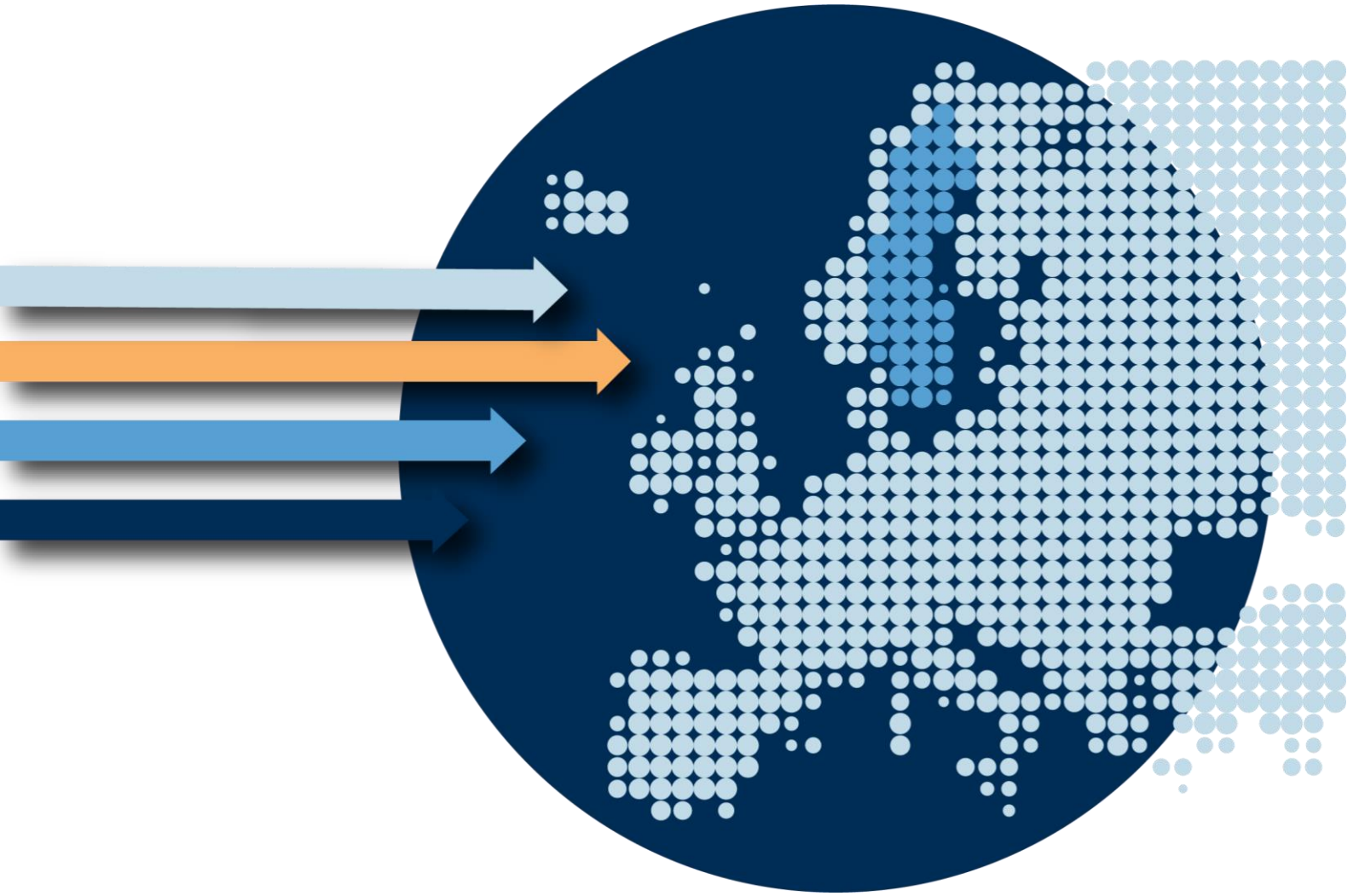
AN OUTCOME-BASED PAYMENT MODEL FOR BIOLOGIC AGENTS IN PSORIASIS



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Foreword

An outcome-based payment model need to meet the, sometimes conflicting, needs of multiple stakeholders. These include patients need for access to new innovative medical technologies, payers need for cost control, and the industries incentives for further innovation. This report is the result of a project funded by AbbVie, Eli Lilly, Novartis and Janssen. The purpose of the project was to discuss how an outcome-based payment model in psoriasis could be developed. A round table discussion was held with stakeholders representing clinical dermatologists, manufacturers, and regional and national payer representatives. The meeting was held on October 3rd, 2017 at Läkaresällskapet, Klara Östra Kyrkogata 10, in Stockholm.

Lund, June 2018

Peter Lindgren
Managing Director at IHE

1. Introduction

When the first innovative biologic drugs for psoriasis were introduced about 15 years ago it was a breakthrough in the treatment for psoriasis patients. Etanercept (Enbrel) and infliximab (Remicade) were reimbursed in Sweden 2003 and recommended as second line treatment for moderate to severe psoriasis in 2004. Since then several effective biologic drug treatments have been introduced, including adalimumab (Humira) and ustekinumab (Stelara). Recently biosimilars to the TNF-alpha inhibitors infliximab (Inflectra, Remsima) and etanercept (Benepali, Erelzi) have been developed and a biosimilar for adalimumab is expected in Europe in 2018. Furthermore, several interleukin-17-inhibitors, have become available for the treatment of psoriasis, including secukinumab (Consentyx), ixekizumab (Taltz), brodalumab (Kyntheum) and guselkumab (Tremfya). Several other interleukin-inhibitors are expected in the near future (risankizumab, tildrakizumab).

A recent study suggests an unmet patient need in the current treatment praxis as one in five psoriasis patients have insufficient response to systemic treatment [1]. With biosimilar drugs entering the market, there is a potential for increased competition and lower prices for biosimilars as well as for original products. Lower prices provide a potential to increase the number of treated patients. A report from The Dental and Pharmaceutical Benefits Agency (TLV), conclude that prices of TNF-alpha inhibitors biosimilars are higher, and the uptake is considerably lower, in Sweden compared to other Nordic countries [2].

Switching a patient from a conventional systemic treatment to a biologic agent, biosimilar or a new synthetic treatment, usually comes at a considerable increase in acquisition costs. The payment is made regardless of how well the treatment works. When a new treatment is introduced, there is always an uncertainty about how well new treatments work in clinical practice, and therefore there is a risk that the access to new innovative treatments is restricted.

