Investigating a screening strategy for the early diagnosis of Psoriatic Arthritis

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Contents

1 Introduction

Table 1 List of abbreviations and glossary

DLQI	Dermatology Life Quality Index
SAPASI	Self-Administered Psoriasis Area Severity Index
EQ-5D-5L	Measure Health-related quality of life
HAQ-DI	Health Assessment Questionnaire - Disability Index
PsA	Psoriatic Arthritis
WPAI-GH	Work Productivity and Activity Impairment--General Health
IA	Inflammatory arthritis
HL test	Hosmer-Lemeshow test
PR test	Pulkstenis-Robinson test

1.1 Background

Psoriatic arthritis (PsA) is a type of inflammatory arthritis that affects some people who have psoriasis, a chronic skin condition that causes red, scaly patches. PsA causes joint pain, swelling, and stiffness, and can affect any joint. It often affects the fingers and toes, but can also affect larger joints such as the knees, ankles, and elbows.

Psoriasis (PsO) is a common chronic skin condition that causes skin cells to multiply rapidly, resulting in the formation of thick, red, and scaly patches on the skin. These patches can be itchy, and painful, and may appear on various parts of the body, including the elbows, knees, scalp, and lower back. Psoriasis is considered an autoimmune disorder, meaning that the immune system mistakenly attacks healthy skin cells, causing the excessive growth and inflammation characteristic of the condition.

According to recent studies, it has been shown that more than 90% of patients with psoriatic arthritis (PsA) first develop their arthritis on a background of known psoriasis (Pso). Therefore, Pso certainly is an indicator for PsA but as PsA develops in <30% of those affected with Pso, the presence of Pso alone is insufficient as a means of identifying which patients with Pso will develop PsA. Further comparison between patients with PsO and those with early PsA feature help refine Pso patients destined to develop PsA, such that healthcare for early PsA can be provided and a new era of treatment for PsA can emerge. [1]

Total Burden of Psoriasis TUDOR) is a clinical trial designed to meet the aim of the research discussed above. Specifically, this trial aims to provide an evidence-based framework for recommendations on an effective and acceptable screening strategy for the early identification of psoriatic arthritis in people with psoriasis in primary care and their subsequent management.

Primary care practices and secondary care rheumatology clinics were places where trials were conducted. They recruited patients with PsO but no prior diagnosis of PsA. Participants were managed according to either standard care (SC) or enhanced surveillance by annual rheumatological assessment (ES). GP practices were randomized on a 1:1 basis to either the ES or SC arm, stratified by CCG and GP practice size. A cluster-randomized design (where the cluster is a GP practice) has been chosen to reduce between-arm contamination as the intervention aims to change clinical practice. As GPs identify potential patients and do not directly recruit or assess them, the risk of contamination via interaction of GP practices is considered negligible. [2]

At baseline, 12th-month and 24th-month participants in the ES arm underwent a clinical assessment for the presence of symptoms of inflammatory arthritis. Clinical assessments include Psoriasis assessments, physical examinations, health-related quality of life, nail Psoriasis assessments, and inflammatory arthritis assessments. Any participants with suspected inflammatory arthritis were referred to a local rheumatology outpatient clinic, and then a rheumatologist determined whether they were diagnosed with PsA.

Participants in the SC arm completed postal questionnaires on their psoriasis, health-related quality of life, physical functioning and health resource utilization at baseline and 12th month and underwent a clinical assessment by the assessing clinician at 24 months as described above for the enhanced surveillance arm. Similarly, any participants who at their 24th-month assessment, were suspected of suffering from inflammatory arthritis were referred by the assessing clinician via their GP to the local rheumatology clinic at participating hospitals for assessment by a treating rheumatologist.

The ways that data is collected in two arms are demonstrated in Table 2 below.

Table 2

	Enhanced Surveillance Arm			**Standard care Arm**		
	baseline	12th month	24th month	baseline	12th month	24th month
Demographics	✓	✓	✓	✓	✓	✓
Psoriasis treatment details	✓	✓	✓	✓	✓	✓
DLQI	✓	✓	✓	✓	✓	✓
SAPASI	✓	✓	✓	✓	✓	✓
Health Resource Utilization Questionnaire	✓	✓	✓	✓	✓	✓
WPAI-GH	✓	✓	✓	✓	✓	✓
EQ-5D-5L	✓	✓	✓	✓	✓	✓
HAQ-DI	✓	✓	✓	✓	✓	✓
Medical history screening questions		✓	✓		✓	✓
ASAS inflammatory back pain patient questionnaire	✓	✓	✓			✓

Psoriasis assessment	✓	✓	✓			✓
Nail psoriasis assessment	✓	✓	✓			✓
Inflammatory arthritis assessment	✓	✓	✓			✓

1.2 Motivation

Much research has provided evidence that the diagnostic delay of Psoriatic arthritis causes irreversible damage to joints and hence more pain and disability. A cohort study [3] illustrated late consulters (>6 months delay at first rheumatologist encounter) with PsA had significantly more erosive joint disease and, a number of deformed joints. Fewer patients achieve drug-free remission and worse functional disability. Individuals with diagnostic delay suffer from disability, chronic pain, and difficulty with everyday activities such as walking.

Research shows that there is an obvious advantage that detecting PsA at an early stage. Achieving drug-free remission which may be viewed as a surrogate for successful rheumatological outcome has a significant negative association with a diagnostic delay (>1 year) and a significant positive association with an early rheumatologist encounter of (<6 months). [3]

However, Identifying Psoriatic Arthritis (PsA) at a very early stage is challenging. According to the Journal of Clinical Medicine [4], there are three clinical phases after PsO onset and before PsA development. The initial two phases are asymptomatic and the diverse range of clinical manifestations, suggests that study of PsO phenotypes themselves more closely is needed. This research provides different effects of PsA and PsO on patients from a data perspective, which distinguishes features of PsA and PsO according to data pattern.

1.3 Aims and Objectives

As mentioned in the introduction section, the study aims to provide a screening strategy for the early identification of psoriatic arthritis in individuals with psoriasis in primary care and reduce the suffering of patients with Psoriatic disease. To achieve this aim, there are 7 objectives in the TUDOR project. I performed three objectives of them in this research:

i. To assess the full impact on quality of life for individuals with psoriatic disease
ii. To identify factors associated with the development of PsA in people with psoriasis

In data analysis for objective 1, the risk factors include gender, age, clinical arms, and severity of PsO, It illustrated a full description of how these risk factors influence QoL of patients with PsA or PsO involving physical function, anxiety skin etc. This helps clinicians predict the medical condition of patients and take effective and comprehensive treatment measures to reduce the patient's suffering and improve their QoL through cost-saving measures. For instance, if elderly

individuals experience a lower QoL compared to younger people, more attention and healthcare monitoring should be given to them. Furthermore, the analysis for objective 1 validates whether various intervention in different clinical arms leads to different outcomes in terms of QoL.

In data analysis for objective 2, provides insights into the risk factors (SAPASI, gender, age and smoking history) that link with a diagnosis of PsA, severity of PsO (SAPASI) is a measurement used to describe the PsO, which essentially links one of PsO's features with the onset of PsA. As mentioned above, the mechanisms of PsO developing into PsA are complex. The link between them supplies information on which features of PsA have a relationship with the onset of PsA. if the link is not significant, the feature can be excluded from the consideration. Smoking history offers information on how personal habitat influences the onset of PsA. In a nutshell, objective 2 is an important part of developing a screening strategy for the early recognition of PsA

2 Literature Review

2.1 Data Analysis Plans

Data Analysis Plan for Objective 1

To investigate the impact of psoriatic disease on health-related quality of life and work productivity

Endpoints:

- Dermatology Life Quality Index (DLQI)
- Health-related quality of life questionnaire EQ-5D-5L
- Psoriasis Area Severity Index (SAPASI)
- Work Productivity and Activity Impairment (WPAI)
- Health Assessment Questionnaire and Disability Index (HAQ-DI)

Datapoints sample: The compared data will choose the same arm and the same period, for example, choosing participants in the ES arm and at 12 months, the same number of patients with PsA and without PsA. The severity of psoriasis will be influenced by GP practice size and CCG (diagnostic device etc.), therefore, GP practice size and CCG are stratification factors

Correlation analysis

WPAI is used to measure work productivity, The score is computed by the below function:
(Work hours missed due to health problem)/ (Hours worked)
DLQI is used to investigate health-related quality of life and is a validated patient-reported outcome measure of the effect of skin disease on a patient's daily activities and is widely used. There are 10 questions in this questionnaire, Each question has four options which are not at all, a little, a lot,very much and corresponding scores are 0,1,2,3. The sum of the score of these 10 questions answered by patients represent final score of each participant. The sum of score

has a simple method of score interpretation: no impact (0-1), small impact (2-5), moderate impact(6-10), very severe impact (11-20) and extremely severe impact (21-30).

