Paper SM06

An Experience of Creating Questionnaire ADaMs Using the {admiral} ADQS Vignette

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ABSTRACT

{admiral} R packages are going to revolutionise the way in which we program ADaMs and provide us the tools required to produce these datasets using simple vignettes. The {admiral} ADQS Vignette is a new vignette that can manipulate questionnaire data into ADaMs. The number of questionnaires used in neuroscience is vast, but typically there are some that are more common. With the development of this new vignette, a change in the way we work and lack of templates available, the ADQS vignette could be used to develop some templates. Determination of which templates could be created were based on most commonly used, difficulty of programming and therapeutic areas of most interest. Once determined, initial templates were created and then SPRINTS were set up to develop more. Some difficulties were encountered, but overall the experience was very positive and we now have a basis to reliably create questionnaire ADaMs using R.

INTRODUCTION

The way in which questionnaires are programmed, particularly at Roche is not good enough. By questionnaires, what we are really discussing is anything that is mapped to QS SDTM (and some other domains), which can encompass a variety of measures including (but not limited to): Electronic Clinical Outcome Assessments (eCOAs), Patient Reported Outcomes Measures (PROM) and Digital endpoints. In the CDISC website, these are defined as QRS (Questionnaires, Ratings and Scales) (CDISC, 2023a). As per SDTM v3.3 onwards QRS data is split between QS, FT and RS, depending on the type of assessment, but the general principle of QRS ADaM mapping remains the same. Questionnaires are very often the primary or secondary, safety or efficacy endpoints in Neuroscience clinical trials; they are also key endpoints in many other therapeutic areas. As an example, in a phase 1 trial in Angelmans Syndrome at Roche, there were 19 Questionnaire endpoints. The reason for this is that it was a new disease area for Roche. Although the observed behaviours and symptoms were clearly defined, the scales used to assess these were not and hence multiple questionnaires were used to assess the same behaviour such as cognitive ability or motor skills. After we presented on this therapeutic area to other internal colleagues, other study teams began reaching out, expressing that they had one or multiple of these scales on their study and would like to utilize our code for creation of ADaMs and TLGs. This was only discovered due to word of mouth and we realized that this code is not Findable Accessible Interoperable & Reusable (FAIR). Multiple studies do use the same questionnaires, but we don't have many ways to track this information. We do have the eCOA library, but it's difficult to understand just how frequent they are used and the dependency of entry is on study teams to upload to the library.

As well as a high frequency of questionnaires in clinical trials, there also aren't enough templates. There is some general guidance on how to program ADQS, from CDISC and internally at Roche. Internally, there is some ADQS guidance available from presentations about PROM Data standards and analysis, regarding the structure of ADQS datasets. It is also recommended to split ADQS into multiple ADaMs: one for each questionnaire. There is guidance on ADQS parameter codes and an ADQS template. There are also templates for some frequently used questionnaires such as CSSRS and EQ5D. Overall there are not enough templates, most of the derivations for these scales are complex and most teams are starting from scratch.

On another topic, {admiral} is one part of the Pharmaverse, offering an open source modularized toolbox that enables companies and communities to develop ADaM datasets in R. It is set to revolutionise the way we program, by providing us the tools to be able to effectively and reliably produce ADaMs using R. One vignette that was produced quite recently was the questionnaire ADQS vignette (Ben Straub et al., 2023). At the same time, Roche next gen tools are also coming into effect such as other Botany tools, Pharmaverse and a new environment to enable us to work in R. With the advances of these tools and processes, we want to use this as an opportunity to reshape the way we work by developing templates for these difficult questionnaires. Our proposal was to create some R programming templates for questionnaire ADaMs which can be utilised across the company/industry. This paper will discuss the progress we have made so far into developing these template ADaMs using the {admiral} ADQS vignette. This will include some of the challenges and discussions we approached during the theory phase and what went well with regards to the final output.

THEORY PHASE

OPEN SOURCE OR CLOSED SOURCE?

Before beginning creation of the templates, we entered a theory phase, as there were multiple questions to consider. The first question we had was, once we begun with the templates, how much code could be shared as open source code? {admiral} and the rest of the Pharmaverse is intended to be open source and shared; free to use by any company or individual. Within companies, additional functions and programs can be created to support individual requirements. Within Roche for example, we have a version of {admiral} called {admiral} Roche. These templates we wish to create as open source code and share with as many people as possible. This is where we encountered our first challenge. Many questionnaires aren't designed to be open source and are owned by companies that own the license to these scales. This could include owning the rights to use the questionnaire in any capacity, such as collecting data using it, analysis techiniques or in some cases, the derivation functions themselves. On the CDISC website (CDISC 2023b) you can find which questionnaires are public domain and which you need to collaborate with the organization to be granted permission to use. Due to the issues of these licensing agreements, we decided to keep these template internally for now. If the scale is in the public domain, has been found useful in Roche and is adequately Quality Controlled (QC'd), then we will propose these templates to the {admiral} team.

WHICH TEMPLATE SHOULD WE CREATE FIRST?

The second question we had was which Questionnaire should we design the first templates for. Upon discussion with the {admiral} Roche team, we discovered that they had managed to create some templates for questionnaires we already had standards available for. These included CSSR-S and EQ5D. There were no other plans for more questionnaire templates. We came up with a few criteria for which scales we should focus on. Firstly was which questionnaires were used most frequently by study teams that didn't yet have standards. For this, we used an internal ECOA library tool. The second criteria was which questionnaires were of greatest priority to the company. This was less easy to determine. We determined this by really evaluating which therapeutic areas were of greatest importance to the company, but specifically if a questionnaire was also a key primary or secondary endpoint for studies within that therapeutic area. For this we contacted some key people within the Patient-Centred Outcomes Research (PCOR) department, a department that were specifically focused on Patient Reported Outcome Measures. We also had discussions with therapeutic area leads and standards groups. We are also now part of the questionnaire standards working groups. The third criteria we looked at was, which questionnaires had we used previously within the teams and which were the most difficult to program. The reason for this is that, not only would we have had experience on this programming, but we also had documentation, data and SAS ADaM programs available to be able to do a comparison. Based on all of this criteria, we determined that we should start programming these Scales: Bayley's scale, Clinical Global Impression Scales (CGI), Mini-Mental Status Exam (MMSE), Montreal Cognitive Assessment and Vineland.