There is an international trend that the willingness to pay for pharmaceuticals has shifted from focusing on safety and efficacy to a focus on the outcomes in clinical practice [3]. The development of adaptive licensing, with the purpose of faster access, provides new opportunities for alternative payment models. Decision-makers increasingly require evidence that is not only based on randomized controlled trials, but also on so-called Real-World Evidence.

The landscape of biological drugs for the treatment of psoriasis is undergoing important changes due to the introduction of new biosimilars as well as new efficacious interleukin inhibitors. An alternative payment model that links payment to outcomes could help reduce uncertainty of treatment outcomes, whilst enabling faster uptake of biosimilars as well as new innovative psoriasis treatments.

An outcome-based payment model need to meet the, sometimes conflicting, needs of multiple stakeholders. These include patients' need for access to new innovative medical technologies, payers' need for cost control, and the industries incentives for further innovation. IHE and the manager of PsoReg, Marcus Schmitt-Egenolf, invited several stakeholders to a roundtable meeting to discuss the possibilities for an outcome-based payment model of biologic agents in psoriasis. Present at the meeting were two clinical dermatologists, four representatives from the manufacturers, two representatives from TLV, two representatives for all county councils (NT-council/ SKL) and one representative from the Skåne Region (by phone). Participants are listed in the appendix.

Two examples of outcome-based payment models for biologic agents for psoriasis are presented in this report: one is based on the clinical outcome measure Psoriasis Area Severity Index (PASI) and one model is based on the patient-reported Dermatology Life Quality Index (DLQI). The Swedish register for systemic treatment of Psoriasis, PsoReg, provides a possibility to simulate what the effect would be if the alternative payment models were to be implemented, based on Real-World Data.

In this report, examples of outcome-based payment models for biologic agents for psoriasis are presented and discussed based on input from the roundtable discussion and on simulations on individual-level data from PsoReg.

2. An outcome-based payment model in psoriasis

The benefits of an outcome-based payment model need to outweigh risks and the costs of implementation and data collection for all stakeholders, including patients, payers, clinicians and manufacturers. Based on a round table discussion, on examples simulated using real-world data and based on the existing literature we discuss:

Firstly, whether an outcome-based payment model in psoriasis is needed. Secondly, how outcomes can be measured. Thirdly, how the payment can be linked to the outcomes. Finally, two examples of outcome-based payment models are simulated using real world data from PsoReg.

2.1 Is there a need for an outcome-based payment model in psoriasis?

There are several challenges in current clinical practice of biologically treated patients in psoriasis that might be addressed with an outcome-based payment model. Firstly, TLV concludes that the uptake of TNF-alpha inhibitors biosimilars in Sweden is low, and the prices are high compared to other Nordic countries. Secondly, there is an unmet patient need in the current treatment praxis as one of five patients do not have sufficient response to systemic treatment. Thirdly, the incentives to follow-up patients' treatment outcomes in current clinical practice is low.

Biosimilars provide an opportunity for improved access to biologic treatments. Since biosimilars are provided at a lower cost, and as an increased competition results in lower prices in general, more patients could get access to treatment. A report from TLV, suggest that prices of biosimilars are higher in Sweden than in Denmark, Norway and Finland. The average treatment cost of infliximab is 44 percent lower in Norway and 54 percent lower in Denmark, compared to Sweden. Furthermore, the penetration rate of biosimilars in Sweden is low. In Sweden, the market share of biosimilars to infliximab was estimated to about 30 percent in March 2016. The corresponding share in Denmark was 97 percent, in Finland 87 percent and in Norway 91 percent. Sweden thus has a considerably lower use of biosimilars than our neighboring Nordic countries [2].

During the round table discussion, dermatologists and payers argued that the prescribing physicians have low incentives to prescribe the biosimilar with the lowest cost as they are unaware of discounts and consequently they are unaware of the net prices of the different drugs. Furthermore, dermatologists and payers reasoned, the introduction of additional biosimilars during the coming years will result in even more confidential, complex, and non-transparent agreements.

A recent study based on the national register for systemic treatment of psoriasis, PsoReg [1], showed that one in five psoriasis patients on systemic treatment, that is biologics or conventional agents such as methotrexate, have insufficient response after at least three months of treatment. Whereas patients currently using conventional agents, are likely to benefit from an increased use of biosimilars as the prices decrease; patients with an insufficient response to current biologics need access to new innovative treatment options with improved treatment outcomes. An increased focus on biosimilars and price cuts, dermatologists fear, will result in restricted access to new and more effective treatments.

Furthermore, the dermatologist's perception is that patients with psoriasis are traditionally treated to a certain extent and that the incentives to follow-up patients in clinical practice are low[1]. Patients may receive expensive treatments, but there is no mechanism in the current health care system to follow-up to ensure that the treatments are effective. At the round table discussion, the dermatologists stressed the importance of a new outcome-based payment model that could create incentives to improve the follow-up of patients in clinical practice.

2.2 How could outcomes be measured?

In an outcome-based payment model, the performance of a treatment can be assessed either by the health care providers or by the patients themselves. Since there is no biomarker that can be used to measure the severity of disease in clinical practice, measures of clinical disease severity rely on estimates of the intensity and extent of psoriasis on the body surface. The most common clinical outcome measure in psoriasis is the Psoriasis Area Severity Index (PASI). PASI measures the current severity of psoriasis based on the coverage of four body areas (in percentage of affected area): head, arms, trunk, and legs. In each area, three main signs of psoriasis are assessed: redness, thickness, and scaling [5]. The score is on a scale from 0 (no disease) to 72 (theoretical maximal disease).

Traditionally, the primary endpoint in Randomized Controlled Trials (RCTs) of systemic treatment of psoriasis is the number of people that achieves at least a 75-percentage reduction in the Psoriasis Area and Severity Index (PASI 75) compared to baseline [6-10]. In RCTs of newer biologics, the primary endpoint reported has been raised to PASI 90 or PASI 100 [11-14]. In routine clinical practice an absolute value of PASI is used to measure the current severity of psoriasis. PASI is included in the Swedish register for systemic treatment of psoriasis, PsoReg. Changes in treatment are often requested when PASI scores exceed 5 [15]. An outcome based on PASI percentage change

[1] According to the national patients register, Swedish psoriasis patients are followed-up twice a year on average (4.National Board of Health and Welfare. *[Statistikdatabasen]*. 2017.)

works well in a clinical trial setting, where patients have a "wash-out" period before the trial and a baseline value of the severity of disease. This is not the case in a clinical practice setting, where patients switch directly from one treatment to another or where patients stay successfully treated for a longer time period. Once an initial change has been achieved, an absolute value is needed as a treatment target in clinical practice.