EQ-5D-5L is used to investigate health-related quality of life and have 5 questions that represent 5 dimensions: mobility, self-care, ability to undertake usual activities, pain, anxiety/depression, each question has five options, scored 1-5. [5]

The HAQ is the extent of disability and asks questions about using 8 domains: dressing and grooming, rising, eating, walking, hygiene, reach, grip, and activities. Patients have a choice of 4 responses to each question, scored 0–3, The maximum scores in each domain are summed and the total is divided by the number of domains answered, giving a final score from 0 to 3.

SAPASI: is a structured instrument for the severity of psoriasis. Respondents assess their skin psoriasis by questions listed in a questionnaire to mark areas of psoriasis. There is a SAPASI score calculated according to marks from respondents and recorded in the data set as measurement of psoriasis severity of each patient. The SAPASI is calculated using the product of the weighted area scores and the severity scores.

Match: The two groups of patients have different sex, psoriasis duration and age, the demographic data show in table 1, comparisons between these two groups will be using nonparametric statistics: Mann-Whitney U and chi-square tests. Duration of psoriasis and age, Mann-Whitney U z score; sex, chi-square tests. Null hypothesis test is that patients with PsA and without PsA have no significant different in terms of sex, duration of psoriasis and age, the alternative hypothesis is that they differ in sex, duration and age. Significant level is 0.05
The calculation results will be recorded in table 1 below.
It helps me to identify the difference between these two sample groups so that I can adjust my sample until they are homogeneous.

	PsA diganosed	PsA not diganosed	Statisitic*	P-value
Sex				
Male				
Female				
Duration, yrs				
Mean				
Median				
Range				
Age,yrs				
Mean				
Median				
Range				

I will be calculating the Mann-Whitney U z score after splitting the patients with PsA and without PsA by the severity of psoriasis, the results will be recorded in table 2 below.
If the pattern of impact of two patient groups on quality of life, work productivity and disability

allow to be discerned, splitting the group by severity of psoriasis is good way exclude the impacts of severity.

	PsA diganosed			PsA not diganosed			Statisitic*	P-value
	Mild	Moderate	Severe	Mild	Moderate	Severe		
HAQ Score								
Dressing&grooming								
Rising								
Eating								
walking								
Hygiene								
Reach								
Grip								
Activities								
EQ-5D-5L								
Mobility								
Self-Care								
Usual Activities								
Pain/Discomfort								
Anxiety/Depression								
DLQI Score								
Median								
Work productivity								
Median								

Linear regression

SAPASI score and sum score of DLQI and EQ-5D-5L act for severity of psoriasis and quality of life respectively. These two measurements are continuous variables. To approach the problem on impact of psoriasis on quality of life, I intuitively think severity of psoriasis have linear relationship with SAPASI score, I will use simple linear regression to explore their relationship, The formula is:

$$y_i = \beta_0 + \beta_1 x_i + \varepsilon_i$$

x_i is severity, y_i is quality of life. We assume ε_i~ Normal(0, σ^2), i=1,2,3…n

The preliminary exploration for linearity use scatter plot which provides their strength and direction of relationship, Also, computing their Pearson correlation coefficient is as good as scatter plot to check trend of variables relationship. If The scatter plot shows that it is not a random decomposition and points on the scatterplot closely resemble a straight line, it would be a good starting to use linear regression model.

In my case, severity is not only factors that influence quality of life, for example, age, sex are also factors that might influence quality of life, therefore, I can use this model to explore other factors that have effects on quality of life.

I choose two groups that are homogeneous except for their gender, I can observe how their quality of life varies with severity by two-group plots of female and male.

The alternative model

This is possible that relationship between quality of life and severity of psoriasis is non-linear, which means the scatter plot illustrate a curved trend. In this situation, starting with empirical estimate would make sense. Establish a new model equation as:

$$E(quality\ |severity) = s(severity)$$

$s(severity)$ is unknow regression function.

There are some ways can be used to deal with non-linearity in my case:

Loess fit in R

Loess (Locally Weighted Scatterplot Smoothing) is a non-parametric regression technique. In R, I can estimate $s(severity)$ by loess() function that used to perform a Loess fit. I finally get a smooth curve that describes the relationship between two variables by fitting a series of local polynomial regressions to the data.

The loess() function in R accomplishes this by:

- Dividing the range of the independent variable into a series of equally spaced intervals.
- For each interval, selecting a subset of data points within a specified bandwidth centered on the midpoint of the interval.
- Fitting a low-degree polynomial regression to the selected data points within the bandwidth, with the degree of the polynomial determined by the span argument
- Estimating the predicted value of the dependent variable at the midpoint of the interval by averaging the fitted polynomial values from all the subsets that include that midpoint.

By repeating this process for each interval along the range of independent variable, the loess fit produces a smooth curve that captures the underlying relationship between response variables and independent variables.

The loess fit in R is useful because the relationship is nonlinear and difficult to model parametrically.

Transformation of response variables or explanatory variables

Choosing the appropriate transformation to adjust for non-linearity depends on the relationship between the severity variable and quality of life variable, There are some properties of my data, scores for severity and quality of life are positive and there is no zero. Right, left and zero skewness may occur in a score of severity and quality of life, the reason is the degree of dispersion of the severity and quality of life in people with psoriatic may disperse or gather.

According to the potential properties of the data, some basic methods for transformation can be considered:

- logarithmic transformation
- Square root or cube root transformation
- Box-Cox transformation
- Reciprocal transformation

All transformations aim to produce a reasonably symmetric distribution. This provides a good basis for further statistical techniques. The transformed distribution need not be normal, although if it is, that would enable more confidence in tests based on smaller samples and might simplify statistical modelling.

Data analysis plan for objective 2

To investigate the association between the severity of psoriasis and the development of PsA in people with psoriasis. To explore the extent to which certain candidate risk factors are associated with the development of PsA in people with psoriasis

These two objects can be merged into a model to investigate, the risk factors that are associated with development of PsA in people with psoriasis are obesity, smoking history, age, sex, psoriasis severity and psoriatic disease duration.

Endpoints

- Psoriasis Area Severity Index (SAPASI)
- Sex
- Obesity
- Smoking history
- Age
- Psoriatic disease duration

According to TUDOR protocol[1], in ES arm, the outcome of PsA diagnosis (yes/no) and risk factors data at baseline will be used with PASI and SAPASI respectively, while in SC arm, same part data will be chosen at 24 months with SAPASI

Generalized additive logistics models

There are many predictors(risk factors) in this case. Obesity, age, psoriasis severity and psoriatic disease duration are continuous, while sex and smoking history are categorical. The response variable is the outcome of PsA diagnosis(yes/no) that is binary variable.

The popular method to investigate the relationship between this sort of data set is logistic regression. However, the data must meet assumptions of logistic regression. Otherwise, the model trained from this data is inaccurate, one of the assumptions is the relationship between the independent variables and the log odds of the response variable is assumed to be linear. In my case, there are many predictors. Therefore, choosing a more flexible model would be a better choice. For non-linear models, in particular the logistic model for binary outcomes, additional steps are required[2]

Generalized additive models(GAMs) allows conventional linear relationship of multiple regression to be generalized to permit much broader class of non-linear, but still additive, relationships between response and predictor variables[]. Therefore, I will be using logistic regression GAM to explore my data. The logistic regression GAM can be expressed in equivalent logit(log odds) form as:

$$\log\left[\frac{p_i}{1-p_i}\right] = \beta_0 + f_1(x_{1i}) + f_2(x_{2i}) \ldots + f_j(x_{ji})$$

i= 1, 2, 3….n(n is sample size)

j=1,2,3….m(m is number of predictor)

$\frac{p_i}{1-p_i}$ is odds ratio of binary variable

$f(x_i)$ is the smoother of each predictor, in my case, formula can be:

$$\log\left[\frac{P}{1-p}\right] = \beta_0 + f_1(severity) + f_2(sex) + f_3(obesity) + f_4(smoking) + f_5(disease\ duration) + f_6(age)$$

From the model above, every arbitrary smooth function of each quantitative predictor(apart from smoking and sex) is actually transformed which makes the model accommodate non-linearity.

