTP)**

The CPTP is a cohort made up of five regional studies following 300,000 Canadians aged 30 to 74. Ensuring compatible data across participating studies was the key-stone of the CPTP when it was formed in 2008. To facilitate this objective, the Opal software was used to harmonize questionnaire items, physical measurements and biospecimens-related data across regions. A single point of access to these harmonized datasets is provided via CPTP’s Mica-powered data portal [https://portal.partnershipfortomorrow.ca/]. In addition to real-time retrieval of descriptive statistics, the CPTP portal also gives researchers an overview of the harmonization potential across participating studies and data transformation.
algorithms used to derive common-format variables. Data access requests are also submitted and managed using this online tool.

Usage case 3: InterConnect
InterConnect is an international research network aiming to help explain the difference in the risk of diabetes and obesity between high- and low-risk populations. To facilitate research collaborations, over 100 diabetes-related studies have been documented on InterConnect’s Mica-powered web portal to date. Through a number of exemplar projects addressing research questions of aetiological and public health interest, InterConnect is also making use of the Opal software and DataSHIELD approach to set up a federated database infrastructure and securely co-analyse harmonized datasets across participating studies from around the world, without the need to physically share individual-level data.

Usage case 5: Maelstrom Research
In addition to developing the Mica application, Maelstrom Research and its partner networks have put this software to use by developing the Maelstrom Research Catalogue, a dynamic compendium of epidemiological studies worldwide that provides researchers with a free, user-friendly, web-based solution for data discovery. To date, 174 studies from more than 55 different countries are documented in the Catalogue, 93 of which include fully annotated and searchable metadata on over 660,000 variables. New studies and searchable variable metadata are added to the Catalogue on a weekly basis.

Discussion
The scientific potential of the wealth of data being collected by epidemiological studies is considerable. A higher volume and variety of data can lead to better precision and interpretation of research results. However, much like other domains of scientific enquiry, unlocking the potential of these data requires improving the organization, compatibility and accessibility of research data. The Opal and Mica software packages attempt to address some of these challenges by creating a comprehensive data framework fostering and enhancing the use of epidemiological study data.

New Opal and Mica software features are continuously being developed based on user feedback. Example of current developments include support for genotyping data management and dissemination and for handling STATA and SAS data formats and data query improvements (e.g. number of study participants fulfilling multiple criteria). By incorporating new functionalities in software release...
cycles, they are made available to all current and future users. The Opal and Mica applications are open-source and freely available for download at [www.obiba.org] under a GNU General Public Licence (GPL) version 3. User guides, detailed software/hardware requirements and links to pre-built packages are available at [wiki.obiba.org]. Study and variable metadata models and classification taxonomies developed by Maelstrom Research to accompany the software are available under the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International Public License. We encourage new epidemiological studies and networks to make use of these applications to help them meet their data management, harmonization and dissemination needs.

Supplementary Data

Supplementary data are available at IJE online.

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Conflict of interest: YM owns Epigeny, a company that offers services based on the Opal and Mica software described in this article.