The clinical relevance of PASI to patients has been questioned and PASI is therefore often complemented by a measure of patients' quality of life in both clinical trials and in observational studies of psoriasis. Dermatology Life Quality Index (DLQI) [16] is the most common quality-of-life measure [17] and is included in PsoReg. The DLQI consists of ten questions on a four-point scale relating how the skin disease affects patients' quality of life over the last week [16]. The score ranges from 0 (quality of life not impaired) to 30 (quality of life severely impaired). It has been suggested that objective measures such as PASI could be used to measure outcomes in RCTs, whereas the impact on the patient's HRQoL could be used in clinical practice [18].

The International Society For Pharmacoeconomics and Outcomes Research (ISPOR) Task Force for Performance-based Risk-Sharing Arrangements [19] state that outcomes in outcome-based payment models should be clinically robust, clinically plausible, appropriate and monitorable. However, a major concern for payers in an outcome-based model is the risk of increasing the administrative burden of the health care system by adding complicated assessments and additional visits. The administrative burden has, for example, been raised as one of the major challenges when implementing payment models in multiple sclerosis and cancer drugs in the UK [20, 21], as hospitals did not receive additional funding for more extensive follow-up consultations. At the round table discussion, the risk of introducing additional health care visits was also raised as a concern by payers.

The ISPOR Task Force state that if the outcome is patient reported, there must be a relatively straightforward way to measure a patient's self-reported clinical response [19]. Clinical outcomes reported by the patients are available in psoriasis, e.g. the self-assessed PASI (SAPASI) [22] and the self-assessed Simplified Psoriasis Index (saSPI) [23]. The experience of using these measures is limited. The dermatologists in the round table discussion question the practicality of such measures in a real-world setting, especially since other available measures, such as the DLQI, are well-known and established.

To our knowledge there are no outcome-based payment models based on patient reported outcomes. None of the major guidelines or reviews of performance-based payment models refer to any existing outcome-based payment models based on patient-reported outcomes [19, 24-26].

The advantages of a patient reported outcome is that it does not necessarily require any additional health care visits to assess the treatment response. Patient reported outcomes can be reported in an "app" or on a webpage. A patient reported outcome included in a payment model does not need to be a validated patient reported outcome measure. It may be sufficient with a simple question such as "Do you believe that the treatment has treated your psoriasis disease sufficiently? Yes or No".

All stakeholders in the roundtable discussion, including representatives from payers, dermatologists and manufacturers, agreed that a patient reported outcome seems relevant for an outcome-based payment model in psoriasis. After all, TLV base part of their decision making on Quality-Adjusted-Life-Yeas (QALY), which is based on a patient reported measure of generic HRQoL. Thus, if patients can assess the impact of the psoriasis disease themselves, participant argued, it seems reasonable to use a patient reported outcome. The dermatologists confirm that patients with psoriasis are generally active in their disease management and that they are likely to be positive towards reporting disease activity in a phone/webpage application.

No consensus was reached in the round table discussion on what measure that would be most appropriate for an outcome-based payment model. One dermatologist favored the DLQI as it is well established and included in PsoReg. One dermatologist favored a new measure; the Patient Benefit Index (PBI) [27]. The advantage of such an index is that it is a comprehensive measure that captures several aspects of the treatment that could be relevant for the patient. The experience of PBI is however limited.

At the round table discussion, the county council representatives had the perception that the negotiations and agreements for the hospital administered drug infliximab, worked well for most counties. Furthermore, the county council representatives argued that it would be complex to have a payment model for both outpatient prescribed drugs and for hospital administered drugs. Dermatologists, argued that infliximab is used in a limited extent in psoriasis and that it eventually will be replaced with outpatient prescribed biologics. Based on the round table discussion, an outcome-based payment model is thus only relevant in prescribed outpatient biologic drugs.

2.3 Could payment be linked to outcomes?

Alternative payment models, including outcome-based payment models, have proven challenging to implement, partly due to the high costs of follow-up and data collection [28],[29]. One example of such payment model is for a drug in multiple sclerosis in the UK. Seven years after the agreement to have a scheme, the data was finally collected. The results suggested that there was a lack of delay in disease progression. Prices, however, were not adjusted downward because the evidence was not

conclusive. Due to challenges of this kind, there has been a trend towards minimizing the administrative burden of outcome-based payment models in the last decade [26].

In Italy indication-specific registers are used for alternative payment models, including outcome-based payment models. The Italian Medicines Agency has about 80 registers to collect data on safety and effectiveness in about 70 drugs. For example, for some drugs there is a price reduction for initial treatment until it is clear whether a patient is responding or not. Another approach is when the manufacturer reimburses the payer for non-responders or when 50 percent of the costs of the non-responders are reimbursed by the manufacturer. These alternative payment models have been well received, likely partly due to the reduced transaction costs of the national registers. [19]

The Swedish quality registers, including PsoReg, provides an opportunity for outcome-based payment models based on existing administrative infrastructure. County councils could be refunded based on the average response of patients registered in PsoReg. The register is estimated to cover about 60 percent of the biologically treated population, but the number of follow-up visits for patients is currently limited. If PsoReg is to be used the registration is crucial. The dermatologists in the round table discussion states that the registration in PsoReg is constantly improving. A county council representative points out that it is essential that each health care unit can track the treatment outcome among the patients at the clinic to improve incentives to report to the register. This feature is currently available in PsoReg.

The payment can be linked to the outcome ex-ante or ex-post. The experience from payment models in cancer drugs in the UK, showed that in 47% of hospitals the savings were not passed back to the payers [21]. In Italy, the system of applying an initial discount to all eligible patients at the beginning of treatment has been simpler to administer than the system of a payback mechanism with reimbursement for non-responders.[19]

In an outcome-based payment model in psoriasis, one alternative is that the county council pays the full price initially and then receives a pay-back for the proportion of patients who do not reach a threshold for successful treatment. Another option would be for the manufacturer to take the risk; the county council initially pays the lower price and pay the additional fee for the proportion of patients treated successfully retrospectively. In the round table discussion, a representative for the county councils pointed out that no matter if payment is linked to the outcome ex-ante or ex-post, it could be challenging for the county councils. As it is unclear what the outcome will be, the county councils would have difficulties with the allocation of budget. A middle way would be for the county council initially pays an estimated average price, which is retrospectively adjusted, upwards or downward, based on the outcome.

Another experience from payment models in cancer drugs in the UK, was that 73 percent of hospitals reported they did not have the capacity to manage the payment models due to the additional staff needed to manage, co-ordinate and track them. In the round table discussion this concern was raised by a representative from the county councils, who pointed out that apart from the three larger regions, the county councils do not have the capacity to do the analysis of outcome data and calculate the price of different biologic agents. Today, TLV supports the county councils in the managed entry agreements (sidoöverenskommelserna) by making the calculations for the refunds. A representative from the county councils suggested that it could be the same for an outcome-based payment model.

