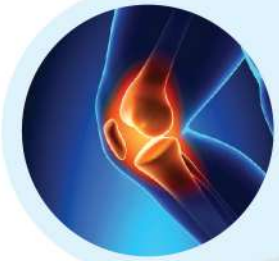
MOH/S/CRC/64.20(RR)

MALAYSIAN SOCIETY OF RHEUMATOLOGY

NIAR & MARBLE
RHEUMATOID ARTHRITIS



Published by:
National Inflammatory Arthritis Registry (NIAR)

(Apr 2009 – Aug 2019)

NATIONAL INFLAMMATORY ARTHRITIS REGISTRY (NIAR)

Published by:

Malaysian National Inflammatory Arthritis Registry (MyNIAR)
Ministry of Health Malaysia

Direct Line : (603) 6126 3333 ext 4167

Fax : (603) 6120 2761

Website : https://www.crc.gov.my

Suggested citation : The suggested citation for this report is as follows:
Dato' Dr Azmillah Rosman
Dr Mollyza Mohd Zain
Dr Shereen Ch'ng Suyin
Dr Habibah Mohd Yusoof
Dr Lau Ing Soo
Dr Liza Mohd Isa
Dr Nor Shuhaila Shahril

ISSN No : 2773-563X

CONTENTS

PAGE

CONTENTS

ACKNOWLEDGEMENTS

The National Inflammatory Arthritis Registry (NIAR) would like to express its sincere thanks and appreciation to all who have supported and contributed to this report.

We would also like to thank Sister Ramlah Shukor and Ms Fadzliza Hafiza Ramli from CRM for their assistance and support. Many thanks too to Dr Mohd Azahadi Omar, Head for the 'Sector for Biostatistics and Data Repository' National Institute of Health, Malaysia and Dr Chin May Chien, Hospital Selayang for their contribution with the statistical analysis.

We thank the following for their support:

- The Ministry of Health, Malaysia
- Clinical Research Centre (CRC)
- Arthritis Foundation Malaysia
- KA Consulting
- Pharmaceutical Industry

STEERING COMMITTEE MEMBERS

Dato' Dr Azmillah Rosman	Hospital Selayang
Dr Mollyza Mohd Zain	Hospital Selayang
Dr Habibah Mohd Yusoof	Hospital Selayang
Dr Lau Ing Soo	Hospital Selayang
Dr Shereen Ch'ng Suyin	Hospital Selayang
Dr Liza Mohd Isa	Hospital Putrajaya
Dato Dr Gun Suk Chyn	Hospital Tuanku Ja'afar
Dr Asmah Mohd	Hospital Tuanku Ja'afar
Datin Dr Asmahan Mohamed Ismail	Hospital Raja Perempuan Zainab II
Dr Chong Hwee Cheng	Hospital Melaka
Dr Lim Ai Lee	Hospital Pulau Pinang

RA SPECIAL INTEREST GROUP MEMBERS

Dr Shereen Ch'ng Suyin	Hospital Selayang
Dr Nor Shuhaila Shahril	Hospital Putrajaya
Dr Sharifah Aishah Wan Mohamad Akbar	Hospital Umum Sarawak
Dr. Malek Faris Reza Jeffrizal	Hospital Selayang

LIST OF CONTRIBUTORS

HOSPITAL PULAU PINANG
Dr Lim Ai Lee
Dr Kan Sow Lai
Dr H'ng Mooi Khin
Dr Nor Hashimah Abu Mansor Matardiah
Dr Ng Choon Seong
Dr Ng Ying Fun
Dr Quake Chuang Tin
Dr Shakira A/P Selvananda

HOSPITAL SELAYANG
Dato' Dr Azmillah Rosman
Dr Lau Ing Soo
Dr Mollyza Mohd Zain
Dr Habibah Mohd Yusoof
Dr Shereen Ch'ng Suyin
Dr Hazlyna Baharuddin
Dr Norliza Binti Zainudin
Dr Malek Faris Reza Jeffrizal
Dr Adrian Mark A/L Masnammany
Dr Avreena Kaur Bhullar A/P Authar Singh
Dr Lim Shiau Li
Dr Chuah Seow Lin
Dr Tay Voon Yaa

HOSPITAL PUTRAJAYA
Dr Liza Mohd Isa
Dr Nor Shuhaila Shahril
Dr Wan Rosmaiza Wan Musa
Dr Azwarina Hanim Ramlan
Dr Azriana Nurfizan Azmi
Dr Mariam Hamid Mustapha
Dr Pradeep V Ravindra Dass
Dr Ravathy A/P Nasadurai
Dr Tan Chou Luan

HOSPITAL KUALA LUMPUR
Dr Ong Swee Gaik
Dr Ding Hui Jen

HOSPITAL TENGKU AMPUAN RAHIMAH, KLANG
Dr Eashwary A/P Mageswaran
Dr Suhaida Ahmad Maulana
Dr Diana Ang Lee Min

HOSPITAL TUANKU JAAFAR, SEREMBAN
Dato' Dr Gun Suk Chyn
Dr Loh Yet Lin
Dr Asmah Mohd
Dr Nadiah Mohd Noor
Dr Chua Siew Houy
Dr Eow Liu Hong
Dr Jasmine Yew Sze Yin
Dr Liau Swee Min
Dr Ng Kooi Heng
Dr Shantene A/P Selvadurai
Dr Wong Phing Sue

HOSPITAL MELAKA
Dr Chong Hwee Cheng
Dr. Hong Hooi Chien
Dr Yap Wee Fang

HOSPITAL RAJA PERMAISURI BAINUN
Dr Ong Ping Seung
Dr Khor Chiew Gek
Dr Noraini Mat Husin
Dr Ng Boon Han

HOSPITAL TAIPING
Dr Lai Ee Ling

HOSPITAL SULTAN ISMAIL
Dr Ng Chun Ruh

HOSPITAL TUANKU NUR ZAHIRAH, TERENGGANU
Dr Siti Mariam Ab Rahim

HOSPITAL RAJA PEREMPUAN ZAINAB II
Datin Dr Asmahan Mohamed Ismail
Dr Gan Syang Pyng
Dr Ng Kiah Loon

HOSPITAL TENGKU AMPUAN AFZAN, KUANTAN
Dr Nurulraziquin Mohd Jamid
Dr Dayang Masyrinartie Suahilai

HOSPITAL KUCHING SARAWAK
Dr Teh Cheng Lay
Dr Sharifah Aishah Wan Mohamad Akbar
Dr Anna Farazilah Mohd Salleh
Dr Benjamin Sachdev A/L Manjit Singh
Dr Cheong Yaw Kiet
Dr Lee Kar Hoo

HOSPITAL SIBU
Dr Ling Guo Ruey

HOSPITAL QUEEN ELIZABETH
Dr Malehah Mohd Noh
Dr Hairul Hadi Ariff

HOSPITAL SULTANAH BAHIYAH
Dr Lim Chong Hong
Dr Ng Seow Ching

INTRODUCTION

National Inflammatory Arthritis Registry (NIAR) was established in 2009, later renamed as Malaysian National Inflammatory Arthritis Registry (MyNIAR) in January 2020. It is a web-based registry that captures Rheumatoid Arthritis (RA) patient's demographics, clinical information, management and outcome. Malaysian Registry for Biologics (MARBLE) is an excel database for the use of biologics for various types of inflammatory arthritis such as Rheumatoid Arthritis, Spondyloarthritis and Psoriatic Arthritis. It was set up in 2012 to look into the utilisation and safety of biologics in Malaysia. However, only RA data were included and analysed in this report (MARBLE-RA).

The majority of hospitals with Rheumatology service under the Ministry of Health (MOH) Malaysia participated in these registries. The information obtained from this registry reflects real life data, hence it will be beneficial to answer some of the clinical questions that may arise with regards to daily practice that are not studied in the randomised control trials. Furthermore, the registry data will also be relevant to stakeholders for budget planning and projection.

OBJECTIVES:

1. To determine the incidence and prevalence of RA in Malaysia.
2. To obtain demographic data
3. To determine disease pattern and manifestations
4. To study the management of patients
5. To assess patients' outcome, disease activity, extent of disability, economic impact and mortality rate

1. DISTRIBUTION OF CASES ACCORDING TO HOSPITAL

Data were obtained from April 2009 to August 2019. Comparing with the data collected in 2009 when NIAR was first started, there was a marked increase in the number of participating hospitals. In 2009, only 3 hospitals participated in the registry as a pilot project. Although the number of patients have also increased, it may not be reflective of the actual number of RA patients in MOH hospitals due to under reporting.

	Hospital	Year	
		2009	2019
1	Hospital Pulau Pinang	NA	1033 (15.79)
2	Hospital Sultanah Bahiyah, Alor Setar	NA	338 (5.17)
3	Hospital Raja Permaisuri Bainun, Ipoh	NA	115 (1.76)
4	Hospital Hospital Selayang	434	1066 (16.29)
5	Hospital Tengku Ampuan Rahimah, Klang	NA	94 (1.44)
6	Hospital Putrajaya	202	513 (7.84)
7	Hospital Tuanku Ja'afar	364	911 (13.93)
8	Hospital Melaka	NA	588 (8.99)
9	Hospital Pakar Sultanah Fatimah, Muar	NA	87 (1.33)
10	Hospital Sultan Ismail, Johor Bahru	NA	751 (11.48)
11	Hospital Tengku Ampuan Afzan, Kuantan	NA	67 (1.02)
12	Hospital Raja Perempuan Zainab II, Kota Bharu	NA	55 (0.84)
13	Hospital Queen Elizabeth, Kota Kinabalu	NA	129 (1.97)
14	Hospital Umum Sarawak, Kuching	NA	558 (8.53)
15	Hospital Sibu	NA	237 (3.62)
	Total	**1000**	**6542**

Table 1. Distribution of cases reported in NIAR according to hospitals

2. DEMOGRAPHICS

i) Age distribution at notification

Majority of the current cohort of patients are in the 40-70 age group.

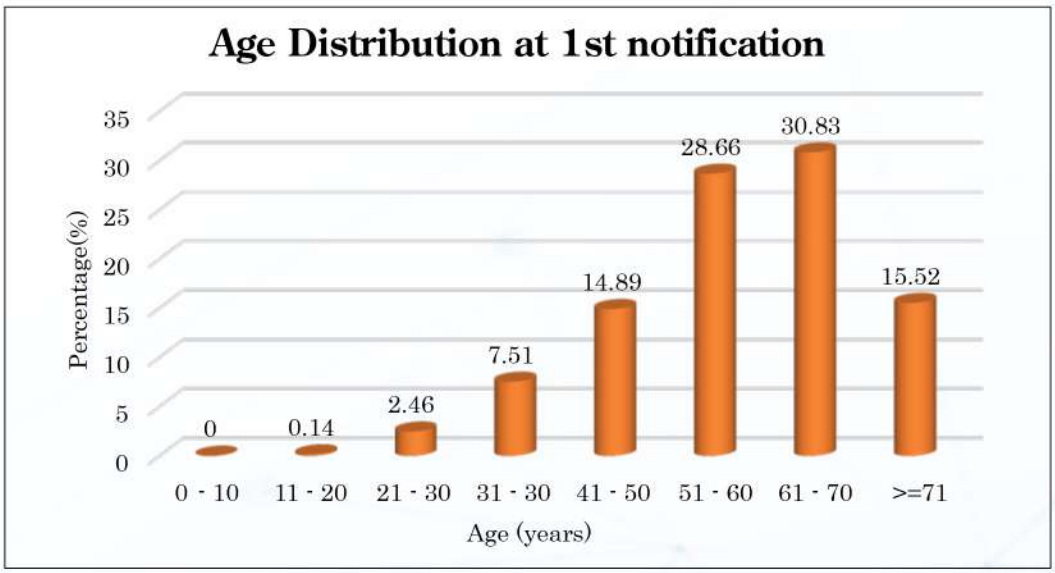


Figure 1: Age distribution at 1st notification

ii) Duration of disease at 1st notification

The majority of patients that were recruited into the registry have established RA with long standing disease.

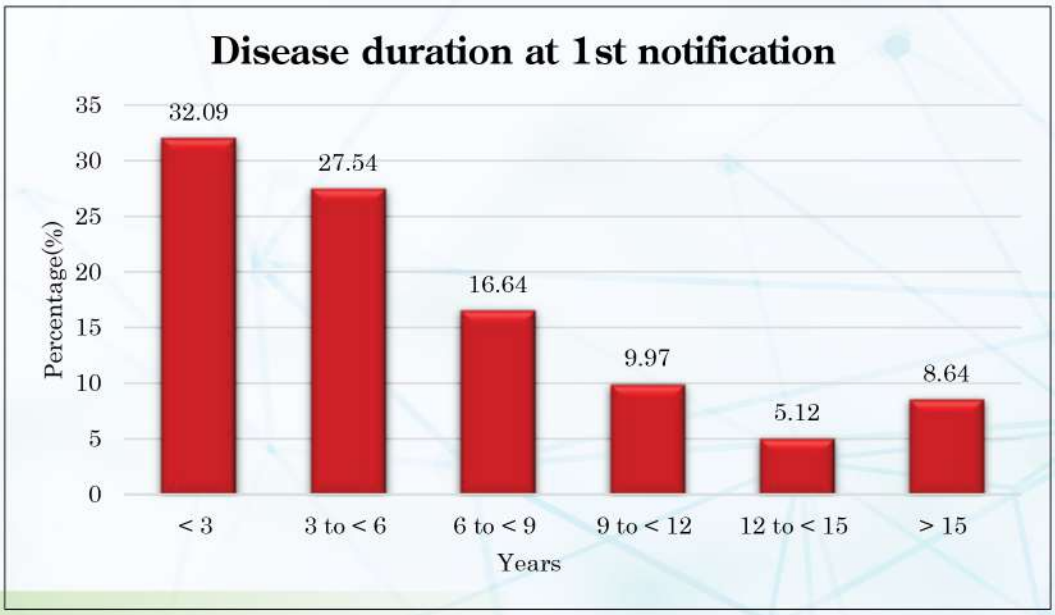


Figure 2: Disease duration at 1st notification

iii) Gender

Rheumatoid arthritis has a female preponderance with approximately 6:1 female to male ratio

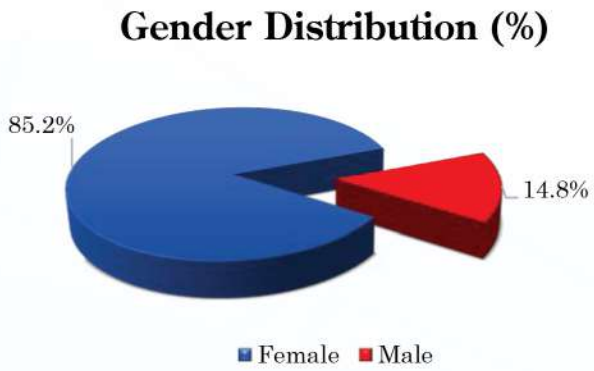


Figure 3: Gender distribution

iv) Ethnic group distribution

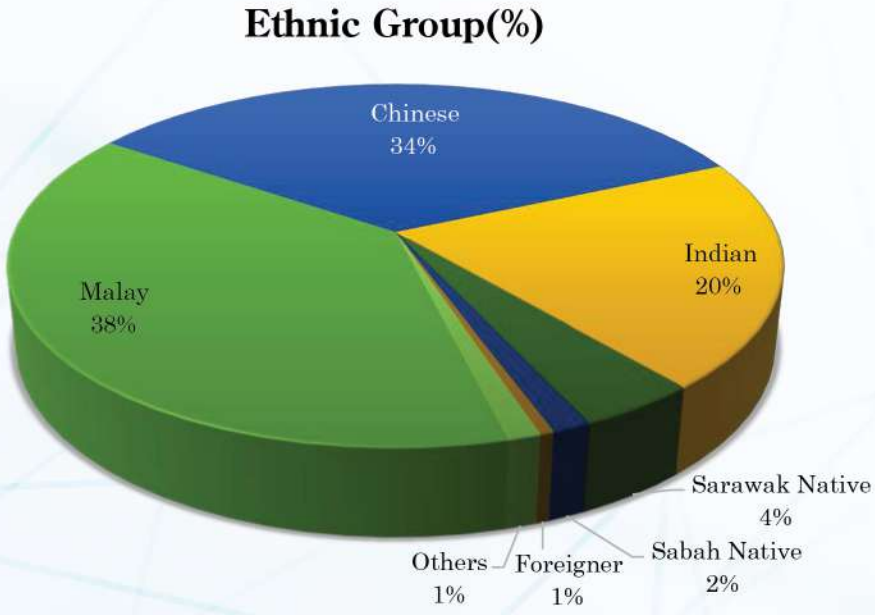


Figure 4: Ethnic group distribution

3. SOCIOECONOMIC STATUS

i) Education level

Seventy percent (70%) of the patients have secondary education level and below. A smaller percentage has no formal education at all.

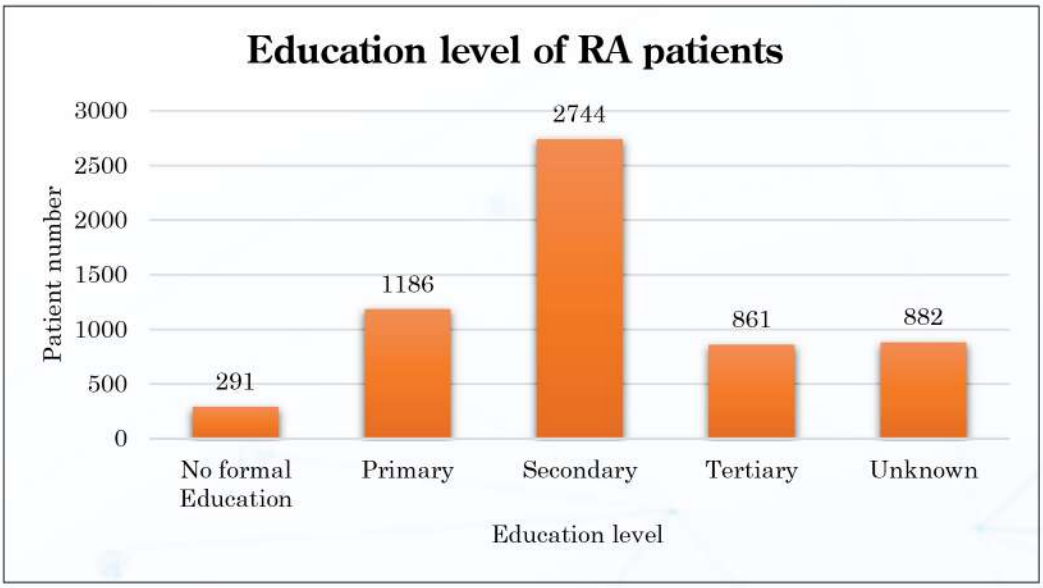


Figure 5: Education level

ii) Employment status

Approximately 11% (n=700) of the RA patients cohort are unemployed. Two third (n=508) of the cause of unemployment is attributed to the disease.

