**Annex 1**

**Database search strategies**

Medline:

1 Huntington Disease/

2 Huntingt\* adj2 (diseas\* or chorea\*)).tw

3 or/1-2

4 Incidence/

5 Incidence\*.tw.

6 or/4-5

7 3 and 6

Embase:

1 Huntington chorea/

2 Huntington\* chorea.tw.

3 Huntington\* diseas\*.tw.

4 1 or 2 or 3

5 prevalence/

6 prevalence\*.tw.

7 5 or 6

8 4 and 7

**Annex 2**

**Studies in discrete populations**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Author ID** | **Location** | **Study year(s)** | **Prevalent cases** | **Population**  **size** | **Prevalence**  **per 100,000**  **(95% CIs)** | **Comments** |
| ***Africa*** |  |  |  |  |  |  |
| Kandil 1994 | Assiut, Egypt | 1988-1990 | 9 | 42,000 | 21.43  (9.80 to 40.68) | Based on a restricted survey |
| Scrimgeour 1981 | Bantu community Tanzania | Approx 1980 | 2 | 28,571 | 7.00  (0.85 to 25.29) |  |
| Hayden 1981 | Mauritius | 1977 | 6 | Whites = 13,000 | 46.15  (16.94 to 100.46) | All patients of European descent |
| Kabore 2000 | Burkina Faso | 1997 | 4 | 10 312 609 | 0.038 (0.011 to 0.099) |  |
| ***Americas*** | | | | | | |
| Kurland 1958 | Rochester, Minnesota  USA | 1955 | 2 | 30,000 | 6.67  (0.81 to 24.08) |  |
| Avila-Giron 1973 | Zulia, Venezuela | Early 1970s | San Luis = 22  Barranquitas = 5  San Isidro = 1 | Unknown | N/A |  |
| Hardt 2009 | Juan de Costa, Colombia | 2009 | Not stated | Not stated | N/A | Population of the town is approx 14,000 |
| Alencar 2010 | Feira Grande,  Brazil | 2005 | 22 | 22,000 | 100.00  (62.67 to 151.40) | Attributes high prevalence to high frequency of consanguineous marriages but no data provided.  “Cluster” |
| ***Asia*** | | | | | | |
| Chen 1968 | Guam | 1963 | 0 | 37,975 | 0  (0 to 9.71) |  |
| ***Central and Eastern Europe*** | | | | | | |
| Kozlova 1986 | Shamkhor, Azerbaijan | 1986 | 23 | 126,800 | 18.14  (11.50 to 27.22) | 19 in one village, 4 in another. Then extrapolated to the whole Shamkor by the authors |
| ***Oceania*** | | | | | | |
| Scrimgoeur 1982 | Papua New Guinea | 1980 (approx) | 11 | 100,000 (approx) | 11 | Denominator by back extrapolation |
| Warren 1990 | Broken Hill, Tasmania, Australia | 1989/1990 | 7 | 23,270 | 30.08  (12.09 to 62.00) |  |
| ***United Kingdom*** | | | | | | |
| Lyon 1962 | Avoch, Scotland  UK | Probably 1960 | 12 | 869 (voters)  1058 (approximate total) | 1134.22  (586.07 to 1981.25) | Not a reliable population estimate.  “Cluster” |
| Brewis 1966 | Carlisle, UK | 1961 | Def = 2  Def+prob = 3 | 71,101 | Def = 2.81  (0.34 to 10.16)  Def+prob = 4.22  (0.87 to 12.33) |  |
| Ratnavalli 2002 | Cambridgeshire,  UK | 2000 | 14 | 72,815 | 19.2  (11.5 to 32.3) | Estimate confined to patients aged 45-67 years |
| Harvey 2003 | West London  UK | 2001/2002 | 9 | 112,309 | 8.01  (3.66 to 15.21 | Confined to ages 30-64 years. Precise year unclear. Prevalence calculated from author’s available data |
| ***Western Europe*** | | | | | | |
| Sjogren 1936 | Sweden | Early 1930s |  |  |  |  |
| Morrison 1993 | Donegal  Ireland | 1991 | 2 | 128,117 | 1.56  (0.19 to 5.64) | Also data for 1926, 1061, 1971,1981 |

