ORIGINAL ARTICLE

# The risk of psoriatic arthritis remains constant following initial diagnosis of psoriasis among patients seen in European dermatology clinics

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## Abstract

**Background** Estimates of psoriatic arthritis (PsA) prevalence among psoriasis patients vary widely (5–40%). The time to development of PsA in patients with plaque psoriasis also remains unclear.

**Objectives** To examine whether length of time since diagnosis of psoriasis affects risk of developing PsA, and to assess differences in quality of life (QoL), work-related issues, comorbidities and healthcare resource utilization (HCRU) for patients with PsA vs. psoriasis.

**Methods** This large cross-sectional observational study was conducted in the UK, Italy, France, Spain and Germany in 2006. Dermatologists who actively treated patients with psoriasis recruited 10 consecutive patients with psoriasis. Presence of PsA, body surface area (BSA) affected with psoriasis and HCRU were recorded; patients completed EUROQoL (EQ5D) and employment disadvantages questionnaires.

**Results** Patients with psoriasis ($n$ = 1560) included 126 with PsA. Ninety per cent of these patients with PsA were seen by dermatologists who involved a rheumatologist in the care of their patients with PsA. Survival analysis indicated that the incidence of PsA among psoriasis patients remained constant (74 per 1000 person-years), while the prevalence increased with time since diagnosis of psoriasis, reaching 20.5% after 30 years. In addition, those with high BSA currently affected by psoriasis were more likely to have developed PsA ($P < 0.028$). PsA patients reported reduced QoL compared with psoriasis patients (EQ5D score: 0.56 vs. 0.82: $P < 0.0005$), as well as more work problems. PsA patients were more likely to be hospitalized (0.27 ± 0.84 vs. 0.14 ± 0.71 per year; $P < 0.0005$) and have additional comorbidities than those without PsA.

**Conclusions** The incidence of PsA was constant after initial diagnosis of psoriasis, leading to a higher prevalence of concomitant PsA over time. PsA is associated with decreased QoL and increased work-related problems, HCRU and comorbidities. Dermatologists should screen for PsA in their patients, especially long-standing patients who did not initially present with PsA.

Received: 12 June 2009; Accepted: 15 September 2009

## Keywords

comorbidities, healthcare resource utilization, incidence, prevalence, psoriasis, psoriatic arthritis, quality of life, work productivity

## Conflict of interest

None declared.

## Introduction

Psoriasis is a common, systemic, inflammatory dermatological disease with a prevalence of between 1.5% and 2.2%.[1–3] Estimates of the prevalence of psoriatic arthritis (PsA) in the psoriatic population vary widely from 5% to 40%.[4–8] The relationship between psoriasis and PsA is not well understood, although most PsA patients develop psoriasis prior to the development of arthritic symptoms[9–11] and some studies have reported a relationship

between both severity and duration of psoriasis and the development of PsA.[4,9]

Both psoriasis and PsA have a negative impact on quality of life (QoL).[2,12–14] On average, psoriasis patients with PsA report significantly lower QoL than those without arthritis.[15,16] In addition, psoriasis and PsA patients are more likely to suffer significant comorbidities, including metabolic and cardiovascular diseases, than the general population.[17–22] Studies report that rates of hospitalization, emergency department visits, outpatient visits, laboratory services and outpatient pharmaceutical use are higher for psoriasis patients than for matched controls.[23,24]

### Objectives

The objective of this study was to explore the relationship between the duration of plaque psoriasis (hereafter psoriasis) and the development of PsA. In addition, this study examined the effect of developing PsA on QoL, employment, comorbidities and healthcare resource utilization (HCRU).

## Patients and methods

The Adelphi Psoriasis Disease Specific Program is a cross-sectional observational study that was conducted in the UK, Spain, France, Italy and Germany in 2006. About 300 dermatologists who actively managed 10 or more psoriasis patients per month were recruited. Each dermatologist enrolled 10 consecutive patients with psoriasis, regardless of type. Results presented here are based on those patients who had plaque psoriasis.

### Data collection

During the single study visit, dermatologists completed a Patient Record Form (PRF) for each patient based on the medical history of the patient, and on the dermatologist's knowledge of the patient. The PRF recorded data on: the type of psoriasis; time since psoriasis diagnosis; whether the patient had PsA and if so, time since PsA diagnosis; BSA affected at the time of the study visit; HCRU during the previous 12 months; and comorbidities. Included in the list of comorbidities, dermatologists were asked if the patient 'suffers from or has suffered from upper GI problems'. Dermatologists also were asked whether they involved a rheumatologist in the care of their PsA patients.