The concept to estimate $f(x_i)$through an iterative procedure called backfitting, the idea of backfitting is that make initial guesses for each of the functions, and use this guess to update the estimate for each function iteratively using the desired fitting process which is local regression[2].
There are two main type smoothers, one is piecewise linear smoothers, other spline smoothers which have more substantial improvement than piecewise linear smoothers.

In practice, R package 'mgcv' facilitate smoothing parameter estimation, *gam()* function is used to train the GAM model, also I can obtain the chi-squared statistic for a GAM using the *summary()* function applied to the fitted model. The summary output will display the chi-squared statistic and its corresponding p-value, and the degrees of freedom for the test.

The chi-squared statistic can be used to test the overall significance of the model. The null hypothesis for this test is that all the smooth functions are zero, indicating that none of the predictors have a significant relationship with the response variable. A smaller p-value for the chi-squared test indicates stronger evidence against the null hypothesis, and therefore stronger evidence for the significance of the model as a whole.

However, there is no single number(p-value) can completely capture the form of the function in terms of interpreting the results of a GAM, graphical analysis is more comprehensive. In R, I can separately visualize the smooth function of each predictor, and interpret the function for one predictor while other predictors are held fixed.

Data analysis plan for objective 3
To investigate the prevalence of inflammatory back pain in people with psoriasis

Endpoints

ASAS inflammatory back pain questions: Detail 5 clinical areas suggestive of inflammatory back pain. If a patient has 4 or more questions positive then inflammatory back pain parameters are fulfilled.

Prevalence of inflammatory back pain

The ASAS data set was collected at baseline and 12 and 24 months in the ES arm, while just collected at 24 months in the SC arm. Two things I will be computing:

The prevalence of inflammatory back pain, together with 95% confidence intervals: using data from the clinical assessments in the ES arm at baseline and 12 and 24 months, and in the SC arm at 24 months in the trial population, together with 95% confidence intervals
The incidence of inflammatory back pain in ES arm, together with 95% confidence intervals: Incident cases of inflammatory back pain will be defined as those with inflammatory back pain documented at the 12-month or 24-month assessment who had no evidence of inflammatory back pain at baseline. Using the data in the ES arm that patients who had no evidence of inflammatory back pain at baseline while onset at the 12 months or 24 months assessment

The denominator for the incidence rates will exclude participants with pre-existing inflammatory back pain and will be calculated as person-time contributing to the trial population.

2.2 Results of Literature Search

Before conducting my data analysis plan for the Total Burden of Psoriasis(TUDOR) clinical trial. After reading the TUDOR protocol, I first searched literature to gain some knowledge on PsA and psoriasis, also, the difficulty and importance of early diagnosis of PsA. [4] gave a good introduction to the relationship between PsA and psoriasis and some clinical concepts, like musculoskeletal issues and, the definition of prediagnosis. I found [5] to provide a good summary of difficulties and needs for conducting pre-diagnosis for PsA that deepened my understanding of the main problems in the pre-diagnosis stage, for example, PsA pre-clinical phases experience asymptomatic phases that are quite hard to identify. [6] introduced a quantitative analysis for the irreversible and destructive outcome of late diagnosis of PsA, this knowledge helps me find the statistical analysis angles that I should spot on to extract useful insights into facilitating early diagnosis of PsA.

Once I had identified the clinical dilemmas in pre-diagnosis and determined my analysis subjects that tackle these potential dilemmas. I started to read the clinical data dictionary from the TUDOR trial, I found many questionnaires are patients self-reported. For example, object 2 in this proposal heavily relies on the outcomes of questionnaires. [2] provide some insights into the features of clinical data sets that distinguish them from other data points, such as repeated measures. I therefore conducted a thorough search of clinical data on wrangling and modelling. These included MathSciNet, Web of Science and Google Scholar.

2.3 The two features of the clinical data set

Two features exist in medical research that are quite common, and these two features are noteworthy and significantly impact the modes of statistical analysis.
First, the outcomes are correlated across observations. Yearly data on a person are more similar to one another than data on other people. Groups of patients from a single center may yield similar responses because of treatment protocol variations from center to center.

The second important feature of this type of data is that predictor variables can be associated with different levels of a hierarchy. For example, a hierarchical dataset with multiple patients clustered within a surgeon and multiple surgeons clustered within a hospital [6]
The insights from this literature give me insights into being careful about my clinical dataset, In my data set, many outcomes potentially come from the same person but different periods. There are period data, that are baseline, 12 months and 24 months. In object 1, if I want to investigate the impact of severity on quality of life, I should not choose data from the same cluster but from a different period. These data are correlated because they come from the same person.

2.4 Demographic

Clinical data can be influenced by demographic factors because demographic characteristics, such as age, gender, race, and ethnicity, can have an impact on various aspects of health, disease, and medical treatment. For example, in my case, older individuals may be more likely to be influenced by the severity of PsA than the younger, this is a kind of luring variable in my analysis.

3 TUDOR clinical trial Data Analysis

The code used to produce the results and graphs displayed in this data analysis can be found at: *https://github.com/Alicege007*

3.1 Objective1

In the first objective analysis, five psoriatic disease-related attributes were utilized as independent variables to assess their impact on health-related quality of life (QoL) and physical function, including two clinical arms (Enhanced Surveillance and standard care), age, gender, clinical visits, and severity of Psoriasis (SAPASI). Both clinical arms included a total of three clinical visits(baseline or follow-up time). Indicators of QoL(EQ5D, DLQI) were response variables for the three models below. Initially, I gained a general understanding of these attributes and then analyzed the correlation of them. An accurate depiction of how psoriatic disease impacts the physical function and quality of life (QoL) of patients varies across gender, age, severity of Psoriasis, clinical arms, and clinical visits, as determined through linear regression techniques.

Demographics were obtained through a questionnaire; the demographic questionnaire was posted by the secure print company or GP to potential participants before the participants took clinical trial procedures for the PsA study.

EQ5D-5L measured health-related quality of life; EQ5D-5L was in health economic patient questionnaire packs. All patients were requested to complete EQ5D-5L at each visit, which

means data on EQ5D-5L was collected at baseline, 12th month and 24th month.

Self-administered Psoriasis Area Severity Index(SAPASI) was a measurement of the severity of Psoriasis. Dermatology Life Quality Index (DLQI) was used to assess the impact of Psoriasis on quality of life. All patients completed the DLQI and SAPASI questionnaires at three clinical visits (baseline, 12th month, 24th month).

The data obtained at ES were more closely monitored than those at SC. Because of the greater intervention in the ES arm, we hypothesize that patients' QoL were different at ES and SC. The linear regression model was applied to test this difference.

Table 3 provides a comprehensive description of the variables related to the first Objective.