At the round table discussion, the representative from the county councils stress the importance of a transparent and simple payment model. If all county councils are to agree to implement the model, they also need to understand the mechanisms behind it. The county council representatives question whether a new model may be too complicated as it need to be different for each indication and whether the county councils would be able to manage several outcome-based payment models for the same drugs.

Even if different types of agreements (including risk-sharing schemes, price–volume negotiations, confidential discounts, coverage with evidence developments) are increasing, international reference pricing is used by the majority of European countries [30]. The manufacturers at the round table discussion stated that official list prices are maintained in an outcome-based payment model, due to international reference pricing.

Different biologic drugs are used for somewhat different patient groups. During the round table meeting representatives from the manufacturers raised the concern that this patient selection could be challenging in an outcome-based payment model, as it is directly linked to the outcome and price.

2.4 Examples based on Real World Data

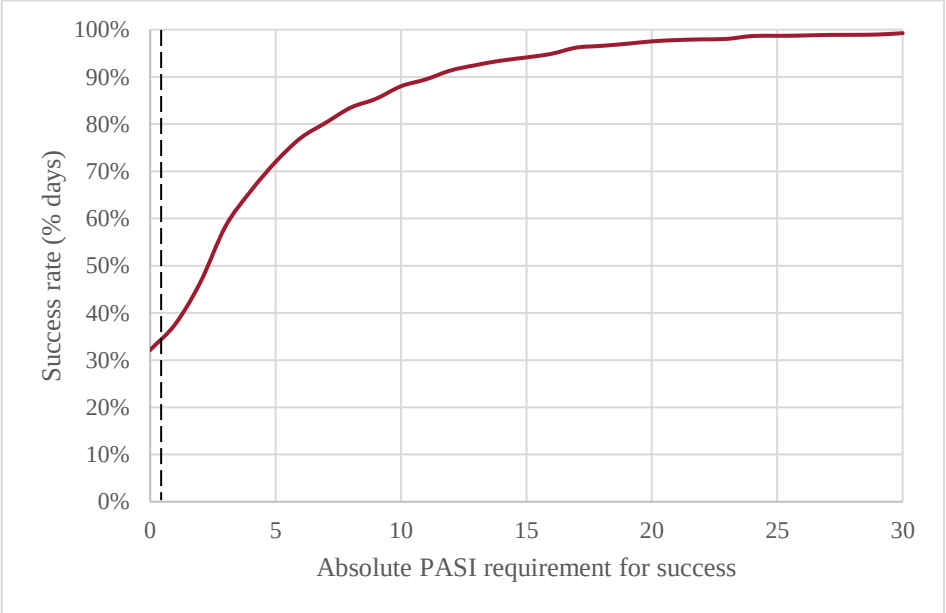
The Swedish register for systemic treatment of psoriasis, PsoReg, provides an opportunity to simulate the consequences of an outcome-based payment model, given that patients in the register are representative of the total population and that patients would be treated in the same way as they are in the current product-based payment system. In this section we present two examples of outcome-based payment models one based on the clinical outcome measure PASI and one model is based on the patient-reported DLQI. The weighted average prices and budgets were simulated based on data from PsoReg, given different price levels.

The simulations are based on data from 1064 patients, registered in PsoReg that used biologic agents during registration. Assessments that were made less than 12 weeks after treatment initiation were excluded. Twelve weeks is in accordance with treatment guidelines, which states that evaluation of the treatment should be made after 3-4 months [31]. Patients who discontinued within the first 12 weeks of treatment were considered treatment failures. The model simulates the number of successfully treated days, were the last value is carried forward. The definition of success can be varied in the model based on different absolute values of PASI or DLQI.

2.4.1 Example based on PASI measure

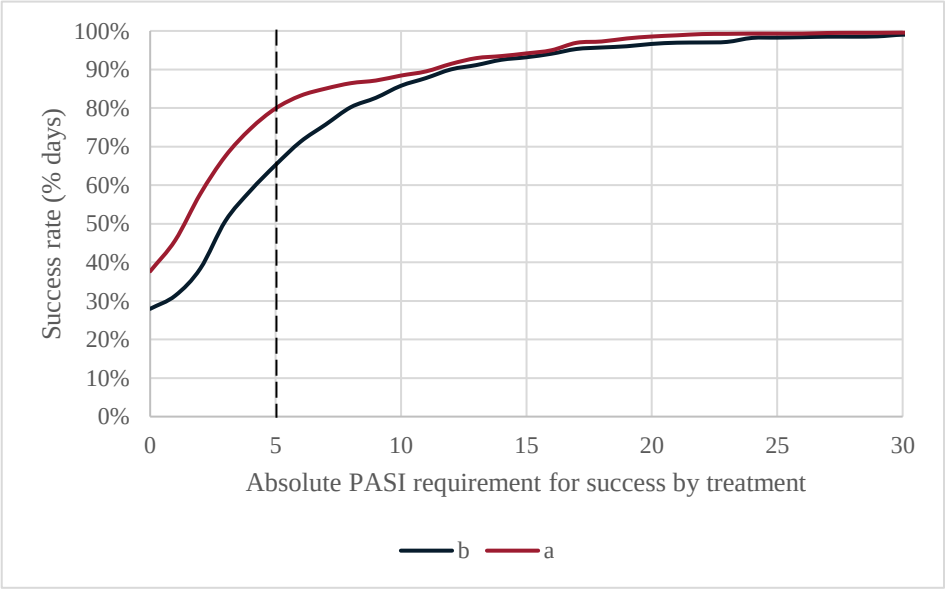
Figure 1 shows the number of successfully treated days in all biologically treated patients in PsoReg. Success is defined as either PASI 75 after switch to a biologic treatment or an absolute PASI level, which is varied on the x-axis. At the threshold of an absolute PASI 5, 72 percent of all patients treated with biologics are successfully treated. In an outcome-based payment model, success could be associated with a higher price and non-success with a low price or zero.

Figure 1: Number of successfully treated days in PsoReg, with success defined as either PASI75 after switch to a biologic treatment or an absolute PASI level (x-axis)



The success rates of two biologic treatments used in PsoReg patients are illustrated in figure 2. At a PASI <5 for the definition of successful treatment, 80 percent of the treated days were successfully treated with Drug A and 65 percent were successfully treated with Drug B.

