DEPARTMENT OF THE AIR FORCE
59TH MEDICAL WING (AETC)
JOINT BASE SAN ANTONIO - LACKLAND TEXAS

21 MAR 2017

MEMORANDUM FOR SGSP
ATTN: MAJ SHAOPING MO SUMNER

FROM: 59 MDW/SGVU

SUBJECT: Professional Presentation Approval

1. Your paper, entitled **Assessing Medication Adherence in Patients with Rheumatoid Arthritis (RA)** presented at/published to **American Pharmacists Association (Journal/Abstract) & American Pharmacists Association Annual Meeting, San Francisco, CA, 24-27 March 2017 (Poster)** in accordance with MDWI 41-108, has been approved and assigned local file #**17154.**

2. Pertinent biographic information (name of author(s), title, etc.) has been entered into our computer file. Please advise us (by phone or mail) that your presentation was given. At that time, we will need the date (month, day and year) along with the location of your presentation. It is important to update this information so that we can provide quality support for you, your department, and the Medical Center commander. This information is used to document the scholarly activities of our professional staff and students, which is an essential component of Wilford Hall Ambulatory Surgical Center (WHASC) internship and residency programs.

3. Please know that if you are a Graduate Health Sciences Education student and your department has told you they cannot fund your publication, the 59th Clinical Research Division may pay for your basic journal publishing charges (to include costs for tables and black and white photos). We cannot pay for reprints. If you are a 59 MDW staff member, we can forward your request for funds to the designated Wing POC at the Chief Scientist's Office, Ms. Alice Houy, office phone: 210-292-8029; email address: alice.houy.civ@mail.mil.

4. Congratulations, and thank you for your efforts and time. Your contributions are vital to the medical mission. We look forward to assisting you in your future publication/presentation efforts.

Linda Steel-Goodwin

LINDA STEEL-GOODWIN, Col, USAF, BSC
Director, Clinical Investigations & Research Support

# PROCESSING OF PROFESSIONAL MEDICAL RESEARCH/TECHNICAL PUBLICATIONS/PRESENTATIONS

## INSTRUCTIONS

**USE ONLY THE MOST CURRENT 59 MDW FORM 3039 LOCATED ON AF E-PUBLISHING**

1. The author must complete page two of this form:
   a. In Section 2, add the funding source for your study [ e.g., 59 MDW CRD Graduate Health Sciences Education (GHSE) (SG5 O&M); SG5 R&D; Tri-Service Nursing Research Program (TSNRP); Defense Medical Research & Development Program (DMRDP); NIH; Congressionally Directed Medical Research Program (CDMRP) ; Grants; etc.]

   b. In Section 2, there may be funding available for journal costs, if your department is not paying for figures, tables or photographs for your publication. Please state "YES" or "NO" in Section 2 of the form, if you need publication funding support.

2. Print your name, rank/grade, sign and date the form in the author's signature block or use an electronic signature.

3. Attach a copy of the 59 MDW IRB or IACUC approval letter for the research related study. If this is a technical publication/presentation, state the type (e.g. case report, QA/QI study, program evaluation study, informational report/briefing, etc.) in the "Protocol Title" box.

4. Attach a copy of your abstract, paper, poster and other supporting documentation.

5. Save and forward, via email, the processing form and all supporting documentation to your unit commander, program director or immediate supervisor for review/approval.

6. On page 2, have either your unit commander, program director or immediate supervisor:
   a. Print their name, rank/grade, title; sign and date the form in the approving authority's signature block or use an electronic signature.

7. Submit your completed form and all supporting documentation to the CRD for processing (59crdpubspres@us.af.mil). **This should be accomplished no later than 30 days before final clearance is required to publish/present your materials.** If you have any questions or concerns, please contact the 59 CRD/Publications and Presentations Section at 292-7141 for assistance.

8. The 59 CRD/Publications and Presentations Section will route the request form to clinical investigations, 502 ISG/JAC (Ethics Review) and Public Affairs (59 MDW/PA) for review and then forward you a final letter of approval or disapproval.