Recruited patients were asked to complete a QoL questionnaire and an employment disadvantages questionnaire. The EuroQoL 5D (EQ5D) assesses QoL, where a score of 1 represents perfect health, a score of 0 represents death and a change in score of 0.05 is considered clinically meaningful.[25] The employment disadvantages questionnaire assesses the impact of psoriasis on everyday tasks, work problems, current employment and days of work missed. The effect of disease on everyday tasks is scored on a scale from 1 to 5, where 5 represents a severe effect.

### Statistical analysis

Patients were categorized into two groups based on the presence or absence of a PsA diagnosis. Using *t*-tests or Fisher's exact test, age, gender, psoriasis duration and BSA affected by psoriasis were compared.

Survival analysis was used to calculate incidence and prevalence of PsA over time, based on the length of time a patient had had psoriasis at the time of PsA diagnosis. Kaplan–Meier life table techniques were used to calculate the cumulative risk of developing PsA during each year with psoriasis. Patients diagnosed with PsA prior to, or concomitantly with, a diagnosis of psoriasis were excluded from the survival analysis.

To determine whether the incidence is constant over time, a piece-wise exponential model was used. The data were divided into several time periods since psoriasis diagnosis. The incidence, or hazard rate, was assumed constant within each time period using an exponential regression model with time period dummy variables included as explanatory variables. This model was compared with a model assuming a constant hazard rate through time using a likelihood ratio test. This tested the null hypothesis that the two models are the same, i.e. the incidence of PsA is constant for all observed time.

Logistic regression was used to analyse whether BSA is associated with the development of PsA, controlling for time since psoriasis diagnosis. A subset of patients diagnosed with psoriasis in the last 6 months – and therefore having BSA measurements taken relatively soon after diagnosis – was used in a second analysis.

The impact of age at psoriasis diagnosis on developing PsA was examined by comparing two cohorts of psoriasis patients: those diagnosed with psoriasis before the age 30 years; and those diagnosed after the age of 50 years. Patients diagnosed with psoriasis between the ages of 30 and 50 years were excluded. The presence of PsA was compared between these two populations using Fishers Exact test, and logistic regression was used to control for time since psoriasis diagnosis and gender. The robustness of this approach was examined by treating age as a continuous variable and including patients of all ages.

Comorbidities, HRCU, QoL and work problems were compared for patients with PsA vs. patients with psoriasis alone using *t*-tests, Fisher's Exact test, or Mann–Whitney *U*-test. Logistic or linear regression analyses were used to control for age and gender.

## Results

Of the 2962 patients with any type of psoriasis who were recruited for this study, 2290 (77%) had plaque psoriasis, and 1560 of those had no missing values for relevant questions from the PRF and were included in these analyses. Of these, 126 were diagnosed with both psoriasis and PsA (Table 1). Patients with PsA and psoriasis were significantly older than those with psoriasis alone, were more likely to be male, had a longer duration of psoriasis, and a larger BSA affected. Prevalence of PsA across this population of patients with psoriasis was 8.1%.

**Table 1** Demographics and clinical characteristics of patients with psoriasis alone or with psoriasis and PsA

| Characteristics | Psoriasis ($n$ = 1434) | Psoriasis and PsA ($n$ = 126) | $P$-value |
|---|---|---|---|
| Age (mean years ± SD) | 45.6 ± 15.6 | 49.1 ± 13.8 | 0.018 |
| Gender (% male) | 57.8 | 68.3 | 0.024 |
| Psoriasis duration (mean years ± SD) | 11.0 ± 11.3 | 17.3 ± 11.3 | <0.0005 |
| BSA affected (mean percentage ± SD) | 17.2 ± 16.9 | 26.6 ± 19.9 | <0.0005 |

BSA, body surface area; PsA, psoriatic arthritis; SD, standard deviation.

A majority of the PsA patients studied (66.3%) were seen by dermatologists who co-managed PsA patients with a rheumatologist, and a further 24.2% of the PsA patients studied were seen by dermatologists who consulted with a rheumatologist for the treatment of their PsA patients. Only 9.5% of patients with PsA were seen by dermatologists who did not involve a rheumatologist in the care of PsA patients. Therefore, although the presence of PsA was reported by dermatologists, involvement of rheumatologists in the care of 90% of these PsA patients supports the accuracy of the diagnosis.