Table 3

Variable Name	Description	Summary Statistics
SAPASI	SAPASI is a tool used to measure the severity of Psoriasis(0-72). A SAPASI score of 5 to 10 is considered moderate disease, and a score over 10 is considered severe. A 75% reduction in the SAPASI score is the current benchmark for most clinical trials in Psoriasis and the criterion for the efficacy of new Psoriasis treatments approved by the FDA [6].	**24th month**: Mean：4.62 SD：5.30 (Min, Max): (0,39)
EQ5D-5L	EQ5D-5L questionnaire has five questions representing five dimensions, namely mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each question(each dimension) has 5 level options, levels 1 to 5 represent no problem, slight problem, moderate problem, severe problem, and unable to do respectively. Levels 1 to 5 are scored from 1 to 5, the higher the score, the lower health-related quality of life.	**Mobility：** Mean：1.35 SD：0.7 (Min, Max): (1,4) **Self-care:** Mean：1.14 SD：0.45 (Min, Max): (1,4) **Activity:** Mean：1.36 SD：0.7 (Min, Max): (1,5) **Discomfort:** Mean：1.89 SD：0.8 (Min, Max): (1,5) **Anxiety:** Mean：1.58 SD：0.8 (Min, Max): (1,5)
DLQI	The impacts of skin disease caused by	**24th month:**

Variable Name	Description	Summary Statistics
	psoriatic disease on QoL. This measurement method provides a different perspective from EQ5D, this one emphasizes the influence of skin problems There are 10 questions. Each question has five options, scores 1 to 5 represent very much, a lot, a little, not at all, not relevant. The DLQI is calculated by summing the score of each question resulting in a maximum of 50 and a minimum of 0. The lower the score, the more quality of life is impaired. Interpret meaning of DLQI scores: 39-50 no effect at all on the patient's life 35-38 Small effect on patient's life 30-34 moderate effect on patient's life 20-29 very large effect on patient's life 0-19 extremely large effect on patient's life	Mean:37.7 SD:3.9 (Min, Max): (18,45)
Clinical arms	Either Enhanced Surveillance(ES) or Standard Care(SC) 1 represent ES and 0 represent SC (SC is a reference)	**24thmonth**: (ES, SC): (64.1%, 35.9%)
Gender	The gender of patients 1 represents women and 0 represents men (men is a reference)	**24thmonth**: (Female, Male): (47.9%, 52.1%)
Age	The age of patients	**24th month**: Mean：53.9 SD： 12.3 (Min, Max): (17,73)

Method

Data collection was described at the beginning of the data description. DLQI and EQ5D-5L were both used to measure the participants' QoL, but they focused on different aspects of quality of life. The DLQI emphasizes the QoL related to skin, while the EQ5D emphasizes the QoL related to mobility. For example, the questions on the questionnaire regarding DLQI were "Did skin affect sports?", "Did skin influence clothes?", "Did skin create problems with a partner?". The questions on the questionnaire regarding EQ5D-5L were such as "Did you have problems walking?", "Did you have problems doing your usual activities? PsA incorporates not only skin problems but also arthritic issues, therefore, DLQI and EQ5D gave various perspectives corresponding to these two aspects. Due to the different interventions between the ES arm and SC arm, research regarding the effect of these arms on QoL provides further insight into using clinical ways to reduce the trauma of PsA.

Statistical analysis

Scatterplot, boxplot and frequency distribution histogram were utilized to observe the interaction and distribution of clinical arms, age, gender and SAPASI. Spearman correlation was applied when examining relationships of continuous variables. Log transformation for SAPASI increased the normality in the linear regression model. The core model is a multivariable linear regression model that was used to evaluate the combined effects of clinical arms, age, gender, and severity of Psoriasis on QoL. The residual-fitted value plot was used to observe outliers and variance heterogeneity of residuals. QQ-plot was employed to check the normality. Cook distance was calculated to examine whether outliers have an unduly large influence on the model fit.

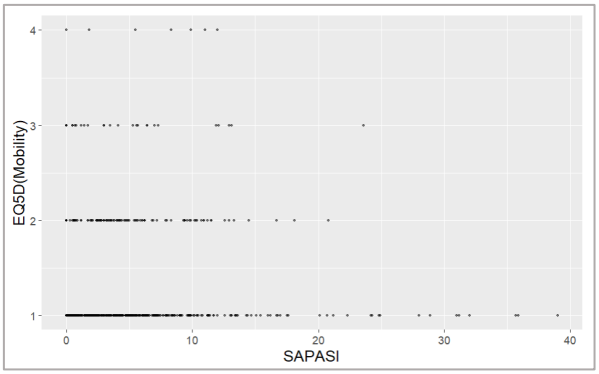
In this research, only two dimensions of EQ5D were investigated. Effects of predictors on mobilityEQ5D were investigated through the ordinal regression model. The anxietyEQ5D variable was dichotomized as “no problem” (level 1) and “problem”(levels 1 to 5). A logistic regression model was used to study independent variables’ effect on anxietyEQ5D.

EQ5D is the scores with natural ordering consisting of discrete values ranging from 1 to 5 (Figure 1), natural ordering refers to a type of categorical data where the categories have a logical order. For example, the categories like "no problems" (level 1), "slight problems" (level 2), "moderate problems"(level 3), "severe problems"(level 4), and "extreme problems"(level 5) of EQ5D represent a natural ordering of health states. The data type like EQ5D as a response variable is suitable for the ordinal regression model.

A crucial assumption for the ordinal regression model is the proportional odds assumption. The ordinal regression model assumes that odds ratios comparing outcome groups based on different cut-points are the same at all cut-points. For instance, in my research, there were three cut-points, namely Y<=1, Y<=2, and Y<=3 (4 levels in MobilityEQ5D). Under the proportional odds assumption, the OR comparing Y<=1 and Y>1 is the same as the OR comparing Y<=2 and Y>2.

Two approaches were used to test the proportional odds assumption in this research. ORs comparing categories were calculated, and then they were observed to determine whether they were invariant. After calculating by hand, Brant-Wald was also used to test if the proportional odds assumption is tenable. In the ***proportional odds assumption*** section, more details were discussed. As for the model diagnostics, Hosmer-Lemeshow(HL) and Lipsitz goodness-fit tests were utilized.

Figure 1



Description of Data

Relationship between EQ5D and Age

From Table 1, the mean values at the 24th month of 5 dimensions, mobility, self-care, activity, discomfort, and anxiety all lay in 1 to 2 which was between no problems and the slight problem of health-related quality of life (QoL). No one reached level 5 (unable to) regarding self-care and mobility dimension. EQ5D index is the score consisting of discrete values ranging from 1 to 5, Due to this nature, calculating the percentage of each EQ5D level within various age ranges was an effective way to illustrate the correlation between age and EQ5D. The numeric age variable was discretized into four age groups: 17-30, 31-45, 46-60, and 60+. The bar plots display the proportion of individuals of 1 to 5 levels against the age range; each bar plot represents a dimension. (Figure 2)

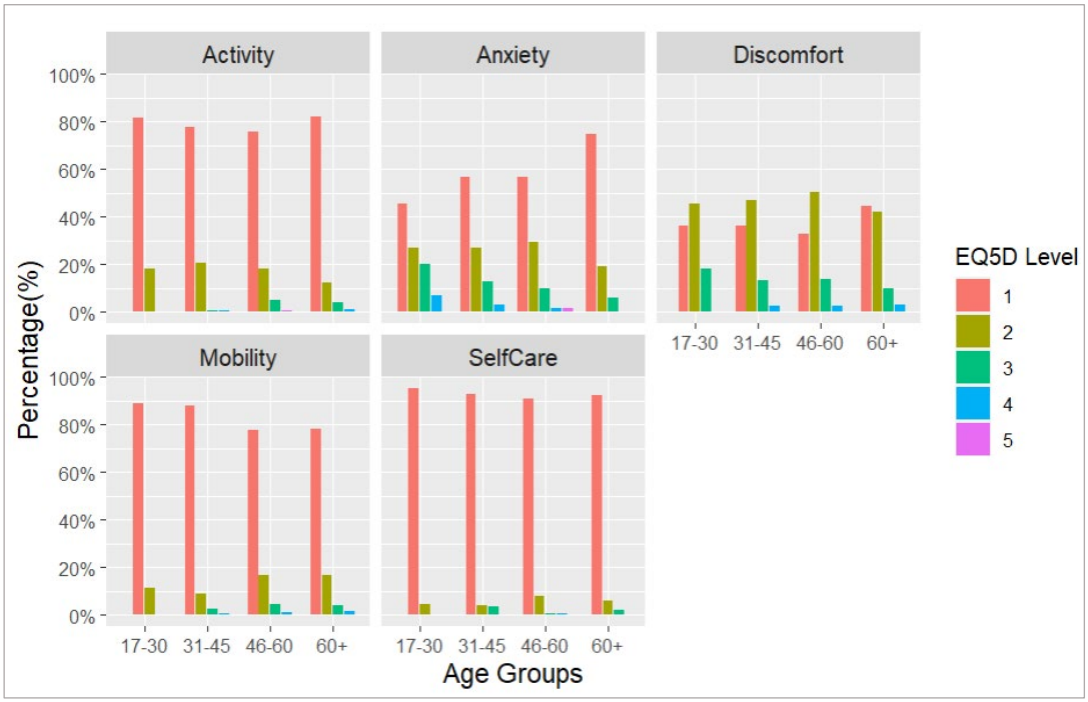
The dichotomy was used to discuss graphical information here; level 1 indicates “no problem”, and levels 2 to 5 indicate “problem” in terms of health-related QoL. Regarding the issue of taking care of themself, mobility, carrying out usual activities (work, study, housework, family leisure activities), and anxiety, most patients had no problem; the no-problem portion of these four dimensions exceeded 85%, 77%, 75%, and 48% respectively. The percentages of no problems with taking care of themselves and usual activities were almost evenly across different age groups. While the fraction of no problems was inversely proportional to age in terms of mobility, the 60+ age group had a minimum fraction of no problems. This means the older they age, the higher their level of difficulty with mobility. Anxiety level had the opposite trend; the older patients get, the lower their anxiety levels. (Figure 2)

As for discomfort, slight problems accounted greater part than the no-problem part for all age groups. Moderate problem parts constituted a higher fraction than the other 4 dimensions (self-care, anxiety, usual activities and mobility).

