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A model to determine the cost-effectiveness of screening psoriasis patients for psoriatic arthritis

Running title: cost-utility of psoriatic arthritis screening

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Abstract

Objective: Screening psoriasis patients for psoriatic arthritis (PsA) is intended to identify patients at earlier stages of the disease. Early treatment is expected to slow disease progression and delay the need for biologic therapy. This paper determines the cost-effectiveness of screening for PsA in patients with psoriasis in Canada.

Methods: A Markov model was built to estimate the costs and quality-adjusted life-years (QALYs) of screening tools for PsA in psoriasis patients. The screening tools included the ToPAS, PEST, PASE; and EARP questionnaires. Health states were defined by disability levels as measured by the Health Assessment Questionnaire (HAQ). State transitions were modelled based on annual disease progression. Incremental cost-effectiveness ratios (ICERs) and Incremental net monetary benefits (INMBs) were estimated. Sensitivity analyses were undertaken to account for parameter uncertainty and test model assumptions.

Results: Screening was cost-effective compared to 'no screening'. The EARP had the lowest total cost ($2,000 per patient per year saved compared to No Screening) and highest total QALYs (additional 0.18 per patient compared to No Screening). The results were most sensitive to test accuracy and DMARD efficacy. 'No Screening' was cost-effective (at $50,000 per QALY) relative to screening when DMARDs failed to slow disease progression.

Conclusions: If early therapy with DMARDs delays biologic treatment, implementing screening in patients with psoriasis in Canada is expected to represent cost-savings of $220 million per year and improve quality of life.

Significance and innovation

1. Canada currently lacks an organized psoriatic arthritis screening program.

2. Screening psoriasis patients for psoriatic arthritis is expected to delay the initiation of biologic therapy.

3. An organized screening program for psoriatic arthritis is expected to improve quality of life and save
$2000 per patient, annually.

Introduction

Psoriatic arthritis (PsA) is a chronic inflammatory arthritis that affects the skin and the musculoskeletal system (1). PsA is associated with psoriasis, a chronic skin disease characterized by red plaques that often appear on the elbows, knees, and scalp (2). Manifestations affect the skin, nails, joints, entheses, or the axial skeleton (3,4). The prevalence of PsA is estimated around 0.3% in the general population (1) and 30% for patients with psoriasis (5). Close to 20% of cases suffer from severe pain and deformation of the joints resulting in impairment and deteriorating quality of life (1).

The cost and health burden of PsA is considerable. The average annual total cost of treatment per patient was estimated around US$15,000 in Europe (6). Furthermore, late stages of PsA are associated with worse health outcomes and higher treatment costs mainly due to biologic therapy (7). The introduction of biologics is expected to result in a 3- to 5-fold increase in direct costs (6). Consequently, early treatment with affordable first-line disease-modifying anti-rheumatic drugs is intended to slow disease progression towards late and severe stages of PsA where biologics are often required (8). As such, organized screening programs are expected to increase the proportion of patients identified and treated during early stages of disease. However, these programs are expensive to implement due to additional resource utilization and significant start-up costs.

Currently, Canada lacks an organized screening program for PsA. However, recent efforts have been directed towards understanding the effect of PsA screening. A meta-analysis compared the accuracy of the most widely used PsA screening tools (9). Additionally, the National Institute for Health Research (NIHR) is conducting a trial to evaluate the effect of screening for PsA on health outcomes

(10). However, there is a knowledge gap regarding the health economic impact of implementing an organized screening program. Consequently, this study evaluates the cost-effectiveness of screening for PsA using different validated tools (11–14) among psoriasis patients in Canada.

Methods

Target population, perspective, and time horizon

A hypothetical cohort of 45-year old patients with psoriasis and without PsA under dermatological surveillance was modelled. At model initiation patients have mild psoriasis with a baseline Psoriasis Area Severity Index (PASI) of 3.5 and are receiving topical treatment or Disease Modifying Anti-Rheumatic Drugs (DMARDs) for their skin condition (15). The evaluation was conducted from the Canadian publicly funded health care payer's perspective and followed a 40-year time horizon with annual cycles.

Comparators

Screening tools were compared between themselves and against the current standard care (no screening). 'No screening' refers to the clinical pathway that the typical PsA patient (with a previous psoriasis diagnosis) follows in Canada. Since patients are not routinely screened, they are diagnosed following self-referral, once their arthritis symptoms become evident and difficult to ignore (14). In Canada, the majority of patients with PsA start treatment with methotrexate (a DMARD) and initiate biologics if the disease progresses and DMARDs are no longer effective (8).