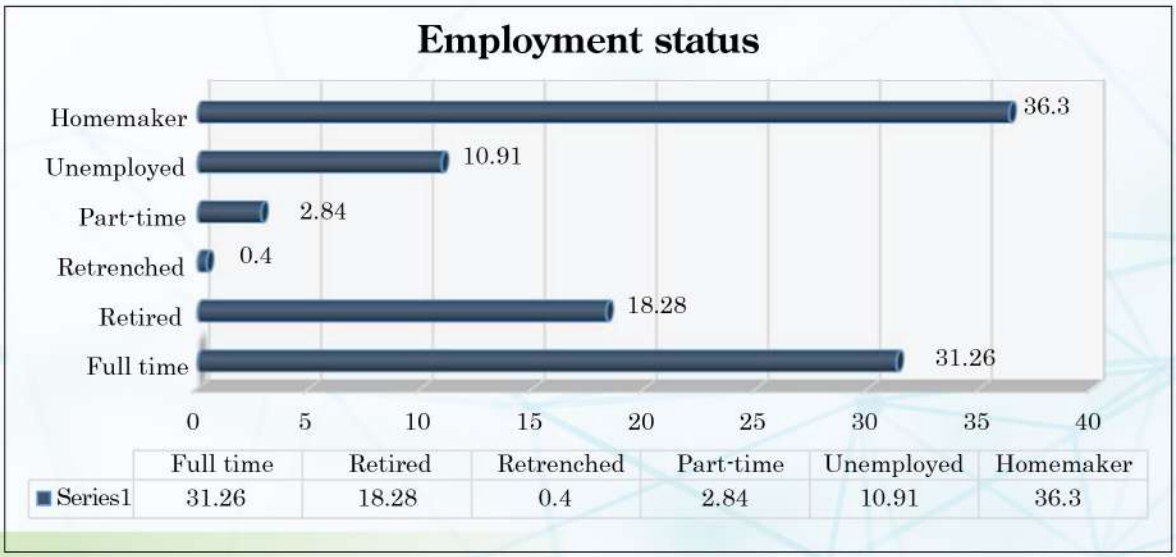


Figure 6: Employment status at 1st notification

iii) Household income

About half of the patients fall under the National Poverty Line Income *(PLI)) category, based on the revised PLI in July 2019 (The Star 2020).
*PLI = RM 2208.00/month

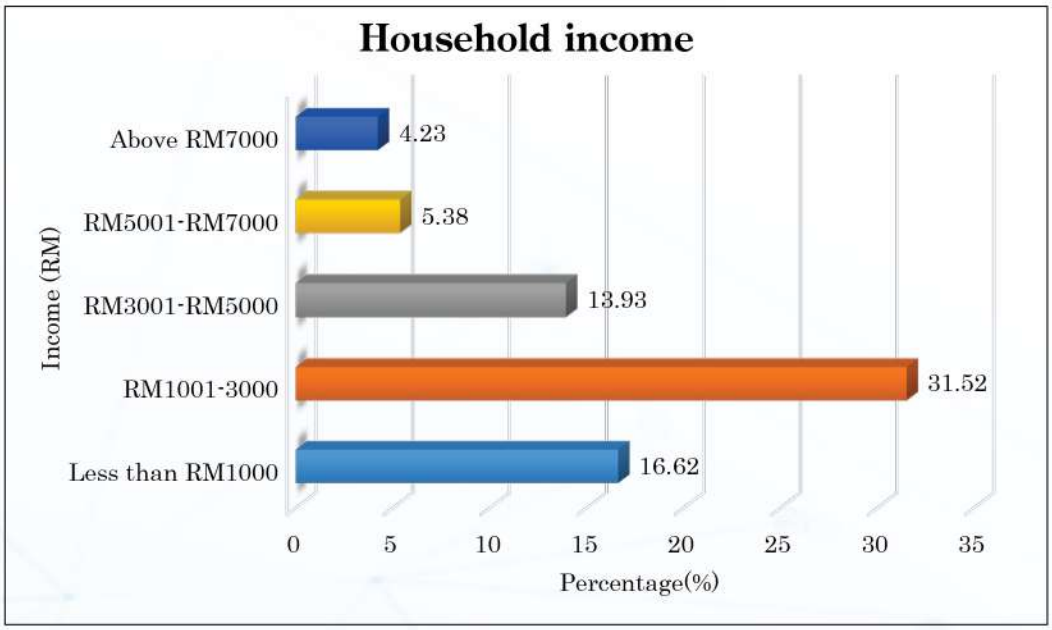


Figure 7: Household income at 1st notification

iv) Personal medical insurance

Majority of the patients do not have personal medical insurance. As our data is mainly from major public hospitals in Malaysia, perhaps inclusions of patients from the private and university hospitals who may have different socio economic background will give a more accurate picture.

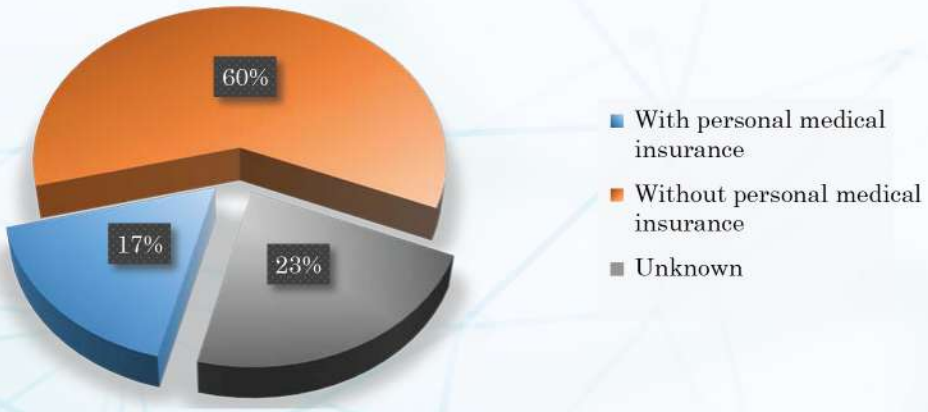


Figure 8: Personal medical insurance

4. DISEASE PATTERN

i) New cases of RA in MOH hospitals

There is an increased number of newly diagnosed RA over time due to higher disease awareness and improved rheumatology service across the country. The number of new cases plateau after 2010 with an average of 780 new cases every 2 years. However, there was a drop in the numbers in 2017-2018 which is most likely due to under reporting. In 2019, we transitioned to another web-based system, hence, the reduction in numbers of reported cases. In order to obtain an accurate epidemiologic trending of incidence of RA cases, vigorous data collection and timely analysis is required.

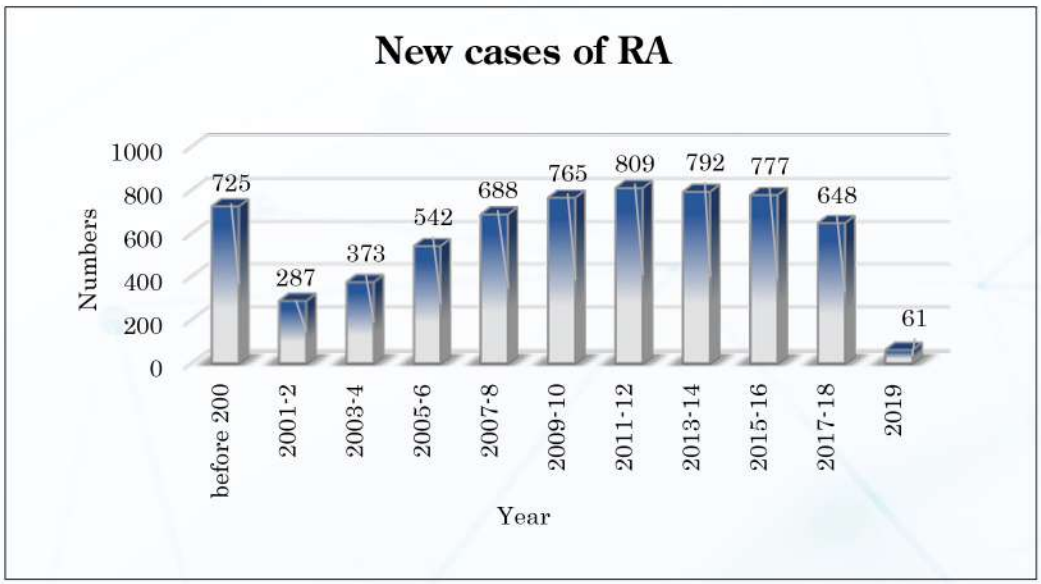
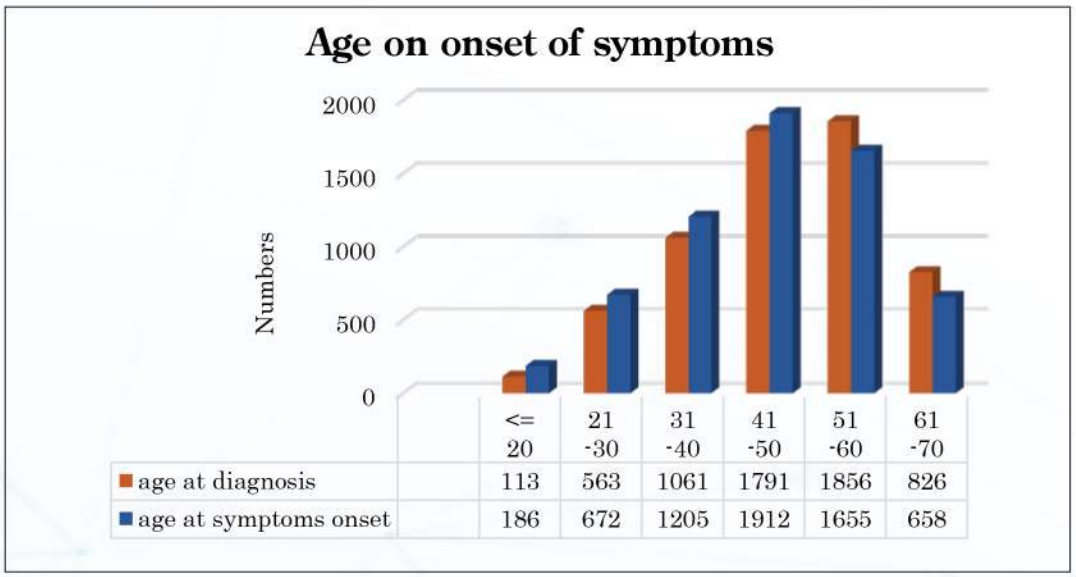


Figure 8: New cases of RA

ii) Age at disease onset.

Majority of the patients were diagnosed with RA at the age of 40-60 consistent with peak incidence worldwide (Bathon J 2008). The peak age of diagnosis is in the 50 years age group but the onset of symptom peaks in the 40s.



	<= 20	21 -30	31 -40	41 -50	51 -60	61 -70
age at diagnosis	113	563	1061	1791	1856	826
age at symptoms onset	186	672	1205	1912	1655	658

Figure 9: Age at onset of symptoms compared with age at diagnosis

More than 50% of the patients are within the productive age group when the symptoms occurred or diagnosis made.

iii) Duration of symptoms prior to the first rheumatology visit

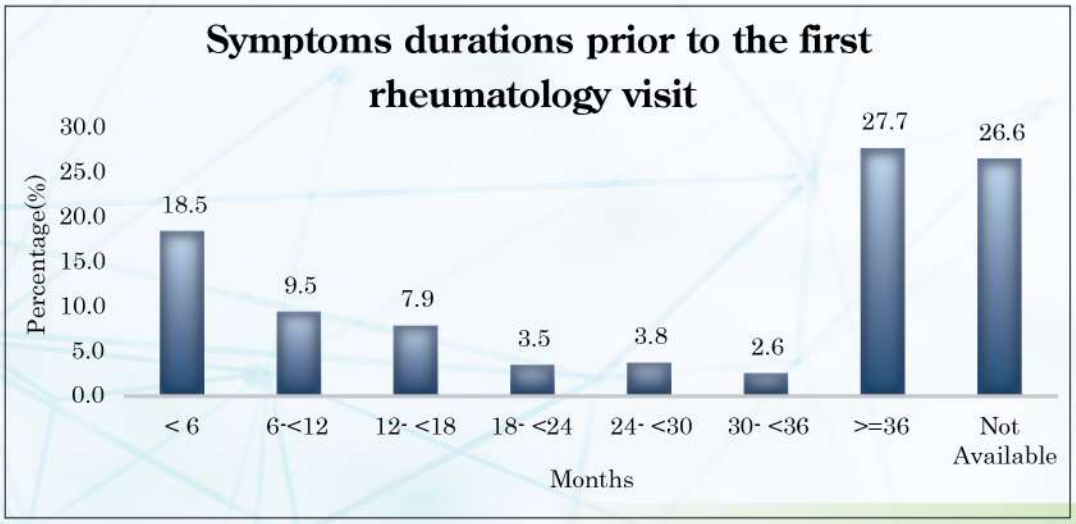


Figure 10: Symptoms duration prior to the first rheumatology visit

Less than 20% of patients with RA were seen by Rheumatologist within 6 months of their symptoms. Forty five percent of patients presented to the rheumatologist after 1 year of symptoms onset.

iii) Duration of symptoms before diagnosis

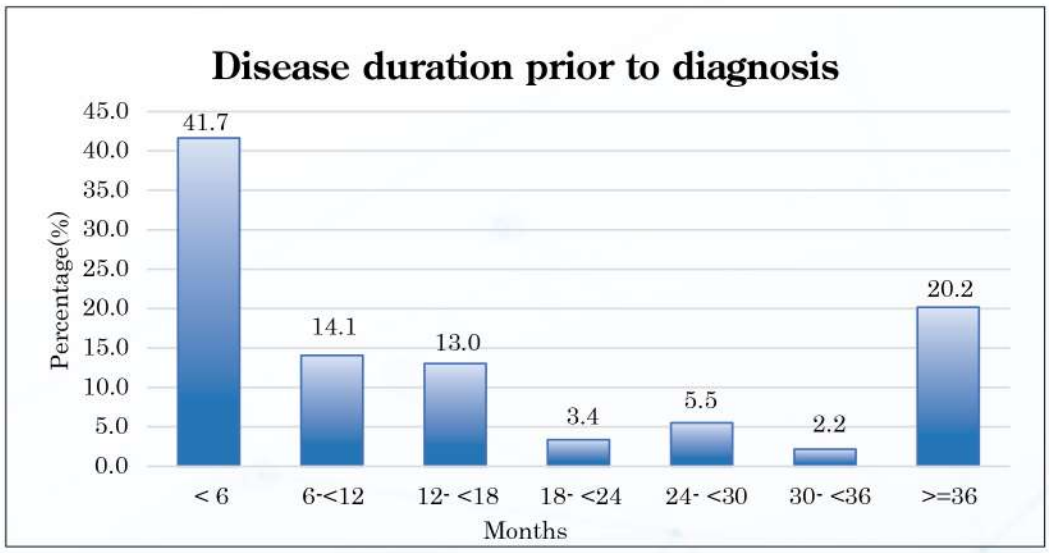


Figure 11. Duration of symptoms prior to diagnosis

Almost 42% of patients have been diagnosed within 6 months of the onset of symptoms in keeping with early diagnosis. However, 20% of patients were only diagnosed after 3 years of symptom onset.

iv) American College of Rheumatology (ACR) criteria at presentation

More than 90% of patients presented with symmetrical arthritis with more than 3 joints involvement and slightly more than a third have radiological changes.

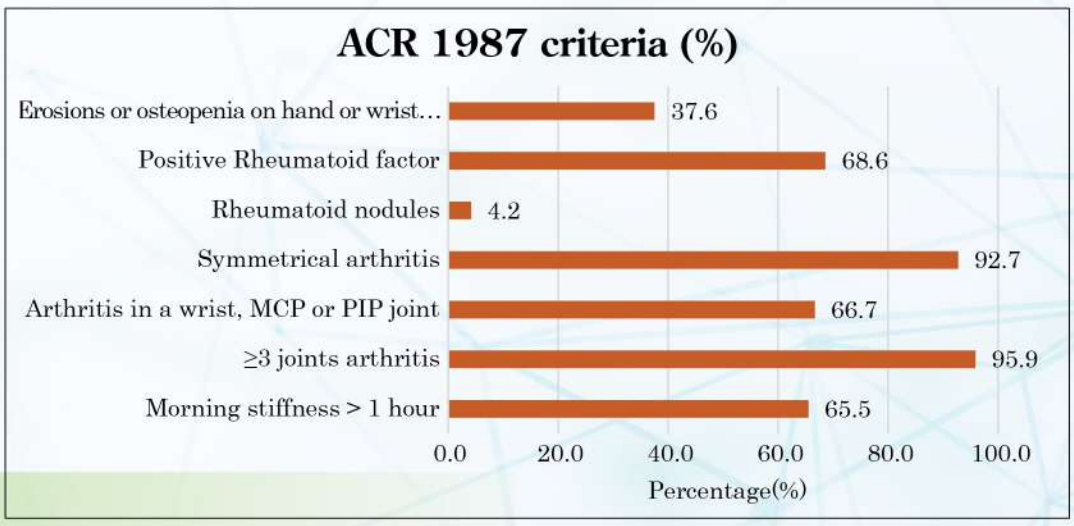


Figure 13: Percentage of patients with ACR 1987 criteria

v) Number of patients fulfilling ACR 1987 criteria for diagnosis of RA

Approximately 74 percent of patients fulfilled the ACR criteria at diagnosis. A patient is said to fulfil the criteria if at least 4 of the 7 criteria is fulfilled.