**Annex 3**

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**Annex 4**

**Excluded studies**

|  |  |
| --- | --- |
| **Study ID** | **Reasons for exclusion** |
| Adams 1988 | No population estimate of prevalence of HD. |
| Aiyesimoju 1984 | Prevalence expressed in relation to all hospital admissions and not a population-based prevalence study) |
| Alonso 2009 | No estimate of population prevalence. |
| Anon 2010 | Review. No original data. |
| Barbeau 1964 | No population estimate of prevalence of HD. |
| Bayulkem 1961 | Describes features of 35 patients with HD admitted to hospital from 1947 until 1959.. Denominator used is the total number of hospital admissions for estimated prevalence over the period. |
| Bell 1934 | No estimate of prevalence |
| Botha 1983 | Review of likely sources of a variety of genetic diseases in Africans people. |
| Brothers 1949 | Description of HD in Tasmania indicating a common ancestor. No prevalence data. |
| Cameron 1967 | No estimate of prevalence is provided.. |
| Carter 1983 | No estimate of prevalence |
| Cchutani 1957 | Description of cases of HD in Punjab but no attempt to estimate prevalence. |
| Cendrowski 1962 | Not a prevalence study or specifically focused on HD. |
| Cendrowski 1964 | Not a prevalence study. |
| Chang 1994 | Duplicate of Leung 1992 |
| Conneally 1984 | Literature review with no new/original data on prevalence. |
| Craig 2005 | This primarily report of patients with spinocerebellar atrophy type 17 (SCA17). HD patients were only included in order to avoid missing those with HD-like symptoms who really had SCA17. |
| Critchley 1934 | Not a population-based study |
| Cruz-Coke 1994 | A mixture of patients reported in the literature supplemented by hospital data. Double counting cannot be excluded. |
| Ekestern 2005 | Data confined to mortality rates. No prevalence data. |
| Gajdusek 1982 | Review only |
| Gatto 2009 | No estimate of prevalence. |
| Gatto 2010 | Genetic analysis of CAG repeats in a sample of Argentinean HD patients and normal subjects. No estimate of prevalence reported from the survey. |
| Guo 2010 | Analysis of clinical features of previously published case reports. No attempt at estimating prevalence. |
| Harper 1981 | No data on prevalence of HD. |
| Harper 1992 | Review of previous prevalence studies. No new data. |
| Harvey 2003 | Estimates of prevalence of a variety of conditions associated with cognitive impairment but confined to people under 65 years. |
| Hayden 1981 | Not a population based study |
| Hecimovic 2002 | Uncertain as to whether this is a point or period prevalence estimate |
| Hemminki 2006 | Study is of hospitalisation rates and not population prevalence rates |
| Hendricks 2009 | Not a prevalence study. |
| Hofman 1987 | Prevalence of undifferentiated “dementia” |
| Hook 1993 | A theoretical account of capture-recapture methods in epidemiology using Folstein’s HD as an example. No new data. |
| Hoppitt 2010 | Full report published by Sackley 2011. |
| Hoppitt 2011 | Review. No original data |
| Huifang 2010 | Part review and part case-series. No prevalence data. |
| Husquinet 1973 | Prevalence estimated (in decades) from 1861 to 1920 based on number of HD patients in psychiatric hospital registers. |
| Husquinet 1985 | Uses data from psychiatric registers and expresses prevalence in relation to live births. |
| Imaizumi 1993 | Concerned solely with mortality rates based on death certification. |
| Jader 2007 | Review of the prevalence of a range of neurological disorders in Wales. No original data. |
| Kirilenko 2004 | Prevalence of hereditary CNS diseases general and no specific estimate for HD |
| Korenyi 1973 | No prevalence estimate |
| Kovalchuk 2010 | Breakdown of the underlying pathology in 1000 patents attending a movement disorders clinic. No population prevalence estimate. |
| Krause 2008 | Review. No original data |
| Kurtze 1979 | Review. No original data. |
| Laccone 1999 | No prevalence estimate |
| Lawal 2009 | No data relating to prevalence/incidence |
| Lekoubou 2014 | Systematic review of the epidemiology of dementias (including HD) in sub-Saharan Africa. No original data. |
| Loy 2010 | No new data but an estimate of the likely increase based on “population structure” in Australia. |
| Ma 2010 | No estimate of prevalence |
| Marx 1973  Mattsson 1985 | Study of genetic fitness. No estimate of prevalence.  Same prevalence estimate as in Mattson 1974. |
| Mercy 2008 | Not a population study (limited to adults aged 45 to 64 years) |
| Minski 1938 | No estimate of prevalence provided. |
| Molon 2010 | Review. |
| Morrison 2010 | Provides a prevalence estimate for 2001 but is in a letter to the Lancet and full details are given in Morrison 2011. |
| Myrianthopoulous 1966 | Review – no original data on prevalence |
| Nakashima 1995a | Duplicate publication of Nakashima 1995b |
| Nakashima 1996 | Duplicate publication of Nakashima 1995b |
| Narabayashi 1973 | Review only. No original data. |
| Panse 1942 | Nazi eugenicist |
| Pavoni 1990 | Duplicate publication of Govoni 1988. |
| Peppa 2010 | Review with no original data. |
| Petrin 1997 | No estimates of the prevalence of HD. |
| Pleydell 1954 | Fuller details in Pleydell 1955 and updated by Reid 1960 and Oliver 1970 |
| Pleydell 1955 | Updated by Reid 1960 and Oliver 1970 |
| Pramanik 2000 | No estimate of prevalence |
| Pridmore 1990b | No data. Comment on Warren 1990 |
| Quarrell 2009 | No original data on prevalence |
| Raskin 2000 | No prevalence estimate. |
| Reid 1960 | Supercede by Oliver 1970 |
| Roccatagliata 1976 | No of estimate prevalence. |
| Roccatagliata 1979 | Population size estimated by extrapolation equals 300,000 but the population of Genoa in 1971 was 600,000. Impossible to reconcile the data and as this estimate of prevalence is the highest ever recorded it must be regarded as unreliable. |
| Roos 2010 | Review – no original data. |
| Roy 2010 | Case report only |
| Rubinstein 1994 | No data on prevalence |
| Saleem 2003 | No original data on prevalence |
| Schoenberg 1979 | Review only. No original data. |
| Scholefield 2007 | No data on prevalence |
| Scrimgeour 1992b | Commentary. No new data on incidence/prevalence. |
| Shaw 1982 | No original data on prevalence |
| Siesling 1997 | No estimate of the prevalence. |
| Singer 1962 | No estimate of prevalence |
| Spillane 1937 | No estimate of prevalence |
| Spinney 2010 | Review with no original data. |
| Squitieri 1994 | No estimate of prevalence. |
| Tanner 1994 | Review only. No original data |
| Teive 2011 | Review only. No original data |
| Thomsen 2010 | Review only. No original data |
| Tibben 2007 | Review of the psychology, sociology and demographics of predictive testing. No prevalence data. |
| Vázquez-Mojena 2013 | A study of the epidemiology of the molecular genetics of HD in a Cuban population. No estimate of prevalence. |
| Walker 1981 | A duplicate of Harper 1978 |
| Wallace 1973 | A duplicate publication of Wallace 1972. |
| Wallace 1979 | Not new data but re-working of data by Wallace 1972 and 1973 |
| Warby 2011 | No new prevalence data |
| Watt 1995 | A critique of Shiwach 1994. No new data. |
| Whittier 1973 | No estimate of prevalence |
| Wider 2006 | Review only. No original data |

**Annex 5**

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**Annex 6**

**Methods for case ascertainment and diagnosis of HD:  
Africa**

|  |  |  |
| --- | --- | --- |
| **Author ID** | **Case finding method(s)** | **Diagnostic criteria** |
| ***South Africa*** | | |
| Hayden 1977 | Records of the Dept Med Genetics plus home visits plus search of neurological and psychiatric records plus personal approach to neurologists, psychiatrists and physicians. | “Diagnosis made by a neurologist or psychiatrist’ |
| Hayden 1980 | Records of Med Genetics department, records of Groote Schurr Hospital, letters to neurologists and psychiatrists and selected GPs; letters to directors of all mental health institutions and departments of neurology and psychiatry | Progressive motor disability plus psychiatric disturbance plus positive family history |
| ***Zimbabwe*** | | |
| Scrimgeour 1992a | Apparently serendipitous finding of an HD family plus two other (non-related) patients | Clinical features |