9. Once your manuscript, poster or presentation has been approved for a one-time public release, you may proceed with your publication or presentation submission activities, as stated on this form. **Note:** For each new release of medical research or technical information as a publication/presentation, a new 59 MDW Form 3039 must be submitted for review and approval.

10. If your manuscript is accepted for scientific publication, please contact the 59 CRD/Publications and Presentations Section at 292-7141. This information is reported to the 59 MDW/CC. All medical research or technical information publications/presentations must be reported to the Defense Technical Information Center (DITC). See 59 MDWI 41-108, *Presentation and Publication of Medical and Technical Papers,* for additional information.

11. The Joint Ethics Regulation (JER) DoD 5500.07-R, *Standards of Conduct*, provides standards of ethical conduct for all DoD personnel and their interactions with other non-DoD entities, organizations, societies, conferences, etc. Part of the Form 3039 review and approval process includes a legal ethics review to address any potential conflicts related to DoD personnel participating in non-DoD sponsored conferences, professional meetings, publication/presentation disclosures to domestic and foreign audiences, DoD personnel accepting non-DoD contributions, awards, honoraria, gifts, etc. The specific circumstances for your presentation will determine whether a legal review is necessary. **If you (as the author) or your supervisor check "NO" in block 17 of the Form 3039, your research or technical documents will not be forwarded to the 502 ISG/JAC legal office for an ethics review.** To assist you in making this decision about whether to request a legal review, the following examples are provided as a guideline:

    For presentations before professional societies and like organizations, the 59 MDW Public Affairs Office (PAO) will provide the needed review to ensure proper disclaimers are included and the subject matter of the presentation does not create any cause for DoD concern.

    If the sponsor of a conference or meeting is a DoD entity, an ethics review of your presentation is not required, since the DoD entity is responsible to obtain all approvals for the event.

    If the sponsor of a conference or meeting is a non-DoD commercial entity or an entity seeking to do business with the government, then your presentation should have an ethics review.

    If your travel is being paid for (in whole or in part) by a non-Federal entity (someone other than the government), a legal ethics review is needed. These requests for legal review should come through the 59 MDW Gifts and Grants Office to 502 ISG/JAC.

    If you are receiving an honorarium or payment for speaking, a legal ethics review is required.

    If you (as the author) or your supervisor check "YES" in block 17 of the Form 3039, your research or technical documents will be forwarded simultaneously to the 502 ISG/JAC legal office and PAO for review to help reduce turn-around time. If you have any questions regarding legal reviews, please contact the legal office at (210) 671-5795/3365, DSN 473.

**NOTE:** All abstracts, papers, posters, etc., should contain the following disclaimer statement:
***"The views expressed are those of the [author(s)] [presenter(s)] and do not reflect the official views or policy of the Department of Defense or its Components"***

**NOTE:** All abstracts, papers, posters, etc., should contain the following disclaimer statement for research involving humans:
***"The voluntary, fully informed consent of the subjects used in this research was obtained as required by 32 CFR 219 and DODI 3216.02_AFI 40-402."***

**NOTE:** All abstracts, papers, posters, etc., should contain the following disclaimer statement for research involving animals, as required by AFMAN 40-401_IP :
***"The experiments reported herein were conducted according to the principles set forth in the National Institute of Health Publication No. 80-23, Guide for the Care and Use of Laboratory Animals and the Animal Welfare Act of 1966, as amended."***

## PROCESSING OF PROFESSIONAL MEDICAL RESEARCH/TECHNICAL PUBLICATIONS/PRESENTATIONS

| 1. TO: CLINICAL RESEARCH | 2. FROM: (Author's Name, Rank, Grade, Office Symbol) | 3. GME/GHSE STUDENT: | 4. PROTOCOL NUMBER: |
|---|---|---|---|
| | Shaoping Mo Sumner, Major/O-4, SGSP | ☒ YES ☐ NO | C.207.024e |

5. PROTOCOL TITLE: (**NOTE:** For each new release of medical research or technical information as a publication/presentation, a new 59 MDW Form 3039 must be submitted for review and approval.)