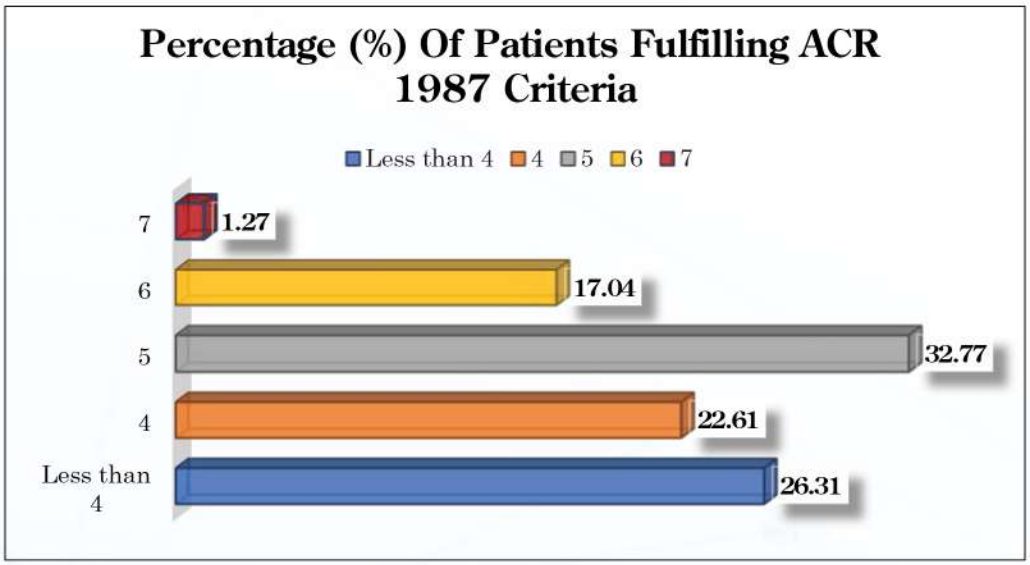


Figure 12: Percentage of patients fulfilling ACR 1987 criteria at diagnosis

vi) Extra articular manifestations

Seventy five percent (75%) of patients had extra articular manifestations at notification.

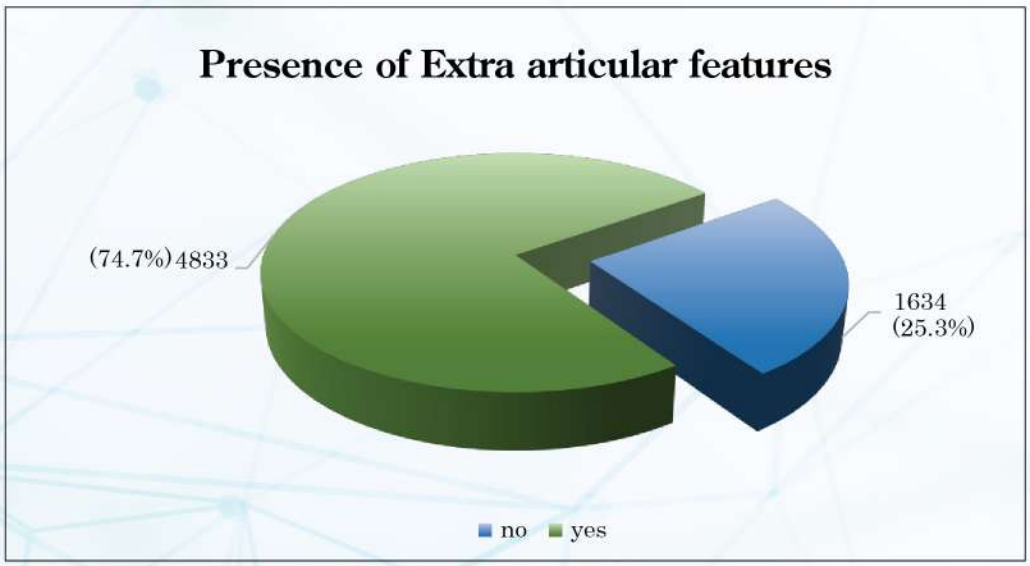


Figure 14: Number of patients with extra articular manifestation

The commonest manifestations were keratoconjunctivitis sicca, followed by interstitial lung disease, rheumatoid nodules and anaemia.

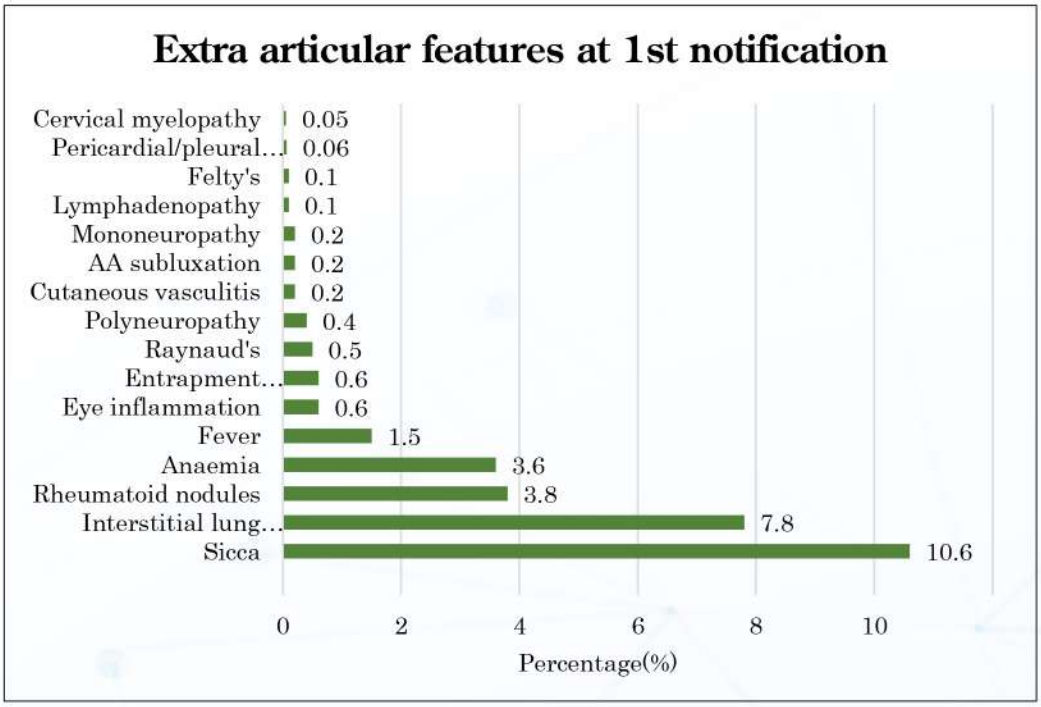


Figure 15: Types of extra articular manifestations

5. ASSOCIATED COMORBIDITIES

Sixty eight percent of RA patients have associated comorbidities.

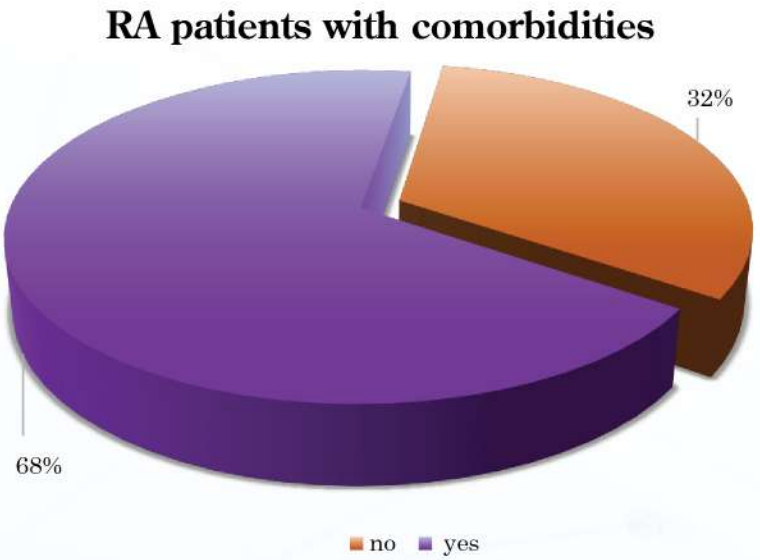


Figure 16: Presence of associated Comorbidities

i) Medical comorbidities

Hypertension is the most frequent comorbidity in this cohort followed by hyperlipidaemia and diabetes mellitus.

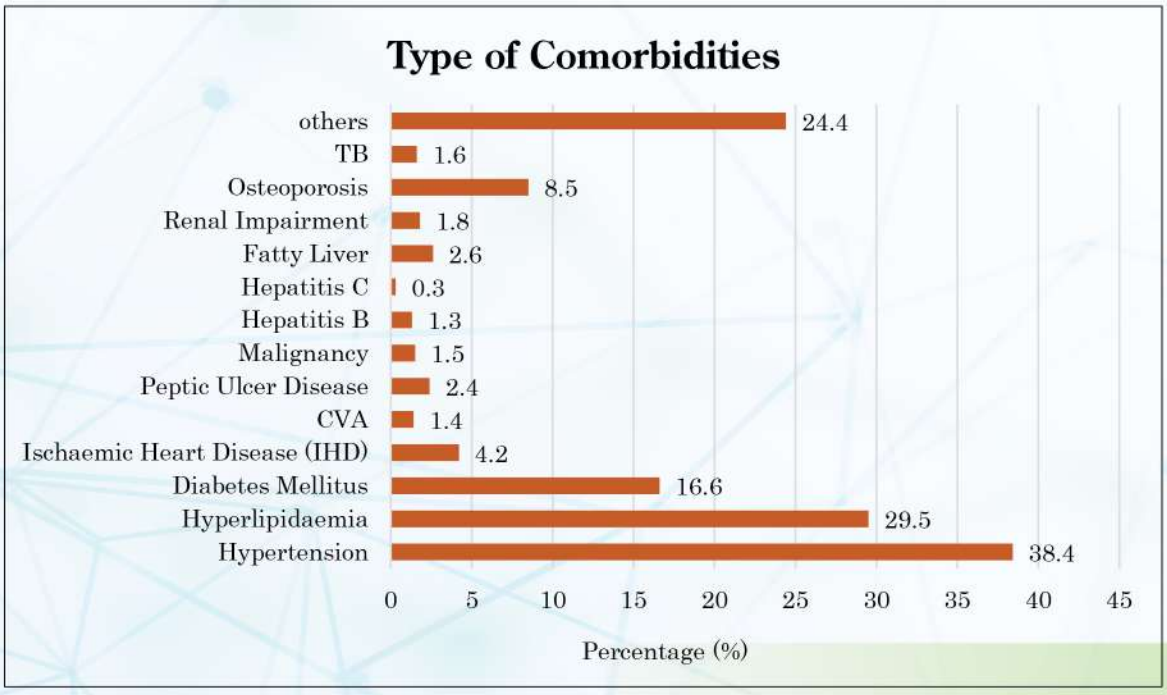


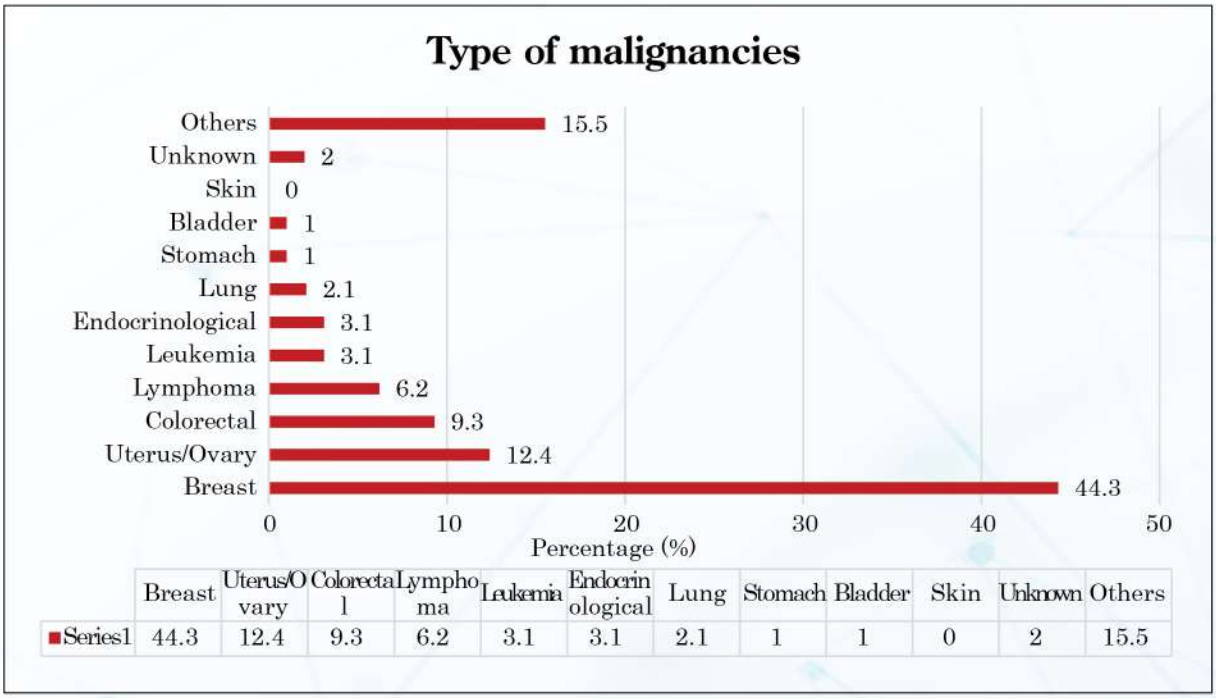
Figure 17: Type of comorbidities

ii) Tuberculosis (TB)

There were 1.6 % of TB cases reported in the registry which is higher than the national TB prevalence rate. In 2018, national TB prevalence was reported at 92 cases of TB notification per 100,000 population (The World Bank 2020).

iii) Malignancies

Prevalence of malignancy is 1.4% (n=94). This corresponds to the incidence rate of 0.14 per 100 patient years which is lower than the reported incidence rate of malignancy among RA population across the world. The crude incidence rate of malignancy in 5 other RA registries is estimated at 0.6-1.3 per 100 patient years (Simon TA 2015). The commonest malignancy is breast cancer followed by uterine and ovarian cancer.



	Breast	Uterus/Ovary	Colorectal	Lymphoma	Leukemia	Endocrinological	Lung	Stomach	Bladder	Skin	Unknown	Others
Series1	44.3	12.4	9.3	6.2	3.1	3.1	2.1	1	1	0	2	15.5

Figure 18: Type of malignancies

SUB-ANALYSIS ON DISEASE ACTIVITY STATUS AND TREATMENT

There were only 65% (n=4176) from the registry cohort who had the data for disease status and drug management.

1. DISEASE ACTIVITY STATUS

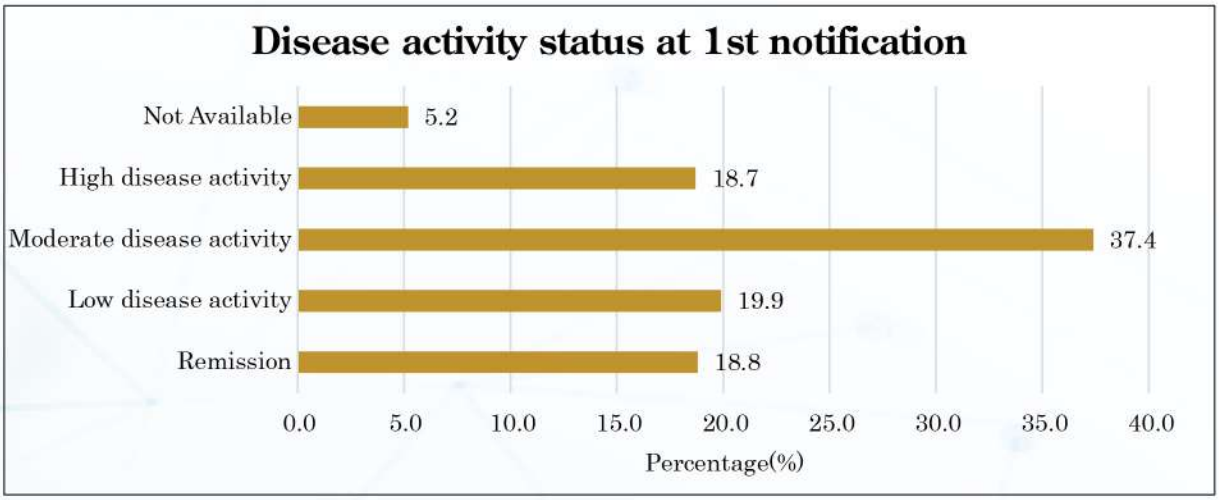


Figure 17: Disease activity status at 1st notification

At notification, 56% were still in moderate to high disease activity status whilst 38% were in low disease activity and remission. Of those who were in the moderate and high disease activity categories, almost half had been diagnosed for more than 5 years.