**Annex 7**

**Methods for case ascertainment and diagnosis of HD:  
Americas**

|  |  |  |
| --- | --- | --- |
| **Author ID** | **Case finding methods** | **Diagnostic criteria** |
| ***Canada*** | | |
| Shokeir 1975 | Hospital records, enquiry of private physicians, including neurologists and family practitioners, nursing homes, senior citizen homes, mental hospitals, society for crippled adults, rehabilitation centres and the Department of Veterans Affairs. Once a patient was recognized, the immediate family and distant relatives were followed-up and other cases, if any, thereby identified. | The diagnosis was accepted only after two experienced clinicians had confirmed it. |
| Fisher 2014 | Centre for Huntington’s Disease in Vancouver, Victoria General Hospital (VGH) Medical Genetics, the Huntington Society of Canada (HSC), BC General Practitioner (GP) and Neurologist records, the HD family community, BC nursing homes, and the DNA diagnostic laboratory at Children and Women’s Hospital in Vancouver. | Clinical features (Unified Huntington’s disease rating scale of >2) +/- CAG repeats >36. |
| ***United States of America*** | | |
| Pearson 1955 | First admissions to state hospitals and hospital admissions due to HD in Minnesota. | Not stated |
| Reed 1958 | Trained field-workers reviewed the d files of all State Hospitals (for mental patients) in Michigan and compiled a list of persons living or dead, with firm or possible diagnoses of Huntington's chorea. The files of the Veterans Administration hospitals in Detroit and Battle Creek were also reviewed. Lists of all choreics seen in University Hospital of the University of Michigan, and Wayne County General Hospital (which serves Detroit largely), and a number of County Infirmaries were also obtained. Kindreds already on file in the Heredity Clinic, University of Michigan, were incorporated into the study. Enquires of HD families | Not stated explicitly but included patients with negative family history. |
| Wright 1981 | Examined seven blacks from four kindreds with HD supplemented by reliable reports on nine other affected relatives. A survey of all geneticists, neurologists, and mental health centers in South Carolina yielded only one case of a black with HD not previously known. Six blacks with HD are currently registered with the Neurology Service; in addition, two choreic relatives of our patient group presently reside in South Carolina. | Not explicitly stated but from the text it appears that they all had typical motor and psychiatric features. |
| Folstein 1981 | From all persons and agencies or institutions that may have been providing care or services to HD patients. Includes general hospitals discharge diagnoses, genetics clinics, medical specialists, rural physicians, Departments of Social Services, voluntary organisations and radio/newspaper spots. | Mainly clinical evaluation by the investigators. Probable HD = chorea plus positive family history; possible HD = chorea without positive family history. |
| Kokmen 1994 | Scrutiny of records of hospitals, nursing homes, private practitioners, state mental hospital. | Definite HD = documented record of progressive choreiform movement disorder; evidence of autosomal dominant inheritance; progressive cognitive, behavioural, and/or emotional dysfunction. Probable HD = 2/3 of the above criteria |
| ***Venezuela (except Zulia)*** | | |
| Paradisi 2008 | Patients referred by neurologists to the Laboratory of Human Genetics at Instituto Venezolano de Investigaciones Cientıficas | Clinical features by referring neurologists |

**Annex 8**

**Methods for case ascertainment and diagnosis of HD:  
Asia**

|  |  |  |
| --- | --- | --- |
| **Author ID** | **Case finding methods** | **Diagnostic criteria** |
| ***Hong Kong*** | | |
| Leung 1992 | Not stated | Patients examined by a neurologist and psychiatrist. Diagnosis based on +ve family history; insidious progressive chorea; progressive cognitive impairment and often psychiatric disturbances. Caudate atrophy on CT supported diagnosis.  Conditions mimicking HD excluded by appropriate lab tests. |
| Chang 1994 | Computer search of all major hospitals records. Announcement in HK Medical Association Newsletter asking for information about known or suspected cases. Enquiry of all neurologists and psychiatrists in HK | All patients examined by a neurologist plus a psychiatrist. Diagnosis based on positive family history plus insidious progressive disorder with chorea, cognitive impairment and often psychiatric disturbance. |
| ***Japan*** | | |
| Kishimoto 1957 | Patients identified through the co-operation of physicians of the Prefecture Medical Association and the registration officers of the local government. | Not stated |
| Kanazawa 1983 | Not stated | Not stated |
| Nakashima 1995 | Not stated | Clinical criteria plus imaging (caudate atrophy) and genetic test. One patient with clinical features but no expanded repeat was excluded (later diagnosed with acanthosis nigricans). |
| Adachi 1999 | Not stated | Not stated |
| ***Taiwan*** | | |
| Chen 2010 | Outpatient and inpatient claims from the National Health Insurance Research Database (NHRDB) covering 96.1% (in 2000) to 98.6% (2007) of population. | Search of NIHRD for ICD-9 code 333.4. |