In a nutshell, the severe level of discomfort and anxiety was higher than that of other dimensions. According to the exploration above, age is a meaningful risk factor that is closely linked to mobility and anxiety levels, indicating that age should be included in the model. The relationships between age and various dimensions were different. In this research, I explored the associations between anxiety and mobility dimensions. The samples of anxiety and

mobility laying in level 1 to level 5 that were used to build models were 694 and 692 respectively, however, no data points laying in level 4 or level 5 were beyond 5 which was quite a small sample size, this might lead to not reliable research results, I, therefore, did not discuss the situation of EQ5D within level 4 and level 5 in this research.

Figure 2



Relationship between DLQI and SAPASI, Age

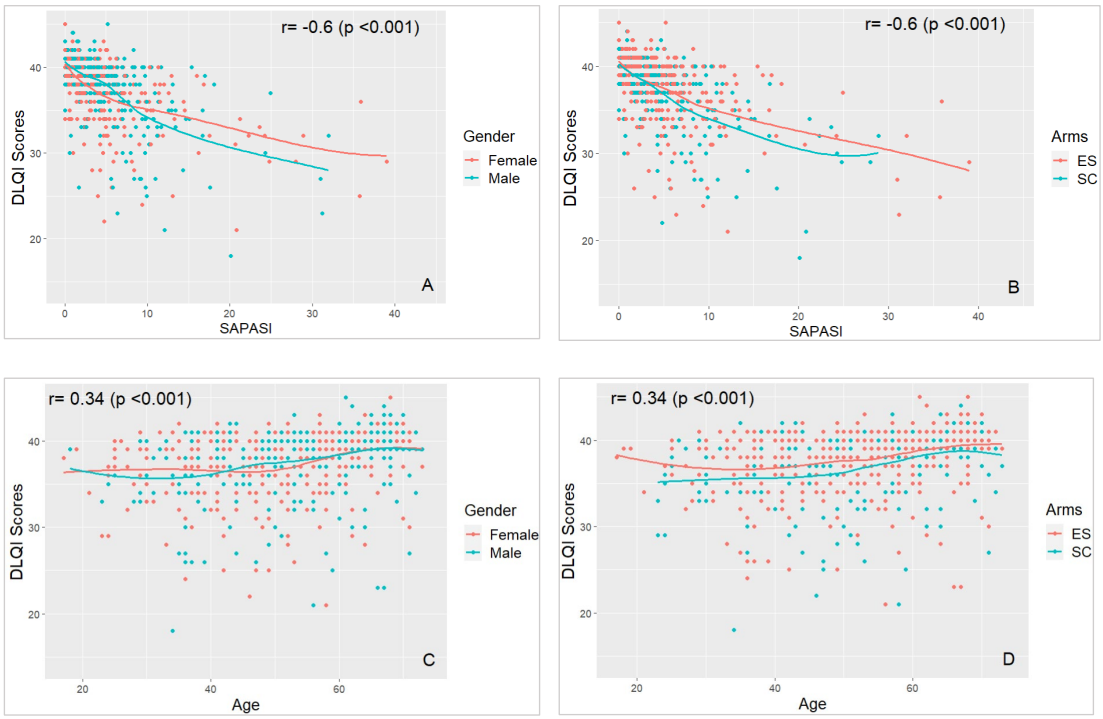
There was a moderate positive correlation between DLQI and age (Spearman r=0.33, P<0.001; Figure 3C). There was no interaction between sex and age in the sense that the trend on LOESS lines in the effect did not vary radically (Figure 3C). Since this is a randomized trial, the pattern between age and DLQI was identical in both arms which also can be observed in LOESS fits. Patients in the ES arm had slightly higher QoL than those in the SC arm (Figure 3D).

A stronger negative correlation was found between SAPASI and DLQI score (r=-0.59, P<0.001; Figure 3A). The LOESS fit of female and male trends was similar, indicating that no interaction between sex and severity of Psoriasis in terms of DLQI; Both trends showed that the severity of Psoriasis increased with the level of QoL decrease. Also, the trend between SAPASI and DLQI was the same in both clinical arms. (Figure 3B).

LOESS fit and Spearman coefficient both showed a dominant pattern between QoL and SAPASI where QoL drops as the severity of Psoriasis grows. However, there were a few patients whose QoL were low while the severity of Psoriasis was not at a high level (Figure 3A; DLQI less than 30 and SAPASI less than 10). This means these a few patients had the opposite trend from the dominant pattern. This opposite trend did not be explained by additional other features in my dataset. As a result, I excluded these a few data points from my multivariable linear regression model (equation 1). The underlying reason that a few patients presented different trends from

the majority of people might be because patients' responses to the QoL and SAPASI questionnaires sometimes were subjective [7]. For example, some individuals perceive pain and discomfort differently from the majority of people.

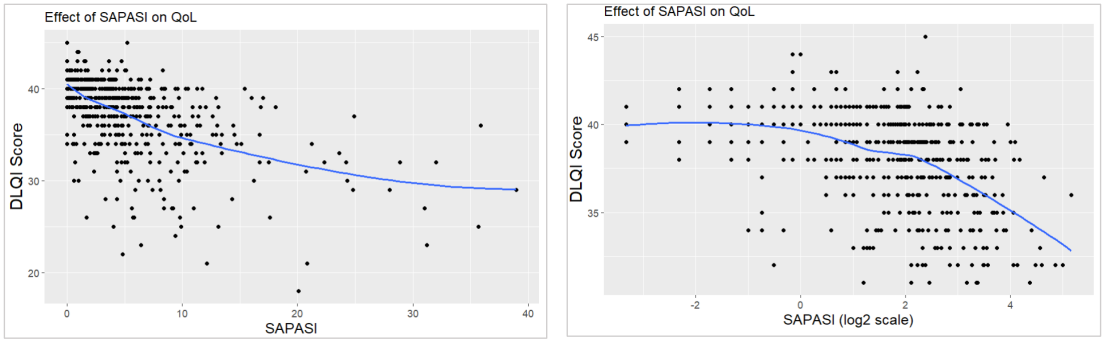
Figure 3: Scatter plots and corresponding LOESS fit

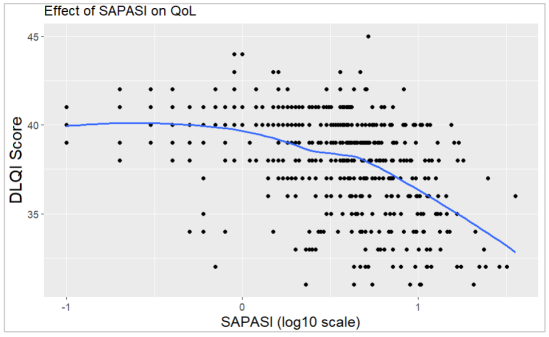


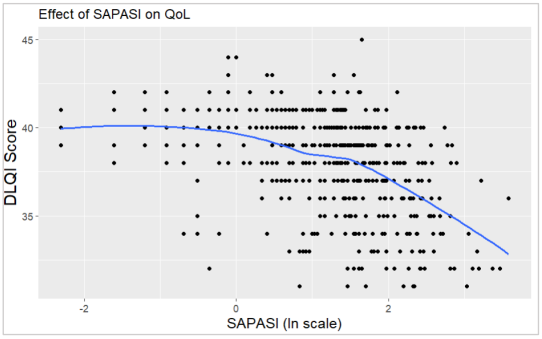
Transformation

In my linear regression model, I transformed SAPASI to increase the normality of the model. $log_2 SAPASI$ was chose to included in the model. The plots of the SAPASI in the log2 scale, log10 scale or in the ln scale against DLQI are identical (Figure 4), indicating the choice of transformation base for the SAPASI did not make a difference. For easier interpretation, log2 was used in my model.