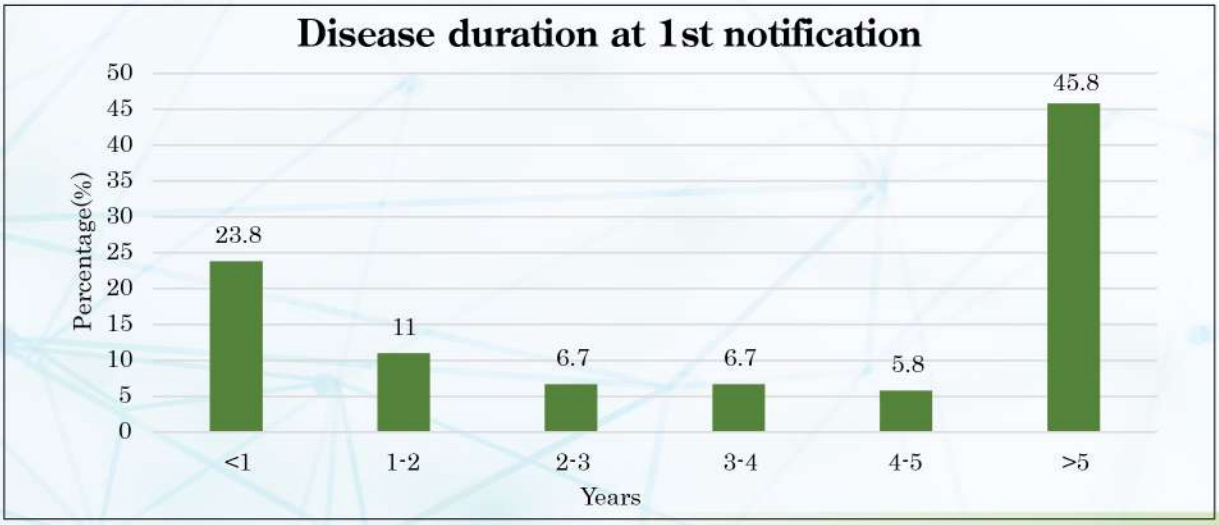


Figure 18: Disease duration at 1st notification in the moderate to high disease activity cohort

2. STANDARD OF CARE

i) Time to initiate disease modifying anti-rheumatic drugs (DMARDs) after diagnosis

More than three quarter of the patients were initiated on DMARDs within the first month of diagnosis.

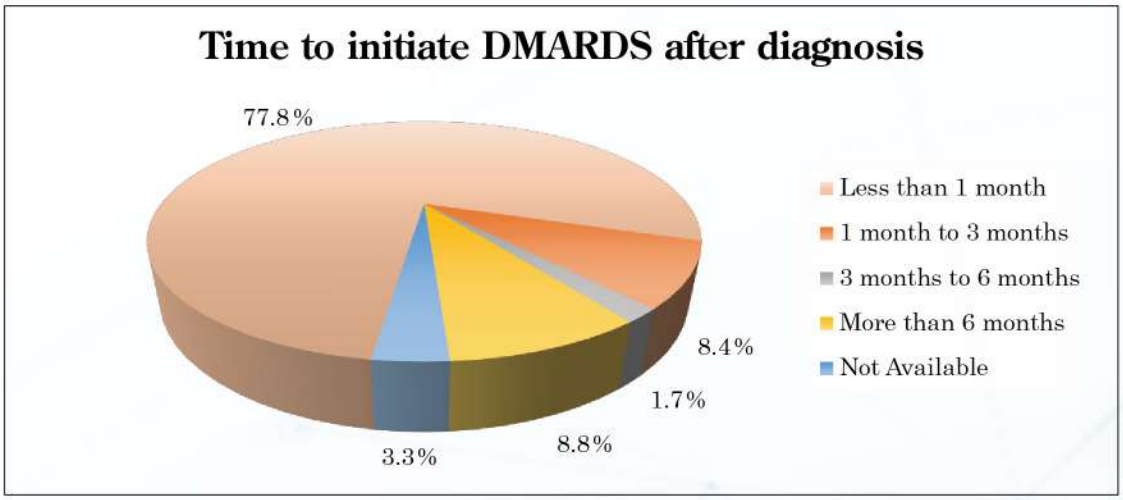


Figure 19: Time to initiate DMARDS after diagnosis

ii) Types of medical therapy

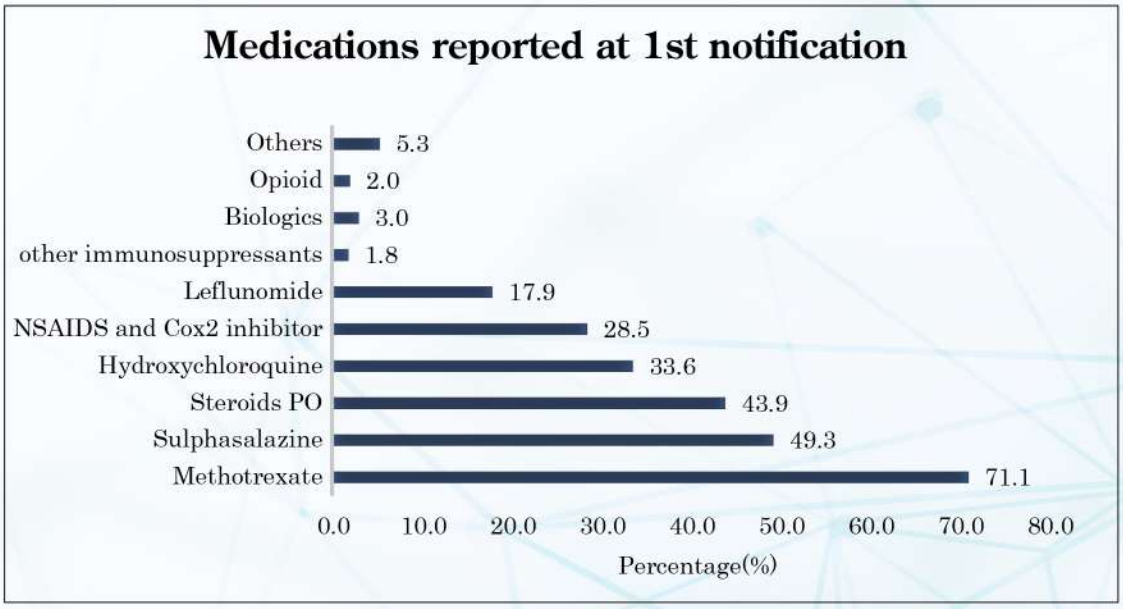


Figure 20: Types of medical therapy

Methotrexate is the commonest DMARD used followed by sulphasalazine and hydroxychloroquine.

Biologic usage in the cohort is rather low at 3%. This is partly attributed by the fact that only Infliximab, Etanercept, Adalimumab and Rituximab use are captured in the registry. The relatively newer biologics and targeted synthetic DMARDs such as Golimumab, Certolizumab, Tocilizumab and JAK inhibitors were not available when the registry was designed. The MARBLE-RA registry will be able to provide a better picture on biologic use in RA.

iii) Use of oral steroids

Oral steroids are being used in 44% of cases.

iv) Types of joint surgery

A total of 392 patients underwent joint surgery, of which, 301 had arthroplasty, while 32, 30 and 29 patients had arthrodesis, spinal surgery and synovectomy respectively.

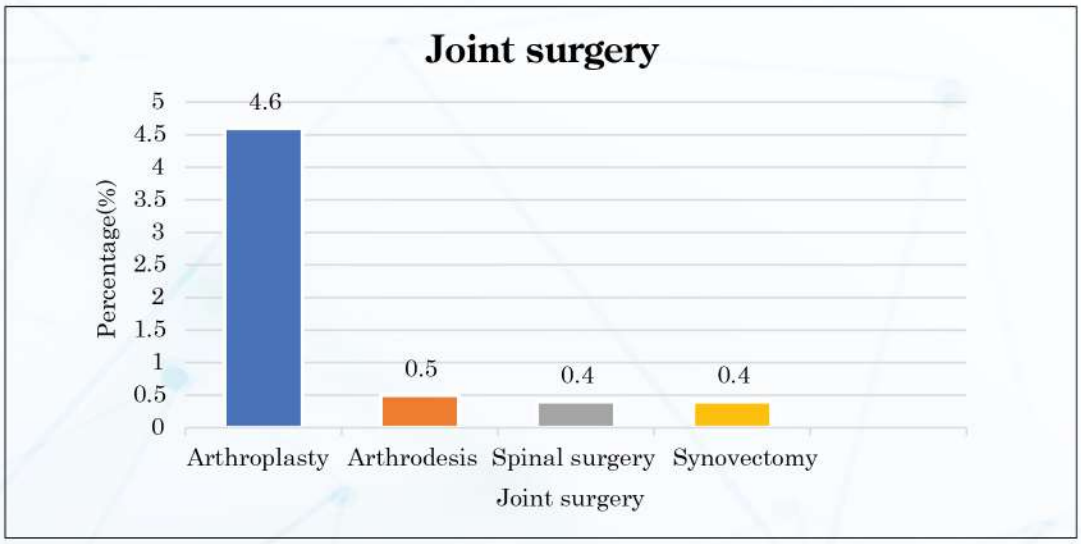


Figure 21: Types of joint surgery among RA cohort

MARBLE – RA REGISTRY

INTRODUCTION

Malaysian Rheumatology Biologic Registry (MARBLE) for RA was developed in the year 2003 with several objectives as stated below.

OBJECTIVES

1. To determine the pattern of biologic use in Rheumatoid Arthritis
2. To analyse the source of biologic funding
3. To study the prevalence of TB
4. To analyse the retention rate of biologic therapy

METHODOLOGY

Data collection was done in a standard excel database. All RA patients, above 18 years old, started on biologics from 2003 to 2019 were included in this registry, including patients who participated in clinical trials. There were no exclusion criteria.

1. NUMBER OF PATIENTS EVER ON BIOLOGICS

There was a total of 600 RA patients who received biologic therapy. However, amongst these patients, many may have received more than one biologic due to switching of therapy.

The term 'Biologic' in this report includes anti-tumour necrosis factor (anti-TNF), anti-interleukin 6 (anti-IL6), antiCD20 and targeted synthetic DMARDs.

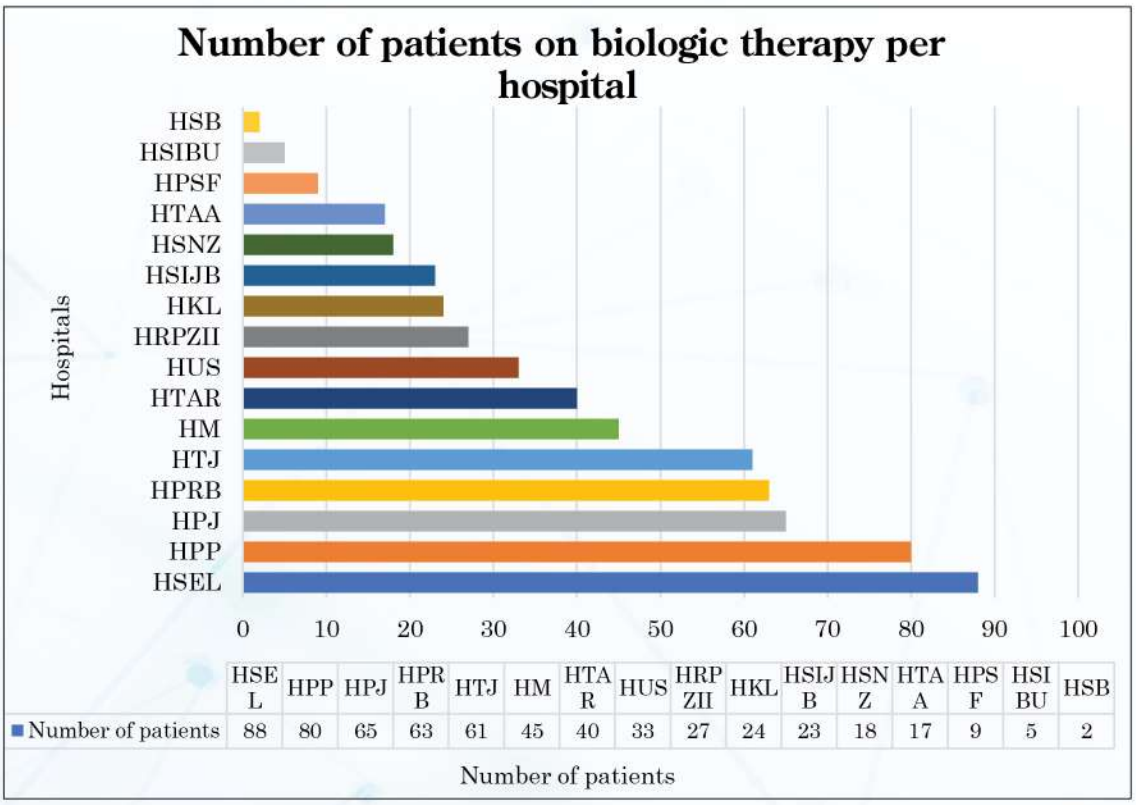


Figure 22: Number of patients on biologic therapy per hospital

The estimated usage of biologics among RA patients is about 8.5% over the last 15 years (total number of patients on biologics (n=558 – excluding two centres with unavailable data in NIAR) divided by total number of patients in NIAR). This figure is very likely an overestimation as the numbers of patients registered in NIAR is under-reported.

2. BIOLOGICS USED IN MOH HOSPITALS

Anti-TNF drugs are the commonest biologic therapy used. These group of drugs include Infliximab, Etanercept, Adalimumab, Golimumab and Certolizumab. Infliximab, Adalimumab and Etanercept were the first few anti-TNFs introduced in Malaysia. Certolizumab is no longer being marketed in Malaysia.

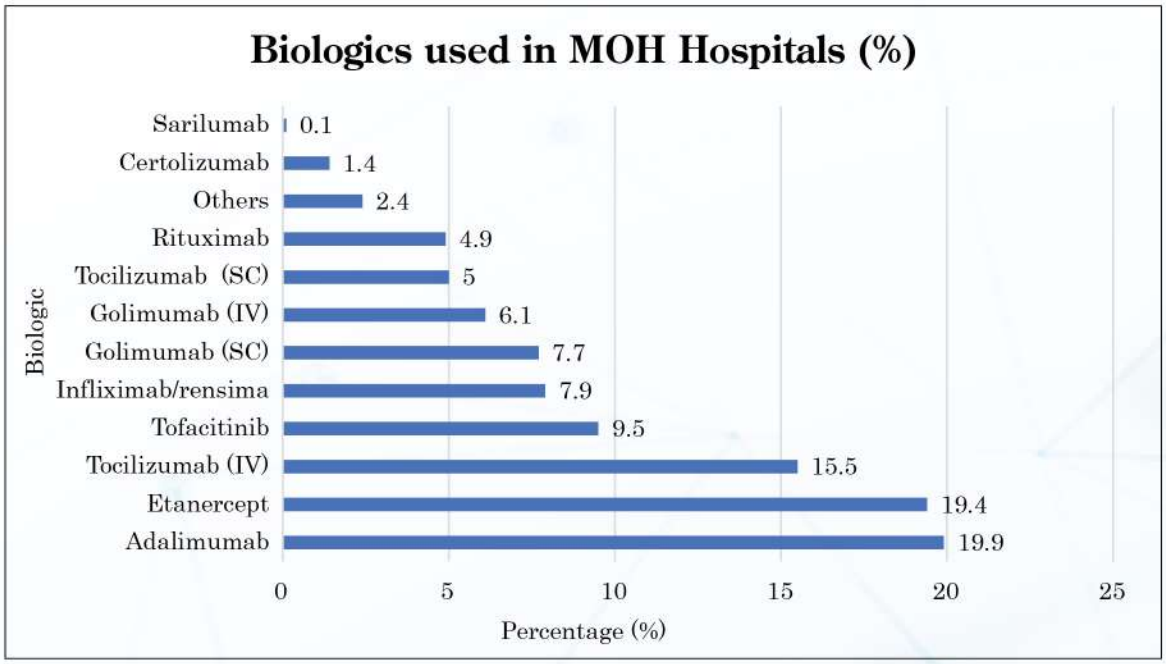
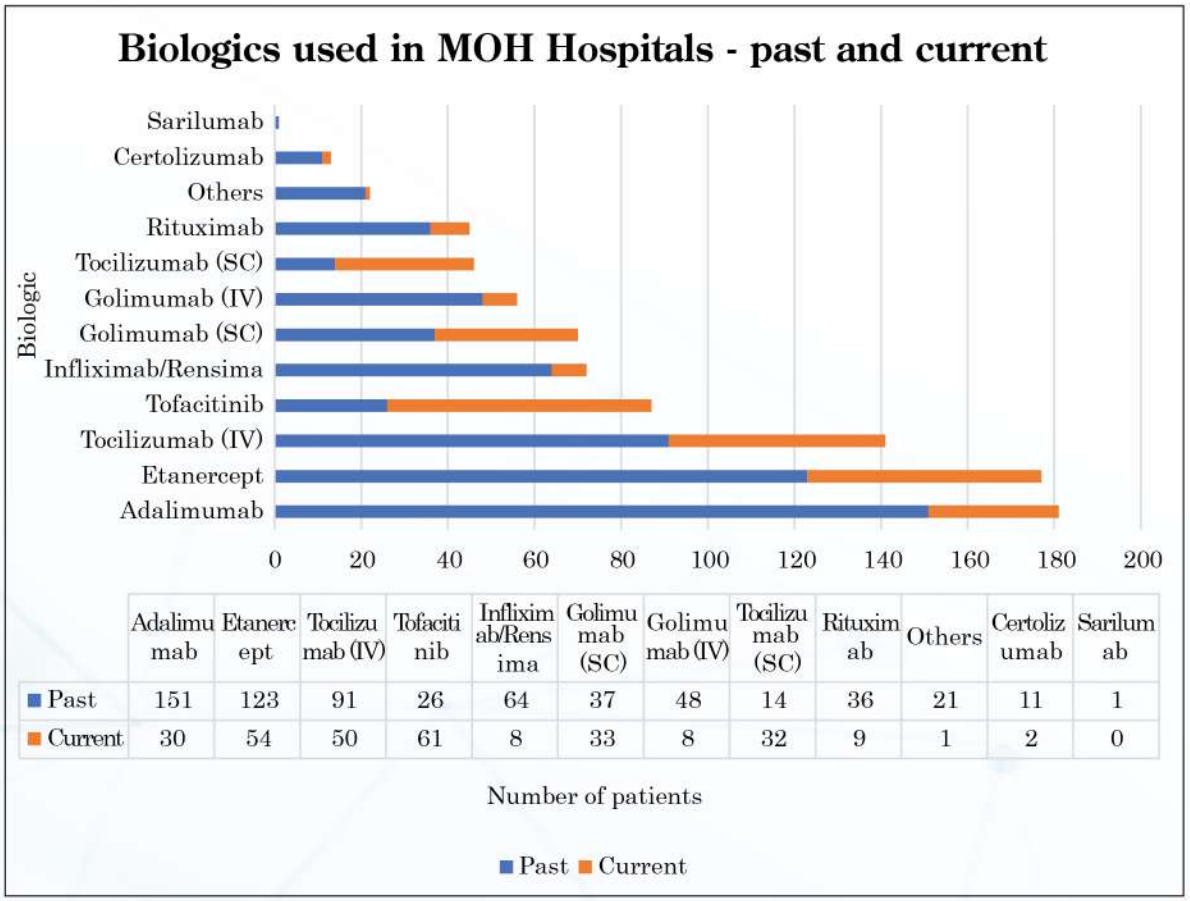


Figure 23a: Biologic therapy used in MOH hospitals

The percentage of current biologic therapy use is 2.9% (n=288). Adalimumab and etanercept were the commonest biologic used but the current use has reduced. Tocilizumab which is an anti-IL6 inhibitor was introduced in Malaysia in 2009 but has the highest overall use compared to the other biologics. This is followed by Tofacitinib, a targeted small molecule janus kinase (JAK) inhibitor which was introduced in 2015. Tofacitinib is the only oral agent available in the MOH drug formulary at present.



