Healthcare disparities in vitiligo: UK population-based cohort study

Author names: Viktoria Eleftheriadou[1], Alia Ahmed[2,3], John Nesnas[4], Ranjit Nagra[4]

Author affiliations:

[1] Department of Dermatology, The Royal Wolverhampton NHS Trust, Wolverhampton, UK

[2] Frimley Health NHS Foundation Trust, Frimley, UK

[3] Barts Health NHS Trust, London, UK

[4] Pfizer Ltd, Walton Oaks, Walton on the Hill, Tadworth, Surrey, UK

Date of the document: August 25, 2023

1. Contents

2. List of abbreviations

Abbreviation	Full Form
ADEPT	Anonymised Data Ethics & Protocol Committee
BMI	Body Mass Index
CIOMS	Council for International Organizations of Medical Sciences
EMA	European Medicines Agency
ENCePP	European Network of Centres for Pharmacoepidemiology and Pharmacovigilance
EQUATOR	Enhancing the QUAlity and Transparency Of health Research)
GEP	Good Epidemiological Practice
GP	General Practitioner
GPP	Guidelines for Good Pharmacoepidemiology Practices
IAPT	Improving Access to Psychological Therapies and psychiatric reviews
ICD10	International Statistical Classification of Diseases and Related Health Problems 10th Revision
IEA	International Epidemiological Association
IMD	Index of Multiple Deprivation
IQR	Interquartile Range
ISPOR	International Society for Pharmacoeconomics and Outcomes Research
OPCRD	Optimum Patient Care Research Database
SD	Standard Deviation
SES	Socio-Economic Status
SNOMED CT	Systemized Nomenclature of Medicine – Clinical Terms
UK	United Kingdom

3. Introduction

3.1 Background

Vitiligo is an acquired, non-contagious skin disorder characterised by depigmented patches of skin that may appear in a localised or very generalised distribution, and affecting 0.5-2.0% of the global population.(1) The exact cause of the loss of functioning melanocytes in vitiligo remains unknown, but is likely to be resulted from the complex interplay of genetics, oxidative stress, and autoimmunity.(2)

Although vitiligo is typically asymptomatic, recent Pfizer-funded research has demonstrated the condition substantially affects psychological wellbeing.(3) This previous study showed that people with vitiligo have a considerable excess mental health burden when compared with people without vitiligo. It also showed that, in people with vitiligo, mental health comorbidity is associated with higher levels of healthcare utilisation, time off work, and unemployment.(3) This increased burden could be due to the unpredictable prognosis, the current lack of cure, the perception and emotional burden associated with the visibility of vitiligo, or a combination of these factors.

There is substantial scope to extend the initial analysis, with a comprehensive assessment of sociodemographic disparities in healthcare utilisation and in the burden of mental health comorbidity in people with vitiligo. Whilst the previous Pfizer-funded study demonstrated a difference by ethnicity in the mental health impacts of vitiligo (with vitiligo associated with a greater mental health burden in people of non-white ethnicity), the study was not designed to assess this as a primary outcome. Further analysis is required to fully understand these potential relationships as well as provide critical information on whether there is a socio-economic (SES) gradient in the mental health impacts of vitiligo. The previous study did not assess other potential disparities in management, such as healthcare utilisation of primary care encounters or dermatology services.

There is also substantial scope to expand on the previous study to provide, for the first time, a greater understanding of the total burden of vitiligo across the population, including reporting lifetime risk estimates for vitiligo, across sociodemographic groups. It is likely that substantial disease burden differences exist across these groups.

A comprehensive assessment of potential disparities in healthcare utilisation in vitiligo, mental health and social impact, and lifetime risk are needed. This research would both strongly complement previous Pfizer-funded work and support the use of newer therapies in vitiligo.

3.2 Purpose of Analysis

This study will provide the first estimate of the cumulative lifetime risk of vitiligo in the population overall, and by important sociodemographic groups, including age, sex, ethnicity and SES, which will prevalent key data to show the relative burden of vitiligo across the aforementioned groups. These approaches allow creation of cumulative lifetime risk plots which provide an excellent and accessible way to display the relative disease burden across groups.

This study will provide a detailed assessment of any sociodemographic disparities in comorbidities and social impact that occurs in people with vitiligo. This will include any differences in mental health impact of vitiligo by sociodemographic. It will also include a description of any sociodemographic disparities in time off work ("sick leave") or unemployment in people with vitiligo.

This study will also provide a detailed assessment of any sociodemographic disparities in healthcare utilisation in people with vitiligo with comparison across sociodemographic. This will include analysis of utilisation of primary care services, mental health referrals as well as referrals to secondary care (dermatology).

4. Study objectives and endpoints

4.1 Study Objectives

The overall purpose of the study is to provide an estimate of the lifetime risk of vitiligo in the population overall and by important sociodemographic groups. Moreover, to do a subgroup analysis in the vitiligo population to identify health-related disparities across people in different sex, age, deprivation and ethnicity.

4.2 Primary Objectives

4.2.1 Objective 1

Describe the total burden of vitiligo (cumulative lifetime risk) across sociodemographic subgroups.

4.3 Secondary Objectives

4.3.1 Objective 2

Describe any disparities in the burden of mental health outcomes, including depression and anxiety in people with vitiligo across sociodemographic subgroups.

4.3.2 Objective 3

Describe any disparities in the association of vitiligo with parasuicide/suicide attempts, adjustment disorder and sleep disturbances associated with vitiligo across sociodemographic subgroups.

4.3.3 Objective 4

Describe any disparities in vitiligo-associated healthcare utilisation across sociodemographic subgroups.

4.3.4 Objective 5

Describe any disparities in vitiligo-associated work impact (time off work for illness and unemployment) across sociodemographic subgroups.

4.4 Primary Endpoints

Objective	Endpoints
1	An incident diagnosis of vitiligo is the date of the first diagnosis code in the record and no alternative diagnosis that merits exclusion (other causes of skin hypopigmentation) diagnosed within a one-year period (six months before or after their first vitiligo diagnosis code).

Table 1: Primary endpoints.

4.5 Secondary Endpoints

Objective	Endpoints
2	Mental health condition outcomes will be assessed up to two years post-vitiligo diagnosis, including history of prior mental health condition and will comprise of depression (record of any depressive episodes and/or major recurrent depression diagnosis) and anxiety disorders, defined by the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD10) classification, and identified using algorithms validated for use in UK primary care data (See previously published codes lists: (4))
3	Other mental health condition outcomes will be assessed up to two years post-vitiligo diagnosis and will comprise of parasuicide/suicide attempts, adjustment disorder and sleep disturbance, defined by the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD10) classification, and identified using algorithms validated for use in UK primary care data (See previously published codes lists: (4))

4	Healthcare utilisation outcomes will comprise primary care visits, dermatology referrals, mental health referrals (including but not limited to those via IAPT; Improving Access to Psychological Therapies and psychiatric reviews) in the two years post-vitiligo diagnosis.
5	Unemployment in the two years post-vitiligo diagnosis will be identified using Read codes relating to unemployment recorded in the primary care record or the issuing of IB113 or ESA113 forms (See previously published codes lists: (4)). Time off work in the two years post-vitiligo diagnosis will be indicated by the issuing of Med 3 certification from primary care (Statement of Fitness for Work certification) (See previously published codes lists: (4)).

