Economic Burden and Quality of Life in Prurigo Nodularis: A Systematic Literature Review

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BACKGROUND

- Prurigo nodularis (PN) is a chronic inflammatory skin condition characterised by the presence of symmetrically distributed, intensely itchy nodules, which have a negative impact on a patient's quality-of-life (QoL).[1,2]
- PN is often associated with severe comorbidities and contributes to a significant clinical and healthcare burden.[3,4]
- Overall, the economic impact of PN is under-reported, with limited estimates available on healthcare resource use and costs.

OBJECTIVES

- This systematic literature review (SLR) examined the published evidence on economic evaluations, utility estimates, healthcare resource use and costs in PN.

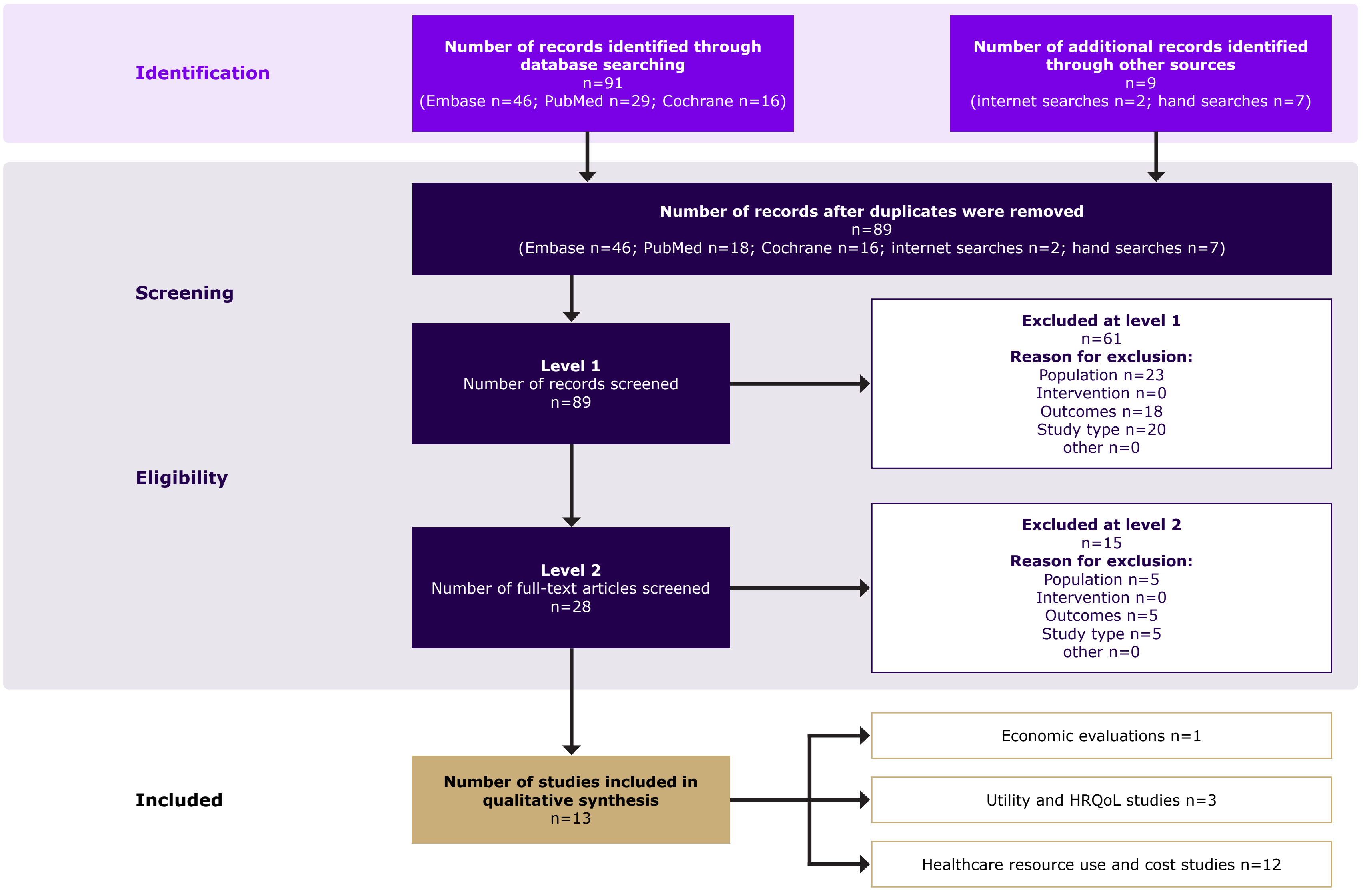
METHODS

- The systematic literature search was conducted in July 2021, not limited by date, geography or language.
- Following databases were used: Embase, MEDLINE, Cochrane-library, Centre for Reviews and Dissemination, National Health Service Economic Evaluation Database, School of Health and Related Research Health Utilities Database and EconLit.
- Searches on congress proceedings and abstracts were conducted between 2019 and 2021, using medical literature databases and specific congress and Health Technology Assessment (HTA) agency websites.
- Key inclusion criteria: Studies on economic analyses (cost-effectiveness, cost-utility, cost benefit, cost-consequence, and cost-minimisation analyses), utility estimates (including studies where mapping has been used), resource use, or costs in patients with PN were included.
- The screening and selection of eligible studies were performed by two independent reviewers. Quality check and data extraction were performed by one independent reviewer each.