Figure 2: Number of successfully treated days of two existing treatments (A, B) in PsoReg, with success defined as either PASI75 after switch to a biologic treatment or an absolute PASI level (x-axis)



If the pharmaceutical price for a successfully treated day is SEK 500 and the price for non-success is SEK 100, the weighted average price per patient for drug A would be ((0.8x500) + (0.2x100)) SEK420 (*Table 1*) The annual budget for 1000 patients (weighted average price *365 days *1000 patients) would be 153 M SEK. If the same level of success and price levels are used for both treatments the weighted average for drug B would be ((0.65x 500) + (0.35x 100)) SEK 360 and the annual budget for 1000 patients would be 131 M SEK *(Table 2.)*

Table 1 Weighted cost per patient and day for drug A in SEK and annual budget impact (MSEK in brackets) of 1 000 psoriasis patients depending on price in SEK per day for success defined as either PASI75 after switch to a biologic treatment or an absolute PASI level 5

PASI75 or PASI 5	**Price success: Drug A (80 %)**		
Price non-success: Drug A (20%)	**400**	**500**	**600**
0	320 (117)	400 (146)	480 (175)
100	340 (124)	**420 (153)**	500 (183)
200	360 (131)	440 (161)	520 (190)
300	380 (139)	460 (168)	540 (197)
400	400 (146)	480 (175)	560 (204)

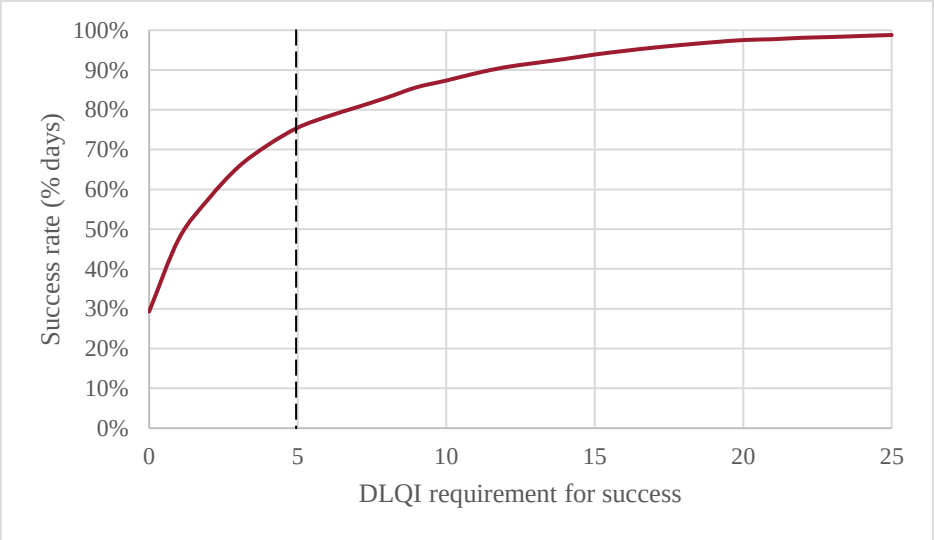
Table 2 Weighted cost per patient and day for drug B in SEK and annual budget impact (MSEK in brackets) of 1 000 psoriasis patients depending on price in SEK per day for success defined as either PASI75 after switch to a biologic treatment or an absolute PASI level 5

PASI75 or PASI 5	**Price success: Drug B (65%)**		
Price non-success: Drug B (35%)	**400**	**500**	**600**
0	260 (95)	325 (119)	390 (142)
100	295 (108)	**360 (131)**	425 (155)
200	330 (120)	395 (144)	460 (168)
300	365 (133)	430 (157)	495 (181)
400	400 (146)	465 (170)	530 (193)

2.4.2 Example based on DLQI measure

The overall success rates of treated days in PsoReg based on different DLQI levels is illustrated in figure 3. At a DLQI <5 the proportion of successfully treated days among all patients in PsoReg were about 75 percent. A DLQI of 0-1 is interpreted as "no effect at all on patient's life", 2-5 "small effect on patient's life", 6-10 "moderate effect on patient's life", 11-20 "very large effect on patient's life" and 21-30 "extremely large effect on patient's life".

Figure 3: Number of successfully treated days in PsoReg, with success depending on an absolute DLQI level (x-axis)



At a DLQI <5 for the definition of successful treatment, 78 percent of the treated days were successfully treated with Drug A and 73 percent were successfully treated with Drug B (*Figure 4*). If the price per day for success is SEK 500 and the price for non-success is SEK 100 the weighted average price per patient for Drug A would be ((0.78x500) + (0.22x100)) SEK 412 and the annual budget for 1000 patients would be 150 M SEK (*Table 3*). If the same level of success and price levels are used for drug B the weighted average for Drug B would be ((0.73x 500) + (0.27x 100)) SEK 392 and the annual budget for 1000 patients would be 143 M SEK (*Table 4*).

Figure 4: Number of successfully treated days of two existing treatments (A, B) in PsoReg, with success defined as an absolute DLQI level (x-axis)

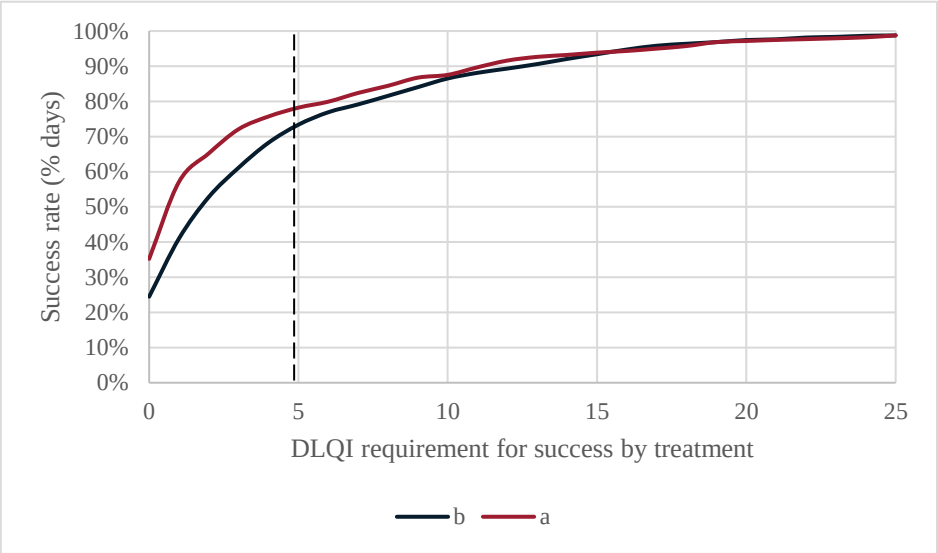


Table 3 Weighted cost per patient and day for drug A in SEK and annual budget impact (MSEK in brackets) of 1 000 psoriasis patients depending on price in SEK per day for success defined as an absolute DLQI level 5