Table 2: Secondary endpoints.

5. General Study Design and Plan

The study will use retrospectively collected anonymised data from all eligible people contributing to the Optimum Patient Care Research Database (OPCRD)(5) at the date of data extraction. A matched-cohort design will be used for incident (and prevalent) vitiligo related healthcare utilisation, mental health conditions and work impacts. Lifetime risk will be calculated using adapted survival analysis to account for the competing risk of death and will be estimated for the population overall and separately in sociodemographic subgroups of interest.

All adults and adolescents (aged 13+ for disparity objectives 2-5 inclusive) contributing to OPCRD during the study period (January 1, 2004 and December 31, 2020 inclusive). People who have opted out of record data sharing will not be included (approximately 1.8% of the adult population) and have not been uploaded to the OPCRD database.

Cumulative lifetime risk of vitiligo will be estimated (using the method described in the statistical methods below) using cases of incident vitiligo occurring during the observational study period (January 1, 2004 and December 31, 2020 inclusive). A matched-cohort design will be used for incident (and prevalent) vitiligo related mental health conditions, healthcare utilisation and work impacts. For all analyses, the overall result including both adults (aged 18+) and children (aged 13-17) will be published, with stratification by age, sex, deprivation and ethnicity.

5.1 Study design

This is a non-interventional study.

5.2 Total disease burden; cumulative lifetime risk

A cross sectional design (incidence) will be used to assess the total disease burden of vitiligo, stratified by sociodemographic groups.

5.3 Disparities in the impact of vitiligo on mental health, healthcare utilisation and work impact

A matched-cohort design will be used for incident (and prevalent) vitiligo related: Mental health conditions; work impact; healthcare utilisation.

5.4 Data Source and Read codes

The OPCRD(5) is a well-established primary care network in the UK. The database contains complete data on all events and clinical entities coded in UK primary care. These include sociodemographic factors and demographic information, clinical diagnoses, laboratory test results, primary care issued prescriptions, process of care codes (e.g. specialist dermatology reviews), and anthropometric measurements (e.g. BMI), and are coded using the Read coding and Systemized Nomenclature of Medicine – Clinical Terms (SNOMED CT) coding systems.(6)

5.5 Data Governance

This study is based wholly on data from the OPCRD (www.opcrd.co.uk) obtained under a limited license from Optimum Patient Care Limited and its execution is approved by recognised experts affiliated to the Respiratory Effectiveness Group.

Data from the OPCRD are available under license for clinical research which is subject to relevant approvals. For additional information visit: www.opcrd.co.uk.

5.6 Data Extraction

Individual patient data was anonymised at the point of data extraction. All data will remain in anonymised form and will be held on a secure server operated by Momentum Data. The data will not be used for any purposes other than for the research which is described in the respective protocols and which has been approved by the OPCRD ADEPT Committee.

5.7 General Study Population

5.7.1 Vitiligo Definition

People diagnosed with vitiligo will be identified using diagnostic Read and SNOMED CT codes which are specific to vitiligo. (Appendix 1) A diagnostic algorithm will be used to facilitate robust case identification, identifying anyone with a specific diagnosis code followed by exclusion of anyone with a diagnosis code for an alternative depigmenting

disorder coded within a one-year period (six months before or after their first diagnosis code). The list of alternative depigmenting disorders is shown in Appendix 2.

Incident cases will be defined as people with a first ever diagnosis code of vitiligo during the study period. People with a diagnosis of vitiligo prior to the study period will be excluded. Each case will be assigned an index date at the time of their vitiligo diagnosis.

5.7.2 Sociodemographic subgroups

Age, sex, deprivation and ethnicity will comprise the sociodemographic factors used for stratification of the outcome measures.

Age will be stratified into four age categories: 13-17 (adolescents), 18-20, 30-49, 50+.

Ethnicity will be grouped using the standardised definitions of major UK ethnic groups: White, Black, Asian, mixed, and others. (7)

Deprivation will be defined using the national deprivation measure; index of multiple deprivation (IMD) and stratified into quintiles of deprivation according to the national distribution. (8) IMD is calculated at the point of data extraction, using patient postcode (practice postcode where patient postcode is not available).

6. Sample Size Calculations

A sample size calculation is only applicable to the incidence of mental health conditions of anxiety and depression in people diagnosed with vitiligo.

Assuming 80% power, a 5% level of statistical significance and a background population prevalence of 15% for anxiety and 10% for depression,(9), our anticipated sample size for vitiligo (n = 8,000) will be sufficient to detect a risk difference of 1.11% in anxiety between those with and without vitiligo, and 1.12% difference in depression between those with and without vitiligo. Sample size calculations were performed in OpenEpi,(10) results are presented using methods of Kelsey.(11)

7. Populations to be Analysed

7.1 Inclusion Criteria

People must meet all the following inclusion criteria to be eligible for inclusion in the study:

- The cohort for the endpoint analysis will consist of all adults and adolescents (aged 13+) contributing to OPCRD during the study period.

- The cohort for the lifetime risk analysis will consist of all people contributing to OPCRD during the study period.
- The vitiligo cohort consists of people newly diagnosed with vitiligo at any point during the study period.

7.2 Exclusion Criteria

People meeting any of the following criteria will not be included in the study:

- People with the alternative non-vitiligo diagnoses (other hypopigmenting conditions).
- People with vitiligo diagnosis within 6 months of practice registration.
- People without vitiligo with less than 1 year of follow up within the dataset.
- People over the age of 95 (for those reaching age 95 during the follow up period, follow up was censored at age 95).

People who have opted out of record sharing are not included (approximately 1.8% of the adult population).

7.3 Matching Process

For objectives 2-5, controls for each vitiligo case will be identified from the pool of people without a vitiligo diagnosis registered in the OPCRD database at the time of vitiligo diagnosis for the case. Vitiligo cases will be eligible as controls up until the date of their vitiligo diagnosis (at which date their follow-up will be censored if selected as a control).

Each case will be assigned an index date at the time of their vitiligo diagnosis. Corresponding controls assigned to each case will have the same index date.

Each individual with vitiligo will be matched at their index date with up to four unaffected controls. Controls cannot be diagnosed with vitiligo at the date of matching and will require at least one year of follow-up time to minimise the risk of a non-recorded existing diagnosis of vitiligo. Time-updated exact matching will be performed by age, sex, ethnicity and deprivation, selected from the pool of eligible people registered in the same GP practice.

If required, a combination of time-dependent propensity score matching and exact matching will be performed to create a baseline matched dataset.

The matching process is subject to change depending on the feasibility of the mentioned matching process during the initial exploration of the data. The produced baseline matched dataset will be used for all analyses for objective 2-5.