- A quality assessment was performed using the Drummond Checklist.[5] For utility estimates, an assessment of compliance with the National Institute of Health and Care Excellence (NICE) reference case was performed.

RESULTS

- A total of 13 PN studies were identified and included in the analysis (n=1, economic evaluation [United States], n=3, utility and health-related QoL analysis [2, United States; 1, Denmark], n=12, healthcare resource and utilisation and costs [10, United States; 2, Europe]): studies could be included in multiple categories **(Figure 1).**
- The details of each eligible study are provided in **Table 1.**

Figure 1: PRISMA flow chart



Identification

Number of records identified through database searching
n=91
(Embase n=46; PubMed n=29; Cochrane n=16)

Number of additional records identified through other sources
n=9
(internet searches n=2; hand searches n=7)

Screening

Number of records after duplicates were removed
n=89
(Embase n=46; PubMed n=18; Cochrane n=16; internet searches n=2; hand searches n=7)

Level 1
Number of records screened
n=89

Excluded at level 1
n=61
Reason for exclusion:
Population n=23
Intervention n=0
Outcomes n=18
Study type n=20
other n=0

Eligibility

Level 2
Number of full-text articles screened
n=28

Excluded at level 2
n=15
Reason for exclusion:
Population n=5
Intervention n=0
Outcomes n=5
Study type n=5
other n=0

Included

Number of studies included in qualitative synthesis
n=13

Economic evaluations n=1

Utility and HRQoL studies n=3

Healthcare resource use and cost studies n=12

HRQoL, health-related quality of life
3 studies were included in two categories. Out of the 12 studies reporting cost or resource-use data, 9 were unique references, and 3 were secondary reports