The incidence and cumulative prevalence of PsA over time were examined in this population of psoriasis patients, using Kaplan–Meier survival analysis (Fig. 1). The number of patients at risk for developing PsA declined over time, from 1453 patients at Year 0 to 128 at Year 30, because of the low number of patients with a long history of psoriasis as well as the number of patients who developed PsA earlier in the course of their psoriasis. Patients diagnosed with PsA prior to psoriasis ($n$ = 6), or diagnosed with psoriasis and PsA concomitantly ($n$ = 12), were excluded, as were patients initially diagnosed with psoriasis on the day of the survey ($n$ = 89). The incidence of PsA in the population of patients with psoriasis remained relatively constant, largely below 1% per year during the 30 years examined (74 per 1000 person-years; Fig. 1). A statistical test for a trend of either increasing or decreasing incidence of PsA failed to reject the null hypothesis of no trend ($P$ = 0.409). Prevalence of PsA increased steadily with disease duration, reaching 20.5% among patients with a 30-year history of psoriasis.

Patients with a higher BSA affected were significantly more likely to have developed PsA [odds ratio (OR): 1.020 for a 1% increase in BSA; 95% confidence interval (CI) 1.012–1.029; $P < 0.0005$] when time since psoriasis diagnosis was taken into account. The BSA observed was the current BSA affected, not that at the time of diagnosis. In a subset of patients diagnosed with psoriasis in the last 6 months ($n$ = 148) – thus having BSA measured relatively soon after psoriasis diagnosis – higher BSA remained predictive of developing PsA (OR: 1.068 for a 1% increase in BSA; 95% CI: 1.007–1.133; $P < 0.028$].

Genetic evidence suggests that psoriasis may be two separate diseases with similar symptoms, one that presents in adolescence/early adulthood and one that presents later in life.[26,27] The propensity of psoriasis patients to develop PsA was examined with regard to the age at which a patient was first diagnosed with psoriasis. Patients with early onset psoriasis (diagnosed before age 30, $n$ = 684) were compared with those with late onset (diagnosed after age 50, $n$ = 267). While there was a trend for patients with early onset psoriasis to be more likely to have PsA than those with late onset (9% vs. 6%; $P$ = 0.086), this difference was not significant. Furthermore, patients with early

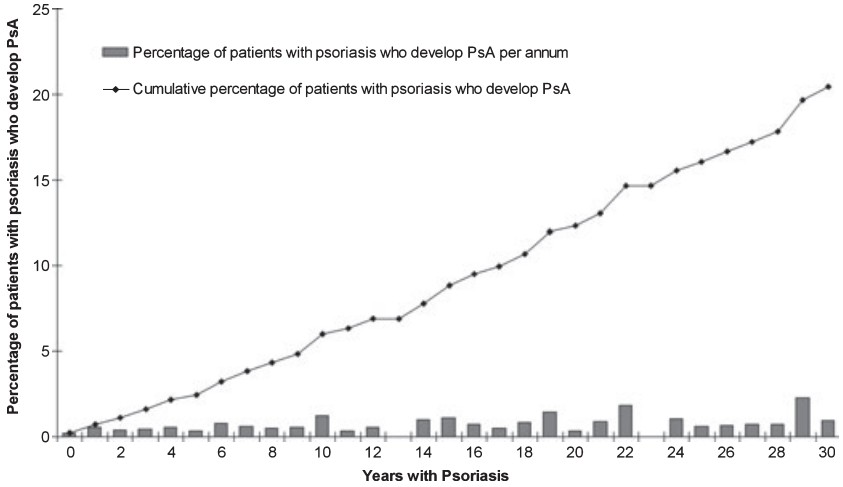


**Figure 1** The incidence and cumulative prevalence of psoriatic arthritis (PsA) over time in the population of psoriasis patients.

onset psoriasis in this dataset had psoriasis for more years than late onset patients (mean length of time with psoriasis: 14.7 ± 13.6 years vs. 5.2 ± 5.5 years; $P < 0.0005$). Because length of time with psoriasis may predict the development of PsA, logistic regression was used to compare PsA occurrence in early onset vs. late onset psoriasis patients controlling for years since psoriasis diagnosis. In this adjusted comparison, patients with early onset psoriasis were no more likely to develop PsA than those with late onset of disease (OR: 1.053; 95% CI: 0.560–1.980; $P = 0.872$). Finally, a logistic regression with age as a continuous variable using data from the whole study group – including 30- to 50-year-old patients – also found that age at psoriasis diagnosis did not predict whether a patient would develop PsA [OR: 1.000 for an additional year of age; 95% CI: 0.987–1.014; $P = 0.983$).