	Adalimumab	Etanercept	Tocilizumab (IV)	Tofacitinib	Infliximab/Rensima	Golimumab (SC)	Golimumab (IV)	Tocilizumab (SC)	Rituximab	Others	Certolizumab	Sarilumab
Past	151	123	91	26	64	37	48	14	36	21	11	1
Current	30	54	50	61	8	33	8	32	9	1	2	0

Figure 23b: Biologic therapy used in MOH hospitals – past and current

3. DURATION OF BIOLOGIC USE

Among the various biologics, there is a wide variation in the duration of biologic used. The biologic with the longest duration of use is Etanercept at 131 months, followed by Adalimumab at 113 months. For Etanercept and Adalimumab, the median duration of use was 59 (Interquartile range, IQR: 39-79) and 53 (IQR: 16-89) months respectively.

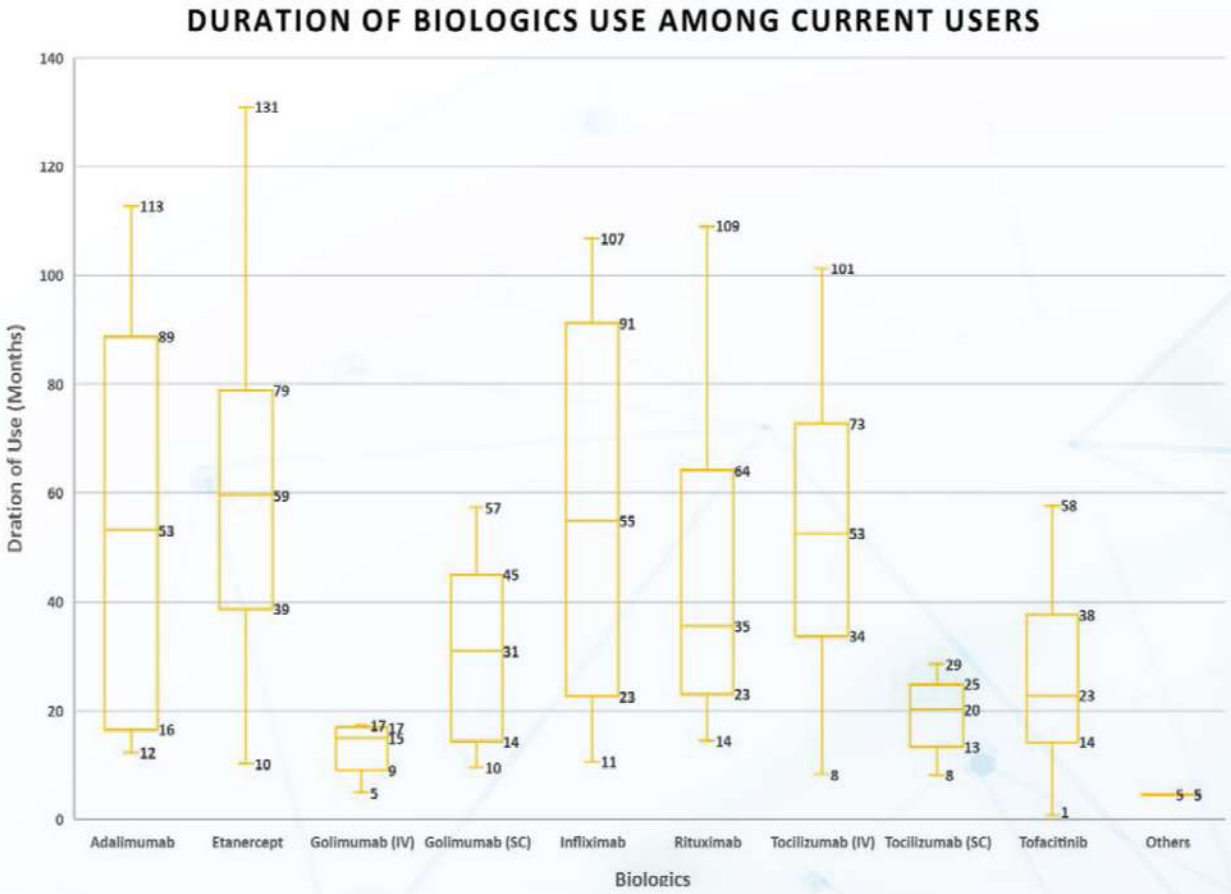


Figure 24: Duration of biologic use among current user

The shortest duration of use is less than 1 month due to adverse events. There are various reasons for cessation of biologic therapy used, which are explained in Figure 26.

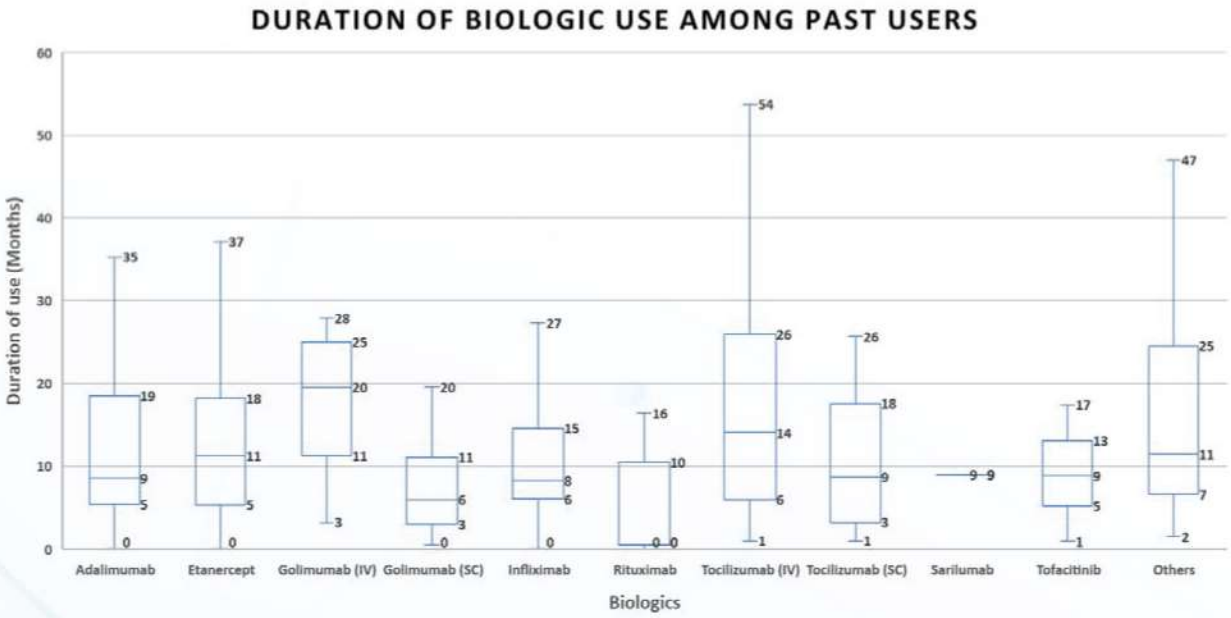


Figure 25: Duration of biologic use among past user

4. REASON FOR STOPPING BIOLOGIC THERAPY

In our cohort, 50% of patients had to stop treatment due to adverse events or inefficacy. Lack of funding contributed to nearly 15% of patients who had to stop therapy.

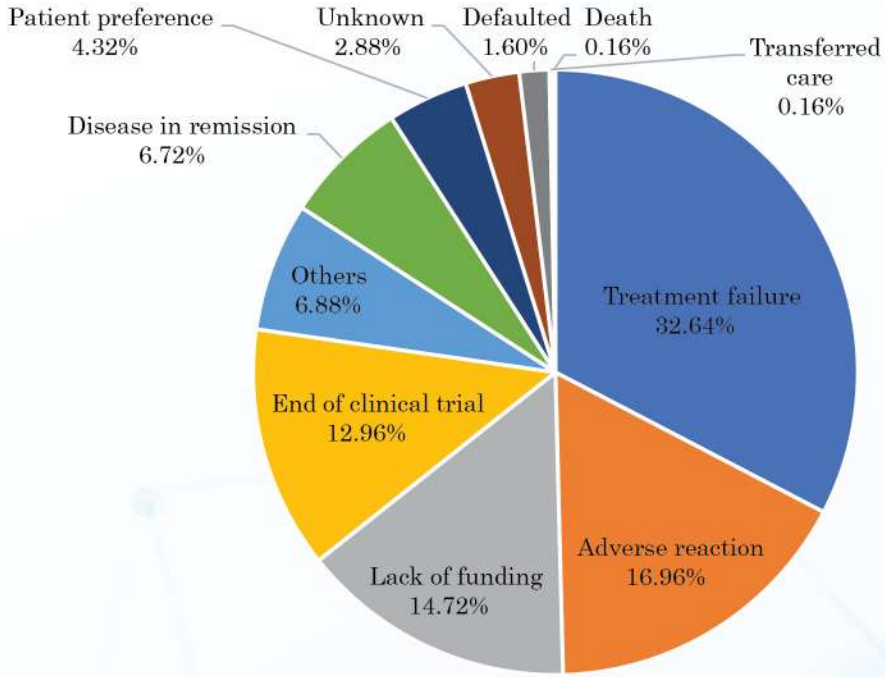


Figure 26: Reasons for stopping biologic therapy

Treatment failure includes both primary and secondary failure. Primary failure is defined as failure of patient to respond to therapy within the first 3 to 6 months from initiation whereas secondary failure is defined as loss of efficacy after the initial response to therapy. In this cohort, the percentage of treatment failure in individual biologic drugs ranges from 4.3% to 53.8%.

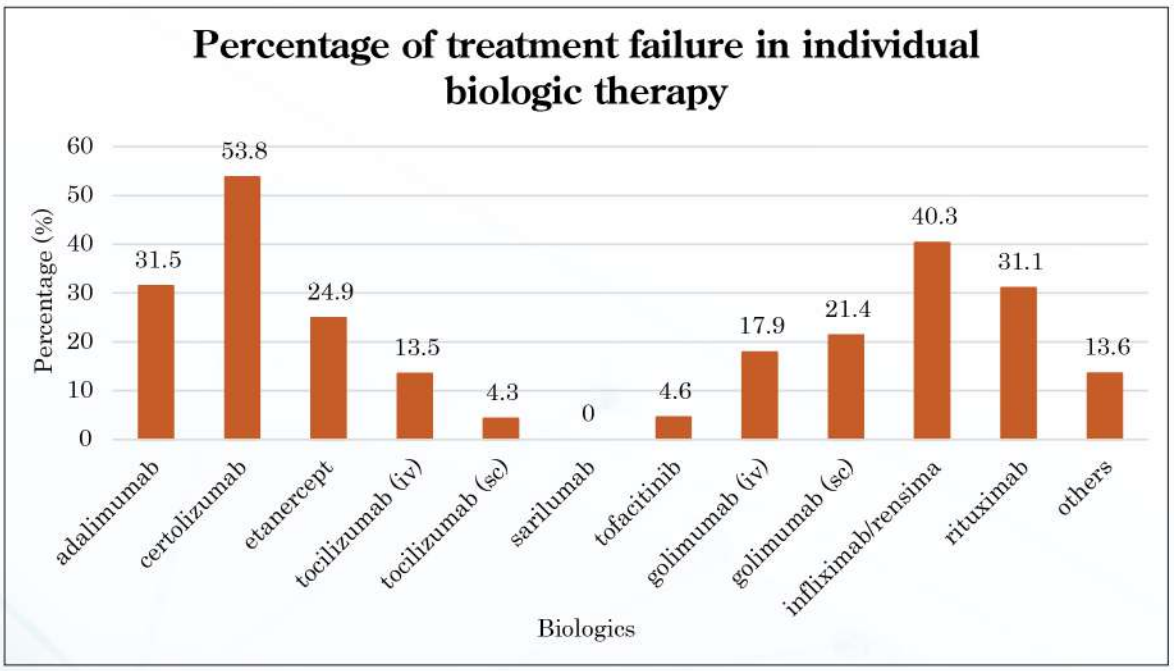


Figure 27: Treatment failure in individual biology therapy

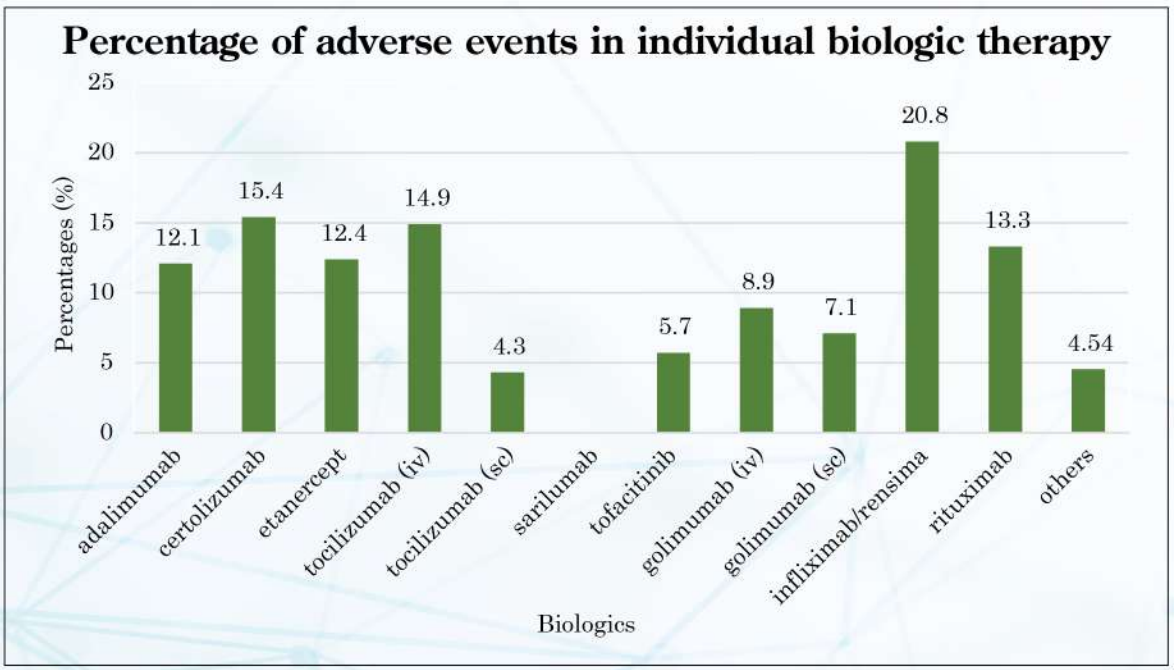


Figure 28: Adverse event in individual biologic therapy

5. SOURCE OF FUNDING FOR BIOLOGIC THERAPY

Sources of funding were mainly (62%) contributed by various government agency, for example from hospital funds, MOH Medical Relief Fund ("Tabung Bantuan Perubatan", TBP) and the Public Service Department ("Jabatan Perkhidmatan Awam", JPA). In some circumstances, an individual patient may receive funding from various sources to ensure continuity of treatment. The majority of patients are not able to afford biologic treatment with their own funds (only 1.8% self-funded), hence, they will need financial support. Only 1.7% of the patients have insurance coverage.

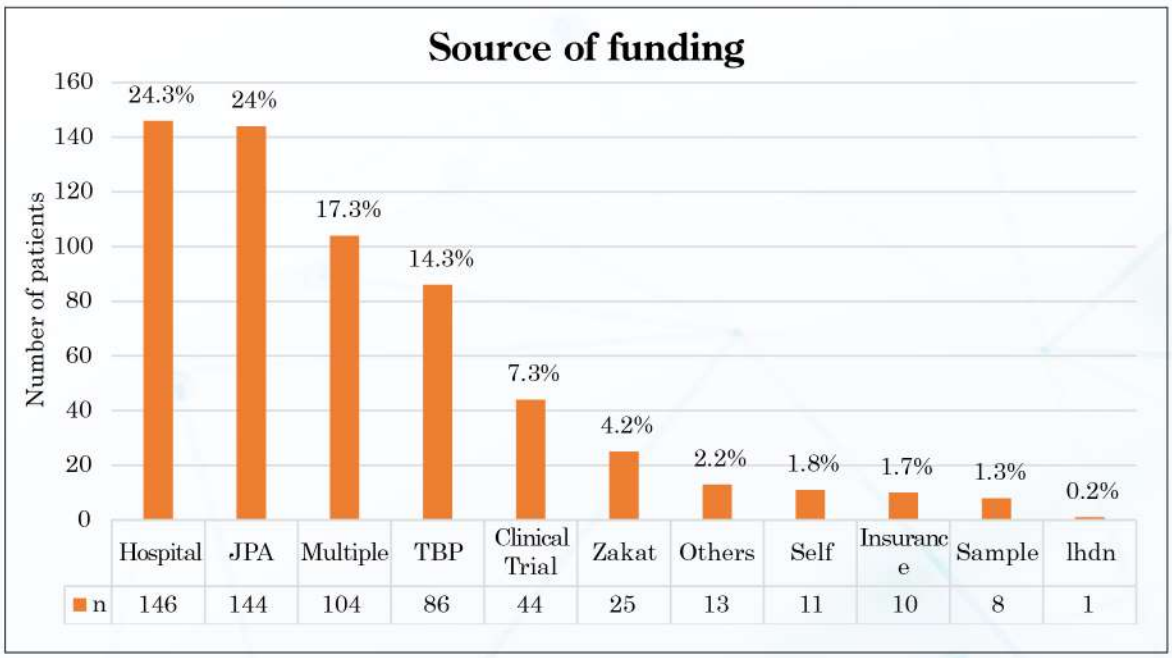


Figure 29: Source of bDMARDs funding

*lhdn – "Lembaga Hasil Dalam Negeri" (Inland Revenue Board)

Multiple sources of funding were required in 17.3% of the patients. Slightly more than half (56%) of the multiple funding sources were contributed by hospital funding, TBP and JPA, which are all government related agencies.