8. Statistical Analysis

8.1 Statistical Principles

Mean, standard deviation (sd) and any other statistical measures, will be reported to one decimal place. Continuous data will be summarised in the form of means, sd, median, interquartile range (IQR) and range as appropriate. Categorical data will be summarised using the frequencies and proportions. Chi-squared and t-tests will be performed to compare the frequency of dichotomous variables and the values of continuous variables where relevant. 95% CIs will be reported for main effect sizes. Statistical significance will be assessed using $p<0.05$. Actual p-values will be reported except for p-values less than 3 decimal places which will be reported as "<0.001". P-values >0.1 will be reported to one decimal place, p-values between 0.01 and 0.1 will be reported to 2 decimal places, and p-values between 0.001 and 0.01 will be reported to three decimal places.

The assessment of any associations with baseline characteristics and the outcomes of interest (objectives 2-5) will be assessed using logistic regression (prevalent and incident outcomes), Cox proportional hazards (time to event outcomes) and Poisson regression (repeated event outcomes) models. Three different adjustment sets will be used for each endpoint analysis. These include: an unadjusted model, a sex and age adjusted model, and a multivariable model with an adjustment set of: age, sex, BMI, smoking status, alcohol use, and common comorbidities: type 2 diabetes, hypertension, atrial fibrillation, angina, acute myocardial infarction, stroke, heart failure, chronic liver disease, dementia, rheumatoid arthritis, asthma, chronic obstructive pulmonary disease, chronic kidney disease stages 3-5, malignancy and inflammatory bowel disease.

Assumptions of statistical approaches will be assessed, and transformations used if necessary.

8.2 Primary Endpoint Analysis

Objective 1

Lifetime risk of vitiligo will be calculated for the population as a whole and by sex, ethnicity, and SES. Ethnicity will be grouped using the standardised definitions of major UK ethnic groups: white, black, Asian, mixed, and other.(7) SES will be defined using the national deprivation measure; IMD.(12)

Lifetime risk will be calculated using methods to estimate cumulative lifetime risk recently published in the Lancet,(13, 14) accounting for the competing risk of death. Key outputs will be lifetime risk plots, presenting the cumulative risk of vitiligo against age for the whole population and for sociodemographic subgroups. At a particular age, the cumulative risk estimate can be interpreted as the lifetime risk of vitiligo up until and including the year of age in question. Age of 80 is considered to be the approximate

lifetime expectancy in the UK,(15) and will be the point of comparison at which the lifetime risk of vitiligo will be compared across sociodemographic subgroups.

8.3 Secondary Endpoint Analysis

Objective 2

Anxiety and depression outcomes will be captured if occurring prior to, or within two years of, an individuals' study index date. Binary outcome logistic regression model outputs will be used to compare the burden of anxiety and depression in vitiligo cases compared to matched controls. Furthermore, additional analyses for new onset anxiety and depression outcomes will be conducted, excluding people with a previous record of the respective mental health condition. Anxiety and depression outcomes will be defined by the first occurrence of a relevant code in the primary care record up to two years post index-date. Cox proportional hazards regression will be used to estimate the excess risk of anxiety and depression outcomes in vitiligo cases versus controls. Results will be described as hazard ratios.

Objective 3

Parasuicide/suicide attempts will be defined by the first occurrence of a relevant code in the primary care record up to two years post index-date. People with a previous record of parasuicide/suicide attempt will be excluded from the calculations. Cox proportional hazards regression will be used to estimate the excess risk of parasuicide/suicide attempts in vitiligo cases versus matched controls. Results will be described as hazard ratios.

Adjustment disorder and sleep disturbance will be defined by the first occurrence of a relevant code in the primary care record up to two years post index-date. People with a previous record of the adjustment disorder will be excluded from the from the adjustment disorder endpoint analysis. Cox proportional hazards regression will be used to estimate the excess risk of the relevant condition in vitiligo cases versus matched controls. Results will be described as hazard ratios.

Objective 4

Dermatology referral and mental health referral or reviews will be defined by the first occurrence of a relevant code in the primary care record up to two years post index date. Cox proportional hazards regression will be used to estimate the excess risk of these outcomes in vitiligo cases versus matched controls.

For primary care encounters reviews, defined as a rate of encounters within two years after the index date, will be compared using generalised linear models with time-at-risk as an offset. Results will be described as incidence rate ratios.

Objective 5

Only cases and matched controls aged 18-65 will be considered for this analysis. Work impact outcomes (unemployment and time off work for illness) will be defined by the first occurrence of a relevant code in primary care record up to two years post index date. Cox proportional hazards regression will be used to estimate the excess risk of these outcomes in vitiligo cases versus matched controls. Results will be described as hazard ratios.

8.4 Sensitivity Analysis

To evaluate the magnitude of potential bias from including, as matched controls, people who are registered with GP practices but who do not attend their practice, we will also repeat the primary analysis for mental health, healthcare utilisation and work-related outcomes including only matched controls with at least one primary care encounter in the year preceding their index date.

We will also repeat the primary analysis for mental health, healthcare utilisation and work-related outcomes extending the outcome period to four years.

To assess the impact of missing ethnicity data, we will repeat the ethnicity sociodemographic subgroup analysis amending missing ethnicity entries to white.

8.5 Missing Data

These studies will use the missing indicator variable method as missing data are considered likely not to be missing at random, meaning multiple imputation approaches will lack validity.

Patients will need to be excluded from analyses based on a matched design if they have incomplete data in the fields (age, sex) required to run the matching process. In similar studies, the exclusion rate due to incomplete data has been very low. (23, 24)

How missing data is handled will be dependent on exploratory and sensitivity analyses and is subject to change.

9. Study Limitations

Disparities between sociodemographic subgroups will be interpreted based on the assumption of the primary/secondary outcomes being related to the vitiligo. We have no definite way to identify that every occurrence of an outcome is related to vitiligo in the context of healthcare utilisation and work impact outcomes and therefore causal interpretation is not possible.

This is an ecological study limited to the UK population and may not be generalisable to other populations.

We expect some missing data for the ethnicity variable, this is a limitation of the dataset itself and could result in bias. Necessary sensitivity analyses will be undertaken to circumvent this and limit any impact this could have in interpretation of results in our analysis.

We expect low number of occurrences for the outcomes of referrals for adjustment disorder and parasuicide/suicide, thus reporting of the results for these two endpoints will depend on the sufficiency of numbers available.

10. Statistical Software

All statistical analyses will be performed using R version 4.2.3 or higher.

11. Ethics

The study will be conducted in accordance with legal and regulatory requirements, as well as with scientific purpose, value and rigor and follow generally accepted research practices described in:

- Guidelines for Good Pharmacoepidemiology Practices (GPP). Public Policy Committee, International Society of Pharmacoepidemiology. Pharmacoepidemiology and Drug Safety 2016; 25:2-10.
- Good Practices for Outcomes Research issued by the International Society for Pharmacoeconomics and Outcomes Research (ISPOR)
- Good practices for real-world data studies of treatment and/or comparative effectiveness: Recommendations from the joint ISPOR-ISPE Special Task Force on real-world evidence in health care decision making
- International Ethical Guidelines for Epidemiological Studies issued by the Council for International Organizations of Medical Sciences (CIOMS)
- European Medicines Agency (EMA) European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) Guide on Methodological Standards in Pharmacoepidemiology
- The ENCePP Code of Conduct for scientific independence and transparency in the conduct of pharmacoepidemiological and pharmacovigilance studies
- Good Epidemiological Practice (GEP) guidelines issued by the International Epidemiological Association (IEA).
- Study reporting will be conducted in accordance with the relevant EQUATOR (Enhancing the QUAlity and Transparency Of health Research) guidelines.