**Annex 9**

**Methods for case ascertainment and diagnosis of HD:  
Central and Eastern Europe**

|  |  |  |
| --- | --- | --- |
| **Author ID** | **Case finding methods** | **Diagnostic criteria** |
| ***Croatia*** | | |
| Sepcic 1989 | Scrutiny of an HD register (Department of Neurology & Psychiatry, University of Rijeka, 1946-1981); HD register (Department of Neurology & Psychiatry, University of Pula, 1961-1980); “poll of primary care at health institutions”. | Criteria of ad hoc Committee on Classification of Extrapyramidal Disorders |
| Hecimovic 2002 | Referrals for genetic testing | Expanded CAG repeat (n=44). Clinical diagnosis by neurologists (n=65) |
| ***Russian Federation*** | | |
| Khomenko 1993 | 1st phase: Reviewing archives of Neurological clinics, Nursing homes, State Disability Examination records, Military Disability Commission for 35 years. 2nd Local examination and interviewing, recording of family history. | Not stated |
| Shkurat 2003 | Medical records of hospitals and polyclinics; family histories. Attempted to survey the whole of Rostov | Medical geneticist clinicians made the diagnosis. |
| Baryshnikova 2002 | Records of neurological hospitals, outpatient clinics, medical sanitary units, the medico-social examination bureau for the period from 1994 to 1999, and from the Medical Genetic Counseling register. | Clinical criteria plus genetic test in some (not sure how many). |
| Kirilenko 2004b | Enquiry of polyclinics, neurological departments of hospitals, medical and sanitary stations and the regional medical genetic counseling service of Volgograd town. | Clinical criteria plus genetic test in all. |
| Nikolaeva 2009 | Records of all hospitals, Polyclinics, and enquiry of families with HD | Clinical features plus genetic testing (done in Japan) |
| ***Slovenia*** | | |
| Peterlin 2010 | Ascertained from: Central database at the Institute of Medical Genetics in Ljubljana, Clinical Departments of Neurology of the University Medical Centers Ljubljana and Maribor, the Registry of the Slovene Associations of HD patients, the Slovene Registry of patients with extrapyramidal diseases, as well as from the medical records of regional outpatient clinics. clinically or genetically established diagnosis of HD. Study included those with and without a family history. | No clinical criteria given. Appears that cases defined on genetic basis only (CAG repeat size > 36) |

**Annex 10**

**Methods for case ascertainment and diagnosis of HD:  
Oceania**

|  |  |  |
| --- | --- | --- |
| **Author ID** | **Case finding methods** | **Diagnostic citeria** |
| Brothers 1955 | Not stated | Not stated |
| Parker 1958 | Not stated | Not stated but includes those without a family history |
| Brothers 1964 | Patients admitted to mental hospitals; patients supplied by private psychiatrists and neurologists, by the various teaching hospitals in Melbourne, notifications from the Commonwealth Pensions Department | Not stated |
| Wallace 1972 | Part based on the families identified by Parker 1958 but also by contacting to all psychiatrists, neurologists, geriatricians. Appeal for cases also through the RCGPs and a personal search of the wards of the State’s psychiatric institutions plus individual approaches to the medical and nursing staff and to convalescent homes. Visits to families in their homes. | Clinical examination wherever possible (numbers not stated) by the author. Specific criteria not stated. |
| Teltscher 1972 | Not stated | Not stated |
| Pridmore 1990 | Records of Tasmnian hospitals and nursing homes; Departments of Pathology and Community Health (University of Tasmania); medical practitioners with an interest in the field; GPs via RACGPs’ newsletter; publicity in newspapers and TV; Registrar-General’s records; family members of HD patients; Australian HD Association. | Positive family history; plus physical and psychological manifestations of HD. Diagnoses all by medical professionals and most by a specialist. |
| McCusker 2000 | Records of the HD Service. Records of the major general and chronic psychiatric hospitals in NSW. Questionnaires to adult and paediatric neurologists in NSW, to psychiatrists, to genetic counsellors, to clinical geneticists. | Definite = chorea or ataxia with a positive +ve family history or expanded CAG repeat; or would have had a signs of HD and would have had a diagnosis of definite HD Probable = suspected by an expert with motor signs but positive family history and no genetic test. |