The PsA screening program is expected to identify disease earlier compared to 'no screening'. PsA patients who are screened and diagnosed earlier follow the same treatment pathway as diagnosed patients under 'no screening', but a few years earlier. This head start is expected to translate to increased time on DMARDs and a delay to receiving biologic therapy. This study compares the following screening questionnaires for PsA: The Toronto Psoriatic Arthritis Screen (ToPAS), the Psoriasis

Epidemiology Screening Tool (PEST), the Psoriatic Arthritis Screening and Evaluation tool (PASE), and the Early Psoriatic Arthritis Screening Questionnaire (EARP), which are all validated for patients with psoriasis (11–14). Although the tools are similar in terms of structure and content, there are a few differences among them: the EARP identifies pain and swelling of specific joints (i.e. does your Achilles tendon swell?), while the remaining three are more general (i.e. my joints hurt) (9). Furthermore, the ToPAS and PEST have additional visual resources like mannequins or skin and nail images to aid patients identify the affected joints. Finally, since all tools are comprised of different items, their maximum score and cut-off values vary (9). All questionnaires were assumed to be delivered in dermatology clinics.

Figure 1: Markov model structure

Model structure

The Markov model is summarized in **Figure 1**; it models the progression of the average PsA patient through different health states. Patients start with psoriasis but not PsA. Each year, based on the annual incidence rate of PsA for psoriasis patients in Canada (16), 2.7% of patients are expected to develop PsA. After PsA onset (T_0), the degree of disability is assumed to increase at a higher rate if left untreated. A steady-state model was generated by filling the first health states (HAQ scores) according to the annual PsA incidence rate. This ensured that the screening interventions would identify a proportion of currently prevalent and undiagnosed cases. Tunnel states were used to model progression through HAQ states.

In the screening arms, psoriasis patients are screened annually for PsA. It was assumed that the screening tools were not sufficiently sensitive to identify PsA between T_0 and T_1. Patients could only be identified after their disease had progressed to T_1. Positive screening tests are followed by the gold standard rheumatological assessment, with 100% sensitivity and specificity. False positives are usually diagnosed with similar rheumatological conditions but remain PsA-free. Therefore, PsA is ruled out in false positive patients and they remain in the model as population at-risk in T_0. Furthermore, patients with PsA who were missed by the screening tool (false negatives) are eventually identified at T_2 or the

time to average diagnosis. Therefore, the period T_2-T_1 represents the sojourn time, or pre-clinical symptom phase. The base case assumed that screening tools were effective 2 years prior to normal identification, i.e. the sojourn time is 2-years.

Following diagnosis; late or early PsA, treatment was modelled based on the EULAR and Canadian recommendations (17,18). DMARDs are used as first line treatment, with biologics initiated after ineffective used of DMARDs, due to loss of efficiency. Biologics were assumed to have a 5-year period of effectiveness. This was based on an annual 16.5% biologic withdrawal rate (19). Patients that withdrew due to either loss of effect or adverse events rebound to the HAQ score that would have been expected had they not initiated biologic therapy (20). A second biologic therapy was modelled to account for the potential switch between anti-TNF therapies to IL-17-inhibitors. Additionally, if the second biologic failed, patients started palliative care as modelled by Bojke et al., where HAQ progressed at a rate of 0.078 per year (20). Biologics and DMARDs were considered as bundles instead of individual drugs, i.e. an average effect and cost was applied to DMARDs and biologics, instead of modelling response to individual treatments.

Model inputs

Common with previous cost-effectiveness models for PsA (20–22), we used the HAQ to describe patient's progression through different PsA health states. Health states were defined by the degree of disability as measured by this multidimensional index that focuses on physical function, pain, and discomfort (23). For each functional activity, an overall score between 0-3 is calculated across the different domains, where 0 represents no impairment and 3 complete impairment (23). Thus, a higher HAQ score represents more severe disease. The average HAQ score at which PsA patients were diagnosed after being identified by self-referral (T_2) was assumed to be 0.71 (24). Patients not identified by screening were diagnosed at this point. Furthermore, based on several Randomized Controlled Trials for PsA, the average HAQ at which patients initiated biologic therapy was estimated to be 1.05 (25).