Table 1. Study description

	Country/ Region	Type of data collected	Study type	Population characteristics	Key outcomes assessed
Whang et al (2021)[6]	United States	Economic evaluation and utility data; cost-year not explicitly stated, but assumed 2017 USD	PN patient survey at Johns Hopkins Itch Clinic	Patients with a dermatologist-confirmed PN diagnosis; mean age: 56.3 years; 75% females; N=36	QoL using HUI3 scores; individual lifetime costs and average QALYs lost, estimated by comparing the HUI3 scores of patients with PN versus controls.
Whang et al. (2020)[7]	United States	Utility data; no cost-year provided	A survey in patients with chronic pruritis	Patients with chronic pruritis; N=95	HUI3 scores stratified by race; total lifetime costs
Todberg et al (2020)[8]	Denmark	Utility data and healthcare resource utilisation	A survey in patients at Department of Dermatology and Allergy, Herlev and Gentofte Hospital, Copenhagen	Patients aged ≥18 years and had a diagnosis of PN between 2006 and 2016; mean age: 64.4 years; 67.3% females; N=52	VAS and DLQI scores; drug utilisation and productivity loss
Whang et al (2019b)[9] (secondary to Whang etal 2019a)[10]	United States	Healthcare costs and utilisation; cost-year not explicitly stated, but assumed 2016 USD	A cross-sectional study of the 2016 National Inpatient Sample (representative of 20% of hospital discharges nationally)	Patients with a PN diagnosis; 52.1% were males; men age: 55.2 years; N=265	Direct costs, hospitalisations, and length of stay
Sutaria et al (2021)[11]	United States	Healthcare costs and utilisation; cost-year not explicitly stated, but assumed 2016 or 2017 USD	A cross-sectional study, using the 2016-2017 National Inpatient sample which contains ~20% of all United States hospitalisations for infectious disease among patients with PN.	Infectious disease hospitalisations in patients with PN; N=3,040	Direct costs and health care resource utilisation
Huang et al (2020b)[12] (secondary references: Huang et al., 2020a[13]; Huang et al., 2020c)[14]	United States	Healthcare costs and utilisation; cost year not explicitly stated, but assumed 2015 or 2016 USD	A claims database study, using data on patients with PN from the IBM® MarketScan Commercial Claims database, between October 2015 and December 2016	Patients with PN aged 18–64 years; N=7,095	Mean total health care spending per patient; cost ratios comparing PN with matched controls; health care utilisation
Aggarwal et al (2021)[15]	United States	Health care resource utilisation; no cost data	A survey study conducted between 13 August and 13 September 2019	patients with PN; mean (SD) age of 52.3 (13.2) years; 93% females; N=171	Patient demographics, duration and distribution of pruritus, pruritus severity, healthcare utilisation, comorbidities and QoL
Wongvibulsin et al, (2021)[16]	United States	Healthcare resource utilisation; no cost data	A claims database study, using data from private insurance claims, between October 2015 and December 2019	Patients with PN defined as individuals with ≥2 medical claims for PN; N=2,658	Estimates of health care utilisation based on number of visits/year/person
Nguyen et al (2020)[17]	United States	Healthcare resource utilisation; no cost data	Data from 2007 to 2016 were collected via NAMCS (nationally representative estimates of United States ambulatory medical care)	Patients with PN were identified using ICD-9 CM 698.3 code/ICD-10-CM codes L28.0 and L.28.1	Annual per capita estimates of PN ambulatory visits
Pereira et al (2021)[18]	Europe	Indirect cost and health care resource utilisation	Prospective, cross-sectional, cohort study of patients with CNPG from 5 regions across Europe, using data between March 2017 and June 2019	Patients with CNPG; median age: 63 years, 61.8% females; N=406	Drug utilisation and out-of-pocket costs

CNPG, chronic nodular prurigo; DLQI, Dermatology Life Quality Index; HUI3, Health Utility Index score; ICD, International Classification of Disease; PN, prurigo nodularis; QALY, quality-adjusted life year; QoL, quality of life; VAS, Visual Analog scale

Economic evaluation

- A life-time cost of $323,292/patient and quality-adjusted life-year (QALY) loss of 6.5 years/patient were reported for patients with PN versus the general population in the United States.[6]

Utility and health-related quality of life analysis

- All studies (United States and Europe) showed a substantial impairment in the QoL of patients with PN **(Table 2).**
- Racial differences in health-related QoL and financial burden in patients with chronic pruritus with a PN diagnosis were reported in a study by Whang et al, with a greater financial and health-related QoL impact seen in the black patient subgroup.[7]
- Dermatology Life Quality Index scores indicate a moderate effect of disease on patients' QoL in a patient population with moderate-to-severe disease as determined by a pruritis Visual Analog scale.[8]

Table 2: Studies reporting utility data and health-related quality of life in patients with PN

Study	Country/ Region	Measure	Results
Whang et al (2021)[6]	United States	HUI3	The HUI3 score reduced significantly by 0.34 points ($p<0.01$) in patients with PN versus general population (mean total HUI3 score [SD]: 0.86 [0.003] versus 0.52 [0.06], respectively)
Whang et al (2020)[7]	United States	HUI3	HUI3 score was lower in the black subgroup versus white patients (coefficient −0.49; 95% CI [−0.98 to −0.01]). QALY loss: 7.66 years in black patient subgroup versus 6.18 years in white patient subgroup; $p=0.003$
Todberg et al. (2020)[8]	Denmark	DLQI and VAS	Mean (SD) DLQI score, 7.0 (5.6) and mean (SD) VAS score, 6.6 (2.4) in patients with PN

CI, confidence interval; DLQI=Dermatology Life Quality Index; HUI3, Health Utility Index score; PN, prurigo nodularis; QALY, quality-adjusted life year; SD, standard deviation; VAS, Visual Analog scale