Comorbidities were compared for patients with PsA vs. those with psoriasis alone (Table 2). Patients with PsA were significantly more likely to have hypertension, or upper gastro-intestinal (GI) tract problems, even after controlling for age and gender ($P \leq 0.033$). Other comorbidities such as physician reported obesity, elevated cholesterol, depression, type II diabetes, body mass index (BMI) >30 and renal impairment occurred more often in PsA patients, but did not reach statistical significance.

Healthcare resource use was compared for patients with PsA vs. patients with psoriasis alone (Fig. 2). Patients with PsA had significantly more disease-related visits per year to their own dermatologist (5.3 ± 3.8 vs. 3.8 ± 3.7: $P < 0.0005$), other specialists (2.1 ± 5.1 vs. 0.8 ± 2.2: $P < 0.0005$) and primary care physicians (1.9 ± 2.2 vs. 1.2 ± 1.9; $P < 0.0005$). Patients with PsA were also more likely to be hospitalized for treatment of their psoriasis (0.37 ± 0.84 vs. 0.14 ± 0.71; $P < 0.0005$). These significant differences remained after controlling for age and gender using linear regression.

Of the 1560 patients, 554 (including 53 PsA patients) returned completed EQ5D and employment disadvantages questionnaires. Patients with PsA had significantly lower QoL – as measured by EQ5D – than those with psoriasis only (Table 3). Patients with PsA also reported more difficulty with everyday tasks and more work problems because of disease. These differences remained significant after controlling for age and gender using linear

**Table 2** Comorbidities of patients with PsA vs. patients with psoriasis alone

| Comorbidity | Psoriasis ($n$ = 1434), % | Psoriasis and PsA ($n$ = 126), % | $P$-value | Adjusted for age and gender, OR (95% CI) |
|---|---|---|---|---|
| Hypertension | 15.6 | 25.4 | 0.008 | 1.745 (1.10–2.77) |
| Physician-reported obesity | 8.4 | 12.7 | NS | 1.534 (0.87–2.70) |
| Elevated cholesterol | 10.0 | 12.7 | NS | 1.108 (0.62–1.97) |
| Depression | 8.3 | 10.3 | NS | 1.318 (0.72–2.42) |
| Upper GI impairment | 2.2 | 5.6 | 0.033 | 2.381 (1.02–5.54) |
| Renal impairment | 1.3 | 3.2 | NS | 2.268 (0.74–6.91) |
| Diabetes type II | 5.9 | 7.1 | NS | 1.071 (0.51–2.25) |
| BMI>30 | 11.9 | 14.3 | NS | 1.162 (0.68–1.97) |

BMI, body mass index; CI, confidence interval; GI, gastrointestinal; NS, not significant; OR, odds ratio.

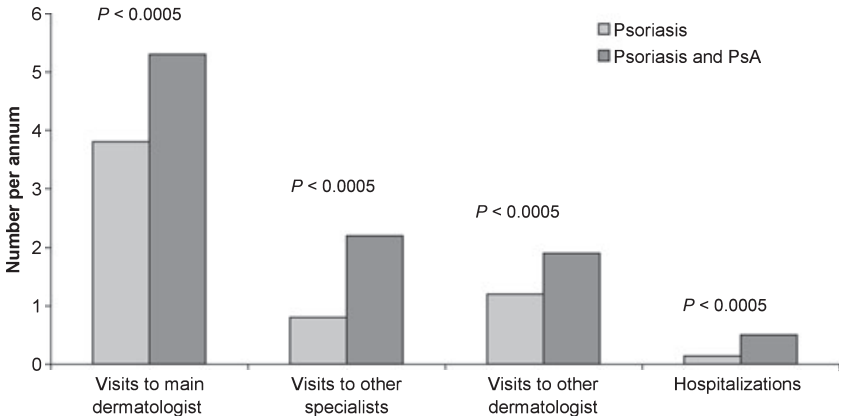


**Figure 2** Healthcare resource use in the last 12 months by patients with psoriasis and those with both psoriasis and psoriatic arthritis (PsA). $P$-values shown are from linear regressions controlling for age and gender.