The progression of PsA (measured as the change in HAQ score) was modelled according to the line of treatment. The annual progression of PsA was 0.07 if left untreated (25). Conversely, patients

treated with DMARDs and biologics progressed at a rate of 0.026 and 0.0001 per year, respectively (25). Patients who progress slower will take longer to reach a HAQ of 1.05 when the average patient switches to biologic therapy. Table 1 summarizes the model inputs such as incidence rates, disease progression, total costs, and utilities.

Table 1: Aggregated model inputs

Costs

Only direct health care costs were included. Each health state had an associated cost relating to screening, diagnostic testing, and treatment. Annual drug costs were estimated from the Alberta Blue Cross and Ontario Drug Benefit Formularies. Annual dosage was estimated considering the product information provided by individual manufacturers. Clinical, non-drug related costs were included with an algorithm where a unit increase in HAQ was associated with $993 (27). Costs were converted and inflated from 2006 GBP to 2017 CAD.

Diagnosis was modelled based on clinical assessment by a rheumatologist, laboratory tests and diagnostic imaging. Screening costs were obtained based on physician time (29–31). Furthermore, the cost associated with implementing a screening program (training, patient support, start-up, and administrative costs) was extrapolated from a Breast Cancer screening program in Canada (26). Mittman et al. estimated that the cost per breast cancer screen (mammography) was close to $200 (2017 CAD) in Canada. After accounting for the physician fees associated with the screening tests, we assumed that the administrative costs per screen were close to $120 per screen. This is likely a conservative estimate, considering that implementing a questionnaire-based screening program for PsA is likely to cost less than a mammography screening program. Appendix 1 provides a summary of disaggregated costs for treatments (topical therapy, DMARDs, biologics), screening, diagnostic testing,

and consultation fees. All costs were transformed to 2017 Canadian Dollars (CAD) using the Bank of Canada consumer price index (CPI).

Health-Related Quality of Life

Health states have associated utilities that measure the health-related quality of life (HRQoL) of being in that state. The average linear correlation between HAQ and utility was estimated to be -0.248 (25). These utilities were derived from the EQ-5D based on a mapping exercise from HAQ scores (25). On the other hand, the average linear correlation between PASI (skin domain) and utility was estimated to be -0.003 (25). The severity of the psoriasis of the skin, as measured by the PASI, was assumed constant at a level of 3.5 (25). Based on the utility and HAQ regression, the base case utility score (at time 0) is 0.884 (25).

Expected utility = 0.884 – (0.248×HAQ score) – (0.003×PASI score)

Finally, a discount rate of 1.5% was applied to both costs and health outcomes (QALYs) (32). To determine the cost-effectiveness of the different strategies, the incremental cost-effectiveness ratio (ICER) was estimated and compared to the commonly cited threshold of $50,000 per QALY.

Assumptions

In line with previous economic models in this area, a few assumptions were made:

- This model assumes a linear relationship between disease duration and HAQ progression for symptomatic and asymptomatic disease (25).
- Following previous models, all-cause and PsA-related mortality rates were assumed constant regardless of line of therapy (biologics, DMARDs, and no treatment) (20) and were not modelled.

The following are the assumptions relevant to the screening and diagnostic components of the study:

- 3.2% of psoriasis patients progressed to DMARD therapy annually for treatment of their skin due to loss of effectiveness of topical treatment (28).
- Screening questionnaires are assumed effective at identifying PsA patients in dermatology clinics during a 2-year sojourn time.

- All patients who test positive undergo diagnostic testing to confirm the disease. False positives are ruled out upon further diagnosis using EULAR and clinical guidelines and remain in the model as population at risk.
- For the base case probabilistic analysis, patients must spend at least two years in DMARD therapy before starting treatment with biologics. This was assumed to ensure that biologics were not initiated before DMARDs in the base case.
- This study assumed 100% sensitivity and specificity for diagnosis (rheumatological assessment).

Sensitivity analyses

Sensitivity analyses were conducted on the base case analysis to account for parameter uncertainty.

(i) A threshold analysis was also conducted to determine the values at which specific model inputs rendered screening more expensive compared to no screening.

(ii) A univariate sensitivity analysis was carried out to determine the threshold at which specific model inputs modified conclusions as measured by the Incremental net monetary benefit (INMB).

(iii) A two-way sensitivity analysis was carried out to determine the effect of sensitivity and specificity over the cost-effectiveness estimates.