CONNECTION WITH THE {ADMIRAL} COMMUNITY

The final main question was, what have the {admiral} team and {admiral} Roche team done so far and how can we support one another? As mentioned previously, the {admiral} team have created a template for ADQS and the {admiral} Roche team have created a couple of templates for specific questionnaires. Neither team has plans to go any further than this. The proposals of these templates were discussed with the {admiral} Roche team and we discovered it also linked with another initiative. We should not just focus on questionnaires and we should develop an area where code can be shared and templates can be created across the Roche {admiral} Community. This led to a second proposal to create an {admiral} Community Gitlab repository for collaboration of the community as the basis of standards in the future. Non-standard code will be shared to this repository from studies and used in a collaborative approach to create templates. If these are frequently used and QC'd, they can be then used to build in standard templates. We will start with questionnaires as our focus on the proof of concept.

PRACTIAL PHASE

THE FIRST SPRINT

There were a few initial setup tasks prior to programming the templates. After the selection of questionnaires, we identified teams where we could access their data, programs and specifications as a guide. We setup the Gitlab area with a templates folder and created a List of Planned outputs (LoPO) and ADaM specification (DAP M3) for each questionnaire. We built a team of 4 colleagues with support from the {admiral} Roche team. After these tasks, we decided to work in a Sprint-like fashion and assign each individual a different questionnaire, with the task of reconvening after 2 weeks to go through our challenges and assign ourselves the next task of QC. We are in the midst of this first Sprint now, so we can only provide limited information.

PROGRAMMING

We programmed these templates using the ADQS vignette (Straub, B. et al., 2023b) and other key functions from {admiral}. In order to build the templates we've needed to upskill in {admiral} & Roche next gen tools. Overall the experience of {admiral} programming has been very intuitive. The code is easier to read as opposed to previous Roche templates, as it uses a modular toolkit. This means that code is more visual and you can utilize existing code as building blocks to develop the ADaM. In this sense we can use the ADQS vignette to program in a likeminded fashion. For more information on the ADQS vignette and some of the functions, please see the Pharmaverse {admiral} website (Straub, B. et al., 2023a)

NEXT STEPS

The work so far is just the beginning. Once this first sprint is complete and the first templates are created, we have multiple future aims. Firstly with the Roche Community Gitlab page, we aim for this to be an area where all colleagues can contribute to {admiral} templates. In order for this to happen, we need to define the workflow better with documentation. This would include defining the QC process, who would QC and how we would QC all of these templates. There would also need to be documentation on information regarding naming conventions, where to save, what happens if a new version of the questionnaire is available, what occurs with new versions of r, {admiral}, ect. The expectation would be that {admiral} and {admiral} Roche would be the first place to look for templates and functions, and if not available then it would be to look in the {admiral} Roche community repository. Furthermore the expectation for the development of any new ADaMs would be to upload new code into the community and also to update any existing code upon review and adaptation of standards. This will not be validated like other {admiral} or {admiral} Roche, but would be a useful resource for a starting place where code isn't available. Frequently used and standard templates from the {admiral} Community would hopefully eventually be submitted to our Data Standards and Governance Group (DSG) and then end up in {admiral} Roche after approval. Once templates have been used multiple times and there is a push to get it standardized, this could be a starting point for templates in {admiral}.

The next step would be to start producing templates on other questionnaires, through other sprints, particularly with the Neuroscience team. Although the ADQS vignette was discussed earlier in this paper, what was failed to mention is that the {admiral} team do have plans to create some templates in the future. As per the {admiral} website "At the moment, {admiral} does not provide functions or metadata for specific questionnaires nor functionality for handling the vast amount of questionnaires and related parameters, e.g. a metadata structure for storing parameter definitions and functions for reading such metadata. We plan to provide it in future releases." (Ben Straub et al., 2023). So the next plans would be to get in contact with the {admiral} team to discuss future releases and then discuss internally about our questionnaire requirements. This has been a really useful learning experience, but we plan to improve our abilities with {admiral} and begin to develop more complex questionnaires.

A final point is from working on this project, we now have developed a deeper network regarding standards and questionnaires. We will be using this platform to integrate better with the DSG, PCOR and {admiral} groups, to help develop questionnaire standards.

CONCLUSION,

The task of creating ADQS templates using R has lead the team down many paths. We have been able to utilize the ADQS vignette to draft some templates for internal use. We have also developed a gitlab repository for the {admiral} community to collaborate on {admiral} code. We've also been able to build links with other members or the organization, develop questionnaire standards further and grow our knowledge of {admiral}. That being said, we are very much in the early stages of development and we have plenty of outstanding tasks, such as: working with {admiral} and {admiral} Roche, develop more templates, build on our skills with R and {admiral} and increase the uptake of the community repository.
This has been a really useful learning experience and my take home recommendation for all would be to experiment in {admiral} and the extended Pharmaverse, now. It is really intuitive and easy to program, if R programming skills are already present. The more we develop now, together, the better {admiral} will be in the future. Consider creating templates for your own use and the potential of having a collaborative community code sharing area outside of {admiral}, because this could lead to providing more standardization for {admiral} overall.

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