Assessing Medication Adherence in Patients with Rheumatoid Arthritis (RA)

6. TITLE OF MATERIAL TO BE PUBLISHED OR PRESENTED:

Assessing Medication Adherence in Patients with Rheumatoid Arthritis (RA)

7. FUNDING RECEIVED FOR THIS STUDY? ☐ YES ☒ NO FUNDING SOURCE:

8. DO YOU NEED FUNDING SUPPORT FOR PUBLICATION PURPOSES: ☒ YES ☐ NO

9. IS THIS MATERIAL CLASSIFIED? ☐ YES ☒ NO

10. IS THIS MATERIAL SUBJECT TO ANY LEGAL RESTRICTIONS FOR PUBLICATION OR PRESENTATION THROUGH A COLLABORATIVE RESEARCH AND DEVELOPMENT AGREEMENT (CRADA), MATERIAL TRANSFER AGREEMENT (MTA), INTELLECTUAL PROPERTY RIGHTS AGREEMENT ETC.?
☐ YES ☒ NO **NOTE:** If the answer is YES then attach a copy of the Agreement to the Publications/Presentations Request Form.

11. MATERIAL IS FOR: ☒ DOMESTIC RELEASE ☐ FOREIGN RELEASE
CHECK APPROPRIATE BOX OR BOXES FOR APPROVAL WITH THIS REQUEST. ATTACH COPY OF MATERIAL TO BE PUBLISHED/PRESENTED.

☒ 11a. PUBLICATION/JOURNAL (List intended publication/journal.)
American Pharmacists Association

☒ 11b. PUBLISHED ABSTRACT (List intended journal.)
American Pharmacists Association

☒ 11c. POSTER (To be demonstrated at meeting: name of meeting, city, state, and date of meeting.)
American Pharmacists Association Annual Meeting, San Francisco, CA, 24-27 March 2017

☐ 11d. PLATFORM PRESENTATION (At civilian institutions: name of meeting, state, and date of meting.)

☐ 11e. OTHER (Describe: name of meeting, city, state, and date of meeting.)

12. HAVE YOUR ATTACHED RESEARCH/TECHNICAL MATERIALS BEEN PREVIOUSLY APPROVED TO BE PUBLISHED/PRESENTED?
☐ YES ☒ NO ASSIGNED FILE # _____ DATE _____

13. EXPECTED DATE WHEN YOU WILL NEED THE CRD TO SUBMIT YOUR CLEARED PRESENTATION/PUBLICATION TO DTIC
**NOTE:** All publications/presentations are required to be placed in the Defense Technical Information Center (DTIC).

| DATE | |
|---|---|
| March 21, 2017 | |

| 14. 59 MDW PRIMARY POINT OF CONTACT (Last Name, First Name, M.I., email) | 15. DUTY PHONE/PAGER NUMBER |
|---|---|
| Sumner, Shaoping, M shaoping.m.sumner.mil@mail.mil | 916-3455; pager 210-228-6002 |

16. AUTHORSHIP AND CO-AUTHOR(S) List in the order they will appear in the manuscript.

| LAST NAME, FIRST NAME AND M.I. | GRADE/RANK | SQUADRON/GROUP/OFFICE SYMBOL | INSTITUTION (If not 59 MDW) |
|---|---|---|---|
| a. Primary/Corresponding Author<br>Shaoping Mo Sumner | O-4/Major | 959 CSPS | 59 MDW |
| b. Annabel L Schumaker | GS | BAMC Army | USARMY MEDCOM |
| c. Thomas Shank | O5 (retired) | N/A | Pfizer |
| d. | | | |
| e. | | | |

17. IS A 502 ISG/JAC ETHICS REVIEW REQUIRED (JER DOD 5500.07-R)? ☐ YES ☐ NO

I CERTIFY ANY HUMAN OR ANIMAL RESEARCH RELATED STUDIES WERE APPROVED AND PERFORMED IN STRICT ACCORDANCE WITH 32 CFR 219, AFMAN 40-401_IP, AND 59 MDWI 41-108. I HAVE READ THE FINAL VERSION OF THE ATTACHED MATERIAL AND CERTIFY THAT IT IS AN ACCURATE MANUSCRIPT FOR PUBLICATION AND/OR PRESENTATION.