(iv) Probabilistic sensitivity analyses were conducted, in which all parameters were varied simultaneously (through 5,000 Monte Carlo simulations) according to assigned probabilistic distributions for each model input (Table 1). Probabilities were assigned beta distributions due to their (0-1) range (33). Normal distributions were assigned to parameters obtained through linear regression. Gamma distributions were assigned to costs and HAQ progression rates (33). A truncated bivariate normal distribution was used to simulate 5,000 pairs of sensitivity and specificity estimates to account for their correlation (33). Cost-effectiveness acceptability curves (CEACs) were used to assess conclusions at given different cost-effectiveness thresholds.

Scenario analyses

Scenario analyses were conducted to account for the uncertainty around specific model parameters and assumptions such as the sojourn time, DMARD efficacy, and first-line treatment.

(i) We built a scenario in which patients started biologic therapy as first-line therapy, which has recently been proposed in the American College of Rheumatology's (ACR) guidelines (34). It was expected that screening would increase early therapy with biologics, thus increasing total costs relative to 'no screening'.

(ii) A scenario in which DMARDs failed to slow disease progression was built. Screening would no longer delay the initiation of biologic therapy.

(iii) Reduced sojourn time (1 year) was expected to reduce the cost-effectiveness of screening relative to 'no screening'. A smaller proportion of PsA patients would be identified early, thus minimizing the benefits of a screening program.

Validation

The model was validated iteratively throughout its development according to the CADTH guidelines for Economic Evaluations (32). The face validation was ensured by the active participation and judgment of content experts throughout the entire process. Duplicate review was undertaken with experts in modelling psoriatic and rheumatoid arthritis. The mathematical and statistical assumptions were evaluated and validated. A member of the development team of the NICE Health Technology Assessment report for Biologic therapy for PsA (20,25) evaluated the HAQ, utility, and costs algorithms that were adapted from these previously validated models. Furthermore, the coding accuracy was validated by testing extreme and zero values, as well as with univariate sensitivity analyses.

Results

Base case scenario

Results for the base case are summarized in **Table 2**. Screening for PsA among psoriasis patients with the EARP, ToPAS, and PEST was cost-saving compared to 'no screening'. All screening tools were cost-effective relative to 'no screening' at a threshold of $50,000 per QALY. Although screening tools had similar costs and QALYs, the EARP yielded the lowest total cost per patient ($104,889) and the highest QALYs (24.242). All results are presented per patient over a 40-year time horizon. The 'No Screening' arm was both more expensive in terms of costs ($1,989 incremental costs) and forgone health (-0.176 incremental QALYS), relative to the EARP. All screening tools were more effective compared to 'No Screening'. The EARP dominated every other alternative by having the most QALYs for the lowest cost.

The probabilistic analysis was summarized in **Table 3**. Screening for PsA (with any screening tool) had a probability of 0.94 of being cost-effective at a $50,000 per QALY threshold. Additionally, the EARP had the highest probability of being cost-effective at any threshold (from 0 to $100,000 per QALY). The cost-effectiveness acceptability curves summarize the probability of each alternative of being cost-effective at different willingness-to-pay thresholds (**Appendix 2**). The conclusions were maintained compared to the deterministic base case: The EARP had the lowest total cost ($99,264) and the highest QALYs (24.362).

Table 2: Deterministic results of the base case per patient -full incremental analysis

Table 3: Probabilistic results of the base case

Univariate sensitivity analyses for the base case

A threshold analysis determined the value of each parameter for which 'No Screening' became less expensive compared to the EARP. The monetary advantage of the EARP relative to 'No Screening' due to reduced biologic therapy was offset whenever the screening, diagnostic, and DMARD-related costs were increased by $87, $1,628, and $5,275, respectively. 'No screening' was less costly than EARP when the annual cost of biologics per patient was below $10,000.

The univariate sensitivity analysis was conducted for the deterministic base case between the EARP and the 'No Screening' arm only. Screening was no longer cost-effective relative to 'No Screening' given the following:

(i) Biologics were initiated before DMARDs.

(ii) The HAQ progression under DMARDs increased to 0.059 per year (compared with the 0.03 base case).

Conclusions were robust to the variation of several inputs, such as the PsA incidence among psoriasis patients, the cost of screening, diagnosis and biologic therapy, and the cost-effectiveness threshold.

Bivariate sensitivity analysis for test accuracy

Table 4 summarizes the different combinations of sensitivity and specificity for 0.1 increments, and their respective INMBs. For the screening tool to be cost-effective relative to 'No Screening', it had to have at least a 0.7 specificity (for any sensitivity level), or a 0.6 sensitivity (for any specificity level).