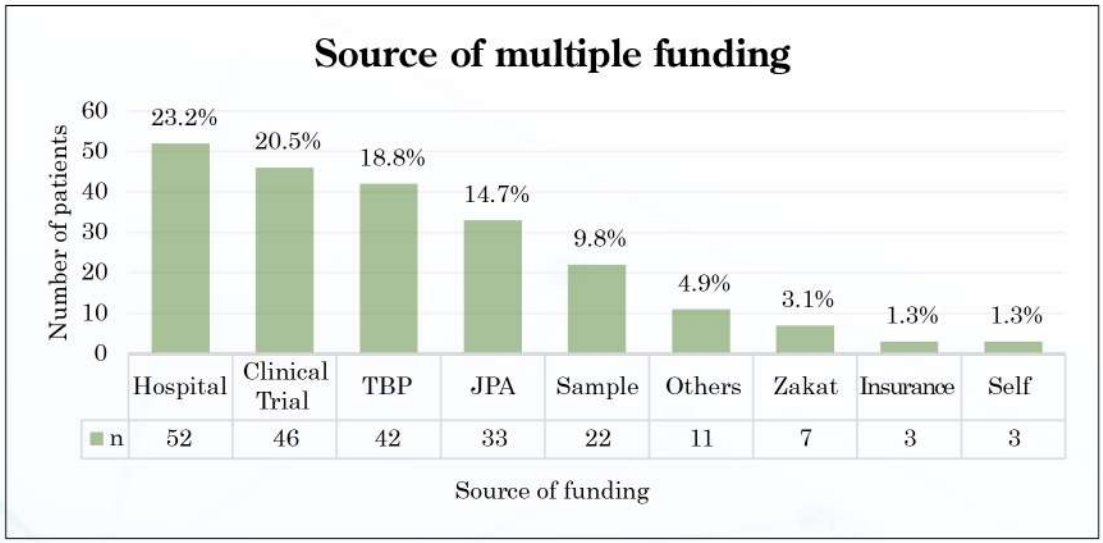
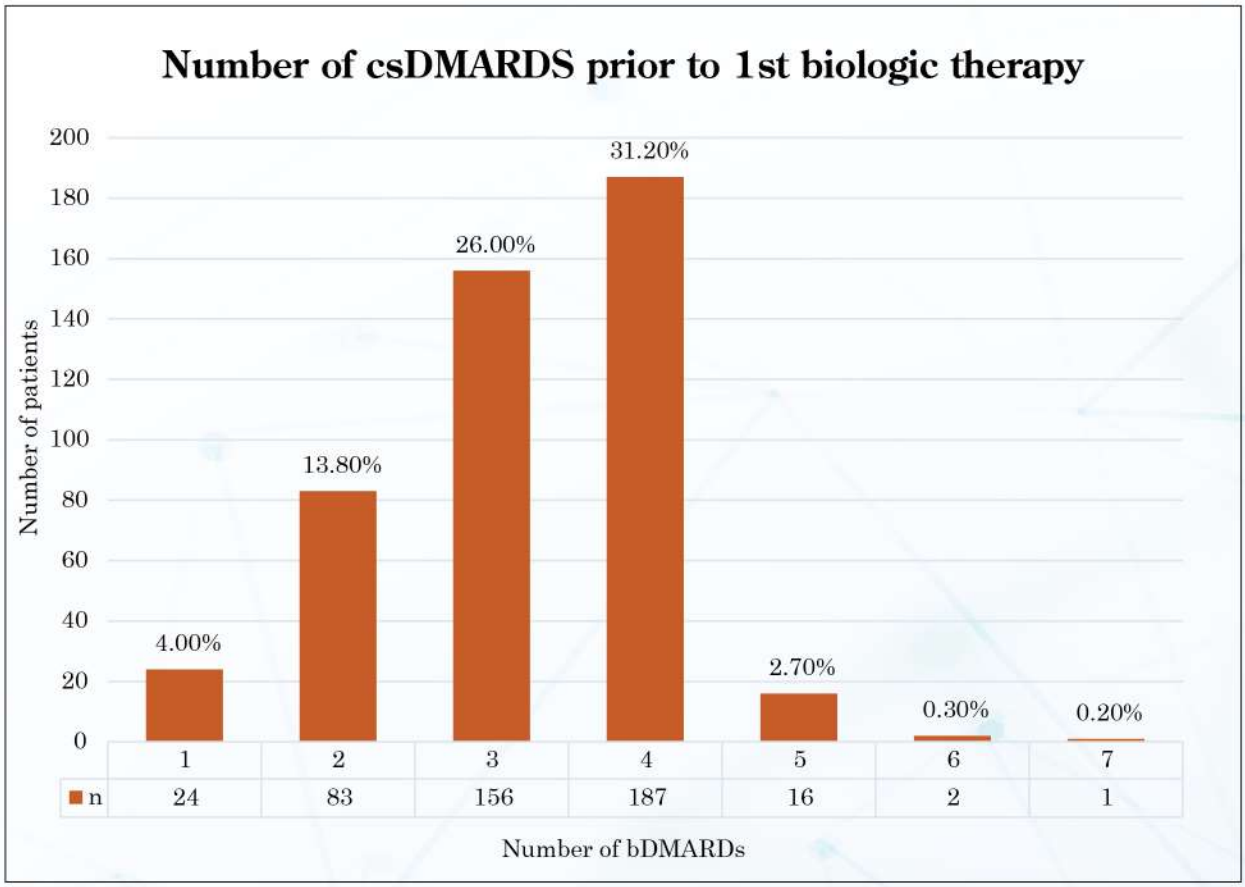


Figure 30. Source of bDMARDs multiple funding

6. NUMBER OF CONVENTIONAL SYNTHETIC DMARDS (CSDMARDS) EVER USED PRIOR TO FIRST BIOLOGIC DMARDS (BDMARDS)

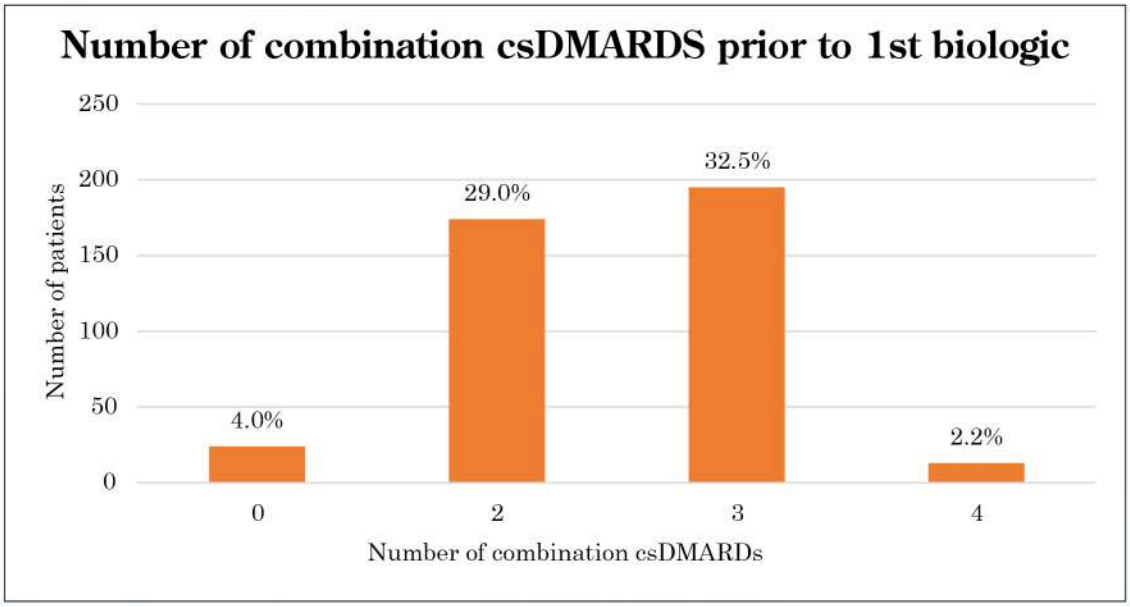
Slightly over 60% of patients had already failed or were intolerant to at least 3 csDMARDs.



Note: 21.8% missing data

Figure 31: Number of csDMARDS ever used prior to 1st biologic therapy

The majority of patients were on 2 to 3 combination csDMARD prior to the 1st biologic therapy. The usual combinations used are triple therapy with Methotrexate, Sulphasalazine and Hydroxychlroquine. Methotrexate and Leflunomide or Sulphasalazine is also a common combination. However, other combinations may also be utilised.



Note: 32.3% missing data

Figure 32: Number of combination csDMARDS prior to 1st biologics

7. PREVALENCE OF TB ON BIOLOGICS

There were 16 cases (2.8%) of TB in the MARBLE registry (n=600), of which 13 cases were pulmonary TB (PTB) and the other 3 were extrapulmonary TB. Of the 16 cases, 6 patients were on anti-TNF, 5 on tocilizumab and 2 on rituximab. The median time of TB diagnosis after exposure to biologics was 13 (range 1.5-74) months for anti-TNF and 7 (range 4.5-44) months for tocilizumab. Patients who were on Rituximab developed TB 5-8 months after the first cycle of Rituximab and both of them had prior exposure to anti-TNF approximately 17-24 months before the diagnosis of TB. There were no deaths due to TB.

DISCUSSION

NIAR began in 2009 with just 3 participating hospitals and has now expanded to 16 participating hospitals with rheumatology services over the last 10 years. The numbers captured in this registry may not reflect the actual numbers of RA patients in Malaysia because patients included are only limited to MOH hospitals. Furthermore, it is also not reflective of the actual numbers of patients at MOH hospitals because of under-reporting. Factors contributing to under-reporting includes non-mandatory notification, newer rheumatology centres, and limited resources at the hospital level. Thus, true national prevalence and incidence of RA cannot be calculated.

There was an increasing trend in the numbers of newly diagnosed RA patients with time, consistent with increased disease awareness and expanding rheumatology services across the country. Nevertheless, the numbers seemed to plateau after 2010 which could possibly be due to plateauing of incidence and under-reporting.

Malaysia consists of a multi-ethnic population with 3 major ethnic groups i.e. Malay, Chinese and Indians. Similar to our 2009 report, the Indians are over-represented even after including other ethnic groups from Sabah and Sarawak. Data from the Department of Statistics showing current population estimates in 2019 indicate that Indians comprise 6.9% of the population (Department of Statistics Malaysia 2020). The percentage of Indian patients in this registry is 20%. This could be explained by various factors including, relatively more Indian patients who seek treatment from public hospitals or higher prevalence of RA among Indians. Additional studies will be needed to look into whether there is ethnic preponderance contributing to the development of RA.

RA is more prevalent in women with 6:1 female to male ratio. The peak age of diagnosis in this registry cohort is in the 50s, and the onset of symptom peaks in the 40s which is the prime age in terms of work productivity. Thus, these patients need to be diagnosed and treated early to prevent disability so that they will be able to contribute to the economy.

Malaysia is classified by the World Bank as an upper middle-income country. The Department of Statistics Malaysia has revised the national Poverty Line Income (PLI) in 2019 under the 11th Malaysia Plan from RM 908 to RM 2208 in July 2019 (The Star 2020). Hence, nearly half of the patients in the registry cohort fall under the National Poverty Line.

DISCUSSION

Seventy percent of the patients have secondary education level and below. Almost half are earning RM3000 and below while 16.6% are earning below RM1000, which falls under the hard-core poverty category. Majority do not have any medical insurance. This poses a challenge when advanced therapy is needed and may also affect other issues including compliance to therapy and access to health services. Malaysia has an excellent healthcare system where everyone has access to good healthcare services irrespective of their socioeconomic background. The public health care system consists of primary health care centres, secondary and tertiary hospitals which are tax-funded. Patients with poor socioeconomic background are provided with easily accessible and good healthcare.

Despite this, there are limitations with availability of certain therapies in view of the cost of certain expensive drugs which are necessary to treat patients to achieve low disease activity or remission, consistent with international standards.

Patients who are from lower socio-economic background may also have other difficulties that prevent them from accessing available healthcare services. They may not be able to afford transportation or take time off work to keep to their hospital appointments due to financial limitations. Hence, social welfare and health support services also need to be enhanced at the community and hospital level.

Primary care doctors play an important role in identifying inflammatory arthritis at initial presentation. In our cohort, 41.7% of patients were diagnosed within 6 months of the onset of symptoms in keeping with early diagnosis. However, less than 20% of patients with RA were seen by a rheumatologist within 6 months of their symptoms. Early diagnosis and treatment can affect disease course, prevent the development of joint erosions or retard progression of erosive disease (Finckh A 2006) (Goekoop-Ruiterman YP 2007). Hence, early referral of RA patients for specialised rheumatology care is of utmost importance.

Hospitals with Rheumatology services in this country are limited to the main hospital of each state except in the Klang Valley where there are 5 major hospitals providing this tertiary service. Rheumatic diseases are generally rare diseases, with patients needing specialised care. In order to maximise the utilisation of human and financial resources, specialised rheumatology services at designated major centres should be provided. However, for patients to access the care, services at the community level also needs to be developed. This may be complemented by the service provided by rheumatology specialist nurses.

DISCUSSION

The commonest presentation of these patients include symmetrical arthritis, more than 3 joints arthritis, early morning stiffness and involvement of the wrist and small joints of the hands. Two thirds of the patients have positive Rheumatoid factor and slightly more than a third have radiological changes. The 1987 ACR revised criteria for the classification of RA was developed using a population of RA patients with established disease. In our cohort, approximately 74% of patients fulfilled the criteria at diagnosis. The 1987 ACR classification criteria may fail to diagnose some patients with early RA who might benefit most from the initiation of early, aggressive treatment. The newer EULAR-ACR criteria for RA diagnosis will be able to capture early RA patients that would benefit early therapeutic intervention to prevent structural damage and permanent functional limitation (Aletaha D 2010). This criteria has been included in the revised MyNIAR registry.

Comorbidities have been shown to be common among RA patients (Michaud K 2007). More than two thirds of patients in this cohort have associated comorbidities. This is not surprising, since nearly 75% of the patients in this cohort are over 50 years of age. Hypertension is the most prevalent comorbidity among RA population followed by hyperlipidaemia and diabetes mellitus. Prevalence rates of hypertension (38.4%) and hyperlipidaemia (29.5%) are both much higher than the national prevalence of 15.9% and 13.5% respectively for adult population above 18 years old in the 2019 National Health and Morbidity Survey (NHMS 2019). The prevalence rate of diabetes mellitus is also higher at 16.6% compared to the national rate in the NHMS survey which is 9.4% (NHMS 2019).

Patients with RA have a modest increased risk of overall malignancy as well as an increased risk of lung cancer and lymphoma when compared with the general population (Simon TA 2015). Prevalence of malignancy among our RA patients is 1.4%. This corresponds to the incidence rate of 0.14 per 100 patient years which is lower than the reported incidence rate of malignancy among RA patients globally. The crude incidence rate of malignancy in 5 other RA registries is estimated at 0.6-1.3 per 100 patient years (Simon TA 2015). The commonest malignancy reported was breast cancer and cancers of the female reproductive organs. Hence, screening for these cancers should be encouraged among RA patients.

Sub-analysis on disease outcome showed that 38% achieved low disease activity or remission at first notification which is the primary target. However, 56% of the patients still have moderate to high disease activity and half of them have been diagnosed with RA for more than 4 years. Timely referral to rheumatologist for specialised management plan may improve patients' outcome. More in depth study may need to be undertaken to look into the factors contributing to poor RA control in this group.

CsDMARDs are the first line of therapy in RA and should be commenced as soon as the diagnosis of RA is established. More than three quarter of the patients

DISCUSSION

were initiated on DMARDs within the first month of diagnosis in keeping with standard guidelines. Methotrexate being the gold standard csDMARD is being used in 71% of cases. Other DMARDs used include Sulphasalazine, Hydroxychloroquine and Leflunomide. Oral steroid use was common at 44% and may have been used as bridging therapy (short-term use at initiation of csDMARDs) or during flares.

Biologic usage is rather low at 3%. This is partly attributed by the fact that only Infliximab, Etanercept, Adalimumab and Rituximab use are captured in the registry. The relatively newer biologics such as Golimumab, Certolizumab, Tocilizumab and JAK inhibitors were not available when the registry was designed.

The MARBLE-RA registry was initiated to collect data regarding the use of all available biologics in Malaysia in RA patients.

The numbers of biologic use per hospital varies depending on the duration of rheumatology service in that particular hospital and availability of funding resources. Although Infliximab, a chimeric monoclonal antibody was the first biologic introduced in Malaysia but the usage is currently reducing in favour of the genetically engineered fully humanized biologic therapy available currently.

A significant number of patients discontinued bDMARD due to adverse events or inefficacy. This is higher than rates reported in another study, in which 30–40% of bDMARD treated patients experience drug discontinuation due to inefficacy or adverse events (Favalli EG 2017). The current bDMARD consensus in Malaysia requires the use of at least 2 csDMARDs sequentially or in combination before being eligible for bDMARD therapy. However, more than half of the patients received more than 2 csDMARDs while a third of the patients were on 3 combination csDMARDs before receiving a bDMARD.

Tuberculosis was reported in 1.6% of RA patients in the NIAR cohort. This figure is much higher than the national TB prevalence rate of 92 cases per 100,000 population (The World Bank 2020). Possible reasons for the increased prevalence may be related to the underlying disease, treatment or patients' comorbidities.

Of concern, the prevalence of TB in the MARBLE cohort was even higher at 2.8% despite TB screening protocol prior to initiation of bDMARD. All patients are screened for TB prior to biologic initiation, with Chest X-ray, TB Quantiferon test and/or Mantoux test. Patients with latent TB are treated with at least 2 to 4 weeks of Isoniazid prior to initiation of biologic therapy and treatment is generally continued for 6-9 months. Thus, further studies are needed to analyse the factors associated with TB prevalence in RA patients.