| 18. AUTHOR'S PRINTED NAME, RANK, GRADE | 19. AUTHOR'S SIGNATURE | 20. DATE |
|---|---|---|
| Shaoping Mo Sumner, Major/O-4 | SUMNER.SHAOPING.MO.1383922212 | 03/15/2017 |
| **21. APPROVING AUTHORITY'S PRINTED NAME, RANK, TITLE** | **22. APPROVING AUTHORITY'S SIGNATURE** | **23. DATE** |
| John A Bouchard, Capt/O-3 | BOUCHARD.JOHN.A.1392707685 | 03/20/2017 |

## PROCESSING OF PROFESSIONAL MEDICAL RESEARCH/TECHNICAL PUBLICATIONS/PRESENTATIONS

**1st ENDORSEMENT (59 MDW/SGVU Use Only)**

| TO: Clinical Research Division<br>59 MDW/CRD<br>Contact 292-7141 for email instructions. | 24. DATE RECEIVED<br>March 20, 2017 | 25. ASSIGNED PROCESSING REQUEST FILE NUMBER<br>17154 |
|---|---|---|
| 26. DATE REVIEWED<br>March 21, 2017 | | 27. DATE FORWARDED TO 502 ISG/JAC |

28. AUTHOR CONTACTED FOR RECOMMENDED OR NECESSARY CHANGES: ☒ NO ☐ YES If yes, give date. _____ ☐ N/A

29. COMMENTS ☒ APPROVED ☐ DISAPPROVED

Presentation of IRB approved research with appropriate disclaimers. approved

| 30. PRINTED NAME, RANK/GRADE, TITLE OF REVIEWER | 31. REVIEWER SIGNATURE | 32. DATE |
|---|---|---|
| Kevin Kupferer/GS13/Human Research Subject Protection Expert | KUPFERER.KEVIN.R.1086667270 | March 21, 2017 |

**2nd ENDORSEMENT (502 ISG/JAC Use Only)**

| 33. DATE RECEIVED | 34. DATE FORWARDED TO 59 MDW/PA |
|---|---|

35. COMMENTS ☐ APPROVED (In compliance with security and policy review directives.) ☐ DISAPPROVED

| 36. PRINTED NAME, RANK/GRADE, TITLE OF REVIEWER | 37. REVIEWER SIGNATURE | 38. DATE |
|---|---|---|
| | | |

**3rd ENDORSEMENT (59 MDW/PA Use Only)**

| 39. DATE RECEIVED | 40. DATE FORWARDED TO 59 MDW/SGVU |
|---|---|
| March 21, 2017 | March 21, 2017 |

41. COMMENTS ☒ APPROVED (In compliance with security and policy review directives.) ☐ DISAPPROVED

| 42. PRINTED NAME, RANK/GRADE, TITLE OF REVIEWER | 43. REVIEWER SIGNATURE | 44. DATE |
|---|---|---|
| Kevin Iinuma, SSgt/E-5, 59 MDW Public Affairs | IINUMA.KEVIN.MITSUGU.1296227 613 | March 21, 2017 |

**4th ENDORSEMENT (59 MDW/SGVU Use Only)**

| 45. DATE RECEIVED | 46. SENIOR AUTHOR NOTIFIED BY PHONE OF APPROVAL OR DISAPPROVAL<br>☐ YES ☐ NO ☐ COULD NOT BE REACHED ☐ LEFT MESSAGE |
|---|---|

47. COMMENTS ☐ APPROVED ☐ DISAPPROVED

| 48. PRINTED NAME, RANK/GRADE, TITLE OF REVIEWER | 49. REVIEWER SIGNATURE | 50. DATE |
|---|---|---|
| | | |

# Assessing Medication Adherence in Patients with Rheumatoid Arthritis (RA)

Maj. Shaoping M. Sumner, Pharm.D, USAF, BSC; Annabel L Schumaker, BCPS; BROOKE ARMY MEDICAL CENTER (BAMC); San Antonio, TX; Thomas C Shank, Pfizer, TX