**Table 3** Quality of life and employment related problems

| | Psoriasis ($n$ = 501) | Psoriasis and PsA ($n$ = 53) | $P$-value* |
|---|---|---|---|
| Quality of life (EQ5D score) | 0.82 | 0.56 | <0.0005 |
| Effect on everyday tasks (1–5 scale) | 2.34 | 2.85 | 0.001 |
| Work problems caused by disease | 11.2% | 32.1% | <0.0005 |
| Currently employed | 58.3% | 41.5% | 0.083 |
| Days of work missed | 1.2 | 2.5 | 0.164 |

*$P$-value for $H_0$: no difference between groups from logistic or linear regression (as appropriate), controlling for age and gender.

regression. Fewer patients with PsA were currently employed and patients with PsA who were employed missed more days of work in the previous 3 months than those with psoriasis, although these differences were sensitive to controlling for age and gender.

## Discussion

While the incidence of PsA among the psoriatic population in this study remained constant in any given year after diagnosis of psoriasis, the prevalence of PsA increased over the 30-year span of the analysis – reaching 20.5% after 30 years. The development of PsA appears to occur at a constant rate during each year following psoriasis diagnosis, resulting in a steady increase in PsA prevalence. The longer a patient has psoriasis, the more likely he/she also has PsA.

Although the apparent constant rate of developing PsA in a psoriasis population has not been widely studied, it has been observed that most PsA patients (60–65.5%) develop psoriasis prior to the development of arthritic symptoms.[9–11] A recent retrospective study in the US using the Olmstead county registry, a population-based cohort of subjects with psoriasis, reported a cumulative incidence of 5.1% for new-onset PsA at 20 years following psoriasis incidence, with an increasing prevalence of PsA by time since psoriasis diagnosis.[8] For comparison, the cumulative incidence of PsA in this study of psoriasis patients seen in European dermatology clinics was 13% at 20 years.

Prevalence of PsA among all patients with psoriasis in this study was 8.1%, i.e. near the low end of reported prevalence rates (5–40%). The 8.1% estimate may be lower than other estimates because the study was conducted in dermatology clinics rather than rheumatology clinics. Moreover, mild psoriasis patients were included. Estimates likely would be higher if only patients with moderate to severe psoriasis were included. However, prevalence of PsA in this study was well above the estimated PsA prevalence in the general population of about 1%, suggesting that the two diseases are related.[28]

Overall, BSA affected was higher in the group of patients with PsA. BSA predicted developing PsA when controlling for time since psoriasis diagnosis. Our findings support those of a US study that shows that the prevalence of PsA among patients with psoriasis increases significantly on the basis of the BSA involved with psoriasis.[4] In that population-based study, 6% of patients with minimal psoriasis had PsA compared with 18% of those with 3–10% BSA and 56% of those with BSA > 10%.

The decrease in QoL for patients with PsA has been well documented.[4,16,29] We provide a direct comparison of QoL between patients with PsA and those with only psoriasis. Patients with psoriasis alone reported an EQ5D score of 0.82, indicating a similar level of impairment to those with chronic obstructive pulmonary disease (EQ5D of 0.83).[30] By comparison, patients with PsA reported an EQ5D score of 0.56, slightly worse than that reported for patients in a rheumatoid arthritis registry (EQ5D is 0.60).[31] The difference in EQ5D between patients with PsA and those with psoriasis only was about five times the established clinically meaningful threshold of 0.05.[25]

We compared comorbidities in PsA patients with those in psoriasis. Patients with PsA had higher levels of comorbidities than patients with psoriasis alone. Hypertension and upper GI problems were significantly more prevalent among PsA patients compared with psoriasis only patients. Previous studies showed a link between psoriasis and increased risk of cardiovascular disease,[21,32] obesity, hypertension, dyslipidaemia and diabetes,[17,19–21] as well as Crohn's disease[19] and pustular disorders of the skin.[19] Two recent studies reported that patients with PsA were significantly more likely than healthy controls to have underlying diabetes, hypertension and a higher BMI,[33] and that based on traditional risk factors alone, patients with PsA without cardiovascular disease have on average a 10% chance of a cardiac event over a 10-year period.[34] Our hypertension results are consistent with these earlier findings. An unanticipated result of the present study was increased upper GI tract problems in patients with PsA compared with psoriasis only patients (OR: 2.381, $P$ = 0.044). Patients with PsA were more likely to take oral medications – including traditional systemics, angiotensin-converting enzyme inhibitors, anti-depressants and traditional non-steroidal anti-inflammatory drugs – which may help explain the increase of these symptoms.[35] Unfortunately, dermatologists were not given an opportunity to elaborate on this issue.