Table 4: Bivariate analysis of sensitivity and specificity versus the INMB of screening relative to 'no screening'

Scenario analyses

The cost-effectiveness results for the scenario analyses are presented in **Table 5**. The first scenario assumed that patients initiated biologic therapy as first-line treatment. The total costs for screening (EARP) were increased compared to the base case. The 'No Screening' strategy had the lowest total cost (-$2,000 compared to EARP), and although it yielded the lowest QALYS, the incremental costs per additional QALY was too high to be deemed cost-effective, considering a $50,000 threshold. Screening (with the EARP) had a probability of 0.05 of being cost—effective.

The second scenario assumed that DMARDs failed to modify disease progression. The 'no screening' alternative was cost-effective relative to screening, with the lowest total cost (-$,5300) and QALYs (-0.01) compared to screening. There was a 0.03 probability of screening (EARP) being cost-effective at a $50,000 threshold.

Finally, a scenario with a modified sojourn time of 1 year was assumed. Overall, the total costs of screening (EARP) were increased and the QALYs reduced compared to the base case. 'No screening' remained unaltered. However, screening (EARP) remained cost-effective with the highest total QALYs (additional 0.078) and lowest total cost (additional $80) compared with 'no screening'. Screening (EARP) had a probability of 0.66 of being cost-effective at a $50,000 per QALY threshold.

Table 5: Cost-effectiveness results of scenario analyses

Discussion

Several studies have suggested that early PsA diagnosis and treatment can potentially improve health outcomes (8,35–37). For example, Haroon et al. concluded that delaying treatment is associated with the development of peripheral joint erosions and worse long-term physical function (38). As a consequence, The EULAR suggested that this 'window of opportunity' constitutes an important aspect of the PsA research agenda (17). Even though there is evidence suggesting that early therapy is clinically

efficacious, to this date, there is no evidence regarding the cost-effectiveness of implementing screening strategies to enable early therapy. Previous economic evaluations have mainly focused on the cost-effectiveness of biologic therapy relative to DMARDs (20,27,39), but have not evaluated where in their disease course patients were diagnosed.

This analysis shows that screening for PsA in psoriasis patients with self-administered questionnaires was cost-effective compared to 'No Screening'. Although the screening questionnaires were similar in terms of accuracy and cost, the EARP represented the best strategy due to slightly better accuracy. Implementing a PsA screening program in Canada would be cost-savings over a 40-year time horizon relative to 'no screening'. Since the average time in biologic therapy per patient is expected to be reduced, the Canadian Health Care System would save around $220 million per year ($2,000 per patient) while improving quality of life.

This evaluation explored the sensitivity of the model results to key parameters and model assumptions through scenario and sensitivity analyses. The total QALYs varied exclusively due to test accuracy, which translated to a slight variation in HAQ scores due to early therapy. Therefore, the EARP always dominated the other screening tools due to its higher accuracy (9). Thus, the sensitivity and scenario analyses only compared the EARP versus 'No screening'. These results could be conservative if early therapy was proven to increase remission rates, which were not included in this model (20). Furthermore, the results suggest that a test with high sensitivity was preferred to one with a high specificity. A high true positive rate increased the proportion of patients starting early therapy, thus improving the cost-effectiveness of the screening tools compared to 'No screening'. A high true negative rate reduced the proportion of unnecessary testing for false positives, which affected the total costs but had no effect over the health outcomes (QALYs). Regarding costs, the sensitivity analysis showed that 'No screening' was expected to be less expensive than the EARP when the cost of biologic therapy was below $10,000 per patient annually. However, screening with the EARP remained cost-effective relative to 'No screening' for any value between $0-$10,000. Therefore, measures that aim to reduce the cost of biologics (i.e. the introduction of biosimilars) would not be expected to modify

conclusions. Finally, it could be argued that patients who are screened and identified early could have a higher probability of starting biologics earlier. This hypothesis was evaluated with a scenario analysis where biologics were included as first-line therapy. Consequently, screening increased the proportion of patients starting early biologic therapy, thus increasing costs considerably.

A number of assumptions were made to allow the cost-effectiveness of screening for PsA to be evaluated. For example, a previously validated algorithm was used to model clinical costs (non-drug) based on HAQ score (27). This algorithm was developed by Bansback et al. based on a linear regression of data collected in 2002. This methodology was used by Rodgers et al. after conducting a thorough comparison of similar costing algorithms (25). The use of this algorithm in our model assumes similar practice patterns of PsA patients in the UK and Canada, this is supported by international clinical guidelines (17,34). Additionally, parameters like psoriasis progression was not modelled. Even though the skin dimension has been previously included in economic evaluations, the utility-HAQ relationship estimated a relatively small utility effect of the PASI (25). Finally, modelling treatment bundles instead of individual treatment responses poses a limitation, since specific DMARD and biologic therapies cannot be compared. However, since this model focuses on PsA screening instead of treatment, all comparators in this model are affected in the same way.