## BACKGROUND

- Rheumatoid Arthritis (RA) is a symmetric, erosive synovitis autoimmune disease
- There are 1-3 million Americans suffering from RA of which 70% are women
- People with RA have higher risk of developing heart disease and stroke
- Oral Disease Modifying Anti-Rheumatic Drugs (DMARDs) are the most used RA medications
- Effectiveness of DMARDs is dependent on patient medication adherence
- Medication adherence is a significant healthcare issue affecting many patients, especially those with chronic diseases and prolonged drug therapy
- Non-adherence rates to DMARDs in RA patients are reported to be up to 80% for correct dosing
- There are different methods to measure how adherent patients are to their medication regimens
- Patient questionnaires/self-reports are thought to be simple, inexpensive, and the most useful method in the clinical setting
- The Morisky Medication Adherence Scale (MMAS) was developed to assess medication adherence intent and has been validated in several common disease but not in RA
- There are several variations of the MMAS but we used the MMAS-8 which has eight questions
- The Compliance-Questionnaires-Rheumatology (CQR) is a rheumatology-specific instrument measuring patient compliance to drug regimens
- CQR identifies factors that contribute to suboptimal patient compliance and could be used to predict future compliance in patients with RA
- CQR is validated in RA but is difficult to score which limits its usefulness in the clinic setting
- The average time to complete the CQR is approximately 12 minutes, compared to less than 1 minute to complete the MMAS-8

## OBJECTIVES

- The primary objective is to determine if there is a correlation between the CQR19, CQR5, and the MMAS8
- The secondary objective is to assess if there is a potential medication adherence issue in patients with RA taking oral DMARDs

## METHODS

### DMARD drugs included in this study

- In this study, patients with RA were asked if they were currently taking one of the following oral DMARD medications: methotrexate, hydroxychloroquine (Plaquenil®), leflunomide (Arava®), sulfasalazine (Azulfidine®), and/or minocycline (Minocin®)

### Hypothesis

- There is a correlation between the CQR-19 and the MMAS-8. The research study would also estimate the extent of medication adherence in patients with RA taking oral DMARDs

### Study population

- Inclusion criteria: anyone that is 18 years and over with a diagnosis of RA, treated with an oral DMARD, treated for RA at the BAMC Rheumatology Clinic, able to read English, and has no cognitive disability

## METHODS (Cont.)

**Exclusion criteria:** Patients not meeting the inclusion criteria

**Sample Size:** An 80% power was used to detect a correlation coefficient of 0.2. Based on the validation studies for the CQR and MMAS, we estimated that between 10% and 20% of surveys will not be evaluable. The estimated sample size for this study is102.

**Data collection methods and processing:** At the time of check-in for a routine appointment in the Rheumatology Clinic, patients were invited to participate in a survey. Patients were provided a questionnaire containing both the MMAS-8 and CQR-19. The CQR and MMAS were used to assess medication adherence, then the CQR and MMAS were compared to assess whether the shorter MMAS could be used to routinely assess medication adherence in patients taking oral DMARDs for RA. The completed surveys were collected in designated drop boxes located at the clinic front desk. At the end of each business day, the primary investigator (PI) for the study collected the completed survey forms for up to 6 weeks.

**Statistical Analysis:** The data were evaluated using descriptive statistics to describe the patient population and normality testing to determine whether we should use Pearson or Spearman correlation. Spearman correlation was used to evaluate the association between the various adherence predictor tools continuous scores. Chi-square tests were used to compare how CQR19, CQR5 and MMAS8 placed patients into adherence groups. The CQR19 places patients into low and high medication taking and dosing compliance groups; the CQR5 places patients into low or high medication adherence groups, and MMAS8 places patients into low adherence (scores < 6), medium adherence (scores of 6 or 7), and high adherence (scores of 8).

**Descriptive Statistics:** Data were collected on 56 patients, but not all patients provided complete data and analyzed using Stata version 14. The descriptive statistics are presented below.