**Annex 11**

**Methods for case ascertainment and diagnosis of HD:  
United Kingdom**

|  |  |  |
| --- | --- | --- |
| **Author ID** | **Case finding method** | **Diagnostic criteria** |
| Bickford 1953 | Patients in Bodmin Mental Hospital plus 6 family members in the community | Not stated |
| Heathfield 1967 | Letter to all chronic institutions and mental hospitals, neurologists, psychiatrists, general physicians, senior partner of all GP practices. | All patients visited at home or seen in hospital outpatients. Cases included all with Huntington’s chorea with and without a family history. Senile chorea excluded. |
| Bolt 1970 | Names of patients contributed by psychiatrists, neurologists, physicians, geriatricians, GPs, MOHs, nurses, social workers. Others from Registrar General and Statistics Branch of the Home and Health Department and searches through records of psychiatric hospitals/units. | All medically examined. All had chorea plus mental symptoms and included both those with or without a family history. Those with chorea alone and without a family history were excluded. |
| Oliver 1970 | Follow-up of the families reported by Pleydell 1954 and Reid 1960 plus any new families/cases | Not stated |
| Heathfield 1971 | Personal cases seen in hospitals; postal enquiry of all GPs, psychiatrists | Chorea +/- family history |
| Glendinning 1975 | Questionnaire sent to all the general practitioners—425-- who had patients in Somerset. 327 replies were received (76%). Also questionnaires were sent to all the consultant psychiatrists, physicians, neurologists and geriatricians, and medical superintendants of mental hospitals in Somerset. The author visited all patients with, or suspected of having, Huntington’s chorea that were reported to him except for two, who died before he could see them. Before including any patient he obtained confirmatory evidence of the diagnosis from consultants who had seen the patient. He also obtained a positive family history where possible. | All patients diagnosed through and by multiple sources: the author, consultant psychiatrists, hospital record, relatives of patient, consultant neurologists, general practitioners. The author does not specify the criteria used to diagnose these specific patients, but he was a general practitioner whose practice included two large families affected by the disease over a period of fifteen years and he was very familiar with the range of symptoms. |
| Stevens 1976 | Request for information sent to1,300 family doctors, 50 psychiatrists, 14 geriatricians and 6 neurologists in the area, as well as to selected general physicians known to have an interest in neurology. In addition, chance discoveries of undiagnosed patients in mental hospitals, tracing pedigrees of known choreics, following up comments made by members of the lay public concerning affected friends or relatives, referrals from gynaecologists of patients who wished for termination of pregnancy on the grounds of Huntington' s chorea | 1. (a) Progressive chorea and dementia with onset in adult life with no other obvious cause.  (b) Progressive chorea or progressive dementia with onset in adult life with no other obvious cause.  (c) Progressive extrapyramidal signs without chorea, with or without dementia, where no other cause is •apparent. (d.) Progressive motor disability with mental deterioration, with or without epilepsy, with onsetin childhood, with- out any other obvious cause. and. 2 (a) A positive family history in which typical choreics as defined in 1 (a) above occur, (b) A negative family history only for patients who conform to 1 (a) above, particularly with respect to the condition that no other obvious cause exists for the symptoms. |
| Caro 1977 | 1) Hand searching all death and discharge records in local mental hospitals since 1947; 2) Indices of local general hospitals ; 3) Letters to all GPs in the area; 4) Death records of all mental hospitals since 1837; 5) Visits to next of kin of patients notified by GPs; 6) Further family tracing using parish registers; 7) Interviews with retired psychiatrists, social workers etc | Not stated |
| Harper 1979 | Complete ascertainment attempted (1971-1978) by enquiry of hospital clinicians, GPs and records of general and psychiatric hospitals in South Wales. | Not stated |
| Quarrell 1988 | North Wales: Cases were sought through general practitioners, psychiatrists, psychiatric records, neurologists, geriatricians and the hospital activity analysis system. Family  members in North Wales were visited and details of pedigree structure obtained. | Not stated |
| Simpson 1989 | Search of the genetics register, Psychiatric Diagnostic Register at the Royal County Hspital, Aberdeen Teaching Hospital Diagnostic Register, Grampian Health Board’s list of general hospital discharges, personal contact with GPs. | All patients seen by the authors or a neurologist. All patients had a DNA test! |
| Shiwach 1990 | Cases of HD were ascertained from our own records and, by telephone and written contact, from all regional and subregional genetics centres in the UK as well as from the National Hospital for Nervous Diseases and the Association to Combat Huntington's Chorea (Combat); all contacted centres responded. In addition, one of us (RSS) checked the records of the Maudsley and Bethlem Royal Hospitals. | The diagnosis in all the cases was based on clinical findings and family history. |
| MacMillan 1991 | A retrospective search of hospital inpatient records, genetic outpatient records, and all electromyography (EMG) records for the health districts of Mid and South Glamorgan for the years 1968 to 1990 was carried out. A family study was instigated by contacting the index patient after obtaining permission from his or her general practitioner. If the index patient had left the study area prior to interview or had died, family members living in the study area were contacted and assessed when possible. If the index patient refused to participate, only that person was included in the prevalence data. | Patients meeting accepted criteria for affected status. |
| Watt 1993 | Letters to all patients/families with HD diagnosis recorded by the Medical Genetics Lab, Churchill Hospital, Oxford followed by visit. | Movement disorder with dementia plus family history. A DNA test appears to have been done at least in some if not all! |
| Shiwach 1994 | Department of Oxford region record linkage scheme; regional nursing homes and psychiatric institutions. Details in Shiwach 1994 | Need to get thesis |
| James 1994 |  |  |
| Morrison 1995 | Enquriy of all GPs, neurologists, psychiatrists, geriatricians. Registers of psychiatric & major teaching hospitals. Registers of Dept Medical Genetics. Intensive search for secondary cases through enquiry of families | Progressive chorea, dementia, psychiatric disturbance plus family history  Atypical cases if a positive positive family history  Typical cases with a negative family history included  Positive DNA test on all 101 living patients |
| Morrison 2011 | Based on follow-up of patients in 1991 survey (Morrison 1994) plus those in Northern Ireland HD register in 2001. | The same as Morrison 1995. All confirmed with genetic test. |
| Sackley 2011 | Read codes for HD and Read codes for HD plus anti-chorea medication, other (unspecified chorea), and a family history of HD in the THIN database | Not stated |
| Evans 2013 | Read codes for HD and Read codes for HD in the CPRD database in patients in patients >20 years. | Not stated |
| Douglas 2013 | Read codes for HD and Read codes for HD in the CPRD database in patients <21 years. | Not stated |