The results of this cost-utility analysis provide a pathway for next steps and further research on PsA screening. This model identified time to biologic start as a key parameter. Therefore, the uncertainty around DMARD-related HAQ progression needs to be further addressed, specifically since there has been controversy around the efficacy of some DMARDs (40). This is important because the cost-effectiveness of screening depends on the ability of DMARDs to slow disease progression and delay the time of biologic start. Consequently, an ongoing trial will provide an estimate of the delay to biologics and the effect of early DMARD treatment (10). A more precise estimate of early DMARD efficacy translates to a more precise cost-effectiveness estimate for the Canadian health care system. Additionally, the long-term effects of biologic therapy remain an uncertainty that needs resolving. Finally, future research should develop new algorithms to understand the relationship between HAQ

and PASI health states and current costs.

In summary, this is the first cost-utility model on screening for PsA among psoriasis patients. Screening for PsA among psoriasis patients with the EARP tool appears to be cost saving compared to the status quo. The ongoing PsA screening trial will provide additional information to account for the parameter uncertainty of the evaluation (10).

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Appendices

Appendix 1: Disaggregated costs for diagnostic tests, screening, therapies, and consultation fees

Appendix 2: Cost-effectiveness acceptability curves for the base case and scenario analyses

Table 1: Aggregated model inputs

Variable	Source	Deterministic value	Standard error	Distribution
Annual PsA incidence among psoriasis patients	Eder et al. 2016 (16)	0.027	0.004	Beta
Cost of topical treatment See **Appendix 1** for details.	Alberta Blue Cross Formulary Ontario Drug Benefit Formulary	$ 226	$76.57	Gamma
Cost of diagnosis See **Appendix 1** for details.	Schedule of Medical Benefits (Alberta Health)	$ 771.	$53.46	Gamma
Cost of screening See **Appendix 1** for details.		$ 78	$29.05	Gamma
Administrative costs of screening (per screen) See **Appendix 1** for details.	Mittmann et al. 2015 (26)	$ 121.45	$ 45.09	Gamma
DMARD cost per year See **Appendix 1** for details.	Alberta Blue Cross Formulary Ontario Drug Benefit Formulary	$ 1,931	$103.95	Gamma
Biologic cost per year See **Appendix 1** for details.		$ 20,559	$2,113.29	Gamma
Palliative care cost per year See **Appendix 1** for details.		$ 3,869	$207.90	Gamma
Direct costs per HAQ score See **Appendix 1**for details.	Bansback et al. 2006 (27)	$ 993	$ 641.23	Normal
Annual adherence to topical treatment	Zaghloul et al. 2004 (28)	0.731	0.038	Beta
HAQ progression palliative care	Bojke et al. 2011 (20)	0.078	0.030	Gamma
HAQ progression under no treatment	Rodgers et al. 2011 (25)	0.0695	0.002	Gamma
HAQ progression under DMARDs		0.026	0.003	Gamma
HAQ progression under biologics		0	0.00	Gamma
Utility and HAQ linear correlation		-0.259	0.009	Normal
Utility and PASI linear correlation		-0.003	0.001	Normal
Baseline Utility		0.884	0.01	Normal
Average HAQ for biologic start		1.05	0.316	Normal
Baseline PASI score for mild psoriasis and topical treatment	Bernstein et al. 2006 (15)	3.54	0.44	Gamma
Average HAQ at diagnosis	Eder et al. 2016 (16) & Kane et al. 2003 (24)	0.71	0.64	Truncated Normal
Discount	CADTH	0.015	NA	NA
Cost-effectiveness threshold	NA	$50,000	NA	NA
Mean time in biologics (years)	Corbett et al. 2017 (19)	5	NA	NA
Progression to natural history	Assumptions	0.026	0.003	Gamma
HAQ rebound		0.130	NA	NA
Progression on 2nd biologic		0	0.00	Gamma
ToPAS sensitivity	Iragorri et al 2018 (9)	0.74	0.04	Bivariate normal
ToPAS specificity		0.79	0.08	Bivariate normal
EARP sensitivity		0.85	0.02	Bivariate normal
EARP specificity		0.85	0.08	Bivariate normal
PEST sensitivity		0.68	0.05	Bivariate normal