The NHS Health Research Authority (NHS HRA) has approved OPCRD for clinical research purposes (REC reference: 20/EM/0148). The protocol for this project was approved by the OPCRD affiliated study approvals committee. The study did not require formal research ethics committee as it used anonymised routinely collected healthcare data, based on outputs from the National Health Service (NHS) Health Research Authority

research decision tool (http://www.hra-decisiontools.org.uk/research/). No patient identifiable information was available to researchers. All patients who chose to opt out of data sharing did not have their data processed. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

The study will be registered on the clinical trial database (clinicaltrials.gov)

12. Acknowledgments

This Study will be based wholly on data from the Optimum Patient Care Research Database (www.opcrd.co.uk) obtained under a limited licence from Optimum Patient Care Limited and its execution is approved by recognised experts affiliated to the Respiratory Effectiveness Group. However, the interpretation and conclusions contained in this report will be those of the author/s alone.

Patients and practices who are members of the OPC network, who allow their data to be shared for surveillance, research, quality improvement, and education. Data access support from the OPCRD team. Statistical input and medical writing from Serhan Bahit (Serhan.bahit@momentumdata.co.uk) and Dr Charlotte Curtis (charlotte.curtis@momentumdata.co.uk) at Momentum Data. Project management support from Emma Jones (emma.jones@momentumdata.co.uk) at Momentum Data.

13. References

1. Steiner D, Bedin V, Moraes MB, Villas RT, Steiner T. Vitiligo. Anais Brasileiros de Dermatologia. 2004;79:335-51.
2. Grimes PE, Miller MM. Vitiligo: Patient stories, self-esteem, and the psychological burden of disease. Int J Womens Dermatol. 2018;4(1):32-7.
3. Thompson AR, Eleftheriadou V, Nesnas J. The mental health associations of vitiligo: UK population-based cohort study. BJPsych Open. 2022;8(6):e190.
4. Macbeth AE, Holmes S, Harries M, Chiu WS, Tziotzios C, de Lusignan S, et al. The associated burden of mental health conditions in alopecia areata: A population-based study in UK primary care. British Journal of Dermatology.
5. Lynam A, Curtis C, Stanley B, Heatley H, Worthington C, Roberts EJ, et al. Data-Resource Profile: United Kingdom Optimum Patient Care Research Database. Pragmat Obs Res. 2023;14:39-49.
6. de Lusignan S, Liaw ST, Michalakidis G, Jones S. Defining datasets and creating data dictionaries for quality improvement and research in chronic disease using routinely collected data: an ontology-driven approach. Inform Prim Care. 2011;19(3):127-34.
7. Tippu Z, Correa A, Liyanage H, Burleigh D, McGovern A, Van Vlymen J, et al. Ethnicity Recording in Primary Care Computerised Medical Record Systems: An Ontological Approach. J Innov Health Inform. 2017;23(4):920.
8. Ministry of Housing, Communities & Local Government,. Department for Communities and Local Government. The English Indices of Deprivation. 2015 [updated 23 September 2019. Available from: https://www.gov.uk/government/statistics/english-indices-of-deprivation-2015.
9. Kessler RC, Chiu WT, Demler O, Merikangas KR, Walters EE. Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. Arch Gen Psychiatry. 2005;62(6):617-27.
10. Dean AG, Sullivan KM, Soe MM. OpenEpi: Open Source Epidemiologic Statistics for Public Health [updated 06/04/2013. Available from: www.OpenEpi.com.
11. Kelsey JL, Whitemore AS, Evans AS, Thompson WD. Methods in Observational Epidemiology. 2nd ed. New York: Oxford University Press; 1996.
12. Department for Communities and Local Government. The English Indices of Deprivation. 2015.2015. Available from: https://www.gov.uk/government/statistics/english-indices-of-deprivation-2015.
13. Gershon AS, Warner L, Cascagnette P, Victor JC, To T. Lifetime risk of developing chronic obstructive pulmonary disease: a longitudinal population study. Lancet (London, England). 2011;378(9795):991-6.
14. Rapsomaniki E, Timmis A, George J, Pujades-Rodriguez M, Shah AD, Denaxas S, et al. Blood pressure and incidence of twelve cardiovascular diseases: lifetime risks, healthy life-years lost, and age-specific associations in 1·25 million people. Lancet (London, England). 2014;383(9932):1899-911.
15. Minton J, Fletcher E, Ramsay J, Little K, McCartney G. How bad are life expectancy trends across the UK, and what would it take to get back to previous trends? Journal of Epidemiology and Community Health. 2020;74(9):741.

14. Appendices

Appendix 1

Codes to be used to identify cases of vitiligo and important exclusion conditions.

Read and SNOMED codes to be used to identify cases of vitiligo

Read V2 Code	**Term ID**	**Description**
M2951	All	Vitiligo
M293.	All	Hypopigmentation disorder
F4E53	All	Vitiligo of eyelid
M295.	All	Leucoderma
M295z	All	Leucoderma NOS
Read CTV3 Code	**Term ID**	**Description**
M2951	All	Vitiligo
M293.	All	Hypopigmentation disorder
F4E53	All	Vitiligo of eyelid
M295.	All	Acquired hypomelanosis
M295z	All	Leucoderma NOS
SNOMED Code	**Term ID**	**Description**
56727007		Vitiligo (disorder)
87666009		Vitiligo of eyelid (disorder)
721539008		Vitiligo of eyelid and periocular area (disorder)
403271008		Kobner vitiligo (disorder)
403270009		Trichrome vitiligo (disorder)
403267005		Localised vitiligo (disorder)
403268000		Segmental vitiligo (disorder)
402621008		Idiopathic vitiligo (disorder)
403269008		Generalised vitiligo (disorder)
330931000119106		Vitiligo of skin of left eyelid and periocular area (disorder)
330931000119104		Vitiligo of skin of right eyelid and periocular area (disorder)
330911000119101		Vitiligo of skin of left upper eyelid and periocular area (disorder)
330881000119101		Vitiligo of skin of right upper eyelid and periocular area (disorder)
726608002		Spastic paraparesis, vitiligo, premature greying, characteristic facies syndrome
23006000		Hypopigmentation of skin (disorder)
89031001		Hypopigmentation (morphological abnormality)
68210006		Hypopigmentation of eyelid
18655006		Dipigmentation
23267004		Achromia of skin (disorder)
402807009		Circumscribed hypomelanosis (disorder)

Read codes and SNOMED codes to be used to identify alternative depigmenting disorders for exclusion