References

1. Castillo T, Gregory A, Moore S et al. Enhancing Discoverability of Public Health and Epidemiology Research Data. London: Wellcome Trust, 2014.
2. Thompson A. Thinking big: large-scale collaborative research in observational epidemiology. Eur J Epidemiol 2009;24:727–31.
3. Piwowar HA, Becich MJ, Bilofsky H, Crowley RS. Towards a data sharing culture: recommendations for leadership from academic health centers. PLoS Med 2008;5:e1315–19.
4. Walport M, Brest P. Sharing research data to improve public health. Lancet 2011;377:537–39.
5. Roger VL, Boerwinkle E, Crapo JD et al. Strategic transformation of population studies: recommendatons of the working group on epidemiology and population sciences from the National Heart, Lung, and Blood Advisory Council and Board of External Experts. Am J Epidemiol 2015;181:363–68.
6. Murtagh MJ, Turner A, Minion JT, Fay M, Burton PR. International data sharing in practice: new technologies meet old governance. BioPreserv Biobank 2016;14:231–40.
7. Wilkinson MD, Dumontier M, Aalbersberg IJ et al. The FAIR Guiding Principles for scientific data management and stewardship. Sci Data 2016;3:160018.
8. Interuniversity Consortium for Political and Social Research (ICPSR). ICPSR. 2016. https://www.icpsr.umich.edu/ (19 December 2016, date last accessed).
9. Consortium of European Social Science Data Archives (CESSDA). CESSDA ERIC. 2017. https://www.cessda.eu (17 August 2017, date last accessed).
10. Michener WK, Allard S, Budden A et al. Participatory design of DataONE—Enabling cyberinfrastructure for the biological and environmental sciences. Ecol Inform 2012;11:5–15.
11. Wichmann H-E, Kuhn KA, Waldenberger M et al. Comprehensive catalog of European biobanks. Nat Biotechnol 2011;29:795–97.
12. CLOSER. CLOSER - Promoting Excellence in Longitudinal Research. 2016. http://www.closer.ac.uk/ (21 December 2016, date last accessed).
13. Gehring U, Casas M, Brunkeef B et al. Environmental exposure assessment in European birth cohorts: results from the ENRICO project. Environ Health 2013;12:8.
14. Centre for Longitudinal Studies. CLS - Centre for Longitudinal Studies. 2016. http://www.cls.ioe.ac.uk/ (21 December 2016, date last accessed).
15. UK Biobank. UK Biobank Data Showcase. 2016. http://www.ukbiobank.ac.uk/data-showcase/ (2 February 2017, date last accessed).
16. Bickerstaffe A, Ranaweer A, Endersby T et al. The Ark: a customizable web-based data management tool for health and medical research. Bioinformatics 2017;33:624–26.
17. Harris PA, Taylor R, Thielle R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap) - a metadata-driven methodology and workflow process for providing translational research informatics support. JM Biomed Inform 2009;42:377–81.
18. OpenClinica. Electronic Data Capture, Randomization and Patient Engagement Made Easy. 2017. https://www.openclinica.com/ (25 May 2017, date last accessed).
19. Crosas M. The Dataverse Network: An open-source application for sharing, discovering and preserving data. d-lib magazine 2011;17:1–2.
20. Norwegian Centre For Research Data. Nesstar. 2016. http://www.nesstar.com/ (21 December 2016, date last accessed).
21. CKAN. CKAN – The Open Source Data Portal Software. 2016. http://ckan.org/ (20 December 2016, date last accessed).
22. International Household Survey Network (IHSN). NADA Microdata Catalogung Tool. 2015. http://www.ihsn.org/home/software/nada (19 December 2016, date last accessed).
23. Pang C, van Enkevort D, de Haan M et al. MOLGENIS/connect: a system for semi-automatic integration of heterogeneous phenotype data with applications in biobanks. Bioinformatics 2016;32:2176–83.
24. Winters K, Netscher S. Proposed standards for variable harmonization documentation and referencing: a case study using QuickCharmStats 1.1. PLoS One 2016;11:e0147795.
25. Fortier I, Raina P, Van den Heuvel ER et al. Maelstrom Research guidelines for rigorous retrospective data harmonization. *Int J Epidemiol* 2017;46:103–05.

26. Wolfson M, Wallace SE, Masca N et al. DataSHIELD: resolving a conflict in contemporary bioscience - performing a pooled analysis of individual-level data without sharing the data. *Int J Epidemiol* 2010;39:1372–82.

27. Gaye A, Marcon Y, Isaeva J et al. DataSHIELD: taking the analysis to the data, not the data to the analysis. *Int J Epidemiol* 2014;43:1929–44.

28. Doiron D, Burton P, Marcon Y et al. Data harmonization and federated analysis of population-based studies: the BioSHaRE project. *Emerg Themes Epidemiol* 2013;10:12.

29. Raina PS, Wolfson C, Kirkland SA et al. The Canadian longitudinal study on aging (CLSA). *Can J Aging* 2009;28:221–29.

30. Borugian MJ, Robson P, Fortier I et al. The Canadian Partnership for Tomorrow Project: building a pan-Canadian research platform for disease prevention. *CMAJ* 2010;182:1197–201.

31. Staff S. Challenges and opportunities. *Science* 2011;331:692–93.