Variable	Source	Deterministic value	Standard error	Distribution
PEST specificity		0.8	0.07	Bivariate normal
PASE sensitivity		0.71	0.04	Bivariate normal
PASE specificity		0.67	0.08	Bivariate normal

* HAQ = Health Assessment Questionnaire; PASI = Psoriasis Area Severity Index; DMARD = Disease Modifying Anti-Rheumatic Disease;

Table 2: Deterministic results of the base case per patient -full incremental analysis

Strategy	Cost	QALY	Incremental Cost	Incremental QALYs	ICER
EARP	$ 104,889	24.242			
ToPAS	$ 105,904	24.226	$ 1,015	-0.015	Dominated
PEST	$ 105,943	24.217	$ 1,054	-0.024	Dominated
No Screen	$ 106,878	24.066	$ 1,989	-0.176	Dominated
PASE	$ 107,445	24.222	$ 2,556	-0.020	Dominated

* ICER = Incremental cost-effectiveness ratio; QALY = quality-adjusted life year

Table 3: Probabilistic results of the base case

Strategy	Cost	QALY	Incremental Cost	Incremental QALYs	ICER	Probability of being CE at $50,000
EARP	$ 99,264	$ 24.362				0.57
No Screen	$ 99,573	$ 24.180	$ 308	-0.182	Dominated	0.06
ToPAS	$ 100,759	$ 24.322	$ 1,494	-0.041	Dominated	0.13
PEST	$ 100,834	$ 24.333	$ 1,569	-0.029	Dominated	0.11
PASE	$ 101,001	$ 24.336	$ 1,737	-0.027	Dominated	0.13

* ICER = Incremental cost-effectiveness ratio; QALY = quality-adjusted life year; CE = cost-effective

Table 4: Bivariate analysis of sensitivity and specificity versus the INMB of screening relative to 'no screening'

Specificity		Sensitivity									
		0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1
	0.1	$ (7,978)	$ (6,358)	$ (4,843)	$ (3,430)	$ (2,122)	$ (917)	$ 184	$ 1,181	$ 2,075	$ 2,865
	0.2	$ (6,759)	$ (5,140)	$ (3,624)	$ (2,212)	$ (904)	$ 301	$ 1,402	$ 2,399	$ 3,293	$ 4,083
	0.3	$ (5,541)	$ (3,922)	$ (2,406)	$ (994)	$ 314	$ 1,519	$ 2,620	$ 3,617	$ 4,511	$ 5,301
	0.4	$ (4,323)	$ (2,704)	$ (1,188)	$ 224	$ 1,532	$ 2,737	$ 3,838	$ 4,835	$ 5,729	$ 6,520
	0.5	$ (3,105)	$ (1,486)	$ 30	$ 1,442	$ 2,750	$ 3,955	$ 5,056	$ 6,053	$ 6,947	$ 7,738
	0.6	$ (1,887)	$ (268)	$ 1,248	$ 2,660	$ 3,968	$ 5,173	$ 6,274	$ 7,272	$ 8,165	$ 8,956
	0.7	$ (669)	$ 950	$ 2,466	$ 3,878	$ 5,186	$ 6,391	$ 7,492	$ 8,490	$ 9,383	$ 10,174
	0.8	$ 549	$ 2,168	$ 3,684	$ 5,096	$ 6,404	$ 7,609	$ 8,710	$ 9,708	$ 10,601	$ 11,392
	0.9	$ 1,767	$ 3,386	$ 4,902	$ 6,314	$ 7,622	$ 8,827	$ 9,928	$ 10,926	$ 11,819	$ 12,610
	1	$ 2,985	$ 4,604	$ 6,120	$ 7,532	$ 8,840	$ 10,045	$ 11,146	$ 12,144	$ 13,038	$ 13,828