DLQI 5	**Price success Drug A (78 %)**		
Price non-success Drug A (22%)	**400**	**500**	**600**
0	312 (114)	390 (142)	468 (171)
100	334 (122)	**412 (150)**	490 (179)
200	356 (130)	434 (158)	512 (187)
300	378 (138)	456 (166)	534 (195)
400	400 (146)	478 (174)	556 (203)

Table 4 Weighted cost per patient and day for drug B in SEK and annual budget impact (MSEK in brackets) of 1 000 psoriasis patients depending on price in SEK per day for success defined as an absolute DLQI level 5

DLQI 5	Price success Drug B (73%)		
Price non-success Drug B (27%)	**400**	**500**	**600**
0	292 (107)	365 (133)	438 (160)
100	319 (116)	**392 (143)**	465 (170)
200	346 (126)	419 (153)	492 (180)
300	373 (136)	446 (163)	519 (189)
400	400 (146)	473 (173)	546 (199)

2.4.3 Example of Hypothetical Drug

For illustrative purposes, imagine a new highly efficacious drug. As there are not yet any Real World Data, the manufacturer estimate the drug to have 30 percent higher effectiveness in terms of absolute PASI compared to an available drug (drug A). In Figure 5, results from PsoReg of two existing drugs and the hypothetical new drug is illustrated. A definition of success of an absolute PASI level of 5, 85% would be successfully treated days. At a success price of 500 SEK and a price of non-success at 100 SEK, the weighted average price per day would be ((0.85 x 500) + (0.15 x 100)) 440 SEK and the total annual budget for 1 000 patients: 161 M SEK (*Table 5*).

Figure 5: Number of successfully treated days of two existing treatments (A, B) in PsoReg and a hypothetic drug (which is 30 percent better than A), with success defined as either PASI75 after switch to a biologic treatment or an absolute PASI level (x-axis)

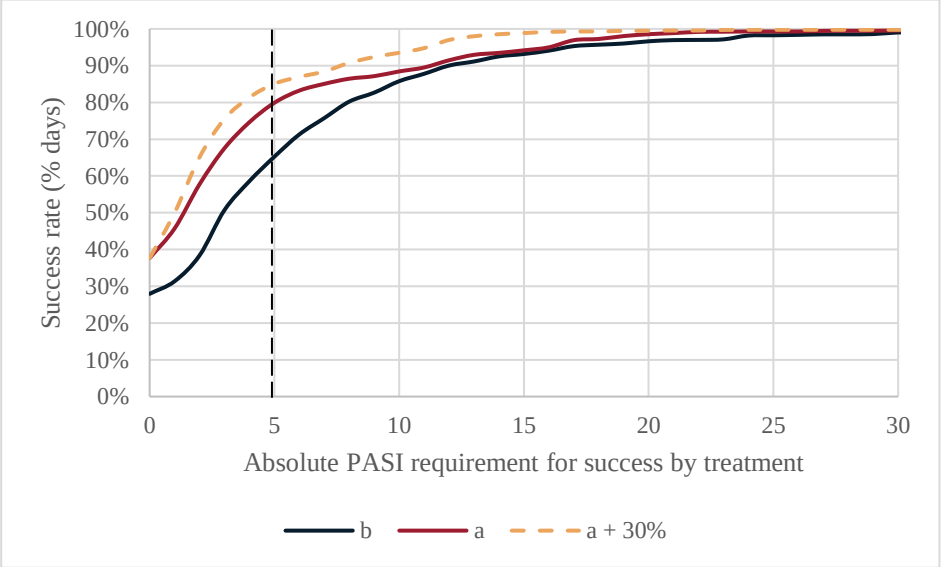


Table 5 Weighted cost per patient and day for a hypothetic drug (which is 30 percent better than A) in SEK and annual budget impact (MSEK in brackets) of 1 000 psoriasis patients depending on price in SEK per day for success defined as either PASI75 after switch to a biologic treatment or an absolute PASI level 5

PASI75 or PASI 5	Price success: Hypothetic drug (85%)		
Price non-success: Hypothetic drug (15%)	**400**	**500**	**600**
0	340 (124)	425 (155)	510 (186)
100	355 (130)	**440 (161)**	525 (192)
200	370 (135)	455 (166)	540 (197)
300	385 (141)	470 (172)	555 (203)
400	400 (146)	485 (177)	570 (208)

In Figure 6, results from PsoReg of two existing drugs and the hypothetical new drug is illustrated. The manufacturer estimate the drug to have 30 percent higher effectiveness in terms of absolute DLQI compared to an available drug (drug A). A definition of success of an absolute DLQI level of 5, 82% would be successfully treated days. At a success price of 500 SEK and a price of non-success of 100 SEK, the weighted average price per day would be ((0.82 x 500) + (0.18 x 100)) 428 SEK and the total annual budget for 1 000 patients: 156 M SEK (*Table 6*).

Figure 6: Number of successfully treated days of two existing treatments (A, B) in PsoReg and a hypothetic drug (which is 30 percent better than A), with success defined for success defined as an absolute DLQI level (x-axis)

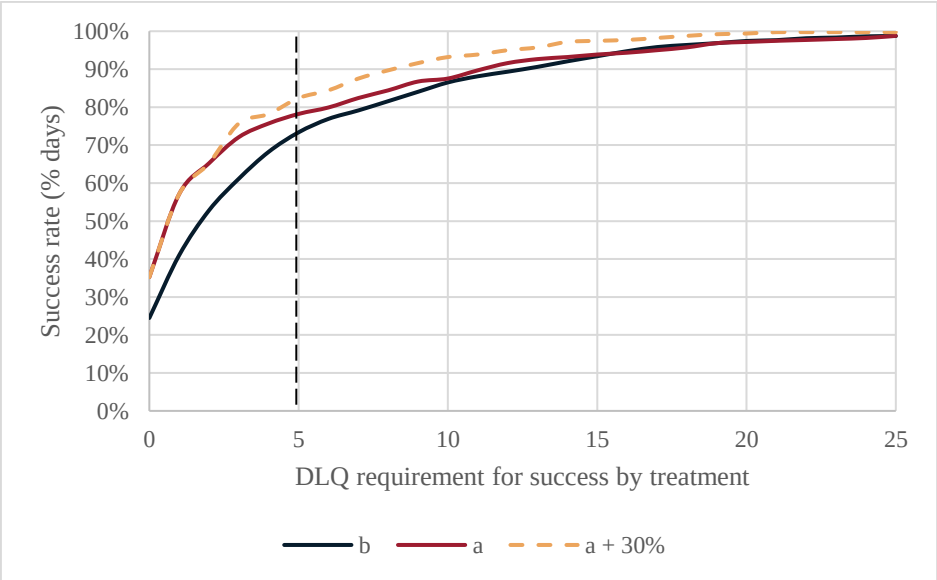


Table 6 Weighted cost per patient and day for a hypothetic drug (which is 30 percent better than A) in SEK and annual budget impact (MSEK in brackets) of 1 000 psoriasis patients depending on price in SEK per day for success defined as an absolute DLQI level 5