CONCLUSIONS

NIAR AND MARBLE registries provide valuable insight on the burden of RA and its management in Malaysia. The registry highlights several findings, including the low usage of biologics compared to developed countries, low socio-economic background, delayed diagnosis and higher TB prevalence. The low usage of biologic is partly contributed by patients' low socio-economic background who are very dependent on government funding. Thus, an alternative source of funding such as the introduction of an insurance scheme will hopefully provide better access to healthcare services. Early diagnosis is crucial for the institution of early treatment to prevent deformity and improve patient's functional outcome. Hence, community based services as well as subspecialised care at the hospitals are essential to provide optimal care. TB is a major concern for patients on biologic therapy in a TB endemic country like Malaysia. Stringent screening and close monitoring for TB infection needs to be implemented to reduce the incidence of TB whilst on biologic therapy.

This registry has provided valuable but limited data as it included patients in public hospitals only. A comprehensive registry would require participation from all hospitals, including institutions from private and universities. Thus, in order to achieve this goal, cooperation and support from all relevant stakeholders are vital.

BIBLIOGRAPHY

Aletaha D, Neogi T et al. 2010. "Rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against RHeumatism collaborative initiative." Arthritis and Rheumatism 62: 2569-81.

Bathon J, Tehlirian C. 2008. "Rheumatoid arthritis clinical and laboratory manifestations ." In Primer on the Rheumatic Diseases, by Stone JH, Croffort LJ et al. Klippel JH, edited by Stone JH, Croffort LJ et al. Klippel JH, 114-121. New York: Springer.

Department of Statistics Malaysia. 2020. Department of Statistics Malaysia Official Portal. July 15. Accessed August 01, 2020. https://www.dosm.gov.my/v1/index.php?r=column/cthemeByCat&cat=155&bul_id=OVByWjg5YkQ3MWFZRTN5bDJiaEVHZz09&menu_id=.

Favalli EG, Raimondo MG et al. 2017. "The management of first-line biologic therapy failures in rheumatoid arthritis: Current practice and future perspectives." Autoimmunity Reviews 16 (12): 1185-1195.

Finckh A, Liang MH et al. 2006. "Long-term impact of early treatment on radiographic progression in rheumatoid arthritis: A meta-analysis. ." Arthritis and Rheumatism (55): 864-72.

Goekoop-Ruiterman YP, de Vries-Bouwstra JK et al. 2007. "Comparison of treatment strategies in early rheumatoid arthritis: a randomized trial." Annals of Internal Medicine (146): 406-15.

Michaud K, Wolfe F, et al. 2007. "Comorbidities in rheumatoid arthritis." Best Practice & Research Clinical Rheumatology 21 (5): 885-906.

NHMS. 2019. Vol I: Non-communicable diseases, risk factors and other health problems. Survey, KL: National Institute of Health, Ministry of Health Malaysia.

Simon TA, Thompson A et al. 2015. "Incidence of malignancy in adult patients with rheumatoid arthritis." Arthritis Research & Therapy 17: 212.

The Star. 2020. Govt revises poverty line income from RM980 to RM2,208. July 07. Accessed August 01, 2020. https://www.thestart.com.my/news/nation/2020/07/10/.

The World Bank. 2020. Incidence of tuberculosis (per 100,000 people). Jan 01. Accessed August 01, 2020. https://data.worldbank.org/indicator/SH.TBS.INCD.

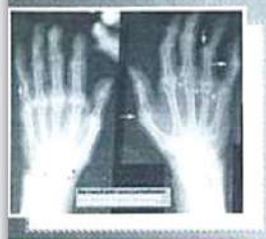
ABBREVIATION

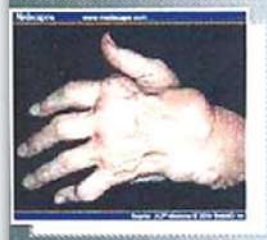
AA	:	Atlanto-axial
ACR	:	American College of Rheumatology
anti-IL6	:	Anti-Interleukin 6
Anti-TNF	:	Anti-Tumour Necrosis Factor-alpha
AZA	:	Azathioprine
bDMARDs	:	biologic Disease Modifying Anti Rheumatic Drugs
COX-2	:	Cyclooxygenase 2
CRF	:	Case Report Form
CRP	:	C-Reactive Protein
csDMARDs	:	conventional synthetic Disease Modifying Anti Rheumatic Drugs
DMARDS	:	Disease Modifying Anti Rheumatic Drugs
ESR	:	Erythrocyte Sedimentation Rate
HCQ	:	Hydroxychloroquine
HKL	:	Hospital Kuala Lumpur
HM	:	Hospital Melaka
HPJ	:	Hospital Putrajaya
HPP	:	Hospital Pulau Pinang
HPSF	:	Hospital Pakar Sultanah Fatimah
HQE	:	Hospital Queen Elizabeth, Kota Kinabalu
HRPB	:	Hospital Raja Permaisuri Bainun, Ipoh
HRPZII	:	Hospital Raja Perempuan Zainab II, Kota Bharu
HSB	:	Hospital Sultanah Bahiyah, Alor Setar
HSEL	:	Hospital Selayang
HSIBU	:	Hospital Sibu
HSIJB	:	Hospital Sultan Ismail, Johor Bharu
HSNZ	:	Hospital Sulatanah Nur Zahirah, Kuala Terenggan
HTAA	:	Hospital Tengku Ampuan Afzan
HTAR	:	Hospital Tengku Ampuan Rahimah, Klang
HTJ	:	Hospital Tuanku Ja'afar
HUS	:	Hospital Umum Sarawak
MTX	:	Methotrexate
NSAIDS	:	Non Steroidal Anti-Inflammatory Drugs
RA	:	Rheumatoid Arthritis
SSZ	:	Sulphasalazine

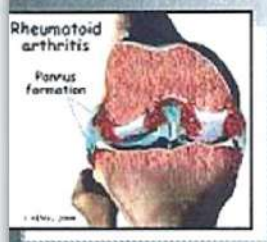
PATIENT CONFIDENTIALITY

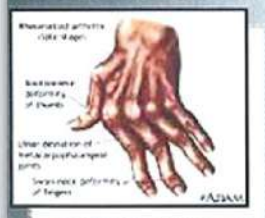
REGISTRI INFLAMASI ARTHRITIS MALAYSIA
NATIONAL INFLAMMATORY ARTHRITIS REGISTRY
(NIAR)

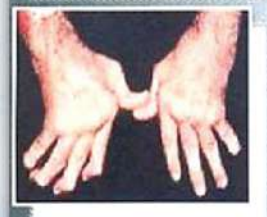
ARTHRITIS FOUNDATION, MALAYSIA











MAKLUMAT KERAHSIAAN PESAKIT

- Niar telah ditubuhkan untuk memantau rawatan bagi pesakit Arthritis Reumatoid serta kesannya.
- Tujuannya adalah untuk meningkatkan taraf penjagaan pesakit.
- Klinik Reumatologi ini turut menyertai registri ini.
- Dalam tempoh penjagaan dan rawatan, kami akan mengumpul maklumat peribadi dan klinikal anda. Ini bertujuan untuk mengurus dan merancang penjagaan kesihatan anda. Maklumat ini berguna untuk menilai kualiti penjagaan yang disediakan serta membantu menaiktaraf perkhidmatan kami.
- Adalah mustahak untuk anda mengetahui bahawa maklumat peribadi dan klinikal anda akan digunakan bagi tujuan ini. NIAR mengamalkan polisi kerahsiaan maklumat pesakit mengikut taraf keselamatan piawaian kebangsaan dan antarabangsa. Tiada maklumat peribadi yang mengenalpasti pesakit akan didedahkan.
- Anda berhak untuk tidak berkongsi maklumat anda dengan NIAR. Sila berunding dengan doktor
- anda untuk maklumat lanjut mengenai registri ini sekiranya anda mempunyai sebarang keraguan.
- Kerjasama dan sumbangan anda amat dihargai.

INFORMATION ON PATIENT CONFIDENTIALITY

- NIAR was started to monitor treatment for Rheumatoid Arthritis and its outcomes.
- The aim is to improve patient care.
- This Rheumatology Clinic participates in NIAR.
- In the course of your care, we collect information about you and your treatment. We use this mainly to plan and manage your care. Some of the information will also be used to measure the quality of care we provide and to carry out work aimed at improving our care and services.
- It is important that you know that your data is being used in this way. NIAR observes strict policies and practices to assure confidentiality that comply with both national and international security standards. No information is published which identifies individual patients.
- You have the right not to share your information with NIAR. Please ask your doctor for more information if you have any doubts on NIAR.
- We appreciate your cooperation and understanding.

Untuk maklumat lanjut, sila hubungi NIAR di:
For further information, please contact NIAR at:

No Telefon/Phone No :03-61203233 ext 4169/4181
No Fax/Fax No :03-61202761
Laman Web/Website :https://app.acrm.org.my/NIAR

NATIONAL INFLAMMATORY ARTHRITIS REGISTRY (NIAR-RA) NOTIFICATION FORM

For Office Use only:
ID: /
Centre:

Instruction: Where check boxes ☐ are provided, check (√) one or more boxes. Where radio buttons ◉ are provided, check (√) one box only.

I. Centre Code: ☐☐☐☐ **Or Reporting centre name:**

II. Date of Notification : (dd/mm/yyyy) ☐☐/☐☐/☐☐☐☐

III. Date 1st visit to rheumatologist: (dd/mm/yyyy) ☐☐/☐☐/☐☐☐☐

SECTION 1 : PATIENT DETAILS & DEMOGRAPHICS

1. Name : * *(Please print in capital letters)*

2. NRIC : *

MyKad/ MyKid: ☐☐☐☐☐☐-☐☐-☐☐☐☐ OR Old IC ☐☐☐☐☐☐☐☐☐☐

Other ID document No:

Specify document type (if others): ◉ Passport ◉ Armed Force ID ◉ Unregistered ◉ Birth Certificate ◉ Police ID ◉ Others

3. Address:

Postcode: ☐☐☐☐ Town / City:

State : ◉ Johor Darul Takzim ◉ Kedah Darul Aman ◉ Kelantan Darul Naim ◉ Melaka ◉ Negeri Sembilan Darul Khusus ◉ Pahang Darul Makmur ◉ Perak Darul Ridzuan ◉ Perlis Indera Kayangan ◉ Pulau Pinang ◉ Sabah ◉ Sarawak ◉ Selangor Darul Ehsan ◉ Terengganu Darul Iman ◉ Wilayah Persekutuan Kuala Lumpur ◉ Wilayah Persekutuan Labuan, Sabah ◉ Wilayah Persekutuan Putrajaya, Selangor ◉ Not applicable - Foreign

4. Contact number: Homephone: ☐☐☐-☐☐☐☐☐☐☐☐ OR H/P: ☐☐☐-☐☐☐☐☐☐☐

5. Gender * ◉ Male ◉ Female

6. Marital status: ◉ Married ◉ Single ◉ Divorced ◉ Widowed

7. Date of Birth: * (dd/mm/yyyy) ☐☐/☐☐/☐☐☐☐ ☐ Estimated/presumed year (autofill if MyKad is available)

If the exact date is not known, please enter 01/07/yyyy & check the estimated year box

8. Age: (autocalculated) ☐☐

9. Ethnic group: *

◉ Malay ◉ Punjabi ◉ Melanau ◉ Bidayuh ◉ Other Malaysian, specify : ◉ Foreigner, specify country :
◉ Chinese ◉ Orang Asli ◉ Murut ◉ Iban
◉ Indian ◉ Kadazan Dusun ◉ Bajau ◉ Orang Ulu ◉ Unknown

SECTION 2 : NEXT OF KIN, EDUCATION, OCCUPATION

1. Next of kin

i.Name:

ii.Contact no.: Telephone:: ☐☐☐-☐☐☐☐☐☐☐ H/P: ☐☐☐-☐☐☐☐☐☐☐

iii.Relationship: → ◉ Parents ◉ Spouse ◉ Children ◉ Siblings ◉ Cousins ◉ Others, specify:

2. Education level : * ◉ No formal education ◉ Primary ◉ Secondary ◉ Tertiary ◉ Unknown

3. Work status: *

◉ Full-time ◉ Retrenched ◉ Part-time → ◉ Retired ◉ Homemaker ◉ Unemployed →

Reason: ☐ Due to disease ☐ Due to family circumstances ☐ Unknown

4. Current occupation : *

◉ Legislator senior officials, managers
◉ Technicians, associate professionals
◉ Service workers, shop and market sales workers
◉ Craft and related trades workers
◉ Elementary occupations
◉ Professionals
◉ Clerical workers
◉ Skilled agricultural, fishery workers
◉ Plant and machine operators and assemblers
◉ Homemaker
◉ Others, specify:
◉ Unknown ◉ Not Applicable

→ ◉ Government ◉ Private Sector ◉ Not Applicable ◉ Unknown

5. Date of last employment: 01/☐☐/☐☐☐☐ dd/mm/yyyy ☐ Unknown

6. Days of sick leave taken due to Inflammatory Arthritides for the past 3 months: ☐☐ ☐ Unknown

7. Household income (RM): *

◉ Less than RM1000 ◉ RM1001 - RM3000 ◉ RM3001 - RM5000 ◉ RM5001 - RM7000 ◉ Above RM7000 ◉ No income → ◉ Unknown

On social welfare: ◉ Yes ◉ No ◉ Unknown

8. Has personal medical insurance? * ◉ Yes ◉ No ◉ Unknown

SECTION 3 : DIAGNOSIS

1. Diagnosis: *

☐ Rheumatoid Arthritis + ☐ Psoriatic Arthritis ☐ Other inflammatory arthritides
☐ Ankylosing Spondylitis ☐ Juvenile Idiopathic Arthritis (irrespective of pattern)

+If Diagnosis = Rheumatoid Arthritis, kindly proceed to complete this form from Page 1b to 4.

NATIONAL INFLAMMATORY ARTHRITIS REGISTRY (NIAR-RA) NOTIFICATION FORM

For Office Use only:
ID: /
Centre:

Instruction: Where check boxes ☐ are provided, check (√) one or more boxes. Where radio buttons ◉ are provided, check (√) one box only.

(Patient identifier for paper CRF)

I. Patient Name: NRIC Number:

II. Centre Code: Or Reporting centre name:

SECTION 4: DIAGNOSIS CRITERIA

1. 1987 ACR * Criteria:	a. Morning stiffness > 1 hour	◉ Yes	◉ No	◉ Unknown
	b. ≥ 3 joints arthritis	◉ Yes	◉ No	◉ Unknown
	c. Arthritis in a wrist, MCP or PIP joint	◉ Yes	◉ No	◉ Unknown
	d. Symmetrical arthritis	◉ Yes	◉ No	◉ Unknown
	e. Rheumatoid nodules	◉ Yes	◉ No	◉ Unknown
	f. Positive Rheumatoid factor	◉ Yes	◉ No	◉ Unknown
	g. Erosions or osteopenia on hand or wrist radiograph	◉ Yes	◉ No	◉ Unknown

2. Date of * diagnosis: (dd/mm/yyyy) / /

3. Date of onset * of symptom: (dd/mm/yyyy) / /

4. Date first Disease * Modifying Anti-rheumatic Drug (DMARD):(dd/mm/yyyy) / / ☐ Not applicable

If the exact date is not known, please enter 01/01/yyyy

SECTION 5: COMORBID CONDITIONS

1. Comorbid conditions: *

◉ No ◉ Yes →

- ☐ Hypertension
- ☐ Hyperlipidaemia
- ☐ Diabetes Mellitus
- ☐ Ischaemic Heart Disease (IHD)
- ☐ CVA
- ☐ Peptic Ulcer Disease
- ☐ Malignancy → Type:
  - ◉ Hematology → ◉ Leukemia ◉ Lymphoma
  - ◉ Others → ◉ Lung ◉ Stomach ◉ Uterus/Ovary ◉ Breast ◉ CNS ◉ Bladder ◉ Colorectal ◉ Liver ◉ Skin ◉ Endocrinological ◉ ENT ◉ Others, specify
  - ◉ Unknown
- ☐ Hepatitis B
- ☐ Hepatitis C
- ☐ Fatty Liver
- ☐ Renal Impairment
- ☐ Osteoporosis
- ☐ TB
- ☐ Others, specify

SECTION 6: EXTRA- ARTICULAR FEATURES

1. Extra-articular features: *

◉ No ◉ Yes →

- ☐ Fever
- ☐ Rheumatoid nodules (autofill)
- ☐ Eye inflammation
- ☐ Sicca → ◉ Eye ◉ Oral Cavity ◉ Both
- ☐ Pleural effusion
- ☐ Interstitial lung disease
- ☐ Pericarditis/effusion
- ☐ Entrapment neuropathy
- ☐ Mononeuropathy
- ☐ Polyneuropathy
- ☐ Cutaneous vasculitis
- ☐ Raynaud's
- ☐ Felty's
- ☐ Lymphadenopathy
- ☐ Amyloidosis
- ☐ AA subluxation
- ☐ Cervical myelopathy
- ☐ Anaemia (due to RA disease activity)
- ☐ Others, specify

NATIONAL INFLAMMATORY ARTHRITIS REGISTRY (NIAR-RA)
JOINT ASSESSMENT (1/2)

For Office Use only:
ID: /
Centre:

Instruction: Where check boxes ☐ are provided, check (√) one or more boxes. Where radio buttons ◉ are provided, check (√) one box only.