Figure 4 LOESS fit and various scales of SAPASI







Proportional odds assumption

Age, gender and SAPASI had significant relationships in the ordinal regression model, thus, only these variables were displayed in Table 4. Based on Table 4, the ORs assessing the effect of age for Y<=1 compared to Y>1, Y<=2 compared to Y>2 and Y<=3 compared to Y>3 were 0.97, 0.96 and 0.95 respectively which were hardly any difference; SAPASI was in the same situation. The OR evaluating the impact of gender for outcome groups of Y<=1 and Y>1 was 0.52. This was slightly lower than the other two outcome groups(0.61 and 0.62). Based on the OR comparisons above, it appears that the proportional odds assumption holds.

In addition, the Brant-Wald test was also employed to assess this assumption, the omnibus was for the whole model, the rest for the individual (table 5). The test results showed that H0: proportional odds assumption holds (P-value > 0.05) which was consistent with the conclusion of OR comparisons above.

In light of the preceding investigation, the crucial assumption for the ordinal regression model is satisfied, the model can be used to investigate the effects of independent variables on mobilityEQ5D.

Table 4 ORs comparing outcomes groups of mobilityEQ5D

	Y<=1 and Y>1 (OR)	Y<=2 and Y>2 (OR)	Y<=3 and Y>3 (OR)
Age	0.97	0.96	0.95
SAPASI	0.96	0.96	0.94
Gender	0.52	0.61	0.62

Table 5 Brant-Wald test for the ordinal regression model

Test for	df	P-value
Omnibus	6	0.99
SAPASI	2	0.84
Age	2	0.89
Gender	2	0.87

Results

Study population

The data used to model was at the 24th-month clinical visit. The sample size was 532. The percentage of males and females was 52.1% and 49.7%, the maximum and minimum ages

were 73 and 17, mean age (SD) was 53.9 (12.3). The participants were on the older side in terms of age. There 64.1% and 35.9% of patients were randomized to the ES arm and Sc arm.

Effect of Age, gender, Clinical arms and SAPASI on DLQI

$$y = \beta_0 + \beta_1 \, log_2 \, SAPASI + \beta_2 Age + \beta_3 Clinical \; Arms \qquad (1)$$

Equation (1) is my best-fitted multivariable model according to AIC and hypothesis test criteria; the response variable is the DLQI score. In my multivariable analysis, the SC arm was a reference.

The average QoL of patients at the 24th month time point was 36.6 (intercept was 36.6); this means that the average effect of Psoriatic disease on patients' QoL was small. When patients in the ES group were the same age and Psoriasis severity as those in the SC arm, their QoL was found to be significantly higher than those in the SC arm. Age exhibited a significantly positive correlation with QoL. while patients' severity of Psoriasis had a significantly negative relationship with their QoL. (P<0.05; Table 6)

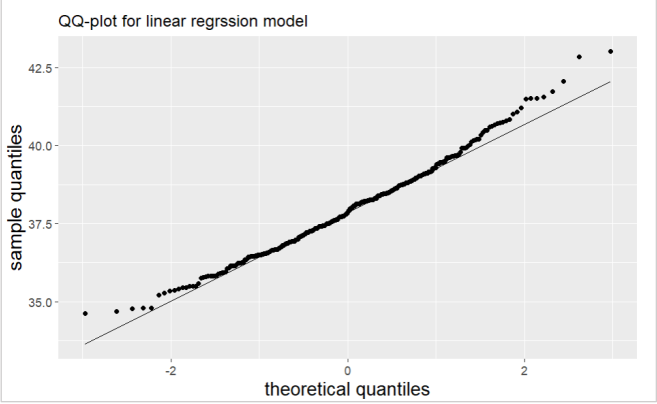
When patients are the same age and SAPASI increases by 10%, the DLQI decreases by $log_2(1 + 10\%) \times \beta_1 = 0.11$. When patients have identical severity of Psoriasis and age increases of 10 years old, the increase in expectation of DLQI score is 0.46.

Table 6 Multivariable model of the effect of DLQI and SAPASI, Age and Clinical arms

	$\boldsymbol{\beta}$**(SE)**	**CI**	**P-value**
Intercept	36.60 (0.64)	(35.96, 37.2)	< 0.01
$\boldsymbol{log_2 \, SAPASI}$	-0.79 (0.086)	(-0.88, -0.7)	<0.01
Age	0.046 (0.01)	(0.04, 0.06)	<0.01
Clinical Arms	0.59 (0.27)	(0.32, 0.86)	0.027

The scatterplot below illustrates the normality of residuals. Figure 5 suggests that residuals follow the standard normal distribution closely; there is no lack of normality.

Figure 5 QQ-plot for linear regression model



Effect of Age, gender, Clinical arms and SAPASI on EQ5D-5L mobility

$$logit\left(P(Y \leq j)\right) = \beta_0 - \beta_1 SAPASI - \beta_2 Age - \beta_3 Gender \qquad j=1,2,3 \qquad (3)$$

Equation (3) is my ordinal regression model. When *j*=1, estimated β_0 =3.6; when *j*=2, estimated β_0 =5.2; when *j*=3, estimated β_0 =6.8 (table 7). Men were a reference. No patients reached level 5 in terms of mobility; thus, there were only three cut points (*j*=1,2,3). In my ordinal regression analysis, the men had 1/exp(-0.66)=1.92 times the odds of Y<=1 than women's Y<=1; this means men had 1.92 times the odds of staying in a "*no problem*" statute compared to women when they were same age and severity of Psoriasis. When discussing Y<=2, men had 1.92 times the odds of staying in a "*no problem*" and a "*slight problem*" status compared to women of the same age and severity of Psoriasis. When discussing Y<=3, women had 1.92 times the odds of progressing to a "*severe problem*" status compared to men of the same age and severity of Psoriasis. In other words, women had lower QoL in terms of mobility than men when men and women were the same age and with severity of Psoriasis.

Patients whose SAPASI were 5 points higher than others had exp(-0.035×5)=0.84 times the odds of Y<=1; more intuitively, patients with SAPASI scores 5 points lower than others had 1/0.84=1.19 times the odds of being "no problem" when they were same gender and age.

When discussing Y<=2, patients with SAPASI scores 5 points lower than others had 1.19 times the odds of being "*no p*roblem" and "slig*ht problem*". When discussing Y<=3, patients with SAPASI scores 5 points higher than others had 1.19 times the odds of having a "*severe problem"*.

Participants were 5 years younger than others of the same age and gender, and the odds of experiencing "*no problem*" with mobility was 1/exp(-0.034×5)=1.19 times. Specifically, young people have higher QoL than older in terms of mobility.

Table 7 Ordinal regression model for EQ5D mobility dimension

	***β*(SE)**	**CI**	**P-value**
SAPASI	0.035(0.02)	(0.02, 0.06)	0.036
Age	0.034(0.009)	(0.03, 0.04)	<0.01
Gender	0.66(0.2)	(0.46, 0.86)	<0.01
Intercept (1 | 2)	3.6(0.55)	(4.15, 3.05)	<0.01
Intercept (2 | 3)	5.2(0.58)	(4.62, 5.78)	<0.01
Intercept (3 | 4)	6.8(0.67)	(6.13, 7.47)	<0.01

Figure 5 and Figure 6 are the predicted probability of equation (3). They give a full description of how SAPASI and age change with a probability of various levels of mobilityEQ5D. Men and women exhibited the same patterns of changes in SAPASI across four probability levels, and the same occurred with age against probability. As age increased, the probability of having 'no problem' with mobility decreased. The risk of being a "slight problem", "moderate problem"

or “severe problem” is raised with age (Figure 7). As SAPASI grew, the likelihood of experiencing “no problem” with movement reduced. The probability of encountering a “slight problem”, “moderate problem” and “severe problem” appeared to grow with SAPASI(Figure 6) Overall, women had a lower probability of experiencing 'no problem' than men, which is consistent with the discussion above.