**Annex 12**

**Methods for case ascertainment and diagnosis of HD:  
Western Europe (excluding the UK)**

|  |  |  |
| --- | --- | --- |
| **Author ID** | **Case finding method** | **Diagnostic criteria** |
| ***Finland*** | | |
| Palo 1987 | Systematic search of all university, central and central mental hospitals. Number of HD patients the same as the number of people receiving pensions because of HD (not possible to undertake linkage though). | Not stated |
| ***France*** | | |
| Leger 1974 | Records of hospitals, clinics and GPs. Enquiry of families | Typical neurological features plus psychiatric symptoms |
| Petit 1985 | Clinics in the region | Chorea with psychiatric symptoms |
| ***Germany*** | | |
| Panse 1942 | Search of the case records of psychiatric and neurological institutions; also spas and old people’s homes. Also from the records of the advisory bureaux concerned with heredity and eugenics (Beratungstellen fur Erb und Rassenpfledge) | Not stated but only those with a positive family history included. |
| Wendt 1972 | Scrutiny of archives of neurological hospitals and care homes; psychiatric institutions; enquiry of psychiatrists; health authority case registries. Follow-up of patients originally identified by Panse. | Not stated – reliant on recorded diagnosis. |
| Przuntek 1987 | All people diagnosed within the catchment area of the neurology department of the Bocum University Hospital | Not stated |
| ***Greece*** | | |
| Panas 2011 | Records of the Laboratory of Neurogenetics, Athens (the only neurogenetics lab in Greece) | Neurological examination including the UHDRS plus CAG repeat length in a subset of patients |
| ***Iceland*** | | |
| Gudmundsson 1969 | Not stated | Not stated |
| Sveinsson 2012 | Medical records and hospital discharge diagnoses of all hospitals including records of neurological, psychiatric and genetic departments. Information from practising neurologists and selected GPs. Information from family members. | Hyperkinetic movement disorder + psychiatric symptoms + progressive cognitive decline +=ve FH or +ve DNA analysis.  Diagnosis verified from hospital records, information provided by families, and results of DNA testing. |
| ***Ireland*** | | |
| Morrison 1998 | Multiple sources including enquiry of geriatricians, neurologists, psychiatrists, GPs, families, lay associations, secondary tracing. | Clinical criteria plus genetic test. |
| ***Italy*** | | |
| Roccatagliata 1979 | Admissions to neurology and psychiatric departments in Genoa and the surrounding regions. | Typical clinical features |
| Groppi 1986 | Enquiry of all neurological/psychiatric facilities; divisions of medicine, geriatrics, long-stay facilities; private hospitals, nursing homes, institutions for the disabled; all neurologists and psychiatrists in the province; 3 leading health centres; small number of GPs. | Positive family history + progressive motor disorder + progressive mental deterioration. Data collected using questionnaire from patients/families. |
| Pavoni 1990 | Records of 1) the hospital departments and clinical institutes of Ferrara and Bologna; 2) Psychiatric Hospital of Ferrara; 3) Non-specialist divisions of the Province of Ferrara; Parish records of the communes of Ferrara; 4) Centres for the disabled and long-stay wards; 5) Telephone surveys of neurologists, psychiatrists, GPs and health workers in the region. | 1) Positive family history; 2) Chorea, not present at birth and progressive; 3) Progressive mental deterioration. |
| Frontali 1990 | All patients admitted to neurological, psychiatric, or geriatric hospitals in the Lazio region.  Field work with affected families to check diagnoses and family histories | 1) presence of motor, mental and psychiatric symptoms with a positive family history of HD; 2) presence of the above symptoms and atrophy of the caudate nucleus assessed at CT scan or post-mortem examination, with unknown family history. Patients with a negative family history were included in a separate group. |
| Leone 1993 | In-patients and out-patients attending Aosta Regional Hospital. No attempt to ascertain patients not attending that hospital. | Presumably assigned by the clinical service? Not specified. |
| ***Malta*** | | |
| Cassar 1967 | Cases seen personally and supplemented by relatives of affected persons, and supplemented by records from Maltese mental hospitals. | Not stated |
| Grassivaro Gallo 1999 | Neurogenetic Clinic of St. Luke's Hospital in Malta | Clinical signs plus DNA analysis |
| ***Netherlands*** | | |
| Tibben 1993 | Leiden register for HD | Not stated |
| Maats-Kievit 2000 | Unknown – based on Leiden roster for HD | Unknown – based on Leiden roster for HD |
| ***Norway*** | | |
| Saugstad 1986 | Admissions to Norwegian psychiatric hospitals supplemented by admissions to Neurological Departments from 1916. | Not stated. Reliant on original diagnoses plus scrutiny of record cards. |
| ***Spain*** | | |
| Calcedo-Ordonez 1970 | Surveys of local doctors, hospital doctors, specialists (neurologists, psychiatrists, neurosurgeons) and records of patients in mental institutions. | Clinical criteria |
| Ruiz 1985 | Not clear but contacted the families of 11 known patients to identify additional ones | Clinical criteria + exclusion of other causes (eg Wilson’s diseases) + CT scan (on some) |
| Burguera 1997 | Used “capture-recapture” method! The sources of information used were clinical histories from the regional hospitals and official figures of registered deaths during the period 1987-1992. | Not stated |
| ***Sweden*** | | |
| Mattsson 1974 | Contact with families previously identified by Ottosson | Occurrence of involuntary movements not due to other causes. Single cases examined by a neurologist or psychiatrist and diagnosis confirmed. |
| ***Switzerland*** | | |
| Zolliker 1959 | Survey of clinics, outpatients and neurologists at the larger hospitals in the country. | Not stated |

**Annex 13**

**Prevalence estimates**

**Africa**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Author ID** | **Location** | **Study year(s)** | **Prevalent cases** | **Denominator(s)** | **Prevalence**  **per 100,000**  **(95% CIs)** | **Comments** |
| ***South Africa*** | | | | | | |
| Hayden 1977 | Cape coloured community  South Africa | 1976 | 26 | 730,306 | 3.56  (2.33 to 5.22) |  |
| Hayden 1980 | South Africa | 1977 | Total =156  Whites = 97  Coloureds = 53  Blacks = 3 | Total = 23,446,000  Whites = 4,367,000  Coloureds = 2,432,000  Blacks = 16,647,000 | Total = 0.67  (0.56 to 0.78)  Whites = 2.22  (1.80 to 2.71)  Coloureds = 2.18 (1.63 to 2.85)  Blacks = 0.02  (0.00 to 0.5) |  |
| ***Zimbabwe*** | | | | | | |
| Scrimgeour 1992a | Manicaland,  Zimabwe | 1988-1989 | 10 | 1,000,000 (approx) | 1.00  (0.48 to 1.84) | All Bantu |

**Annex 14**

**Prevalence estimates**

**Americas**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Author ID** | **Location** | **Study year(s)** | **Prevalent cases** | **Denominator(s)** | **Prevalence**  **per 100,000**  **(95% CIs)** | **Comments** |
| ***Canada*** | | | | | | |
| Shokeir 1975 | Winnipeg & Mannitoba, Canada | Early 1970s | 162 | 1,926,942 | 8.41  (7.2 to 9.8) | Prevalence year not stated |
| Fisher 2014 | British Columbia, Canada | 2012 | Total = 631  Caucasian = 599 | Total = 4,609,659  Caucasian = 3,470,930 | Total = 13.69 (12.64–14.80).  Caucasian = 17.26  (15.90–18.70) |  |
| ***United States of America*** | | | | | | |
| Pearson 1955 | Minnesota USA | 1950 | 162 | 2,982,483 | 5.43  (4.63 to 6.34) |  |
| Reed 1958 | Michigan, USA | 1940 | 203 | 4,932,562 | 4.12  (3.57 to 4.72) |  |
| Wright 1981 | South Carolina USA | 1980 | 9 | 927,835 | 0.97  (0.44 to 1.84) | Study confined to Blacks only |
| Folstein 1987 | Maryland USA | 1980 | Total=217  White=156  Black=61 | Total=4,217,000 White= 3,259,386  Black=957,614  . | Total=5.15  (4.48 to 5.88)  White=4.79  (4.06 to 5.60)  Black=6.37  (4.87 to 8.18) |  |
| Kokmen 1994 | Olmstedt County, Minnesota, USA | 1990 | 3 | 150,754 | 1.9  (0.2 to 6.8) | Includes 2 definite plus 1 probable HD diagnoses |
| ***Venezuela*** | | | | | | |
| Paradisi 2008 | Venezuela (excluding Zulia) | Early to mid-2000s | 88 | 25,251,697 | 0.35  (0.29 to 4.29) | Population derived from VZ census data (2011) |