Congenital and Genetic Hypomelanoses		
Read V2 Code	**Term ID**	**Description**
C302A	All	Piebaldism
PK5..	All	Tuberous sclerosis
PKy54	All	Waardenburg's syndrome
C3029	All	Hermansky-Pudlak
PKy92	All	Menke's syndrome
Read CTV3 Code	**Term ID**	**Description**
X78Ve	All	Hypomelanosis of Ito
XaZqX	All	Piebaldism
PK5..	All	Tuberous sclerosis
X78E7	All	Ash leaf spot, tuberous sclerosis
X78E8	All	Shargreen patch
X78E9	All	Adenoma sebaceum
X20Ex	All	Hermansky-Pudlak syndrome
X20ij	All	Griscelli syndrome with immunodeficiency
PKy92	All	Menkes syndrome
SNOMED Code	**Term ID**	**Description**
218358001		Incontinentia pigmenti achromians syndrome (disorder)
718122005		Piebaldism (disorder)
7199000		Tuberous sclerosus syndrome (disorder)
254243001		Ash leaf spot, tuberous sclerosis (disorder)
36025004		Fibrous skin tumor of tuberous sclerosis (disorder)
254244007		Shagreen patch (disorder)
9311003		Hermansky-Pudlak syndrome (disorder)
37548006		Hypopigmentation-immunodeficiency disease (disorder)
59178007		Menkes kinky-hair syndrome (disorder)
47434006		Waardenburg's syndrome (disorder)
715952000		Waardenburg syndrome co-occurrent with Hirschsprung disease (disorder)
773575001		Ocular albinism with congenital sensorineural deafness (disorder)
765325002		Peripheral demyelinating neuropathy, central dysmyelinating leukodystrophy, Waardenburg syndrome, Hirschsprung disease (disorder)
Post-inflammatory Hypomelanoses		
Read V2 Code	**Term ID**	**Description**
M2920	All	Post inflammatory hypopigmentation
M170.	All	Lichen planus

M1700	All	Lichen planus actinicus
M1701	All	Lichen planus annularis
M1702	All	Lichen planus atrophicus
M1703	All	Lichen planus bullosus
M1704	All	Lichen planus hypertrophicus
M1705	All	Lichen planus linearis
M1707	All	Lichen planus obtusus
M1708	All	Subacute active lichen planus
M1709	All	Follicular lichen planus
M170z	All	Lichen planus NOS
M17y0	All	Lichen ruber moniliforme
M1650	All	Pityriasis alba
M2102	All	Lichen sclerosus and atrophicus
K276.	All	Balanitis xerotica obliterans
Read CTV3 Code	**Term ID**	**Description**
Xa0WM	All	Post inflammatory hypopigmentation
M170.	All	Lichen planus
X507Y	All	Confluent lichen planus
X507Z	All	Micropaplular lichen planus
X507a	All	Guttate lichen planus
X507b	All	Follicular lichen planus
M1703	All	Bullous lichen planus
M1701	All	Annular lichen planus
M1704	All	Hypertrophic lichen planus
M1702	All	Atrophic lichen planus
M1705	All	Linear lichen planus
X507c	All	Zosteriform lichen planus
M1700	All	Acintic lichen planus
X507d	All	Post inflammatory hyperpigmentation in lichen planus
X507e	All	Wickham's striae in lichen planus
X507f	All	Lichen planus - lupus erythematosus overlap
X507g	All	Lichen planus pemphigoides
X507h	All	Site-specific lichen planus
X507i	All	Lichen planus of scalp
X507j	All	Lichen planus of palms and soles
X507k	All	Ulcerative lichen planus of palms and soles
X507n	All	Mutilating lichen planus of fingers and toes
X507l	All	Lichen planus of nail
X507w	All	Genital lichen planus
X408F	All	Lichen planus of vuvla
X507y	All	Erosive lichen planus of vulva
X507z	All	Lichen planus of penis
X5080	All	Lichen planus of glans penis
M1707	All	Lichen planus obtusus

M1708	All	Subacute active lichen planus
M170z	All	Lichen planus NOS
Myu32	All	[X]Other lichen planus
M17y0	All	Lichen ruber moniliforme
M1650	All	Pityriasis alba
M2102	All	Lichen sclerosus
X50FC	All	Genital lichen sclerosus
K276.	All	Balanitis xerotica obliterans
X50FE	All	Lichen sclerosus of vulva
X50FF	All	Extra genital lichen sclerosus
X50FG	All	Guttate lichen sclerosus
SNOMED Code	**Term ID**	**Description**
277787003		Post-inflammatory hypopigmentation (disorder)
403272001		Post-infective hypomelanosis (disorder)
403276003		Acquired hypomelanosis of uncertain etiology (disorder)
4776004		Lichen planus (disorder)
263797007		Lichen planus-like (qualifier value)
4459000		Linear lichen planus (disorder)
6111009		Bullous lichen planus (disorder)
238666005		Lichen planus of lips (disorder)
201001005		Lichen planus obtusus (disorder)
200999007		Actinic lichen planus (disorder)
238658001		Lichen planus of nail (disorder)
238668006		Genital lichen planus (disorder)
201000006		Annular lichen planus (disorder)
238647005		Guttate lichen planus (disorder)
237112004		Lichen planus of vulva (disorder)
400108007		Flexural lichen planus (disorder)
238655003		Lichen planus of scalp (disorder)
44509000		Linear lichen planus (disorder)
25858008		Atrophic lichen planus (disorder)
238670002		Lichen planus of penis (disorder)
238645002		Confluent lichen planus (disorder)
717061002		Lichen planus pigmentosus (disorder)
238648000		Zosteriform lichen planus (disorder)
238653005		Lichen planus pemphigoides (disorder)
68266006		Hypertrophic lichen planus (disorder)
238646001		Micropapular lichen planus (disorder)
64540004		Lichen planopilaris (disorder)
238654004		Site-specific lichen planus (disorder)
238652000		Lichen planus-lupus erythematosus overlap (disorder)
403198004		Lichenoid actinic keratosis (disorder)
723003004		Acute eruptive lichen planus (disorder)
238671003		Lichen planus of glans penis (disorder)

68266006		Hypertrophic lichen planus (disorder)
201002003		Subacute active lichen planus (disorder)
720493003		Annular atrophic lichen planus (disorder)
238651007		Wickham's striae in lichen planus (disorder)
201001005		Lichen planus obtusus (disorder)
402349005		Chronic lichen planus (disorder)
238668006		Genital lichen planus (disorder)
238656002		Lichen planus of palms and soles (disorder)
402352002		Poikiloderma due to lichen planus (disorder)
721171007		Hypertrophic lichen planus of vulva (disorder)
402348002		Köbner reaction from lichen planus (disorder)
238657006		Ulcerative lichen planus of palms and soles (disorder)
238660004		Mutilating lichen planus of fingers and toes (disorder)
726476005		Lichen planus co-occurrent with onycholysis (disorder)
238649008		Post-inflammatory hyperpigmentation in lichen planus (disorder)
402296004		Pityriasis alba (disorder)
402298003		Diffuse pityriasis alba (disorder)
402297008		Localised pityriasis alba (disorder)
25674000		Lichen sclerosus et atrophicus (disorder)
402423004		Adult lichen sclerosus (disorder)
782666006		Lichen sclerosus of anus (disorder)
238934003		Guttate lichen sclerosus (disorder)
238932004		Genital lichen sclerosus (disorder)
700082001		Lichen sclerosus of penis (disorder)
26348009		Lichen sclerosus et atrophicus of the vulva (disorder)
402424005		Childhood lichen sclerosus (disorder)
403566002		Anogenital lichen sclerosus (disorder)
238933009		Extragenital lichen sclerosus (disorder)
402714001		Lichen sclerosus of male genitalia (disorder)
402715000		Lichen sclerosus of female genitalia (disorder)
402422009		Bullous extragenital lichen sclerosus (disorder)
721199003		Prepubertal lichen sclerosus of vulva (disorder)
403568001		Localized extragenital lichen sclerosus (disorder)
402421002		Generalized extragenital lichen sclerosus (disorder)
403564004		Lichen sclerosus of penis, childhood form (disorder)
111023000		Lichen sclerosus et atrophicus, bullous type (disorder)
403565003		Vulval lichen sclerosus, childhood form (disorder)
198033005		Balanitis xerotica obliterans (disorder)
Post Traumatic Leukoderma		
SNOMED Code	**Term ID**	**Description**
402622001		Hypomelanosis due to scarring (disorder)
18655006		Depigmentation (morphologic abnormality)
23006000		Hypopigmentation of skin (disorder)
398656003		Acquired hypomelanotic disorder (disorder)