## Limitations

A limitation of this study was the possible misdiagnosis of PsA by dermatologists. To address this, dermatologists were asked whether they involved rheumatologists in the care of patients with PsA. The majority (90.5%) of PsA patients were identified by dermatologists who reported that they either co-managed PsA patients with a rheumatologist, or consulted a rheumatologist during their care of PsA patients. This indicates that misdiagnosis of PsA should be rare in this study. The exact method dermatologists used to diagnose each patient was not captured.

If PsA patients with significant joint problems but only minor BSA involvement choose to see rheumatologists rather than dermatologists, the correlation between BSA and PsA observed

here may be due to sample selection rather than a physiological relationship between these two manifestations of disease. However, the correlation may remain relevant for practising dermatologists who would see in their clinics a similar population to the one studied here. A further limitation is that BSA was measured at the time of survey, not at the time of diagnosis of either psoriasis or PsA. This limitation is somewhat offset by a confirmatory subgroup analysis on recently diagnosed patients.

If patients with psoriasis only are less bothered by their disease than those with PsA and therefore attend dermatology clinics less frequently, the prevalence of PsA in this study may be a biased estimate of that seen in the larger population of psoriasis patients. Similarly, if PsA worsens over time prompting patients to attend dermatology clinics only after attaining a particular severity threshold, the incidence rate of PsA in this study may be a biased estimate of the rate in the larger population. However, the observed prevalence and incidence rates would remain useful for practising dermatologists who would see in their clinics a similar population to ours.

In these analyses, observed BSA was employed as a marker of underlying psoriasis severity. However, BSA also partly reflects treatment, disease flares and season.

This is not a longitudinal study and therefore it cannot definitively conclude that presence of psoriasis over the long term increases the risk of a given patient developing PsA. However, the retrospective survival analysis, showing the cumulative percentage of development of PsA in patients with psoriasis, overcomes some of the limitations of the cross-sectional nature of the study by providing a risk of developing PsA with duration of psoriasis.

## Conclusions

Patients with a long history of psoriasis are more likely to have PsA than those who have only had psoriasis for a short time. The incidence rate of acquiring PsA after psoriasis diagnosis was constant over time, occurring at 0.74% per year. In addition, patients with a larger BSA affected were also more likely to have developed PsA. PsA is a severe disease associated with similar QoL impairment as rheumatoid arthritis, and patients with PsA have a lower QoL, more work-related problems and higher levels of comorbidity and use more healthcare resources than patients with psoriasis alone. Because of the associated medical and economic burden, dermatologists should consider screening for PsA on a regular basis in their patients with long-standing psoriasis. The need to do so may be especially great because patients may fail to associate their skin and joint symptoms and thereby not discuss joint problems unless prompted.

## Acknowledgements

The authors wish to thank Amitabh Singh, William Shine, Melanie Harrison and Sian Walker. The study was funded by Wyeth Research, USA, and Adelphi Group Products, UK. This article was prepared with the assistance of BioMedCom Consultants Inc, Montreal, Canada.

## Disclosures

Mr Milligan is employed by Adelphi; Drs Molta, Sato and Boggs are employed by Wyeth; Professor Christophers has received a fee as an invited speaker from Wyeth. Professor Barker has been an advisor to Schering-Plough, Wyeth, Abbott, Merck Serono and Janssen-Cilag. Professor Daudén has received research support, or has acted as a consultant or lecturer for Abbott, Merck Serono, Schering Plough, Wyeth, Leo Pharma, Novartis, 3M, Glaxo, Astellas and Janssen. Professor Griffiths has received research support, or has acted as a consultant or lecturer for Abbot, Amgen, Biogen-IDEC, Centocor, Essex Pharma, Galderma, Leo Pharma, Novartis, Novo Nordisk, Schering Plough, Merck-Serono, UCB Pharma and Wyeth.

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