Figure 6

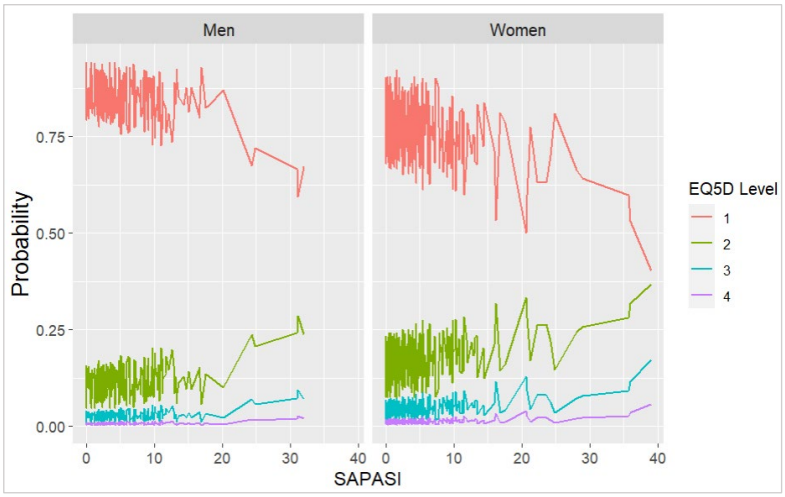
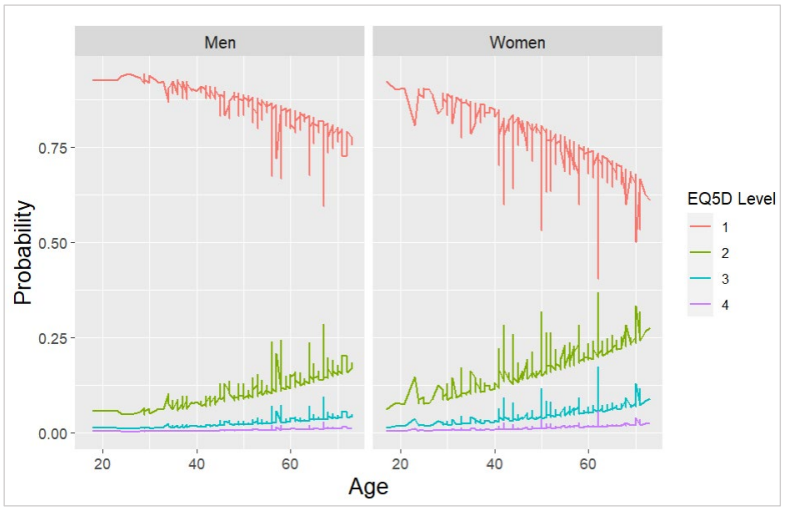


Figure 7



Ordinal regression model diagnostics

In my ordinal regression analysis, there were enough samples to do the HL test, thus, three goodness of fit tests were calculated to assess the overall adequacy of the ordinal regression model. The p-values for all three tests are greater than 0.05; this suggests that null hypothesis H0: which is a good ordinal logistic regression model was accepted (Table 8).

Table 8 Goodness of fit test for Ordinal regression model

Test	**statistic**	**df**	**P-value**
HL (Hosmer-Lemeshow)	24.14	24	0.45
Lipsitz	9.79	9	0.37
PR (Pulkstenis-Robinson)	3.38	7	0.85

Effect of age, gender, clinical arms and SAPASI on EQ5D-5L Anxiety

$$log\left[\frac{P(Y=1)}{1-p(Y=1)}\right] = \beta_0 + \beta_1 Age + \beta_2 SAPASI \quad (4)$$

Equation (4) is the model used to investigate predictors' effect on anxietyEQ5D. As mentioned earlier, categorical levels of anxiety were dichotomized “no problem” (level 1) and “problem” (level 2 to 5). Y=1 means having a problem.

In my logistic regression analysis, gender and clinical arms did not have evident effects on whether patients have problems with anxiety. However, SAPASI and age had a crucial correlation with whether patients have problems with anxiety (Table 9). Patients with SAPASI scores 5 points higher than others of the same age had exp(0.05 × 5)=1.28 times the odds of experiencing problems with anxiety. For participants who were 5 years older than others, the odds of experiencing no anxiety problem were 1/exp(-0.02×5)=1.11 times. In other words, when the SAPASI score is the same level, the older one gets, the less anxiety one tends to feel. The model goodness of fit test was measured by the HL test, the p-value for the test is 0.39 which means the model had no lack of fit.

Table 9 Generalized logistic regression model for EQ5D anxiety dimension

	***β*(SE)**	**CI**	**P-value**
SAPASI	0.05(0.02)	(0.02,0.06)	<0.01
Age	-0.02(0.007)	(0.03, 0.04)	<0.01
Intercept	0.5(0.4)	(4.15, 3.05)	0.2

3.2 Objective2

The second objective is to identify the risk factors that associated with whether patients were diagnosed with PsA. These risk factors include SAPASI, smoking history, duration of Psoriasis, gender, and age.

The data on whether patients were diagnosed with PsA was obtained from the outcome questionnaire. Patients completed the outcome questionnaire after being referred to rheumatology outpatient and PsA diagnosis. This happened at baseline, 12th month and 24th-month clinical visits in both clinical arms in this trial. As referred in the first objective, participants who were suspected of inflammatory arthritis were be referred to a local rheumatology outpatient clinic, and then assessment and diagnosis of PsA made by a treating rheumatologist from the rheumatology outpatients department at participating research sites.

Assessment made according to the Classification Criteria for Psoriatic Arthritis (CASPAR) criteria as part of standard clinical practice. As discussed in the literature, there are no reliable diagnostic criteria but classification criteria for PsA [4]. To date, the most useful are the CASPAR Criteria, which have been validated as a means of classifying PsA for research studies, and have assisted in standardizing the inclusion of patients for clinical trials [4]. X-ray and blood tests

were only undertaken if deemed clinically relevant. For trial purposes, patients either fulfilling the CASPAR criteria or not fulfilling the CASPAR criteria but who do have a clinical diagnosis of PsA will be regarded as having reached a diagnosis of PsA. Clinical diagnosis is the presence of inflammatory articular disease with current Psoriasis or psoriatic nail disease.

Smoking history was collected along with demographic data at all the time points(12^{th},24^{th} month and baseline). Duration of Psoriasis gained from clinical assessment performed by assessing clinician.

The descriptions of gender, age and SAPASI are presented in Table 1, while Table 10 provides the descriptions of the other risk factors used in the model for this objective.

Table 10

Variable Name	Description	Summary Statistics
Whether PsA was diagnosed		**24^{th} month**: (Diagnosed, not diagnosed)= (23%, 77%)
Smoking history	The data recorded the past smokers, current smokers and non-smokers	**The percentage of past smokers, current smokers and non-smokers in the 24^{th} month：** (40%, 48%, 12%)
Duration of Psoriasis		**24^{th} month**: Mean: 22.7 SD：16.3 (Min, Max): (0,67)

Method

Statistical analysis

A logistic regression model was a core model for the analysis. I initially included SAPASI, age, gender, duration of Psoriasis(years) and smoking history predictors in my logistic regression model and gained the estimated coefficients for these independent variables. Wald tests were applied to test significant relationships with the response variable. According to test results, risk factors that had a significant association with response were set as the main variables of the model, the others were set as effects modifiers. The reason for including effect modifiers in the model was that the association between modifiers and main risk factors can be discerned if the association exist. The methods that assess confounders and interactions involve not only observing changes in coefficients but also utilizing visualization techniques, such as boxplots and scatter plots. Evaluation of confounders and interactions combines AIC, and hypothesis test to decide whether to eliminate a risk factor from the model.

The Hosmer-Lemeshow test (HL) and the table of observed and expected cases were employed in combination to diagnose the model performance. Discriminatory performance (DP) of

logistic regression was evaluated, which provides how well the covariates in the model help to predict which subjects will develop PsA (Y=1) and which will not develop PsA. The Receiver Operating Curve (ROC) and Area Under the Curve (AUC) were utilized to measure DP.