Para-Malignant Hypomelanoses		
Read V2 Code	**Term ID**	**Description**
B621.	All	Mycosis fungoides
B6210	All	Mycosis fungoides of unspecified site
B6211	All	Mycosis fungoides of lymph nodes of head, face and neck
B6212	All	Mycosis fungoides of intrathoracic lymph nodes
B6213	All	Mycosis fungoides of intra-abdominal lymph nodes
B6214	All	Mycosis fungoides of lymph nodes of axilla and upper limb
B6215	All	Mycosis fungoides of lymph nodes of inguinal region and leg
B6216	All	Mycosis fungoides of intrapelvic lymph nodes
B6217	All	Mycosis fungoides of spleen
B6218	All	Mycosis fungoides of lymph nodes of multiple sites
B621z	All	Mycosis fungoides NOS
BBI..	All	[M]Mycosis fungoides
BBI0.	All	[M]Mycosis fungoides
BBI1.	All	[M]Sezary's disease
BBIz.	All	[M]Mycosis fungoides NOS
B62xX	All	0th and unspecif peripheral & cutaneous T-cell lymphomas
B62E7	All	Subcutaneous panniculitis like T-cell lymphoma
BBmD.	All	[M]Cutaneous lymphoma
B622.	All	Sezary's disease
B6220	All	Sezary's disease of unspecified site
B6221	All	Sezary's disease of lymph nodes of head, face and neck
B6222	All	Sezary's disease of intrathoracic lymph nodes
B6223	All	Sezary's disease of intra-abdominal lymph nodes
B6224	All	Sezary's disease of lymph nodes of axilla and upper limb
B6225	All	Sezary's disease of lymph nodes of inguinal region and leg
B6226	All	Sezary's disease of intrapelvic lymph nodes
B6227	All	Sezary's disease of spleen
B6228	All	Sezary's disease of lymph nodes of multiple sites
B622z	All	Sezary's disease NOS
BBEA.	All	Amelanotic melanoma
Read CTV3 Code	**Term ID**	**Description**
B621.	All	Mycosis fungoides
XaQbT	All	Poikiloderma vasculare atrophicans
X78hm	All	Mycosis fungoides of skin
B6210	All	Mycosis fungoides of unspecified site
B6211	All	Mycosis fungoides of lymph nodes of head, face and neck
B6212	All	Mycosis fungoides of intrathoracic lymph nodes
B6213	All	Mycosis fungoides of intra-abdominal lymph nodes
B6214	All	Mycosis fungoides of lymph nodes of axilla and upper limb
B6215	All	Mycosis fungoides of lymph nodes of inguinal region and leg
B6216	All	Mycosis fungoides of intrapelvic lymph nodes

B6217	All	Mycosis fungoides of spleen
B6218	All	Mycosis fungoides of lymph nodes of multiple sites
B621z	All	Mycosis fungoides NOS
B622.	All	Sezary's disease
B6220	All	Sezary's disease of unspecified site
B6221	All	Sezary's disease of lymph nodes of head, face and neck
B6222	All	Sezary's disease of intrathoracic lymph nodes
B6223	All	Sezary's disease of intra-abdominal lymph nodes
B6224	All	Sezary's disease of lymph nodes of axilla and upper limb
B6225	All	Sezary's disease of lymph nodes of inguinal region and leg
B6226	All	Sezary's disease of intrapelvic lymph nodes
B6227	All	Sezary's disease of spleen
B6228	All	Sezary's disease of lymph nodes of multiple sites
B622z	All	Sezary's disease NOS
X78hn	All	Sezary's disease of skin
X78hl	All	Cutaneous lymphoma
XaYin	All	Cutaneous follicle centre lymphoma
Xa0Sz	All	Cutaneous/peripheral T-cell lymphoma
XaYjf	All	Subcutaneous panniculitis like T-cell lymphoma
ByuDD	All	[X]0th and unspecif peripheral & cutaneous T-cell lymphomas
XaYjl	All	Primary cutaneous CD30 antigen positive large T-cell lymphoma
XaOCE	All	Amelanotic malignant melanoma of skin
SNOMED Code	**Term ID**	**Description**
90120004		Mycosis fungoides (morphologic abnormality)
118618005		Mycosis fungoides (disorder)
765328000		Classic mycosis fungoides (disorder)
404115006		Bullous mycosis fungoides (disorder)
94714002		Mycosis fungoides of spleen (disorder)
404117003		Spongiotic mycosis fungoides (disorder)
681291000119105		History of mycosis fungoides (situation)
418628003		Follicular mycosis fungoides (morphologic abnormality)
404113004		Tumour stage mycosis fungoides (disorder)
404118008		Syrngotropic mycosis fungoides (disorder)
404112009		Granulomatous mycosis fungoides (disorder)
404114005		Erythrodermic mycosis fungoides (disorder)
404110001		Hypomelanocytic mycosis fungoides (disorder)
404109006		Folliculotropic mycosis fungoides (disorder)
404108003		Pokilodermatous mycosis fungoides (disorder)
404107008		Patch/plaque stage mycosis fungoides (disorder)
404116007		Mycosis fungoides with systemic infiltration (disorder)
94708009		Mycosis fungoides of intrapelvic lymph nodes (disorder)
94707004		Mycosis fungoides of intra-abdominal lymph nodes (disorder)
188627002		Mycosis fungoides of lymph nodes of multiple sites (disorder)
404111002		Lymphomatoid papulosis-associated mycosis fungoides (disorder)