DLQI 5	Price success: Hypothetic drug (82%)		
Price non-success Hypothetic drug (18%)	**400**	**500**	**600**
0	328 (120)	410 (150)	492 (180)
100	346 (126)	**428 (156)**	510 (186)
200	364 (133)	446 (163)	528 (193)
300	382 (139)	464 (169)	546 (199)
400	400 (146)	482 (176)	564 (206)

2.4.4 Summary of Examples

Using the same price levels for success and non-success, the weighted average price was higher for Drug A than Drug B in both examples, as Drug A had higher performance in both measures (*Table 7*). The manufacturer of Drug A would most likely favor the payment model based on PASI as the weighted average price was higher in the PASI payment model compared to the DLQI payment model, given the same absolute value of PASI/DLQI. Likewise, the manufacturer of the hypothetical drug would favor the PASI payment model. In contrast, manufacturer of Drug B would most likely favor the payment model based on DLQI, as the weighted average price was higher in the DLQI payment model compared to the PASI payment model, given the same absolute value of PASI/DLQI.

Table 7 Weighted cost per patient and day for drug A, drug B and a hypothetic drug (which is 30 percent better than A) in SEK and annual budget impact (MSEK in brackets) of 1 000 psoriasis patients depending at a price of SEK 500 per day for success defined with PASI or DLQI

Definition of Success	Drug A	Drug B	Hypothetical drug
PASI75 or PASI 5	420 (153)	360 (131)	440 (161)
DLQI 5	412 (150)	392 (143)	428 (156)

3. Discussion: How could an outcome-based payment model in psoriasis work in practice?

In this report, we present two examples of outcome-based payment models; one based on the clinical outcome PASI and one based on the patient reported measure DLQI. These examples demonstrate that the consequences of an outcome-based payment model may differ depending on the measure used; Drug A had a higher weighted average price using the PASI payment model compared to the DLQI model and drug B had a higher weighted average price using the DLQI model compared to the PASI model. This illuminates the challenge for stakeholders to agree on the design of an outcome-based payment model as different manufacturers may have different preferences.

An outcome-based payment model based on a clinical assessment, such as PASI, would most likely require extra follow-up visits given that Swedish psoriasis patients are only followed-up twice a year on average [4]. Introducing additional health care visits could be challenging based on the international experience of high costs of follow-up and data collection in outcome-based payment models [28],[29] and based on the input from the payer representatives in the roundtable discussion. A patient-reported outcome measure could be relevant in psoriasis, as patients has the possibility to assess the disease themselves, which is not the case in many other disease areas. To our knowledge, there is no experience of outcome-based payment models based, nationally or internationally, on patient reported outcomes.

The examples of outcome-based payment models illustrate how expected outcomes can be estimated based on simulations from PsoReg. The hypothetical example illustrates that the weighted average price of new drugs, that are not yet included in the register, can be estimated. For example, if there is a head-to-head trial of a new drug against an existing drug suggesting superior efficacy, an estimate of the expected real-world effectiveness can be made based on real-world data from PsoReg. The estimated weighted average of a “high price” (successful) and a “low price” (non-success) could be used ex-ante to estimate expected outcomes of the payment model. The estimated weighted average price could then be confirmed depending on actual success rates. The actual weighted average price would only be known ex-post from the outcomes data and consequently, official list prices of drugs could be maintained.

The purpose of the examples of the outcome-based payment models was to illustrate how outcomes can be linked to the price of a drug used in clinical practice. Outcome measures of performance and, levels used to define success/non-success need to be agreed upon based on negotiations between the manufacturers, TLV and the NT-council. The definition of success and non-success could be the same for all biologic treatments for psoriasis, as in the examples in this report. Alternatively,

definitions of success could be product-specific and be defined together with each manufacturer separately. The advantage of a differentiated approach is that success rates in combination with manufacturers' pricing strategies could provide opportunity to have a broad price range for psoriasis treatment, with different products aiming for different patient segments. The disadvantage of a differentiated approach is that it adds complexity and may be difficult to implement in practice.

The weighted average price could be based on the national average response among patients and be applied in all county councils. A second option is that the weighted average price could be based on the average response among patients in a sample or a specific region and be applied in all county councils. A third option is a regional-outcome approach where the county pays a weighted average price based on the outcome among their own patients. The weighted average price would then differ between county councils. The experience from outcome-based payment models internationally, and as pointed out at the round table discussion, smaller county councils may not have the capacity to do the extra analysis needed for such regional-outcome approach.

3.1 Challenges with outcome-based payment model in psoriasis

There is a trade-off between designing the perfect payment model, that could work in theory, and the simplicity needed for successful implementation in practice. Questions remain whether county councils have the capacity to manage the complexity of 1) product-specific success rates, 2) weighted average price based on regional outcomes, and 3) several payment models for same biologics in several indications, as psoriasis is only one disease area among many where these biologic agents are used.

Data collection is a challenging factor in all outcome-based payment models. In its current form, PsoReg may not be sufficient for an outcome-based payment model. The number of visits per patients is limited and the time period between visits for individual patients is often long. Alternative payment models based on the indication-specific registers in Italy, are often considered successful, partly due to the reduced transaction costs. Similarly, PsoReg could provide an opportunity for an outcome-based payment model in psoriasis in Sweden by further developing the existing infrastructure.

Another challenge is that we do not know how the incentives of different stakeholders could change in an outcome-based payment model and how that would impact treatment decisions. Whereas the simulations in this report were based on treatment decisions made in the current system, we can only speculate how those would change with an alternative payment model. For example, an outcome-based payment model may change incentives that affect the patient selection for a particular drug and consequently affect success rates. Even though patients could be followed-up with patient reported measures in an outcome-based payment model, it is unknown how this would impact county

councils' incentives to follow-up patients. County councils may, for example, have low incentives to follow-up patients and to switch them from a non-successful treatment, in order to keep prices low.