Healthcare costs and resource utilisation

- PN was associated with a high healthcare resource utilisation and costs in the United States and Europe **(Table 3).**
- Direct costs were up to ~2 times higher in patients with PN compared with the general population in year 2016-2017 in the United States.[11] PN-related expenditure was mostly attributed to outpatient care ($5,580/patient/year) in the United States.[12,13,14]
- Hospitalisation duration (range: 3.9-16.4 days) and number of physician visits (range: 0.49-2.01 visits/patient/year) were greater in patients with PN compared with the general populations in the United States.[16] As per a study by Aggarwal et al, the mean number of physician visits was 6.3 in patients with PN; ~36.3% patients had ≥10 visits and 14% patients had ≥1 visit to emergency department.[15]
- The patient out-of-pocket costs in the previous 6 months was >€500 for patients with PN in Europe[18]; productivity loss (absenteeism/retirement) was reported in >25% patients in a study in Denmark.[8]

Table 3: Studies on healthcare resource utilisation and costs in patients with PN

	Country/ Region	Measure	Results
Sutaria et al (2021)[11]	United States	Mean costs of care in 2016-2017	$8,240 to $32,433 in patients with PN versus $6,190 to $15,674 in general patients in year 2016-2017; costs varied based on follow up time and presence of infectious disease comorbidities
		Healthcare resource utilisation	Mean length of hospitalisation: 3.9-16.4 days for patients with PN versus 3.5- 6.3 days for general patients
Whang et al (2020)[7]	United States	Costs per patient	Lifetime financial burden: $383,036/patient for black patient subgroup versus $309,011/patient for white patient subgroup
Whang et al 2019b[9] (secondary to Whang etal 2019a)[10]	United States	Care costs for hospitalised Patients with PN in 2016	Total care cost, $18,686,522; Financial burden, $63 million Average cost of care, $14,772 (versus $11,728 without PN)
		Healthcare resource utilisation	Mean length of hospitalisation: 6.51 days for patients with PN versus 4.62 days for patients without PN
Huang et al (2020b)[12] (secondary references: Huang et al., 2020a[13]; Huang et al., 2020c)[14]	United States	Mean total healthcare costs per PN patient in year 2015-2016	Outpatient care= $5,580; Inpatient care= $1,896; Emergency services= $464; Pharmacy/laboratory services= $394
		Cost ratios (patients with PN versus matched controls)	Costs ratio increased: 1.52 for total costs ($p<0.001$), 2.70 for pharmacy/laboratory costs ($p<0.001$), and 1.67 for outpatient costs ($p<0.001$).
		Healthcare resource utilisation	85.9% patients visited dermatologists
Aggarwal et al (2021)[15]	United States	Healthcare resource utilisation	Mean number of visits to physicians: 6.3 ±3.3; ~36.3% patients with PN visited physicians ≥10 times and 14% patients with PN had ≥1 visit to ED in past year. 88.3% patients visited dermatologists, 58.5%, primary care physicians, 43.9%, allergists and 32.7%, psychiatrists.
Wongvibulsin et al (2021)[16]	United States	Healthcare resource utilisation	Estimates based on number of visits/year/person for patients with PN: 2.01, internal medicine, 1.87, dermatology, 1.6, family practice, 0.85, cardiology cardiovascular disease, and 0.49, orthopaedics or orthopaedic surgery
Nguyen et al (2020)[17]	United States	Healthcare resource utilisation	Annual per capita estimates of PN ambulatory visits (year 2007-2016) were 5 of 100,000 white patients, 6 of 100,000 black patients, and 7 of 100,000 Asian American patients.
Pereira et al (2021)[18]	Europe	Out-of-pocket costs for PN	The out-of-pocket costs for PN was >€500 in Europe, which was related to the chronic nodular prurigo treatments in the previous 6 months.
Todberg et al (2020)[8]	Denmark	Impact on quality of life	>25% of patients with PN reported productivity loss, attributed to absenteeism from work and early retirement due to PN.

PN, prurigo nodularis; ED, emergency department

CONCLUSIONS

- This SLR highlights the paucity of high-quality economic data in PN. While more data were available for the United States, European data were scarce.
- There are limited published studies on economic evaluations, resource use and costs for PN and no utility studies using or mapping to EQ-5D.
- Several studies indicate that PN was associated with a high financial burden and a poor QoL, with a disproportionate impact on the black patient subgroup.
- These findings emphasise the need for effective treatments for PN to improve patients' QoL and reduce disease burden.

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CONFLICTS OF INTEREST:

Donia Bahloul and Jules Tavi are employees of Sanofi and may hold stock/stock options in Sanofi. Ryan Thomas is an employee of and stockholder in Regeneron Pharmaceuticals, Inc. Sydney Harold and Emily Moss are employees of RTI Health Solutions. Sean Conlon is an ex-employee of Sanofi.

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