(Patient identifier for paper CRF)

I. Patient Name:	NRIC Number:	
II. Centre Code:	Or Reporting centre name:	
III. Follow up month:	◉ 1st Notification (Month 0) ◉ Month 6 ◉ Month 12	

SECTION 1: JOINT ASSESSMENT

1. Date of Assessment: * / / (dd/mm/yyyy)

2. Joint Evaluation-Upper Extremities

RIGHT SIDE				LEFT SIDE		
Not Evaluable Yes	Tenderness	Swelling	*JOINTS	Not Evaluable Yes	Tenderness	Swelling
☐	◉ Yes ◉ No	◉ Yes ◉ No	Temporomandibular	☐	◉ Yes ◉ No	◉ Yes ◉ No
☐	◉ Yes ◉ No	◉ Yes ◉ No	Sternoclavicular	☐	◉ Yes ◉ No	◉ Yes ◉ No
☐	◉ Yes ◉ No	◉ Yes ◉ No	Acromioclavicular	☐	◉ Yes ◉ No	◉ Yes ◉ No
☐	◉ Yes ◉ No	◉ Yes ◉ No	Shoulder	☐	◉ Yes ◉ No	◉ Yes ◉ No
☐	◉ Yes ◉ No	◉ Yes ◉ No	Elbow	☐	◉ Yes ◉ No	◉ Yes ◉ No
☐	◉ Yes ◉ No	◉ Yes ◉ No	Wrist	☐	◉ Yes ◉ No	◉ Yes ◉ No
☐	◉ Yes ◉ No	◉ Yes ◉ No	MCP1	☐	◉ Yes ◉ No	◉ Yes ◉ No
☐	◉ Yes ◉ No	◉ Yes ◉ No	MCP2	☐	◉ Yes ◉ No	◉ Yes ◉ No
☐	◉ Yes ◉ No	◉ Yes ◉ No	MCP3	☐	◉ Yes ◉ No	◉ Yes ◉ No
☐	◉ Yes ◉ No	◉ Yes ◉ No	MCP4	☐	◉ Yes ◉ No	◉ Yes ◉ No
☐	◉ Yes ◉ No	◉ Yes ◉ No	MCP5	☐	◉ Yes ◉ No	◉ Yes ◉ No
☐	◉ Yes ◉ No	◉ Yes ◉ No	IP1	☐	◉ Yes ◉ No	◉ Yes ◉ No
☐	◉ Yes ◉ No	◉ Yes ◉ No	PIP2	☐	◉ Yes ◉ No	◉ Yes ◉ No
☐	◉ Yes ◉ No	◉ Yes ◉ No	PIP3	☐	◉ Yes ◉ No	◉ Yes ◉ No
☐	◉ Yes ◉ No	◉ Yes ◉ No	PIP4	☐	◉ Yes ◉ No	◉ Yes ◉ No
☐	◉ Yes ◉ No	◉ Yes ◉ No	PIP5	☐	◉ Yes ◉ No	◉ Yes ◉ No
☐	◉ Yes ◉ No	◉ Yes ◉ No	DIP2	☐	◉ Yes ◉ No	◉ Yes ◉ No
☐	◉ Yes ◉ No	◉ Yes ◉ No	DIP3	☐	◉ Yes ◉ No	◉ Yes ◉ No
☐	◉ Yes ◉ No	◉ Yes ◉ No	DIP4	☐	◉ Yes ◉ No	◉ Yes ◉ No
☐	◉ Yes ◉ No	◉ Yes ◉ No	DIP5	☐	◉ Yes ◉ No	◉ Yes ◉ No

3. Joint Evaluation-Lower Extremities

RIGHT SIDE				LEFT SIDE		
Not Evaluable Yes	Tenderness	Swelling	*JOINTS	Not Evaluable Yes	Tenderness	Swelling
☐	◉ Yes ◉ No		Hip	☐	◉ Yes ◉ No	
☐	◉ Yes ◉ No	◉ Yes ◉ No	Knee	☐	◉ Yes ◉ No	◉ Yes ◉ No
☐	◉ Yes ◉ No	◉ Yes ◉ No	Ankle	☐	◉ Yes ◉ No	◉ Yes ◉ No
☐	◉ Yes ◉ No	◉ Yes ◉ No	Tarsus/Mid Tarsal	☐	◉ Yes ◉ No	◉ Yes ◉ No
☐	◉ Yes ◉ No	◉ Yes ◉ No	MTP1	☐	◉ Yes ◉ No	◉ Yes ◉ No
☐	◉ Yes ◉ No	◉ Yes ◉ No	MTP2	☐	◉ Yes ◉ No	◉ Yes ◉ No
☐	◉ Yes ◉ No	◉ Yes ◉ No	MTP3	☐	◉ Yes ◉ No	◉ Yes ◉ No
☐	◉ Yes ◉ No	◉ Yes ◉ No	MTP4	☐	◉ Yes ◉ No	◉ Yes ◉ No
☐	◉ Yes ◉ No	◉ Yes ◉ No	MTP5	☐	◉ Yes ◉ No	◉ Yes ◉ No
☐	◉ Yes ◉ No	◉ Yes ◉ No	IP1	☐	◉ Yes ◉ No	◉ Yes ◉ No
☐	◉ Yes ◉ No	◉ Yes ◉ No	PIP2	☐	◉ Yes ◉ No	◉ Yes ◉ No
☐	◉ Yes ◉ No	◉ Yes ◉ No	PIP3	☐	◉ Yes ◉ No	◉ Yes ◉ No
☐	◉ Yes ◉ No	◉ Yes ◉ No	PIP4	☐	◉ Yes ◉ No	◉ Yes ◉ No
☐	◉ Yes ◉ No	◉ Yes ◉ No	PIP5	☐	◉ Yes ◉ No	◉ Yes ◉ No

4. ACR functional status: *	◉ Normal (I) ◉ Limited in social activites (II)	◉ Limited in avocational/ vocational activites (III) ◉ Wheel-chair or bedridden (IV)
5. Radiographic erosion at assessment: *	◉ Yes ◉ No	◉ Not available / Not Done

NATIONAL INFLAMMATORY ARTHRITIS REGISTRY (NIAR-RA)
JOINT ASSESSMENT (2/2)

For Office Use only:
ID: /
Centre:

Instruction: Where check boxes ☐ are provided, check (√) one or more boxes. Where radio buttons ◎ are provided, check (√) one box only.

(Patient identifier for paper CRF)

I. Patient Name:	NRIC Number:	
II. Centre Code:	Or Reporting centre name:	
III. Follow up month:	◎ 1st Notification (Month 0) ◎ Month 6 ◎ Month 12	

SECTION 2: INVESTIGATIONS (AT NOTIFICATION)

Blood test	Results
1. ESR:	(mm/hr)
2. CRP:	. (mg/L) ☐ Unknown
3. Anti CCP: (at any time)	◎ Positive → ◎ Negative ◎ Unknown

SECTION 3: RA ACTIVITY

(please enter the VAS measurement from the worksheet into section 3)

Activity	Measurement
1. General health * assessment:	(mm)
2. Physician's global assessment of RA Activity:	(mm)

SECTION 4: DAS 28 ESR CALCULATION

Clinical Variable	Value
1. Tender joint count: (Autocalculate)	
2. Swollen joint count: (Autocalculate)	
3. ESR (Autofill)	(mm/hr)
4. General Health Assessment: (Autofill)	(mm)
5. DAS 28 Score: (Autocalculate)	.

(Note: Formula for DAS ESR 28 calculation: [(0.56 x √(Tender Joint Count) + 0.28 x √(Swollen Joint count) + 0.70 x Ln(ESR) + 0.014 x General Health Assessment]

SECTION 5: DAS 28 CRP CALCULATION

Clinical Variable	Value
1. Tender joint count: (Autocalculate)	
2. Swollen joint count: (Autocalculate)	
3. CRP (Autofill)	(mg/L)
4. General Health Assessment: (Autofill)	(mm)
5. DAS 28 Score: (Autocalculate)	.

(Note: Formula for DAS 28 CRP calculation: [0.56 x √(Tender Joint Count) + 0.28 x √ (Swollen Joint Count) + 0.36 x ln(CRP+1) + 0.014 x General Health Assessment + 0.96]
General Health Assessment - disease activity on a 100 mm VAS

NATIONAL INFLAMMATORY ARTHRITIS REGISTRY (NIAR-RA)
TREATMENT

For Office Use only:
ID: ___ / ___
Centre:

Instruction: Where check boxes ☐ are provided, check (√) one or more boxes. Where radio buttons ○ are provided, check (√) one box only.

(Patient identifier for paper CRF)

I. Patient Name:		**NRIC Number:**	
II. Centre Code:	☐☐☐☐	**Or Reporting centre name:**	
III. Follow up month:	○ 1st Notification (Month 0)	○ Month 6	○ Month 12

SECTION 6: TREATMENT

A. Was there any new medication administered?: *(Not applicable for the 1st notification/entry)* ○ Yes ○ No ○ Not applicable

1. Drug				2. Status	3. Reason for Discontinuing	
○ Steroids PO	○ Azathioprine	○ Cyclophosphamide	○ Cox2 Inh	○ Now	☐ Allergy	☐ Others, specify:
○ Steroids IM	○ Hydroxychloroquine(HCQ)	○ Infliximab	○ Opioid	○ Past	☐ Ineffective	
○ Steroids IV	○ Leflunomide	○ Etanercept	○ Others, specify:	○ PRN	☐ Patient refused	
○ Steroids IA	○ Penicillamine	○ Adalimumab			☐ Side effect, specify:	
○ MTX	○ Mycophenolate	○ Rituximab				
○ SSZ	○ Cyclosporine	○ NSAIDS				ADD
○ Steroids PO	○ Azathioprine	○ Cyclophosphamide	○ Cox2 Inh	○ Now	☐ Allergy	☐ Others, specify:
○ Steroids IM	○ Hydroxychloroquine(HCQ)	○ Infliximab	○ Opioid	○ Past	☐ Ineffective	
○ Steroids IV	○ Leflunomide	○ Etanercept	○ Others, specify:	○ PRN	☐ Patient refused	
○ Steroids IA	○ Penicillamine	○ Adalimumab			☐ Side effect, specify:	
○ MTX	○ Mycophenolate	○ Rituximab				
○ SSZ	○ Cyclosporine	○ NSAIDS				ADD
○ Steroids PO	○ Azathioprine	○ Cyclophosphamide	○ Cox2 Inh	○ Now	☐ Allergy	☐ Others, specify:
○ Steroids IM	○ Hydroxychloroquine(HCQ)	○ Infliximab	○ Opioid	○ Past	☐ Ineffective	
○ Steroids IV	○ Leflunomide	○ Etanercept	○ Others, specify:	○ PRN	☐ Patient refused	
○ Steroids IA	○ Penicillamine	○ Adalimumab			☐ Side effect, specify:	
○ MTX	○ Mycophenolate	○ Rituximab				
○ SSZ	○ Cyclosporine	○ NSAIDS				ADD
○ Steroids PO	○ Azathioprine	○ Cyclophosphamide	○ Cox2 Inh	○ Now	☐ Allergy	☐ Others, specify:
○ Steroids IM	○ Hydroxychloroquine(HCQ)	○ Infliximab	○ Opioid	○ Past	☐ Ineffective	
○ Steroids IV	○ Leflunomide	○ Etanercept	○ Others, specify:	○ PRN	☐ Patient refused	
○ Steroids IA	○ Penicillamine	○ Adalimumab			☐ Side effect, specify:	
○ MTX	○ Mycophenolate	○ Rituximab				
○ SSZ	○ Cyclosporine	○ NSAIDS				ADD
○ Steroids PO	○ Azathioprine	○ Cyclophosphamide	○ Cox2 Inh	○ Now	☐ Allergy	☐ Others, specify:
○ Steroids IM	○ Hydroxychloroquine(HCQ)	○ Infliximab	○ Opioid	○ Past	☐ Ineffective	
○ Steroids IV	○ Leflunomide	○ Etanercept	○ Others, specify:	○ PRN	☐ Patient refused	
○ Steroids IA	○ Penicillamine	○ Adalimumab			☐ Side effect, specify:	
○ MTX	○ Mycophenolate	○ Rituximab				
○ SSZ	○ Cyclosporine	○ NSAIDS				ADD

SECTION 7 : OTHER THERAPY

1. Complementary, medicine:	○ Yes ○ No	**2. Acupuncture:**	○ Yes ○ No

SECTION 8 : SURGERY

1. Arthroplasty:	○ Yes ○ No	**3. Spinal surgery:**	○ Yes ○ No	**5. Other surgery, specify:**	○ Yes ○ No
2. Arthrodesis:	○ Yes ○ No	**4. Synovectomy:**	○ Yes ○ No		↳

SECTION 9 : ADMISSION TO HOSPITAL (last 3 admissions)

No.	Date of Admission (dd/mm/yy)	Date of Discharge (dd/mm/yy)	Duration(days) (Auto calculate)	Reason for Admission		
(Autofill)	__/__/__	__/__/__		☐ RA flare ☐ Infections	☐ Cardiovascular ☐ Drug-related	☐ Jt replacement/surgery ☐ Others, specify: ADD
(Autofill)	__/__/__	__/__/__		☐ RA flare ☐ Infections	☐ Cardiovascular ☐ Drug-related	☐ Jt replacement/surgery ☐ Others, specify: ADD
(Autofill)	__/__/__	__/__/__		☐ RA flare ☐ Infections	☐ Cardiovascular ☐ Drug-related	☐ Jt replacement/surgery ☐ Others, specify: ADD

Finalized Version 1.5 last updated on 23/09/2009 (based on 11/09/09 meeting) * mandatory fields Page 4 .

NATIONAL INFLAMMATORY ARTHRITIS REGISTRY (NIAR-RA)
OUTCOME

For Office Use only:
ID: /
Centre:

Instruction: 1. Where check boxes ☐ are provided, check (√) one or more boxes. Where radio buttons ◉ are provided, check (√) one box only.
2. For the 1st notification, kindly also complete this Outcome page
3. For every 6 monthly Follow Up Visit , please complete Page 2 & 3:Joint Assessment, Page 4:Treatment and Outcome page

I. Patient Name:	NRIC Number:
II. Centre Code:	Or Reporting centre name:
III. Date of * Assessment:	(dd/mm/yy) ☐ Not applicable
IV. Follow up month:	◉ 1st Notification (Month 0) ◉ Month 6 ◉ Month 12
V. Estimated date of the next follow up: (dd/mm/yy)	(autocalculate) /

SECTION 1 : PATIENT STATUS

1. Patient status : *

◉ Alive →
- ◉ Remission (< 2.6)
- ◉ Moderate disease activity (>3.2 to 5.1)
- ◉ Unknown
- ◉ Low disease activity (2.6 to 3.2)
- ◉ High disease activity (>5.1)

(autofill based on page 3 Section 4 or Section 5 "DAS 28 score")

◉ Death →
- i) Date of death : * (dd/mm/yy) / /
- ii) Primary cause of death :
  - ◉ RA related → Specify the cause:
  - ◉ Non RA related →
  - ◉ Other causes →
  - ◉ Unknown

◉ Transfer to a new centre →
- i) Date of transfer: (dd/mm/yy) / /
- ii) Centre:
  - a) Centre Code:
  - b) Name of new centre:
- iii) Reason:

◉ Lost to follow up

ADD page for subsequent follow up month(s):
ADD Outcome page, 2,3 and 4

NATIONAL INFLAMMATORY ARTHRITIS REGISTRY (NIAR-RA) WORKSHEET

For Office Use only:
ID: ___ / ___
Centre: ___

Instruction: i) Where check boxes ☐ are provided, check (√) one or more boxes. Where radio buttons ◎ are provided, check (√) one box only.
2) Kindly ensure that the horizontal line of the VAS scales are 100 mm in length

(Patient identifier for paper CRF)

I. Patient Name:		NRIC Number:
II. Centre Code:	☐☐☐☐	Or Reporting centre name:
III. Follow up month:	◎ 1st Notification (Month 0) ◎ Month 6 ◎ Month 12	

(Please enter the VAS measurement from the worksheet into section 3: RA Activity (Page 3))

1. Date of Measurement: (dd/mm/yy) (Date of Follow up / Date of Assessment)	☐☐ / ☐☐ / ☐☐
2. RA Activity	**Measurement (mm)**
General Health Assessment *"How do you feel today?"* **0 (very well)** — **100 (very bad)**	☐☐☐
Physician's global assessment of RA activity **0 (very well)** — **100 (very bad)**	☐☐☐

MARBLE FORM

Patient's name :_____
Patient's ID :_____

1. Name of BIOLOGIC DMARDs (bDMARDs) ever used (past and current)
- can tick more than one.

	Name of current bDMARDs	Current	Past	Date start dd/mm/yyyy	Date stop dd/mm/yyyy	Total duration of use (round up to months) (especially important for patients who use biologic intermittently whereby definite start and stop date cannot be determined)	The primary reason for stopping the said bDMARDs (refer key)
1	s/c Adalimumab						
2	s/c Certolizumab						
3	s/c Etanercept						
4	IV Golimumab						
5	s/c Golimumab						
6	IV Infliximab / Remsima						
7	IV Rituximab						
8	IV tocilizumab						
9	s/c tocilizumab						
10	IV Sarilumab						
11	Tofacitinib						
12	Others 3: specify name: _____						

Key for primary reasons for stopping the said biologics

1	Treatment failure		6	End of clinical trial
2	Adverse reaction		7	Transferred care
3	Patient's preference		8	Patient defaulted follow up
4	Lack of fund		9	Death
5	Disease in remission		10	Others: specify:_____

2. Source of biologic funding (past and current)—can tick more than one.

	Funding	Tick
1	Hospital	
2	Tabung bantuan perubatan (TBP)	
3	JPA	
4	Insurance	
5	Zakat	
6	Self	
7	Sample	
8	Clinical trial	
9	Multiple funding sources	
10	Others: specify	

3. Is the patient **on bDMARDs now**? (circle)

Yes : Name of bDMARDs :_____
No.

4. csDMARDs ever used before **the FIRST bDMARDs** (Tick, can be more than one selection):

csDMARDs	Tick	csDMARDs	Tick	csDMARDs	Tick
MTX		AZA		CYCLOPHOSPHAMIDE	
SSZ		CYCLOSPORIN A		OTHERS 1: SPECIFY_____	
HCQ		PENICILLAMINE		OTHERS 2: SPECIFY_____	
ARAVA		GOLD		OTHERS 3: SPECIFY_____	

5. Was combination of csDMARDs ever used before initiation of **the first bDMARDs** (circle): | Y | N |

- If Yes, what was the highest number of csDMARDs combination at one time?

2	3	4

6. TB diagnosis - Pulmonary Or Extra Pulmonary – [.....]

- Type and duration of biologic prior to TB diagnosis