Another challenge is the county councils need for budget caps. The examples of outcome-based payment models provided in this report aim to ensure that payers get value for money as payers only pay the full price for successful treatments. A limitation of the suggested payment models is that the models do not include county councils' budget impact.

3.2 Opportunities with outcome-based payment model in psoriasis

As psoriasis is a disease that can be assessed by the patients themselves, this provides an opportunity to develop an outcome-based payment model with patient reported outcomes in a phone/webpage application. This would increase the likelihood of actual implementation, as the model does not necessarily require any additional health care visits. Furthermore, in psoriasis there is no disease progression as in e.g. rheumatoid arthritis and other disease areas for which the same biologic agents are used. This is an advantage in an outcome-based payment model where payment is linked to on outcomes over time.

An advantage of an outcome-based payment model compared to a discount is that manufacturers will have incentives to maximize the number of responders, and not only the volume of treated patients. This could e.g. be achieved by providing education on the disease and treatment to patients, or other measures to increase compliance, and thereby the chances of successful treatments.

In the current payment system, there is a challenge with non-transparent prices as physicians do not have information on the discounted prices, whereas manufacturers want to maintain list prices and keep discounts confidential. Even though physicians would not know the weighted average price ex-ante, an outcome-based payment model could provide an opportunity for physicians to make more informed decisions. As physicians could continuously track the clinic's patients and their success rates in the register, they could have an estimate of the weighted average price.

3.3 The way forward

One way forward could be to further develop the existing infrastructure in PsoReg, by developing an application for devices that would allow for patient-reported outcomes. The pilot-testing of a "PsoReg-App" for e.g. monthly or quarterly patient self-reporting of DLQI and EQ-5D is scheduled for spring 2018. This will compensate for the current limitation of PsoReg where reporting of DLQI and EQ-5D is dependent on the less frequent contacts with the care-giver. An application will

provide the opportunity for patients to continuously report data to the register directly, without requiring extra, cost driving, health care visits. This could provide the patients with a tool to monitor their chronic disease over time and it could improve the possibilities for physicians to monitor and adjust the treatment of their patients. Consequently, an application could not only provide data for the payment model but also open up for possibilities to improve management of disease.

Another way forward to implementing an outcome-based payment model in psoriasis in practice could be to perform a pilot study in one region/county council. A pilot could be challenging to perform as a county council is committed to make joint agreements with the other county councils, TLV and the NT-council and not to make separate agreements with manufacturers. The new commission on financing, reimbursement and pricing of pharmaceuticals may shed some light on the future of payment models in Sweden.

3.4 Conclusion

An outcome-based payment model may address some of the challenges with the current "price per mg" payment model, by improving access to biosimilars and new innovative interleukin inhibitors, as well as improving outcomes by better follow-up of patients in clinical practice.

PsoReg is a valuable data source and provides a good starting point for the design of outcome-based payment models and for testing scenarios on patients from clinical practice. The register is currently not rigged for implementation of an actual outcome-based payment model. The application with patient reported outcome measures, linking to the existing infrastructure in PsoReg, provides opportunities for an outcome-based payment model in psoriasis. An application could avoid some of the administrative burdensome of an outcome-based payment model by avoiding extra health care visits. Nevertheless, the challenge is to develop an outcome-based payment model that is effortless enough to be implemented in the county councils, and at the same time sophisticated enough to capture outcomes and to link payment to outcomes.

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Appendix: Round table discussion

A Round Table Discussion was held October 3rd, 2017, at Svenska Läkaresällskapet, Klara Östra Kyrkogata 10, Stockholm

Participants:

Marlene Almqvist, AbbVie

Gustav Befrits, NT-rådet

Sara Dalin, TLV

Dana Enkusson, Janssen

Ulrika Fröbel, Novartis

Kristina Karlsdotter, Eli Lilly

Maj Carlsson, Region Skåne (on the phone)

Douglas Lundin, TLV

Marcus Schmitt-Egenolf, Umeå University, Dermatologist, Registerhållare PsoReg

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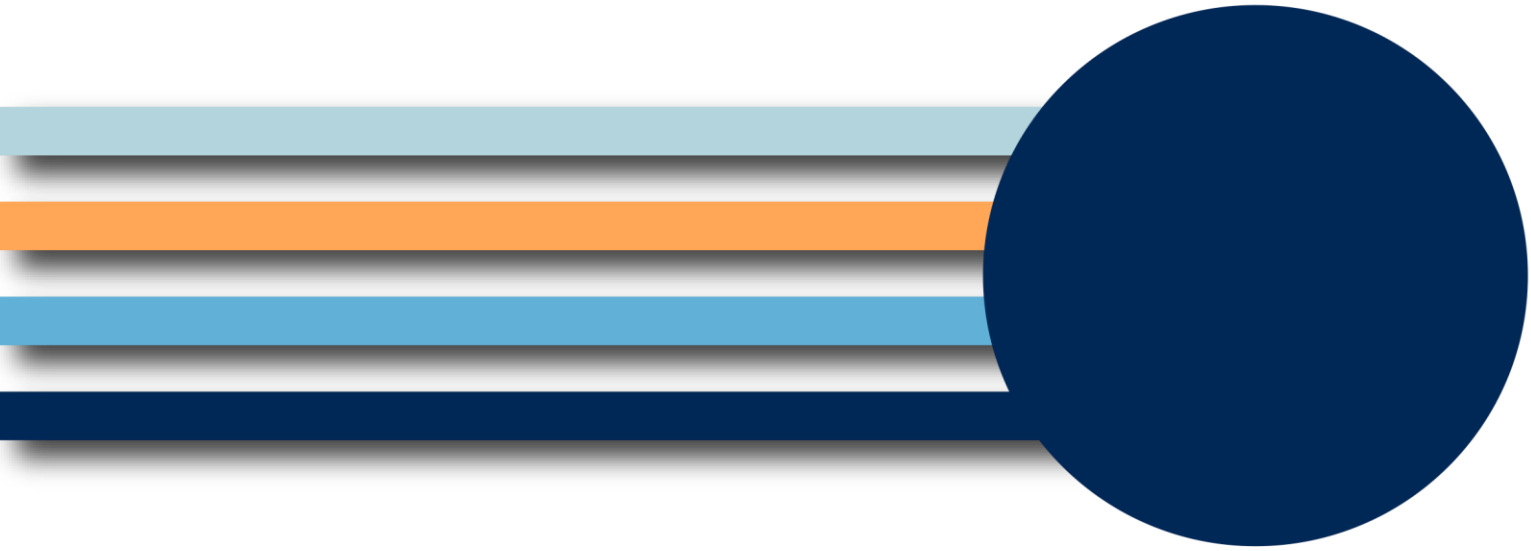

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