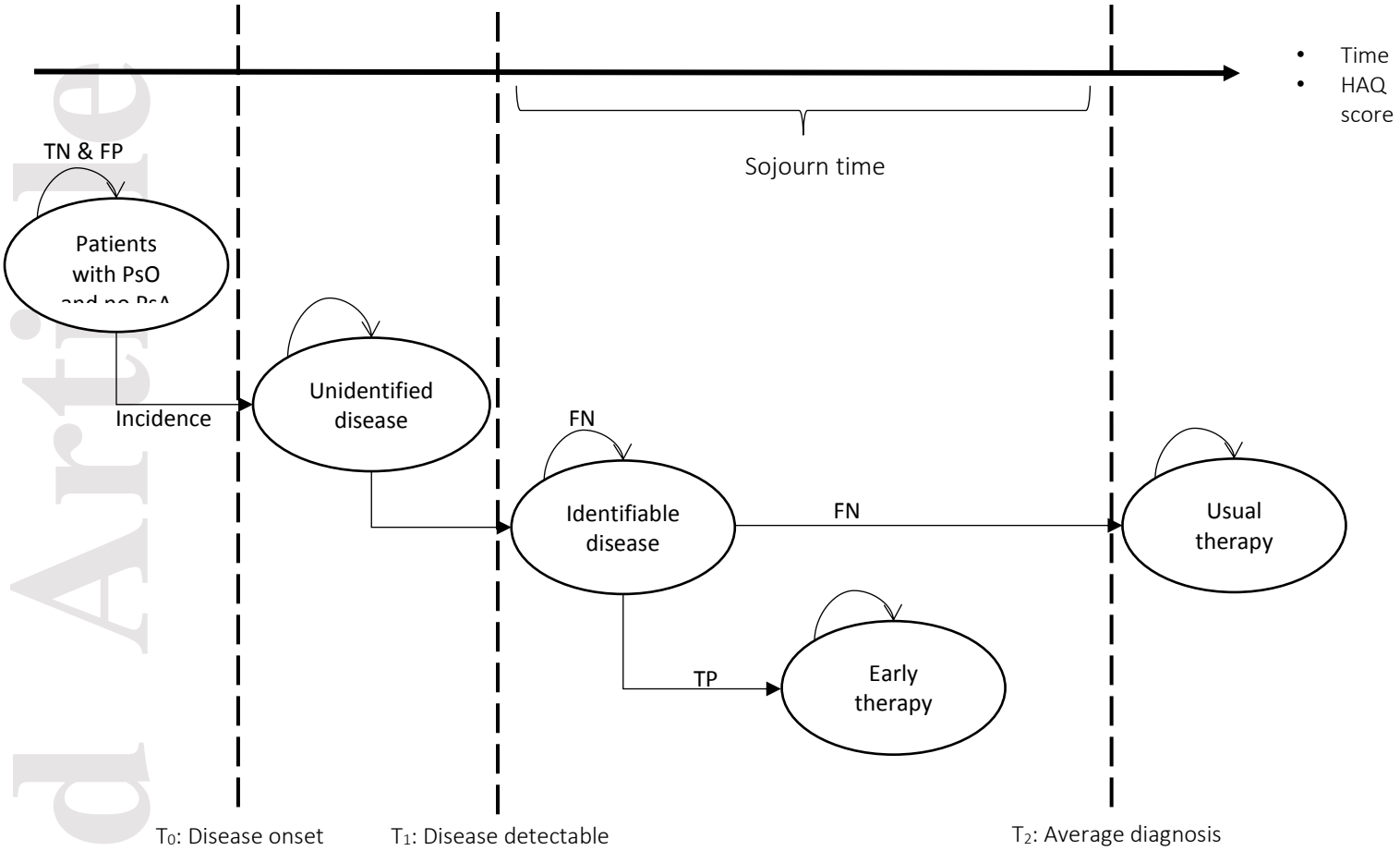
* Screening is cost-effective (at $50,000 per QALY) when the combinations of sensitivity and specificity result in positive INMBs

Table 5: Cost-effectiveness results of scenario analyses

Strategy	Cost	QALY	Incremental Cost	Incremental QALYs	ICER	Probability of being CE
Biologics as first-line therapy						
No Screen	$127,449	23.975	-	-	-	0.95
Screening (EARP)	$135,434	24.057	$7,984	0.082	$97,743	0.05
Ineffective DMARDs						
No Screen	$136,849	22.769				0.97
Screening (EARP)	$142,228	22.779	$5,379	0.01	$516,171	0.03
Sojourn time of 1 year						
No Screen	$106,878	24.066				0.34
Screening (EARP)	$106,958	24.144	$80	0.078	$1,017	0.66

* ICER = Incremental cost-effectiveness ratio; QALY = Quality-adjusted life year; CE = cost-effective

Figure 1: Markov model structure



TN = true negatives; TP = true positives; FP = false positives; FN = false negatives; PsO = psoriasis; PsA = psoriatic arthritis; HAQ = health assessment questionnaire