**Annex 15**

**Prevalence estimates**

**Asia**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Author ID** | **Location** | **Study year(s)** | **Prevalent cases** | **Denominator** | **Prevalence**  **per 100,000**  **(95% CIs)** | **Comments** |
| ***Hong Kong*** | | | | | | |
| Leung 1992 | Hong Kong | 1991 | 14 | 5,550,000 | 0.25  (0.14 to 0.42) | Also includes period prevalence for 1987-1991 |
| ***Japan*** |  |  |  |  |  |  |
| Kishimoto 1957 | Aichi Prefecture, Japan | 1957 | 13 | 3,916,922 | 0.33  (0.18 to 5.69 |  |
| Kanazawa 1983 | Ibaraki Prefecture, Japan | Early 1980s? | 3 | 2,638,280 | 0.11  (0.023 to 0.33 | Prevalence date not stated. |
| Nakashima 1995 | San-in area  Japan | 1993 | 9 | 1,387,000 | 0.65  (0.30 to 1.23) |  |
| Adachi 1999 | San-in Region,  Japan | 1997 | 10 | 1,388,889a | 0.72  (0.35 to 1.32) |  |
| ***Taiwan*** |  |  |  |  |  |  |
| Chen 2010 | Taiwan | 2007 | 97 | 23,0000,000 | 0.42  (0.34 to 0.51)  Needs recalculating | Also includes prevalence data for years 2000-2006 |

a Population size calculated by back extrapolation

**Annex 16**

**Prevalence estimates**

**Central and Eastern Europe**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Author ID** | **Location** | **Study year(s)** | **Prevalent cases** | **Denominator(s)** | **Prevalence**  **per 100,000**  **(95% CIs)** | **Comments** |
| ***Croatia*** | | | | | | |
| Sepcic 1989 | Rijeka District, Yugoslavia (now Croatia) | 1981 | 24 | 536,978 | 4.47  (2.86 to 6.65) |  |
| Hecimovic 2002 | Croatia | 2002  (approx) | 44 | 4,492,049 | 0.98  (0.71 to 1.31) | Prevalence date not reported |
| ***Russian Federation*** | | | | | | |
| Khomenko 1993 | Amur Territory, Russia | Early 1990s? | 33 | 1,092,715a | 3.01  (2.08 to 4.24) |  |
| Shkurat 2003 | Rostov region, Russia Federation | 2002 | 109 | 4,400,000 | 2.48  (2.03 to 2.99) |  |
| Baryshnikova 2002 | Vladimir Oblast  Russia | 1994-1997 | 31 | 1,662,900 | 1.86  (1.27 to 2.65) |  |
| Kirilenko 2004b | Volgograd and Volzhsky, Russian Federation | Early 2000s? | 8 | 1 323 500 | 0.60  (0.26 to 1.19) | Attributes low prevalence to recent migration. |
| Nikolaeva 2009 | Sakha Republic, Russian Federation | 2008 | 5 | 949,972 | 0.53  (0.17 to 1.23) |  |
| ***Slovenia*** | | | | | | |
| Peterlin 2010 | Slovenia | 2006 | 104 | 2,015, 503a | 5.16  (4.22 to 6.25) |  |

a Population calculated by back extrapolation

**Annex 17**

**Prevalence estimates**

**Oceania**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Author ID** | **Location** | **Study year(s)** | **Prevalent cases** | **Denominator(s)** | **Prevalence**  **per 100,000**  **(95% CIs)** | **Comments** |
| Brothers 1955 | Victoria  Australia | 1954 | 57 | 2,452,341 | 2.32  (1.76 to 3.01) | Author did not estimate prevalence or incidence. Denominator data from Australian Bureau of Statistics for 1954 |
| Parker 1958 | Queensland, Australia | 1956 | 31 | 1,347,826a | 2.30  (1.56 to 3.26) |  |
| Brothers 1964 | Victoria  Australia | Early 1960s | 138 | 2,875,000a | 4.80  (4.03 to 5.67) |  |
| Wallace 1972 | Queensland, Australia | 1969 | 111 | 1,751,828 | 6.34  (5.21 to 7.63) |  |
| Teltscher 1972 | Victoria  Australia | Early 1970s | 192 | 3,453,237a | 5.56  (4.80 to 6.40) |  |
| Pridmore 1990 | Tasmania  Australia | 1990 | 54 | 447,000 | 12.08  (9.08 to 15.76) |  |
| McCusker 2000 | New South Wales Australia | 1996 | 380 | 6,038,969 | 1996= 6.29  (5.68 to 6.90) |  |