404104001		Lymphomatoid papulosis type B mycosis fungoides-like (disorder)
94715001		Mycosis fungoides of extranodal AND/OR solid organ site (disorder)
94709001		Mycosis fungoides of intrathoracic lymph nodes (disorder)
94711005		Mycosis fungoides of lymph nodes of head, face AND/OR neck (disorder)
94710006		Mycosis fungoides of lymph nodes of axilla AND/OR upper limb (disorder)
188627002		Mycosis fungoides of lymph nodes of multiple sites (disorder)
94712003		Mycosis fungoides of lymph nodes of inguinal region AND/OR lower limb (disorder)
28054005		Cutaneous T-cell lymphoma, no International Classifcation of Diseases for oncology subtype (morphologic abnormality)
40012207		Primary cutaneous T-cell lymphoma (disorder)
277613000		Cutaneous/peripheral T-cell lymphoma (disorder)
404128004		CD-30 negative cutanoeus T-cell lymphoma (disorder)
419283005		Primary cutaneous T-cell lymphoma - category (morphologic abnormality)
128804002		Primary cutaneous CD30 antigen positive T-cell lymphoproliferative disorder (morphologic abnormality)
450908002		Primary cutaneous gamma-delta T-cell lymphoma (morphologic abnormality)
122571000119106		History of primary cutaneous T-cell lymphoma (situation)
419018000		Primary cutaneous large T-cell lymphoma - category (morphologic abnormality)
402880009		Primary cutaneous large T-cell lymphoma (disorder)
404133000		Subcutaneous panniculitic cutaneous T-cell lymphoma (disorder)
404128004		CD-30 negative cutaneous T-cell lymphoma (disorder)
787198005		Primary cutaneous acral CD8 positive T-cell lymphoma (morphologic abnormality)
397352006		Primary cutaneous anaplastic large T-cell lymphoma, CD30-positive (morphologic abnormality)
733627006		Primary cutaneous gamma-delta-positive T-cell lymphoma (disorder)
404129007		CD-30 negative anaplastic large T-cell cutaneous lymphoma (disorder)
122571000119106		History of malignant cutaneous T-cell lymphoma (situation)
404130002		CD-30 negative pleomorphic large T-cell cutaneous lymphoma (disorder)
404126000		CD-30 positive pleomorphic large T-cell cutaneous lymphoma (disorder)
419283005		Primary cutaneous T-cell lymphoma - category (morphologic abnormality)
450908002		Primary cutaneous gamma-delta T-cell lymphoma - category (morphologic abnormality)
765136002		Primary cutaneous CD8 positive aggressicve epidermotropic cytotoxic T-cell lymphoma (disorder)
128875000		Primary cutaneous CD30 antigen positive large T-cell lymphoma (disorder)
733895005		Primary cutaneous CD8 positive aggressicve epidermotropic cytotoxic T-cell lymphoma (morphologic abnormality)

419586003		Primary cutaneous T-cell lymphoma, large cell, CD30-negative (morphological abnormality)
118611004		Sezary's disease (disorder)
4950009		Sezary's disease (morphologic abnormality)
255101006		Sezary disease of skin (disorder)
95263006		Sezary's disase of spleen (disorder)
188632001		Sezary's disase of intra-abdominal lymph nodes (disorder)
188635004		Sezary's disase of intrapelvic lymph nodes (disorder)
188631008		Sezary's disase of intrathoracic lymph nodes (disorder)
188637007		Sezary disease of lymph nodes of multiple sites (disorder)
95264000		Sézary's disease of extranodal AND/OR solid organ site (disorder)
188633006		Sézary's disease of lymph nodes of axilla and upper limb (disorder)
95260009		Sézary's disease of lymph nodes of head, face AND/OR neck (disorder)
188634000		Sézary's disease of lymph nodes of inguinal region and lower limb (disorder)
95261008		Sézary's disease of lymph nodes of inguinal region AND/OR lower limb (disorder)
419392005		Primary cutaneous lymphoma (morphologic abnormality)
82321000000106		Tumour and germline whole genome sequencing for anaplastic lymphoma kinase negative anaplastic large cell lymphoma including primary cutaneous subtypes (procedure)
403274000		Hypomelanosis surrounding malignant melanoma (disorder)
402563000		Metastatic malignant melanoma with diffuse hypermelanosis (disorder)
276751004		Amelanotic malignant melanoma of skin (disorder)
70594002		Amelanotic melanoma (morphologic abnormality)
404110001		Hypomelanotic mycosis fungoides (disorder)
402623006		Hypomelanosis surrounding melanocytic neoplasm (disorder)
Occupational/drug induced hypomelanoses		
Read V2 Code	**Term ID**	**Description**
M293.	All	Hypopigmentation
Read CTV3 Code	**Term ID**	**Description**
X508z	All	Occupational vitiligo
X78VE	All	Chemically-induced hypomelanosis
X50Gx	All	Drug-induced hypomelanosis
Xa1aV	All	Chemically-induced hypomelanosis
M2950	All	Leucoderma aestivale
M295.	All	Acquired hypomelanosis
SNOMED Code	**Term ID**	**Description**
238713002		Occupational vitiligo (disorder)
280962005		Chemically-induced hypomelanosis (disorder)
402622001		Hypomelanosis due to scarring (disorder)

403807001		Phylloid hypomelanosis (disorder)
398656003		Acquired hypomelanotic disorder (disorder)
238999005		Drug-induced hypomelanosis (disorder)
403698000		Laser-induced hypopigmentation (disorder)
402622001		Hypomelanosis due to scarring (disorder)
280962005		Chemically-induced hypomelanosis (disorder)
403692004		Hypomelanosis due to cryotherapy (disorder)
403744007		Arsenic-induced "rain-drop" hypomelanosis (disorder)
403698000		Laser-induced hypopigmentation (disorder)
201290009		Leukoderma estivale (disorder)
Para-infectious hypopigmentation		
Read V2 Code	**Term ID**	**Description**
AB10.	All	Pityriasis versicolor
Read CTV3 Code	**Term ID**	**Description**
AB10.	All	Pityriasis versicolor
SNOMED Code	**Term ID**	**Description**
56454009		Pityriasis versicolor (disorder)
18097004		Malassezia (organism)
721794002		Infection caused by Malassezia (disorder)
402133004		Malassezia infection of the skin (disorder)
29619007		Malassezia furfur (organism)
Others (including Melasma, Morphoea, Idiopathic guttate hypomelanosis, Xeroderma pigmentosum, Progressive macular hypomelanosis, Nevus depigmentosus, Cutaneous sarcoidosis)		
Read V2 Code	**Term ID**	**Description**
M290.	All	Melasma
M2900	All	Chloasma bronzinum
M2901	All	Chloasma cachecticorum
M2902	All	Chloasma caloricum
M2903	All	Chloasma gravidarum
M2903	All	Chloasma gravidarum
M2903	All	Chloasma gravidarum
M290z	All	Chloasma NOS
M2103	All	Morphoea
M2104	All	Linear Morphoea
M210.	All	Circumscribed scleroderma
M2100	All	Unspecified circumscribed scleroderma
M2101	All	Localised dermatosclerosis
M210z	All	Circumscribed scleroderma NOS
PH322	All	Xeroderma pigmentosum
BBE9.	All	[M]Nonpigmented naevus
AD530	All	Lupus Pernio