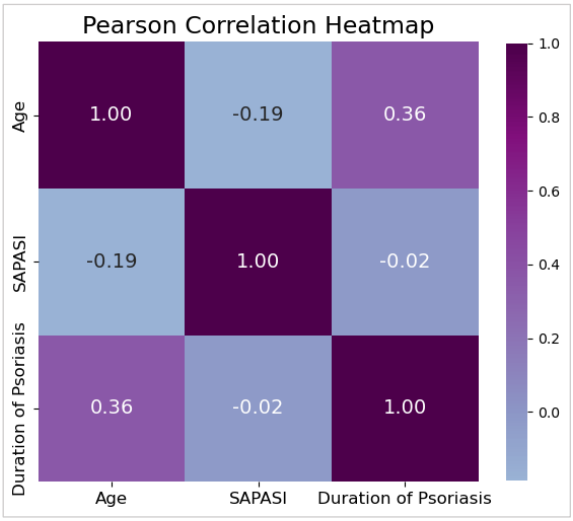
Description of Data

Collinearity and confounder

At the beginning of the modelling process, I will propose an initial model. The initial model included all five risk factors, A univariate simple logistic regression model was first developed to assess the significant effects of these five risk factors (the significance level was set at 0.05), and then the significant effects of five factors in the initial model also be assessed. Gender was the only risk factor found to be significant in either the initial logistic regression model or the univariate simple logistic regression model. The other factors were not significant in both models. The p-value for smoking history was 0.09, which was not significant at a 0.05 significance level. However, its significant effect was higher than the other three variables (duration of Psoriasis, age, and SAPASI). Therefore, smoking history and gender of interest were chosen to be the main risk factors in the initial model.

Before understanding the correlations between these three variables and the main factors (confounders or interaction), assume that these three variables act as effect modifiers of the relationship between the response variable and main risk factors in the initial model. The collinearity of the three effects modifiers was examined, Pearson correlation coefficient of age and duration of Psoriasis was 0.36, indicating there was a moderate linear relationship between them(Figure 8). Due to the collinearity of age and duration of Psoriasis, these variables were not included in the initial model simultaneously when exploring the association between the main effect and modifiers.

Figure 8



In my modelling process, the estimated regression coefficients and corresponding standard error of main factors (gender and smoking) in model 1 (predictors were only gender, smoking), model 2 (predictors were gender, smoking, SAPASI and age) and model 3 (predictors were

gender, smoking, SAPASI and duration of Psoriasis) were almost same, indicating that these three modifiers were neither confounder nor highly correlated with gender and smoking history. Consequently, the modifiers were eliminated from the initial model.

Interaction

After eliminating the SAPASI, duration of Psoriasis, and age factors, only gender and smoking history remained in the model. It was easy to conceive that, generally speaking, men tend to smoke more than women which suggests there might be an interaction between them. I, therefore, used the cross table to investigate whether there is a correlation between gender and smoking history. The odds ratio assessing effect of gender for comparison of non-smokers and current smokers was 0.82 (Table 11; men were the reference) and corresponding confidence interval (CI) was (0.41, 1.23) (CI: $0.82 \pm 1.96 \times 0.43$); the odds ratio for non-smoker and past smokers was 1.44 (Table 12) and corresponding confidence interval was (0.87, 2.01) (CI: $1.44 \pm 1.96 \times 0.29$). According to the CIs, the null hypothesis test H0: OR is 1 was accepted, suggesting that there was no association between gender and smoking history. Thus, the interaction of smoking history and gender is excluded from the model.

Based on the analysis above, the final model included gender and smoking history which was an addictive model.

Table 11 Cross table

	Non-smokers	**Current smokers**	**odds**
Men	42	14	0.33
Women	51	14	0.27

Table 12 Cross table

	Non-smokers	**Past smokers**	**odds**
Men	42	40	0.95
Women	51	70	1.37

Results

Study population

The data used for research was patients at the 24th month time point. The demographic features are 42% men and 58% women, the average age (SD) of patients was 53.6 (11.5). The sample size is 231 with 23% patients with PsA and 77% patients without PsA. The average duration (SD) of Psoriasis was 25.4 (17.1), and the maximum and minimum duration of Psoriasis was 67 and 0 years respectively. For smoking history, non-smokers, past smokers and current smokers accounted for 40%, 48% and 12% respectively. The mean score (SD) of the severity of Psoriasis was.

Effect of Gender and smoking history on diagnosis of PsA

$$log\left[\frac{P(Y=1)}{1-p(Y=1)}\right] = \beta_0 + \beta_1 Gender + \beta_2 Smoking\ history \quad (2)$$

Equation (2) was the final model. In my logistic regression analysis, men and non-smokers were referenced. In the smoking history categorical variable, 1 represents non-smokers, 2 represents past smokers, and 3 represents current smokers. Non-smoking men had a 14% to 41% probability of being diagnosed with PsA. while the Non-smoking women had a 5% to 30% probability of being diagnosed with PsA. This suggests that non-smoker men had 1.37 to 2.8 times the probability of having PsA compared to non-smoker women. Therefore, the chance of being diagnosed with PsA is higher for men than for women (Table 13).
The positive coefficient for smoking history indicates that the odds of developing PsA increase sequentially for non-smokers, past smokers, and current smokers. In other words, smoking increases the risk of developing PsA. The probability ranges of being diagnosed with PsA for non-smokers, past smokers and current smokers were 14% to 41%, 25% to 56%, and 18% to 70%, respectively. Non-smokers had 1.37 to 1.79 times the probability of having PsA compared to past smokers (Table 13)

Table 13 Logistic regression model for *diagnosis of PsA*

	β**(SE)**	**CI**	**P-value**
Gender	-0.80 (0.32)	(-1.12, -0.48)	0.01
Smoking history	0.39 (0.23)	(0.16, 0.62)	0.09
Intercept	-1.46(0.47)	(-1.99, -0.99)	0.2

Model performance
The p-value of the HL test for the logistic regression model was 0.82, suggesting that there is no evidence that the model lacks fit (Table 14). The ROC and AUC are the measurements of discriminatory performance (DP) for a model. A model provides good DP if the covariates in the model discriminate which subjects will develop PsA and which will not develop PsA. The larger the area under the ROC curve (AUC), the better the model's DP

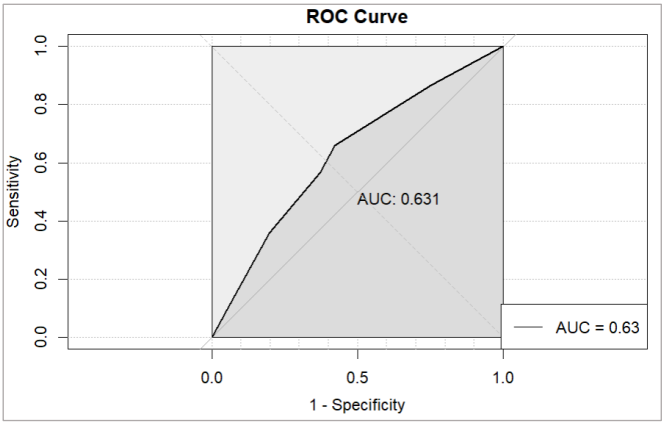
The AUC for this logistic regression model was 0.63 (Figure 9), indicating that the model had poor classification for patients with and without PsA. In the logistic regression full model with all risk factors (SAPASI, smoking history, duration of Psoriasis, gender, and age), the AUC was around 0.66, which was slightly higher than the AUC of 0.63 when only gender and smoking history were included. However, this outcome is not surprising. The onset of PsA is complex involving musculoskeletal disorders. Clinical research claims that the key to recognition of early PsA is entheseal inflammation [4]. Entheseal inflammation is a condition characterized by inflammation at the sites where tendons or ligaments attach to bone. SAPASI is not correlated with the severity of arthritis, these five features do not have strong joint involvement to classify patients with PsA and without PsA. Gender does have a significant relationship with developing PsA and thus demonstrated a certain degree of classification capability (AUC=0.5 suggests no classification capability).

In a nutshell, the logistic regression model provided some information on the effects of risk factors on the diagnosis of PsA but did not perform well in prediction.

Table 14 Hosmer-Lemeshow test results for equation (2)

	Statistic	Degree of freedom	P-value
HL test	1.54	4	0.82

Figure 9 ROC and AUC



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