a Population size calculated by back extrapolation

**Annex 18**

**Prevalence estimates**

**UK**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Author ID** | **Location** | **Study year(s)** | **Prevalent cases** | **Denominator(s)** | **Prevalence**  **per 100,000**  **(95% CIs)** | **Comments** |
| Bickford 1953 | Cornwall  UK | 1950 | 19 | 340,941 | 5.57  (3.36 to 8.70) |  |
| Heathfield 1967 | North East London  UK | 1963 | 81 | 3,271,000 | 2.48  (1.97 to 3.08) |  |
| Bolt 1970 | Western Scotland UK | 1960 | 154 | 2,959,600 | 5.20  (4.41 to 6.09) |  |
| Oliver 1970 | Northamptonshire, UK | 1967-1968 | 27 | 428,000 | 6.31  (4.16 to 9.1) |  |
| Heathfield 1971 | Bedfordshire  UK | 1960-1965 | 30 | 427,970 | 7.01  (4.73 to 10.00) |  |
| Glendinning 1975 | Somerset  UK | 1965 | 33 | 632,000 | 5.22  (3.59 to 7.33) |  |
| Stevens 1976 | West Yorkshire  UK | 1966 | 133 | 3,190,020 | 4.17  (3.49 to 4.94) |  |
| Caro 1977 | Cromer (Norfolk)  UK | 1971 | 54 | 583,000 | 9.26  (7.00 to 12.09) | Also includes prevalence estimates for1941, 1951,1961 |
| Harper 1979 | Gwent & Glamorgan, Wales  UK | 1971 | 130 | 1,720,901 | 7.55  (6.31 to 8.97) |  |
| Quarrell 1988 | South Wales  UK | 1981 | 153 | 1,728,000 | 8.85  (7.51 to 10.37) |  |
| Simpson 1989 | Grampian, Scotland | 1984 | 46 | 462,891 | 9.94  (7.28 to 13.26) |  |
| Shiwach 1990 | UK | 1988 | 17 | 1,260,000 | 1.35  (0.79 to 2.16) | Study confined to UK migrants from the Indian Subcontinent. Population size is “approximate” |
| MacMillan 1991 | South Wales  UK | 1988 | 78 | 939,300 | 8.30  (6.56 to 10.36) |  |
| Watt 1993 | Oxfordshire,  UK | 1988 | 101 | 2,520,000 | 4.01  (3.26 to 4.87) |  |
| Shiwach 1994 | Oxford  UK | 1985 | 138 | 2,437,000 | 5.66  (4.76 to 6.69) |  |
| James 1994 | South Wales  UK | 1994 | 86 | 1,393,900 | 6.17  (4.94 to 7.62) |  |
| Morrison 1995 | N Ireland  UK | 1991 | 101 | 1,569,971 | 6.43  (5.24 to 7.82) | Also estimate for1981 |
| Morrison 2011 | N Ireland  UK | 2001 | 180 | 1,698,113 | 10.60  (9.11 to 12.27) |  |
| Sackley 2011 | UK | 2008 | 177 | 2,964,386 | 6.0  (5.1 to 6.9) | Prevalence data for 2004-2007 also provided. |
| Evans 2013 | UK | 2010 | 432 | 3,515,986 | 12.28  (11.16 to 13.50) |  |
| Douglas 2013 | UK | 1990-2010 | 21 | 1990 = 248,518  2010 = 1167,683 | 0.68  (5.60 to 8.12) | Confined to patients <21 years at diagnosis. Average prevalence1990-2010 |

**Annex 19**

**Prevalence estimates**

**Western Europe (excluding UK)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Author ID** | **Region** | **Study year(s)** | **Prevalent cases** | **Denominator(s)** | **Prevalence**  **per 100,000**  **(95% CIs)** | **Comments** |
| ***Finland*** | | | | | | |
| Palo 1987 |  | 1985-1987 | 26 | 4,900,000 | 0.53  (0.35 to 0.77) |  |
| ***France*** | | | | | | |
| Leger 1974 | Limousin | 1972 | 24 | 341,589a | 7.03  (4.50 to 10.45) |  |
| Petit 1985 |  | 1984 | 158 | 3,900,000 | 4,05  (3.44 to 4.73) |  |
| ***Germany*** | | | | | | |
| Wendt 1972 | West Germany | 1967 | 1,500 | 61,400,000 | 2.44  (2.32 to 2.57) |  |
| Przuntek 1987 | Wurzburg, Northern Bavaria, | 1980 | 57 | 1,190,000 | 4.79  (3.63 to 6.21) |  |
| ***Greece*** | | | | | | |
| Panas 2011 |  | 1995-2008 | 594b | 10,964,020 | 5.42  (4.99 to 5.87) |  |
| ***Iceland*** | | | | | | |
| Gudmundsson 1969 |  | 1963 | 5 | 187,200 | 2.67  (0.87 to 6.23) |  |
| Sveinsson 2012 |  | 2007 | 3 | 311,114 | 0.96  (0.20 to 2.82) |  |
| ***Ireland*** | | | | | | |
| Morrison 1998 |  | 1991 | 96 | 3,525,719 | 2.72  (2.21 to 3.32) |  |
| ***Italy*** | | | | | | |
| Arena 1979 | Tuscany |  | 20 | 857,701a | 2.33  (1.42 to 3.60) |  |
| Groppi 1986 | Florence region | 1979 | 37 | 1,202,013 | 3.08  (2.17 to 4.24) |  |
| Pavoni 1990 | Ferrara region | 1987 | 47 | 1,511,254a | 3.11  (2.29 to 4.14) |  |
| Frontali 1990 | Lazio region | 1981 | 128 | 5,001,684 | 2.56  (2.14 to 3.04) |  |
| Leone 1993 | Aosta | 1982-1991 | 13 | 260,000a | 5.00  (2.66 to 8.55) |  |
| ***Malta*** | | | | | | |
| Cassar 1967 |  | 1966 | 25 | 317,739 | 7.87  (5.09 to 11.61) |  |
| Grassivaro Gallo 1999 |  | 1994 | 40 | 339,173 | 11.79  (8.43 to 16.06) | Also mentions 6 doubtful cases |
| ***Netherlands*** | | | | | | |
| Tibben 1993 |  | 1992 | 676 | 15,070,000a | 4.49  (4.15 to 4.84) |  |
| Maat-Kievit 2000 |  | 1987-1994 | 986b | 15,184,000 | 6.49  (6.09 to 6.91) |  |
| ***Norway*** | | | | | | |
| Saugstad 1986 | Norway | 1950 | 189 | 3,278,546 | 5.75  (4.97 to 6.65) | Also included prevalence estimates for 1930 and 1940 |
| ***Spain*** | | | | | | |
| Calcedo-Ordonez 1970 | Cadiz Province | 1968 | 12 | 909,244 | 1.32  (0.68 to 2.31) | Also included prevalence estimate for 1967 |
| Ruiz 1985 | Salamanca | 1981 | 31 | 368,000 | 8.42  (5.72 to 11.9) |  |
| Burguera 1997 | Valencia | 1987-1992 | 201 | 3,873,812 | 5.42  (4.71 to 6.21) |  |
| ***Sweden*** | | | | | | |
| Mattsson 1974 |  | 1965 | 362 | 7,733,853 | 4.68  (4.21 to 5.19) |  |
| ***Switzerland*** | | | | | | |
| Zolliker 1959 |  | 1930 | 90 | 4.0 million | 2.25  (1.81 to 2.77) | Also includes prevalence estimates for 1900, 1910 and 1920 |

a Population sizes calculated by back extrapolation

b Numbers patients with Huntington’s disease calculated by back extrapolation

**Annex 20**

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