AD53.	All	Sarcoidosis of skin
Read CTV3 Code	**Term ID**	**Description**
M290.	All	Melasma
Xa1aM	All	Drug-induced melasma
M2900	All	Chloasma bronzinum
M2901	All	Chloasma cachecticorum
M2902	All	Chloasma caloricum
M2904	All	Chloasma hepaticum
M2905	All	Chloasma toxicum
M2906	All	Chloasma traumaticum
M290z	All	Chloasma NOS
M2903	All	Melasma of pregnancy
Xa1aM	All	Drug-induced melasma
M2103	All	Morphoea
X7053	All	Generalised morphoea
M2101	All	Localised morphoea
M2100	All	Unspecified circumscribed scleroderma
M210z	All	Circumscribed scleroderma NOS
X7055	All	Linear morphoea
PH322	All	Xeroderma pigmentosum
X78Cz	All	Xeroderma pigmentosum group A
X78D0	All	Xeroderma pigmentosum group B
X78D1	All	Xeroderma pigmentosum group C
X78D2	All	Xeroderma pigmentosum group D
X78D3	All	Xeroderma pigmentosum group E
X78D4	All	Xeroderma pigmentosum group F
X78D5	All	Xeroderma pigmentosum group G
X78D6	All	Xeroderma pigmentosum XP variant
X78D7	All	De Sanctis-Cacchione syndrome
X78D8	All	Xerodermoid, pigmented
X50lw	All	Symmetrical progressive leucopathy
X20GW	All	Cutaneous sarcoid
X20GX	All	Orofacial sarcoid
X20GY	All	Lupus pernio
X5089	All	Acute skin sarcoidosis
X508A	All	Sarcoidosis-induced erythema nodosum
X508B	All	Lofgrens syndrome
X508C	All	Maculopapular sarcoidosis
X508D	All	Chronic skin sarcoidosis
X508E	All	Sarcoidosis in scar
X508F	All	Papular sarcoidosis
X508G	All	Lichenoid sarcoidosis
X508H	All	Nodular sarcoidosis
X508I	All	Angiolupoid sarcoidosis

X00YQ	All	Sarcoid skin of eyelid
X20G5	All	Sarcoid dactylitis
X50Dy	All	Subacute nodular migratory panniculitis
X50Dz	All	Subcutaneous lipogranulomatosis
SNOMED Code	**Term ID**	**Description**
36209000		Melasma
201274009		Chloasma bronzinum (disorder)
201275005		Chloasma cachecticorum (disorder)
201276006		Chloasma caloricum (disorder)
201277002		Chloasma hepaticum (disorder)
201278007		Chloasma toxicum (disorder)
280955001		Drug-induced melasma (disorder)
79840007		Idiopathic chloasma (disorder)
111208003		Melasma gravidarum (disorder)
54397000		Symptomatic chloasma (disorder)
201279004		Chloasma traumaticum (disorder)
201049004		Morphea (disorder)
128458002		Plaque morphea (disorder)
22784002		Linear scleroderma (disorder)
403521006		Guttate morphea (disorder)
201048007		Localised morphea (disorder)
7513007		Generalized morphea (disorder)
403522004		Subcutaneous morphea (disorder)
51156002		Coup de sabre scleroderma (disorder)
403523009		Disabling pansclerotic morphea of children (disorder)
128460000		Diffuse cutaneous scleroderma (disorder)
403524003		Scleroderma-like secondary cutaneous sclerosis (disorder)
1717003		Idiopathic guttate hypomelanosis (disorder)
711154007		Guttate hypopigmentation and punctate palmoplantar keratoderma with or without ectopic calcification (disorder)
44600005		Xeroderma pigmentosum (disorder)
56048001		Xeroderma pigmentosum, group E (disorder)
25784009		Xeroderma pigmentosum, group C (disorder)
36454001		Xeroderma pigmentosum, group G (disorder)
1073003		Xeroderma pigmentosum, group B (disorder)
68637004		Xeroderma pigmentosum, group D (disorder)
42530008		Xeroderma pigmentosum, group F (disorder)
43477006		Xeroderma pigmentosum, group A (disorder)
73663008		Neurologic xeroderma pigmentosum (disorder)
88877002		Xeroderma pigmentosum, variant form (disorder)
7806002		Non-neurologic xeroderma pigmentosum (disorder)
719819004		Xeroderma pigmentosum and Cockayne syndrome complex (disorder)
239083007		Symmetrical progressive leucopathy (disorder)

763368004		Familial progressive hyper and hypopigmentation of skin (disorder)
403541001		Nevus depigmentosus
112680001		Naevus depigmentosus
55941000		Cutaneous sarcoidosis (disorder)
238680003		Papular sarcoidosis (disorder)
238679001		Sarcoidosis in scar (disorder)
402369000		Atrophic sarcoidosis (disorder)
402371000		Verrucous sarcoidosis (disorder)
238681004		Lichenoid sarcoidosis (disorder)
238674006		Acute skin sarcoidosis (disorder)
402370004		Ulcerative sarcoidosis (disorder)
58870009		Sarcoidosis, anular type (disorder)
54515008		Sarcoidosis, plaque type (disorder)
80941006		Subcutaneous sarcoidosis (disorder)
870334009		Palmoplantar sarcoidosis (disorder)
238678009		Chronic skin sarcoidosis (disorder)
238677004		Maculopapular sarcoidosis (disorder)
402368008		Ichthyosiform sarcoidosis (disorder)
402373002		Hypomelanotic sarcoidosis (disorder)
9529007		Sarcoidosis, erythrodermic type (disorder)
72470008		Sarcoidosis, lupus pernio type (disorder)
402372007		Subcutaneous nodular sarcoidosis (disorder)
238675007		Sarcoidosis-induced erythema nodosum (disorder)
238676008		Lofgrens syndrome (disorder)
31541009		Lupus pernio of Besnier
231799005		Sarcoid skin of eyelid (disorder)

Appendix 2

Potential differential diagnoses for vitiligo which will be used as exclusion criteria if they appear as diagnoses in the medical record within six months of the initial diagnosis of vitiligo (six months before or after the vitiligo diagnosis). *As these conditions are extremely uncommon in the UK they will not be used in the exclusion process. Codes for these conditions are listed in Appendix 1.

Condition group	**Conditions/causes included**
Congenital and genetic hypomelanoses	Piebaldism Tuberous sclerosis Hypomelanosis of Ito Waardenburg syndrome Hermanski-Pudlak syndrome Griscelli syndrome Menkes syndrome
Post-inflammatory hypomelanoses	Post-inflammatory leukoderma including after Atopic eczema or Psoriasis
	Lichen planus
	Pityriasis alba
	Lichen sclerosus
Post traumatic leukoderma	Post traumatic leukoderma
Para-malignant hypomelanoses	Cutaneous T-cell lymphoma (mycosis fungoides)
	Melanoma associated depigmentation
Occupational/drug induced hypomelanoses	Occupational vitiligo
	Other induced hypomelanoses
Para-infectious hypopigmentation	Pityriasis versicolor (or tinea versicolor)
	*Leprosy**
	*Leishmaniasis**
Others	Melasma
	Morphoea
	Idiopathic guttate hypomelanosis
	Xeroderma pigmentosum
	Progressive macular hypomelanosis
	Nevus depigmentosus
	Cutaneous sarcoidosis