## PRELIMINARY RESULTS

**Descriptive Statistics**

| Variable | Number of Observations | Statistic |
|---|---|---|
| | | Mean [SD] |
| Age [total cohort] | 52 | 54 [13.7] |
| Females | 40 | 53 [13.6] |
| Males | 12 | 59 [13.7] |
| | | Median [IQR] |
| Number of prescription medications | 48 | 6 [3] |
| Number of oral RA medications | 55 | 2 [3] |
| IQR = Interquartile Range | | |

Before inferential testing, the variables were evaluated to ensure that the assumptions for each proposed test were met. We intended to use Pearson correlation to compare the continuous adherence predictor variables which requires that the variables be normally distributed. Since none of the CQR-19 or CQR-5 predictors were normally distributed, Spearman correlations were employed to determine the strength of association between these variables. These results are provided below.

**Spearman Correlations for Adherence/Compliance Predictor Scores**

| Comparison Groups | N | ρ (rho) | P-value | Interpretation |
|---|---|---|---|---|
| CQR19 Taking - CQR19 Dosing Compliance | 56 | 0.597 | <0.001 | Moderate, significant, positive |
| CQR19 Taking Compliance – CQR5 High Adherence | 56 | 0.289 | 0.031 | Weak, significant, positive |
| CQR19 Dosing Compliance – CQR5 High Adherence | 56 | 0.469 | 0.0003 | Moderate, significant, positive |
| MMAS8 - CQR19 Taking Compliance | 56 | 0.117 | 0.390 | Very weak, nonsignificant, positive |
| MMAS8 Adherence - CQR19 Dosing Compliance | 56 | -0.0058 | 0.966 | Very weak, nonsignificant, negative |
| MMAS8 Adherence – CQR5 High Adherence | 56 | 0.1559 | 0.2513 | Very weak, nonsignificant, positive |

## PRELIMINARY RESULTS (Cont.)

The null hypothesis for chi-square is that the groups are independent. We conducted these tests at the 0.05 level of significance. P-values less than 0.05 would indicate that that the groups are not independent; there is an association between the two variables. For this study, any significant results would mean that the two adherence measures tested generally would be similar in their ability to identify patients' adherence intention. The results of the chi-square test are provided below. The only significant associations were between the two CQR-19 compliance measures and the CQR-5 adherence predictor.

**Chi-Square Tests of Independence (All Adherence/Compliance Groups)**

| Comparison Groups | | Chi-square | P-value |
|---|---|---|---|
| CQR19 Taking Compliance | CQR5 | 18.589 | < 0.001 |
| CQR19 Dosing Compliance | CQR5 | 19.337 | < 0.001 |
| MMAS8 Adherence | CQR19 Taking Compliance | 0.1505 | 0.698 |
| MMAS8 Adherence | CQR19 Dosing Compliance | 0.0008 | 0.977 |
| MMAS8 Adherence | CQR5 | 0.8958 | 0.334 |

## DISCUSSION

- This is a preliminary analysis because the data collection has not been completed
- The CQR19 performance in our patient population was similar to that which was described in the validation study
- The CQR5 high adherence predictor was moderately correlated with CQR19 Dosing compliance
- The MMAS8 was very weakly correlated with both the CQR19 and CQR5
- Both the CQR19 and CQR5 were similar in their ability to place patients into adherence groups
- Neither the CQR19 nor CQR5 were similar to the MMAS8 in their ability to place patients into adherence groups

## CONCLUSION

- Based on the preliminary analysis, the MMAS8 was not able to place patients into adherence groups in a way that was similar to the CQR19, we would not recommend replacing the CQR19 with the MMAS8
- The CQR5 was able to predict adherence as well as both of the CQR19 compliance measures (taking and dosing) and could be used in the clinic setting

## REFERENCES


a. de Klerk E, van der Heijde D, Landewe R, van der Tempel H, van der Linden S. The Compliance-Questionnaire-Rheumatology compared with electronic medication event monitoring: a validation study. J Rheumatol. 2003;30:2469-75.

b. Hughes et al. A 5 item version of the Compliance Questionnaire for Rheumatology (CQR5) successfully identifies low adherence to DMARDs. BMC Musculoskeletal Disorders 2-13;14:286

c. Morisky DE, DiMatteo MR. Improving the measurement of self-reported medication nonadherence. Final response. J Clin Epidemiol. 2011; 64:262-263

StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP.