Hwb Gwyddorau Bywyd Cymru
Life Sciences Hub Wales

Intelligence Report: Rare diseases research landscape in Wales

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Contents

1. Executive summary

Rare diseases, defined as conditions affecting fewer than one in 2,000 individuals, collectively impact over 3.5 million people in the UK, including approximately 170,000 people in Wales. To better understand the position of the UK in rare diseases research, the National Institute for Health and Care Research (NIHR) published the Rare Diseases Research Landscape Project Report (RDRL) in September 2023. The report aimed to map the rare disease research landscape, identifying gaps and priorities for future funding. Using a developed algorithm, the RDRL team analysed data from UK government and charity databases, industry bodies, and research support organisations.

While offering a UK-wide perspective, the RDRL had limited specific analysis of the landscape in Wales. This complementary report interrogates the original datasets provided in the RDRL to assess rare disease research in Wales. The dataset, derived from NIHR and Medical Research Council (MRC) portfolios, covers a five-year period from April 2016 to March 2021. The publicly available dataset was filtered to focus on awards, programmes, and portfolios based in Wales, providing insights into rare disease research funding awarded to Welsh institutions or infrastructure programmes between 2016 and 2021. In addition, this report uses NIHR ‘be part of research’ data to identify live rare disease clinical trials run by industry and non-profit organisations in Wales, and EU Horizon data.

The RDRL analysis of the combined UK NIHR programmes and MRC rare disease research portfolio, spanning 2016-2021, revealed a total of 698 awards with a cumulative value of nearly £627mn. Of these awards, 11 were led by organisations located in Wales and these had a total value of £9.79 mn. Cardiff University secured all awards, with a focus on neurodegenerative diseases, including Huntington’s disease. Wales led or contracted a modest proportion of awards (1.6%) compared with other UK regions. By contrast, London had the highest concentration, overseeing 35.8% of the awards. Wales ranked lower than Scotland in both funding (5.6%) and the number of awards (5.4%), with research organisations in Wales receiving less than one-third of the funding allocated to Scottish counterparts.

Considering the NIHR Clinical Research Network (CRN) portfolio, out of a total of 1,686 rare diseases studies supported by NIHR CRN, 29 were conducted in Wales, representing 1.7% of all supported studies. The largest funder of clinical studies in Wales in this portfolio were English and Welsh charities, constituting 41.4% of the studies.

The Welsh Government champions rare diseases research through initiatives such as Health and Care Research Wales (HCRW), a collaborative network supporting clinical and non-clinical fellowships and overseeing the Rare Diseases specialty. The Sêr Cymru Programme attracts scientific talent to Wales, providing funding for diverse fellowships. Wales Gene Park, funded by HCRW, promotes genetic and genomic research. The Wales Syndrome Without a Name (SWAN) Clinic supports individuals with unnamed rare syndromes, serving as a research platform. Additionally, the Congenital Anomaly Register and Information Service (CARIS) is the rare disease registration system in Wales, recording congenital anomalies and rare diseases.

In addition to Government funding, the RDRL highlights the volume of rare disease research supported by charitable funding using data from 171 charities that were AMRC members during 2016-2021. The UK data shows that 107 charities (both with a specific remit in a particular rare disease, and also those with broader remit) invested £580mn into over 2,300 rare disease research studies. Only 1.1% of this funding went to projects and programmes led by Welsh institutions.

From using the NIHR ‘be part of research’ data, the industry research and development projects on rare diseases in the UK demonstrated the support provided from industry into rare disease research. There were 22 active clinical trials identified, including 7 where the primary contacts were based in Wales. The majority of these clinical trials were active in the Cardiff area.

The RDRL identified the importance of collaborative funding between government, industry and charity for rare disease research in the UK and Wales, including co-funding, complementary infrastructure and activity funding. International research collaboration was also identified as vital given the incidence of each rare disease. While collecting international data was out of scope for this work, European Union funding of rare disease research in Wales was investigated as a potentially important source of funding.

Overall, the data showed Cardiff to be the dominant region in Wales for rare diseases research, with Cardiff University the foremost research organisation. Rare disease research in Wales was more concentrated in Cardiff than broader research for life sciences. Similarly, Wales had a lower percentage of the total rare disease research in the UK than it has for the total of life sciences research. Neurological conditions (including Huntington’s disease) and respiratory conditions (namely cystic fibrosis) were among the rare diseases for which the greatest number of research awards were identified across funder portfolios. Following the collation of the data for the RDRL, the UK Rare Disease Research Platform was established through a £14mn five-year investment from the MRC and the NIHR. Swansea University was chosen as one of the platform’s 11 specialist nodes, with others based at universities across the UK and offering different specialities. This may aid in forming a second hotspot of rare diseases research in Wales.

2. Introduction

2.1. Background the Rare Diseases Research Landscape Project Report (RDRL)

In the UK, a rare disease is defined as a condition which affects fewer than one in 2,000 people[1]. Current estimations are that there are more than 7,000 rare diseases, with new conditions continually identified as research advances. Whilst rare diseases are individually rare, they are collectively common, with one in 17 people affected by a rare disease during their lifetime. This amounts to over 3.5 million people UK-wide, including approximately 170,000 people in Wales[2]. It is important that NHS Wales and other services provide this large and diverse patient population with the best possible care.

In September 2023, the National Institute for Health and Care Research (NIHR) published a report overviewing the rare disease research taking place across the UK over a five-year period between 2016-2021. This '**Rare Diseases Research Landscape Project Report**' (hereafter referred to as 'RDRL') was compiled to better understand the UK's rare diseases research landscape in line with the **UK Rare Diseases Framework** published in 2021 and **England's 2022 Rare Diseases Action Plan**, particularly action 15 within the action plan to "map the rare disease research landscape to identify gaps and priorities for future funding". Using an algorithm developed to identify rare disease relevant research over the five-year period, the RDRL team searched databases from UK government and charity organisations and obtained information from industry bodies and other research support organisations[3]. Administrations in Scotland, Wales and Northern Ireland also provided available data on the research they funded to provide a comprehensive picture of rare disease research taking place across the whole of the UK.

The **Wales Rare Diseases Action Plan 2022-2026**, launched as part of The UK Rare Diseases Framework, aims to address the concerns of sufferers of rare diseases. In Wales, the Rare Diseases Implementation Group oversees the national action plan and supports health boards in executing their local plans[4]. The action plan has four priorities, in line with The UK Rare Diseases Framework: helping patients get a final diagnosis faster, increasing awareness of rare diseases among healthcare professionals, better coordination of care, and improve access to specialist care, treatment and medicines. The action plan pledges to ensure access to research studies for rare diseases patients and includes specific commitments to develop a consent strategy to enable researchers to access routine

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[1] UK Government (9 Jan 2021) The UK Rare Diseases Framework. Available at: https://www.gov.uk/government/publications/uk-rare-diseases-framework/the-uk-rare-diseases-framework (accessed 18 Dec 2023)

[2] NHS Wales Health Collaborative (Jun 2022) Wales Rare Diseases Action Plan 2022-2026. Available at: https://executive.nhs.wales/our-functions/networks-and-planning/rare-diseases/wales-rare-diseases-action-plan-2022-2026/ (accessed 18 Dec 2023)

[3] Rare Disease Research Landscape Steering Group, & Bainbridge, K. (2023). Rare diseases research landscape project report. NIHR Open Research. https://doi.org/10.3310/nihropenres.1115214.1

[4] NHS Wales Executive. National Rare Diseases Implementation Network. Available at: https://executive.nhs.wales/our-functions/networks-and-planning/rare-diseases/ (accessed 18 Dec 2023)

genomic data securely and safely and to engage with Health and Care Research Wales (HCRW) to help increase access to research studies for rare diseases patients[5].

2.2. Aims of this report

The RDRL covers research spanning the whole UK and offers limited analysis of the situation in devolved nations such as Wales. In this complimentary report, the available datasets were searched for data relating to the rare disease research landscape in Wales. The purpose of the exercise is to understand the scope of research taking place in Wales, and to understand gaps and strengths, to aid in determining where Wales sits on rare diseases research in the UK context.

UK-wide rare diseases research data was generated from NIHR and MRC portfolios by the authors of the RDRL. Full details on the generation of the original published dataset is available in the RDRL[6], with published data available at **NIHR Open Data**[7]. The original RDRL focussed on a dataset covering a five-year period from April 2016 – March 2021. The research team subsequently released a six-year dataset extending from April 2016 – March 2022, but for the ease of comparison with the findings in the original report, the five-year dataset was used in analysis for this report. The publicly available dataset was filtered to awards, programmes and portfolios where the lead location was based in Wales. This enabled the identification of rare diseases research funding awarded between 2016 and 2021 to institutions or infrastructure programmes based in Wales.

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[5] NHS Wales Health Collaborative (Jun 2022) Wales Rare Diseases Action Plan 2022-2026. Available at: https://executive.nhs.wales/our-functions/networks-and-planning/rare-diseases/wales-rare-diseases-action-plan-2022-2026/ (accessed 18 Dec 2023)

[6] Rare Disease Research Landscape Steering Group, & Bainbridge, K. (2023). Rare diseases research landscape project report. NIHR Open Research. https://doi.org/10.3310/nihropenres.1115214.1

[7] NIHR Open Data (21 Sep 2023) Rare Diseases Research Landscape Project Datasets. Available at: https://nihr.opendatasoft.com/explore/dataset/rare-diseases-research-landscape-project/information/ (accessed 18 Dec 2023)

3. NIHR programmes and MRC rare disease research portfolio

3.1. NIHR and MRC awards in Wales

The RDRL found (using Dataset 1, available via **NIHR OpenData**) that the combined UK NIHR programmes and MRC rare disease research portfolio comprised 698 awards, with a total value of almost £627mn (equivalent to £125mn per annum) during 2016-2021. Of these awards, 11 were led by organisations located in Wales and these had a total value of £9.79 mn. Programmes in Wales accounted for around 1.6% of the total funds awarded, both in the number of awards and total value (Table 1).

Table 1. Comparison of UK total and Wales data from MRC and NHIR Programmes Rare Disease Combined Portfolio

	Total award value	No. awards	Award value per annum	Median award value
Total UK dataset	£ 626,918,074	698	£ 125,383,615	£ 425,065
Wales	£ 9,785,066	11	£ 1,957,013	£ 687,871
Wales as a % of UK total	1.6 %	1.6 %	1.6 %	-

For all awards, Cardiff University was the research organisation awarded funding, with no others highlighted in the data or searches (Table 2). In some cases, funding was awarded to Cardiff University-affiliated organisations or initiatives, including The Wales Genomic Medicine Centre[8] and Cardiff Fetal Tissue Bank[9]. The awards made to Wales cover several neurodegenerative diseases, including five awards which focus on Huntington's disease. There were four awards worth at least £1mn each. The largest award was approximately £2.4mn for the **AZTEC trial**, a multi-centre, randomised, placebo-controlled trial of azithromycin for preventing chronic lung disease in preterm infants[10].

Out of the 181 career development awards within the NIHR Programmes and MRC Rare Disease Research portfolio, only one career development award was led or contracted by a research organisation in Wales, which was worth £309,744.

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[8] UKRI. The Wales Genomic Medicine Centre. Available at: https://gtr.ukri.org/projects?ref=MC_PC_16035 (accessed 6 Dec 2023).

[9] UKRI. Cardiff Fetal Tissue Bank: Quality assured tissue for biomedical research and clinical trial in neurodegenerative disease. Available at: https://gtr.ukri.org/projects?ref=MR%2FM02475X%2F1 (accessed 6 Dec 2023)

[10] NIHR. AZithromycin ThErapy for Chronic lung disease (AZTEC): A randomised, placebo controlled trial of azithromycin for the prevention of chronic lung disease of prematurity in preterm infants. Available at: https://fundingawards.nihr.ac.uk/award/16/111/106 (accessed 6 Dec 2023)

Table 2. Details of the 11 awards made by the MRC and NIHR programmes to Wales, 2016 to 2022 ordered by award value. One of these awards was a career development award, which is marked with a star (*).

#	Funder Programme	Title	Research Organisation	Awarding body	Award Value
1	Health Technology Assessment	AZithromycin ThErapy for Chronic lung disease (AZTEC): A randomised, placebo controlled trial of azithromycin for the prevention of chronic lung disease of prematurity in preterm infants	Cardiff University	NIHR	£2,361,018
2	MRC SIEBEL	Cell therapy for Huntington's disease: addressing critical knowledge gaps	Cardiff University	MRC	£1,996,455
3	MRC SIEBEL	LIMK1 inhibitors - A novel, disease-modifying approach for the treatment of fragile X syndrome	Cardiff University	MRC	£1,980,780
4	MRC LIS	The Wales Genomic Medicine Centre	Cardiff University	MRC	£1,000,000
5	MRC SIEBEL	How CTIP2 deficiency drives medium spiny neuron degeneration and dysfunction: implications in Huntington's disease pathogenesis	Cardiff University	MRC	£708,068
6	MRC LIS	(Epi)genome editing to combat expanded CAG/CTG repeat disorders	UK Dementia Research Institute at Cardiff University	MRC	£687,871
7	MRC LIS	Understanding the role of neurodegenerative disease risk genes in the ageing nervous system	Cardiff University	MRC	£485,234
8*	MRC SIEBEL	Understanding the role of DNA repair in Huntington's Disease pathogenesis: towards new therapeutic targets	Cardiff University	MRC	£309,744
9	MRC SIEBEL	Cardiff Fetal Tissue Bank: Quality assured tissue for biomedical research and clinical trial in neurodegenerative disease	Cardiff University	MRC	£202,304
10	MRC LIS	Exploring the proteome of CAG/CTG repeat expansions	UK Dementia Research Institute at Cardiff University	MRC	£38,733
11	MRC SIEBEL	Investigating the effects of CAG repeat structure and MSH3 variants on the molecular biology of Huntington's disease	Cardiff University	MRC	£14,859

3.2. Comparing NIHR and MRC awards in Wales with the rest of the UK

The NIHR programmes and MRC rare disease research portfolio included postcode data for the lead or contracted research organisation for each award. In the RDRL, these data were used to compile the total number and value of NIHR Programmes and MRC awards led by or contracted to research organisations within each region of England and the devolved administrations (Table 3). It found that the NIHR programmes and MRC rare disease research portfolio encompassed awards led by or contracted to research organisations across all regions of England, including Scotland, Wales, and Northern Ireland.

Table 3. Breakdown of the proportion of funding and number of awards between 2016 – 2021 by English region/devolved nation.

Region		**Proportion of funding value awarded**	**Proportion of total number of awards**
Scotland		5.6 %	5.4 %
Northern Ireland		0.4 %	0.9 %
Wales		1.6 %	1.6 %
England	North West	5.8 %	8.2 %
	North East	3.5 %	4.6 %
	Yorkshire and the Humber	5.8 %	11.6 %
	West Midlands	2.1 %	3.3 %
	East Midlands	1.6 %	3.0 %
	East of England	10.0 %	6.7 %
	South West	3.3 %	5.0 %
	South East	15.5 %	13.5 %
	London	45.0 %	35.8 %

The majority of awards were led by or contracted to research organisations within England, with the highest concentration in London (35.8%). By contrast, research organisations in Wales (1.6%) and Northern Ireland (0.9%) oversaw or contracted the fewest number of active awards in the given period. Furthermore, research organisations in Wales received less than one-third of the funding received by their counterparts in Scotland (5.6%). Examining the funding distribution, the RDRL noted that the largest total funding was allocated to awards led by or contracted to organisations in London (£282mn). Conversely, the funding awarded to organisations in Wales (£9.8m) was the second lowest, surpassing only Northern Ireland (£2mn)[11].

3.3. Awards by disease names and Health Research Classification System (HRCS)

In the original UK-wide RDRL, data were analysed to determine the Orphanet disease names associated with the highest number of awards. Their analysis showed that amyotrophic lateral sclerosis (ALS) was associated with the highest number of awards (n=44), followed by Huntington's disease (n=35). In the 11 awards that Wales received, Huntington's disease was associated with the highest number of awards (n=6). All other rare diseases that were studied were only associated with a single award (Table 4).

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[11] Rare Disease Research Landscape Steering Group, & Bainbridge, K. (2023). Rare diseases research landscape project report. NIHR Open Research. https://doi.org/10.3310/nihropenres.1115214.1

Table 4. Disease names associated with Wales-based awards April 2016 – March 2021. Note: Some awards were associated with multiple diseases, so it is possible for a single award to appear under more than one category.

Disease name	Number of awards
Huntington's disease	6
Bronchopulmonary dysplasia	1
Cystic fibrosis	1
Rabies	1
Fragile X syndrome	1
Myotonic dystrophy	1
Amyotrophic lateral sclerosis (ALS)	1
Frontotemporal dementia	1

Another way of categorising is by the type of research being funded. The Health Research Classification System (HRCS) serves as a shared terminology among funders to record and assess the nature and scope of funded research. The system, which encompasses classifications for health categories and research activities, is elaborated on in the RDRL (see Annex 1.7.1.1. in the RDRL). HRCS health categories capture the area of health or disease being studied. In the 11 awards that Wales received, the neurological category had the largest proportion of awards (Table 5), both in the number of awards and in apportioned value[12].

Table 5. Apportioned Number and value of Wales-based awards by HRCS category.

HRCS health category	Apportioned number of awards	Apportioned value of awards
Neurological	7	£ 4,240,964
Generic health relevance	2	£ 1,202,304
Infection	0.5	£ 1,180,509
Reproductive health and childbirth	0.5	£ 1,180,509
Congenital disorders	0.5	£ 990,390
Mental health	0.5	£ 990,390
Total	**11**	**£ 9,785,066**

HRCS Research Activity Codes (RAC) capture the type of research taking place. In this case, the largest apportioned number of awards in Wales went to the category of ‘Underpinning research’, whilst the largest apportioned value of awards went to ‘Evaluation of treatments and therapeutic interventions’ (Table 6).

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[12] Apportioning was determined in the same way as in the original RDRL where, if an award is assigned multiple categories in a particular metric, they would be equally apportioned (e.g. two categories would be apportioned 50% each, three categories apportioned 33.3% etc.). See Annex 1.7.1.1.1 in the original RDRL for further details.

Table 6. Apportioned number and value of Wales-based awards by HRCS Research Activity Code.

HRCS Research Activity Code	Apportioned number of awards	Apportioned value of awards
1. Underpinning research	4.25	£ 3,235,439
2. Aetiology	2.75	£ 826,933
3. Prevention of disease & conditions	0	£ 0
4. Detection, screening and diagnosis	0.25	£ 171,968
5. Development of treatments and therapeutic interventions	1.25	£ 2,152,748
6. Evaluation of treatments and therapeutic interventions	1.5	£ 3,359,246
7. Management of diseases and conditions	0	£ 0
8. Health and social care services research	0	£ 0
No code given	1	£ 38,733
Total	**11**	**£ 9,785,066**

3.4. Mapping awards to the Wales Rare Diseases Action Plan 2022-2026

The Wales Rare Diseases Action Plan 2022-2026 lists four key priorities, in line with The UK Rare Diseases Framework:

1. Helping patients get a faster diagnosis,
2. Increasing awareness of rare diseases among healthcare professionals,
3. Better coordination of care,
4. Improve access to specialist care, treatment and medicines.

To better understand how research funded by MRC and NIHR might contribute to advancing these priority areas, assigned each award was assigned to at least one of six categories: the four priority areas, basic science research, or ‘no priority’. These awards were manually assigned using the authors’ best judgement and were based on the criteria set by authors of the RDRL. See Annex 5 of the RDRL for detailed definitions of the categories.

Table 7: Number of awards per key priority in the Wales Rare Diseases Action Plan 2022-2026.

Category	Number of awards
Priority 1: Faster Diagnosis	1
Priority 2: Increased awareness of rare diseases among healthcare professionals	1
Priority 3: Better Coordination of Care	0
Priority 4: Improved access to specialist care, treatment and drugs	3
Basic Science Research	6
No Priority	0

Faster diagnosis

Research relevant to priority 1 was defined as being “specifically focused on improving the rate or process of detection, screening or diagnosis of rare diseases, or on understanding the diagnostic pathway”. There was one award mapped to this priority. The award, supporting Wales’ Genomics Medicine Centre, aims to bring benefit to patients through improved diagnosis, together with improved understanding of rare diseases through the contribution of samples from patients in Wales.

Increased awareness of rare diseases among healthcare professionals

For the purposes of this project, priority 2 was defined as “addressing ‘increased awareness amongst healthcare professionals’ as a specific goal, over and above dissemination of research findings”. There was one award in this priority, awarded to the Cardiff University programme titled “Cell therapy for Huntington's disease: addressing critical knowledge gaps”. This programme aims to improve the knowledge of the use of cell therapy in Huntington’s disease, including using findings to guide clinics in the treatment of Huntington’s disease.

Better coordination of care

Awards relevant to priority 3 were defined as “social or economic research into the needs of rare disease patients for coordinated care; how care for people living with rare diseases could be better coordinated within a health or social care setting, or how technology or innovation could improve coordination of care for people living with rare diseases”. There were no awards in Wales for this priority. This pattern follows overall UK trends, where priority 3 had the lowest number of awards.

Improved access to specialist care, treatment and drugs

Research mapped to this priority was defined as being focused on “the discovery and development of therapeutic interventions for rare diseases, and testing in preclinical, clinical, community or applied settings”. It also included research into improving access to specialist care and treatments. There were three awards mapped to this category. Two of these were clinical studies into novel advanced therapies. One award was for the use of LIMK1 inhibitors, A novel, disease-modifying approach, for the treatment of fragile X syndrome. The other award was for quality assured tissue for biomedical research and clinical trial in neurodegenerative disease and was based at the Cardiff Foetal Tissue Bank. The third award was for a clinical trial to study the use of azithromycin for preventing chronic lung disease in preterm infants.

Basic science research

Basic science research was defined as “any basic science research where rare disease is the primary focus, including the development of *in vitro* and *in vivo* models of rare diseases, and research into understanding the cause and development of rare diseases”. Basic science research was the largest category, with 6 awards. There was a pattern of these awards being awarded for investigative research into neurogenerative diseases. In particular, most awards went to research into Huntington’s disease.

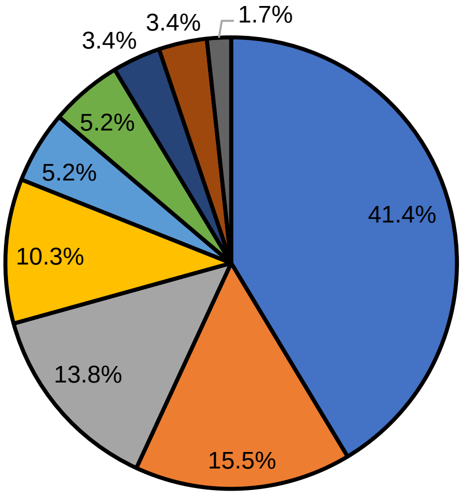
4. NIHR Infrastructure portfolio

The original RDRL considered data and the NIHR Clinical Research Network (CRN) portfolio spanning 2016-2021 (available as Dataset 4 via **NIHR OpenData**). The CRN supports studies funded by the NIHR itself, but also research funded by other partners including UK Research and Innovation (UKRI), medical research charities and industry.

NHIR CRN supported 29 rare diseases studies in Wales, out of 1,686 in total, meaning Wales represented 1.7% of all supported rare diseases studies. A summary of these is available in Appendix 1. The largest funder of clinical studies in Wales fell under the category of ‘Charity – England’ (Table 8). Despite the name however, this category includes charities from both England and Wales. For example, Kidney Wales, Tenovus Cancer Care, and The Jane Hodge Foundation are all Wales-based charities within this category that funded studies in this period.

Table 8. Funder types in NIHR CRN supported rare diseases studies in Wales 2016-2021.

Funder		**Proportion of studies funded**
Charity - England	🟦	41.4%
Devolved Nation Research Funders	🟧	15.5%
Research Council	⬜	13.8%
National Institute for Social Care and Health Research (NISCHR)	🟨	10.3%
Commercial	🟦	5.2%
Government - Overseas	🟩	5.2%
Academic Institution	⬛	3.4%
Royal College	🟫	3.4%
Charity - Overseas	⬛	1.7%



Several other charities provided funding to Wales-based studies including Cancer Research UK and the Wellcome Trust. The second largest category is “Devolved Nation Research Funders”, which consisted entirely of studies funded or part-funded by Health and Care Research Wales (HCRW). The National Institute for Social Care and Health Research (NISCHR), which appears as the 4th largest category, is the precursor to what is now HCRW[13]. Funders appearing in the ‘Commercial’ category included Biomarin Ltd. and Novartis.

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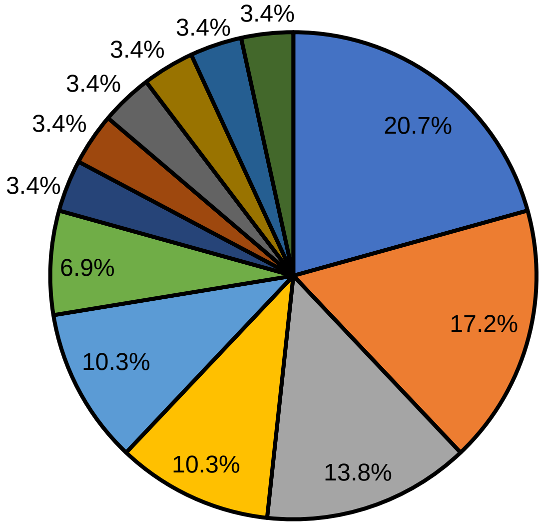
[13] Social Care Wales (2017) Social care research and development strategy for Wales 2018-2023. Available at: https://socialcare.wales/cms-assets/documents/Research-and-development-strategy-2018-23-English.pdf (accessed 13 Dec 2023)

Breaking down the supported studies by clinical specialty, Dementias and Neurodegeneration, Genetics, and Cancer were the three largest categories (Table 9).

Table 9. Clinical specialties in NIHR CRN supported rare diseases studies in Wales

Clinical Specialty		**Proportion of studies funded**	
Dementias and Neurodegeneration	🟦	20.7%	
Genetics	🟧	17.2%	
Cancer	■	13.8%	
Children	🟨	10.3%	
Neurological Disorders	🟦	10.3%	
Respiratory Disorders	🟩	6.9%	
Gastroenterology	■	3.4%	
Haematology	🟫	3.4%	
Health Services Research	■	3.4%	
Metabolic and Endocrine Disorders	🟫	3.4%	
Ophthalmology	🟦	3.4%	
Renal Disorders	🟩	3.4%	

In addition to the CRN portfolio described above, the original RDRL also considered data from the NIHR Infrastructure schemes (available as Dataset 3 via NIHR OpenData), however, there were no infrastructure schemes identified in Wales. All infrastructure schemes identified were in England, so will not be covered here.

5. Industry and charity rare disease research

5.1 Industry and non-profit organisation funded studies

The contribution of UK industry to rare disease research was investigated in the RDRL in an analysis commissioned to Clarivate. This utilised Clarivate's Competitive Intelligence database, as well as access to data from the Association of The British Pharmaceutical Industry (ABPI) and the BioIndustry Association (BIA) to look at industry contribution. No breakdown by devolved nation was available, so it was not possible to determine what proportion of these project were based in Wales.

To gain an impression of the rare disease research landscape funded by industry and charitable sources, study information was gathered through the **NIHR's 'be part of research' database**. Using this source, 22 rare diseases projects were found in Wales, of which 19 were fully sponsored and funded by industry while two were a joint venture between the charity sector and industry, and 1 was fully sponsored by a charity. A summary of these is available in Appendix 2.

Companies sponsoring rare disease activity in Wales include Roche, Sanofi, Novo Nordisk, Daiichi Sankyo, Takeda, Celgene (BMS), and Vertex Pharmaceuticals. Charities and non-profit organisations that have sponsored and funded research activity in Wales include CHDI Foundation, Shire, EspeRare foundation and Pierre Fabre Medicament.

Cardiff was the most common location for industry led research programmes in Wales, with 18 of 22 being active in Cardiff. Cardiff's strong life science cluster, combined with resources such as the Wales Gene Park, the research strengths offered by Cardiff University, and its high-density population (the largest population in Wales) goes some way to explaining Cardiff having the highest number of clinical trials in Wales. One programme was in Swansea and Merthyr Tydfil, respectively. Bangor and Wrexham each were active in one programme where Cardiff was also an active location. Out of the programmes, two were active solely in Wales, while 20 were active across multiple sites across the UK including Wales. A total of 7 programmes had the lead researchers based in Wales.

5.2. Association of Medical Research Charities (AMRC) funding

Third sector organisations, including members of the Association of Medical Research Charities (AMRC), offer a substantial source of funding to life science research. Limited analysis from the original RDRL showed that AMRC funding for rare disease research in Wales was 1.1% of total funding. Wales-based members of AMRC include Cancer Research Wales, Cerebra, and Tenovus Cancer Care[14].

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[14] AMRC member directory. Available at: https://www.amrc.org.uk/Pages/Category/member-directory?Take=3 (accessed 14 Dec 2023)

6. Welsh Government funded rare diseases support

The RDRL described several Welsh Government funded initiatives that support rare diseases research:

- **Health and Care Research Wales (HCRW):** HCRW is a networked organisation supported by Welsh Government, which brings together partners from across Wales to promote research into diseases, treatment and services. HCRW supports both clinical and non-clinical fellowship awards. Additionally, HCRW supports a specialty lead in Rare Diseases, ensuring Wales' active involvement in clinical research portfolio monitoring and research delivery at the UK level[15].
- **Sêr Cymru Programme:** The Sêr Cymru funding programme, initiated in 2012, is a suite of schemes that bring scientific talent into research posts in Wales. The programme is led by the Welsh Government Office for Science. Like HCRW, the Sêr Cymru funding programme provides support for clinical and non-clinical fellowship awards.
- **Wales Gene Park:** Wales Gene Park is an infrastructure support group hosted by Cardiff University’s School of Medicine. Wales Gene Park is funded by the Welsh Government through HCRW and supports and promotes genetic and genomic research across Wales.
- **Wales Syndrome Without a Name (SWAN) Clinic:** Opened in October 2022, the SWAN clinic supports individuals, both children and adults, with syndromes so rare that they lack a name. The clinic also serves as a platform for quality improvement and original research opportunities that can be applied across various rare disease health settings.
- **Congenital Anomaly Register and Information Service (CARIS):** Each UK nation has a population-based congenital anomaly and rare disease registration system. In Wales, this is known as CARIS and it sits within the Knowledge and Research Division of Public Health Wales. First established in 1998, CARIS expanded to include childhood rare diseases in 2013 and began recording rare diseases in people over the age of 18 years from 2020.

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[15] Health and Care Research Wales. Speciality leads. Available at: https://healthandcareresearchwales.org/specialty-leads (accessed 18 Dec 2023)

7. EU Horizon Europe

Though the majority of international research collaboration occurs outside the context of European Union (EU) specific structures, it is important to recognise those EU initiatives that do facilitate cross border collaboration; one of these is research funding. A significant source of funds for health research in the rare disease field comes from European sources such as the Innovative Medicines Initiative and Horizon Europe. These are not solely a source of funding, but also a significant driver in the formation of partnerships across the EU.

Prior to leaving the EU, Wales received funding for life sciences research through the EU Horizon scheme. In September 2023, the UK Government announced that the UK will become an associate country member of the programme, meaning that Wales will continue to benefit from the EU Horizon scheme. The current programme will support Wales in Horizon Europe, running until 2027 with a budget of around €100bn. **Horizon Europe** is the largest ever transnational programme supporting research and innovation. Horizon 2020, Horizon Europe's predecessor, has provided a platform for Welsh researchers and businesses to take part in projects worth over €2.5bn, involving 81 countries and bringing grants worth €153mn to Wales as of September 2023. EU Horizon 2020 involved 178 unique organisations across Wales and produced 1,568 signed grants.

Horizon 2020 has provided numerous opportunities for health, care and third sector organisations in Wales to access significant European and other international funding to support policy development and implementation, research and innovation, leading to better health and wellbeing and enhanced service sustainability. Wales was in a position to increase its involvement in EU funding due to the close fit and coherence between policies, providing a clear opportunity to exploit EU funding streams to add value in Wales.

Whilst rare diseases specific data was not available, information was available on where Wales has contributed to EU life sciences. In total, Wales contributed a net €410.7mn to the EU life sciences sector (Table 10). Of this, €207.9mn of this contribution was from Cardiff and the Vale of Glamorgan, over half of the total of Wales. Southwest Wales contributed the second most at €50.2mn, while Swansea contributed the third largest at €50mn.

Table 10. Net Life Sciences Contribution in Wales by Region from EU Horizon Europe. Source: EU Horizon[16]

Region	Net EU Contribution (€ mn)
Cardiff + Vale of Glamorgan	207.9
Swansea	50.0
South West Wales	50.2
Gwynedd	41.1
Monmouthshire and Newport	16.7
Flintshire and Wrexham	7.8
Central Valleys	11.3
Bridgend and Port Talbot	7.3
Gwent Valleys	4.9
Conwy and Denbighshire	5.2
Powys	4.5
N/A	0.1
Wales Total	**410.7**

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[16] EU Horizon. R&I Country Profiles. Available at: https://dashboard.tech.ec.europa.eu/qs_digit_dashboard_mt/public/sense/app/1213b8cd-3ebe-4730-b0f5-fa4e326df2e2/sheet/0c8af38b-b73c-4da2-ba41-73ea34ab7ac4/state/analysis

8. Concluding remarks

Across government, industry and charity rare disease research portfolios, most of the studies identified were led by, or contracted to, research organisations in the South of Wales, particularly Cardiff. Cardiff University was found to be the dominant lead research organisation in Wales for rare disease research. This is unsurprising, given that Cardiff University is the home of several rare disease research initiatives including Wales Gene Park, Cardiff University Rare Genetic Research Group and Cardiff Rare Genetic Variant Research Programme. Cardiff also houses the SWAN (Syndrome Without a Name) Clinic, giving it a unique area of research to lead from. While there are pockets of research in Swansea, Bangor and Wrexham, these are small compared to the focus of rare disease research in Cardiff.

While Cardiff is home to the largest proportion of life sciences research in Wales, totalling just over half of the EU contribution to the industry from Wales, the proportion that it contributes to the rare diseases landscape is far larger than it does for the rest of life sciences. Swansea University's recent award of one of the UK Rare Disease Research Platform's 11 specialist nodes will give the area a platform to increase its rare disease research landscape in the future[17].

Considering the rare disease research portfolios UK-wide, the RDRL found that most studies were led by, or contracted to, research organisations in London and the Southeast of England. Wales only holds a small percentage of the UK rare diseases research landscape, with only Northern Ireland with a smaller share of research programmes and projects. This is reflective of the broader trends of geographical distribution of research that are seen across UKRI Research Councils collectively, as well as overall NIHR Programme data and AMRC members' charitable expenditure in 2022[18]. However, in the case of rare diseases the lower proportion of research is more pronounced than it is for general life sciences trends.

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[17] Thomas, K. (5 Jul 2023) University Chosen For Specialist Base As Part Of £14m Investment In Rare Disease Research. Available at: https://www.swansea.ac.uk/press-office/news-events/news/2023/07/university-chosen-for-specialist-base-as-part-of-14m-investment-in-rare-disease-research.php (accessed 18 Dec 2023)

[18] AMRC (Jun 2023) 2023: Our sector's footprint. Available at: https://www.amrc.org.uk/our-sectors-footprint-in-2022 (accessed 18 Dec 2023)

Appendix 1. NHIR CRN supported rare diseases studies in Wales 2016-2021

The table below provides summary details of NHIR CRN supported rare diseases studies in Wales 2016-2021. The data was obtained from the Rare Diseases Research Landscape Project 'Dataset 4: NIHR Clinical Research Network supported studies' available at:
https://nihr.opendatasoft.com/explore/dataset/rare-diseases-research-landscape-project/information/
Data was filtered where the NIHR CRN Lead Administration was set to 'Wales'.

CRN ID	Title	Study funder	Study funder type	Managing specialty
3808	Detecting Susceptibility Genes for Late-onset Alzheimer's disease	Medical Research Council	Research Council	Dementias and Neurodegeneration
9014	Experiences of Children with Copy Number Variants	National Institute of Mental Health (NIH NIMH); Wellcome Trust	Government - Overseas; Charity - England	Children
13635	Whole genome/exome sequencing to identify additional Tuberous Sclerosis Complex (TSC) disease causing gene(s) in no mutation identified (NMI) TSC patients	Health and Care Research Wales	Devolved Nation Research Funders	Genetics
13640	A randomised, double blind, placebo-controlled study of RAD001 (Everolimus) in the treatment of neurocognitive problems in tuberous sclerosis.	Novartis Pharma AG; The Tuberous Sclerosis Association	Commercial; Charity - England	Genetics
14615	The contribution of induced sputum sampling to surveillance of lower respiratory tract microbiology in children with Cystic Fibrosis.	NISCHR Academic Health Science Collaboration	NISCHR	Children
14774	Genetic mechanisms in polyposis of the bowel	NISCHR Cancer Genetics Biomedical Research Unit	NISCHR	Genetics
15938	A Trial for Older Patients with Acute Myeloid Leukaemia and High Risk Myelodysplastic Syndrome	Cancer Research UK	Charity - England	Cancer
16305	The collection of Huntington's Disease positive fetal tissue from elective termination of pregnancy	European Huntington's Disease Network (EHDN)	Academic Institution	Dementias and Neurodegeneration
16961	Diagnostic Journeys in Myeloma (DJiM):how long does it take to be diagnosed?	Tenovus Cancer Care	Charity - England	Cancer
18218	Adults with acute myeloid leukaemia or high-risk myelodysplastic syndrome	Cancer Research UK	Charity - England	Cancer
19065	Molecular genetic analysis of duodenal polyposis in the inherited colorectal adenoma and cancer predisposition syndromes (Familial Adenomatous Polyposis and MUTYH-Associated Polyposis)	Health and Care Research Wales	Devolved Nation Research Funders	Genetics
19401	A Study of the Natural History of Renal Disease in TSC2/PKD1 Contiguous Gene Deletion Syndrome.	NISCHR Wales Gene Park	NISCHR	Genetics

20374	An ethnographic study of Leber hereditary optic neuropathy: exploring the experiences and perceptions of children, young adults and their families.	Economic and Social Research Council (ESRC)	Research Council	Ophthalmology
20850	Emotion recognition and oxytocin concentrations in cranial diabetes insipidus	Economic and Social Research Council (ESRC)	Research Council	Metabolic and Endocrine Disorders
31196	A pilot, exploratory study to investigate platelet and microparticle phospholipids in thrombotic and bleeding disorders	British Heart Foundation (BHF)	Charity - England	Haematology
31964	Exploiting 3D scanning technology in lymphoedema for accurate and fast measurements of volume and shape	British Lymphology Society	Charity - England	Cancer
33447	Exploring computerised cognitive training as a therapeutic intervention for people with Huntington's disease.	Health and Care Research Wales; Jacques and Gloria Gossweiler Foundation	Devolved Nation Research Funders; Charity - Overseas	Neurological Disorders
34892	Developing clinical applications for a novel multi-task funcational assessment: The Clinch Token Transfer Test (C3T)	Medical Research Council	Research Council	Dementias and Neurodegeneration
38240	Promotion of physical activity in Huntingtons disease specific clinics	Huntington's Disease Association	Charity - England	Dementias and Neurodegeneration
38376	Developing an occupational therapy intervention for people living with early stage dementia: A qualitative, participatory action research (PAR) study.	Royal College of Occupational Therapists	Royal College	Dementias and Neurodegeneration
39379	A single site, open label, phase I study to assess the safety and feasibility of foetal stem cell transplants in the striatum of people with Huntington’s Disease.	Health and Care Research Wales	Devolved Nation Research Funders	Dementias and Neurodegeneration
39384	Calibration and Cross-Validation of Accelerometry in youth and adults with Cystic Fibrosis	Cystic Fibrosis Trust	Charity - England	Respiratory Disorders
40213	Investigating the inflammatory response to a 6-week exercise programme in children and adolescents with Cystic Fibrosis.	European Commission	Government - Overseas	Children
41812	A pilot study investigating the effects of a manuka honey sinus rinse on sino-nasal outcome test scores in cystic fibrosis patients	The Jane Hodge Foundation	Charity - England	Respiratory Disorders
44910	Using 3D organoid models to explore the genetic causes of duodenal polyposis by comparing affected patients with healthy volunteers	Health and Care Research Wales	Devolved Nation Research Funders	Gastroenterology
45091	Cerliponase alfa Observational Study	Biomarin (U.K.) Ltd.	Commercial	Neurological Disorders
48503	A prospective cohort study of adults with hereditary angioedema to assess the feasibility of using a wearable fitness tracking device to investigate relationships between attack frequency and physical activity.	HAEUK	Charity - England	Health Services Research
50305	Covid-19 Immune Response and Vaccine Efficacy in Patients with Renal Disease and/or Transplantation	Kidney Wales Charity	Charity - England	Renal Disorders
52190	Welsh Advanced Neuroimaging Database in Juvenile Myoclonic Epilepsy (WAND-JME)	Wellcome Trust	Charity - England	Neurological Disorders

A. Breakdown of funding organisation names and types of NHIR CRN supported rare diseases studies in Wales 2016-2021.

Funding Organisation Name	Organisation Type	Apportioned No. Studies	Proportion of studies
Academic Institution		**1**	**3.4%**
European Huntington's Disease Network (EHDN)	Academic Institution	1	3.4%
Charity - England		**12**	**41.4%**
Cancer Research UK	Charity - England	2	6.9%
Wellcome Trust	Charity - England	1.5	5.2%
British Heart Foundation (BHF)	Charity - England	1	3.4%
British Lymphology Society	Charity - England	1	3.4%
Cystic Fibrosis Trust	Charity - England	1	3.4%
HAEUK	Charity - England	1	3.4%
Huntington's Disease Association	Charity - England	1	3.4%
Kidney Wales Charity	Charity - England	1	3.4%
Tenovus Cancer Care	Charity - England	1	3.4%
The Jane Hodge Foundation	Charity - England	1	3.4%
The Tuberous Sclerosis Association	Charity - England	0.5	1.7%
Charity - Overseas		**0.5**	**1.7%**
Jacques and Gloria Gossweiler Foundation	Charity - Overseas	0.5	1.7%
Commercial		**1.5**	**5.2%**
Biomarin (U.K.) Ltd.	Commercial	1	3.4%
Novartis Pharma AG	Commercial	0.5	1.7%
Devolved Nation Research Funders		**4.5**	**15.5%**
Health and Care Research Wales	Devolved Nation Research Funders	4.5	15.5%
Government - Overseas		**1.5**	**5.2%**
European Commission	Government - Overseas	1	3.4%
National Institute of Mental Health (NIH NIMH)	Government - Overseas	0.5	1.7%
NISCHR		**3**	**10.3%**
NISCHR Academic Health Science Collaboration	NISCHR	1	3.4%
NISCHR Cancer Genetics Biomedical Research Unit	NISCHR	1	3.4%
NISCHR Wales Gene Park	NISCHR	1	3.4%
Research Council		**4**	**13.8%**
Economic and Social Research Council (ESRC)	Research Council	2	6.9%
Medical Research Council	Research Council	2	6.9%
Royal College		**1**	**3.4%**
Royal College of Occupational Therapists	Royal College	1	3.4%

Appendix 2. Studies on NIHR 'Be Part of Research' with locations in Wales

Summary details of studies on NIHR 'Be Part of Research' with locations in Wales

Title	Base	Locations	Sponsor/Funder
Atypical Hemolytic-Uremic Syndrome (aHUS) Registry	Manchester	London, Manchester, Exeter, Southampton, Newcastle, **Swansea**	Roche
A Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of DNL593 in Healthy Participants and Participants With Frontotemporal Dementia (FTD-GRN)	Merthyr Tydfil	**Merthyr Tydfil**	Takeda
Safety Study of CC-93538 in Adult and Adolescent Participants With Eosinophilic Esophagitis	Chorley	Birmingham, **Cardiff**, Hexham, Liverpool, Manchester, Belfast, Hardwick, Southampton, Chorley, Cambridge	Celgene
Clinical Study of Cannabidiol in Children, Adolescents, and Young Adults With Fragile X Syndrome	Manchester	London, **Cardiff**, Manchester, Leicester	Zynerba Pharmaceuticals
CD64 as a marker of prosthetic joint infection	Manchester	London, Newcastle, Oxford, Cambridge, Plymouth, Birmingham, Frimley, Leeds, **Cardiff**	Shire; Takeda Development Center Americas, Inc
Hereditary Angioedema (HAE) is a genetic condition characterised by swelling of tissues. These swellings can occur on any part of the body.	Leeds	Frimley, Birmingham, Leeds, Cambridge, London, **Cardiff**	KalVista Pharmaceuticals Ltd
Intraamniotic Administrations of ER004 to Male Subjects With X-linked Hypohidrotic Ectodermal Dysplasia	Cardiff	**Cardiff**	EspeRare Foundation; Pierre Fabre Medicament; Iqvia Pty Ltd.
Avatrombopag for the Treatment of Thrombocytopenia in Pediatric Subjects With Immune Thrombocytopenia for ≥6 Months	Liverpool	Birmingham, Liverpool, London, Manchester, Sheffield, **Cardiff**	Sobi, Inc.
A Study to Evaluate the Effect of SAGE-718 on Cognitive Function in Participants With Huntington's Disease (HD)	Leeds	Plymouth, Leeds, Southampton, London, Aberdeen, **Cardiff**, Birmingham, Newcastle	Sage Therapeutics
Study of WVE-003 in Patients With Huntington's Disease	Liverpool	**Cardiff**, Liverpool, Newcastle, Exeter, Glasgow	Wave Life Sciences Ltd.
A Study to Evaluate the Safety and Efficacy of PTC518 in Participants With Huntington's Disease (HD)	Manchester	Manchester, Leeds, **Cardiff**, London, Birmingham	PTC Therapeutics
Safety and Efficacy of AMT-130 in European Adults With Early Manifest Huntington's Disease	Cardiff	**Cardiff**, London	UniQure Biopharma B.V.
A Phase 2b, Study of Linsitinib in Subjects With Active, Moderate to Severe Thyroid Eye Disease (TED)	Cardiff	**Cardiff**, London, Camberley	Sling Therapeutics, Inc.

ELEVATE, a Registry of Patients With Acute Hepatic Porphyria (AHP)	Cardiff	**Cardiff**, London	Alnylam Pharmaceuticals
A study to evaluate the safety and efficacy of PTC518 in participants with Huntington's disease (HD)	Cardiff	**Cardiff**, European Locations	PTC Therapeutics
Pompe Disease Registry Protocol	Salford	Salford, **Cardiff**, London, Cambridge, Birmingham, Glasgow, Manchester, Newcastle	Genzyme, a Sanofi Company
Evaluation of Elexacaftor/Tezacaftor/Ivacaftor (ELX/TEZ/IVA) in Cystic Fibrosis (CF) Participants 12 to Less Than 24 Months of Age	Liverpool	Leeds, London, Liverpool, **Cardiff**	Vertex Pharmaceuticals Incorporated
Evaluation of VX-121/Tezacaftor/Deutivacaftor in Cystic Fibrosis (CF) Participants 1 Through 11 Years of Age	Cardiff	**Cardiff**, London	Vertex Pharmaceuticals Incorporated
Treatment With Bempedoic Acid and/or Its Fixed-dose Combination With Ezetimibe in Primary Hypercholesterolemia or Mixed Dyslipidemia	Manchester	Manchester, Darlington, Torquay, London, Lincoln, Bath, Truro, Southend, Nottingham, Telford, Chippenham, Southampton, Watford, Craigavon, Belfast, **Cardiff**, Dartford, Middlesborough, Plymouth, Salford, Staffordshire, Trowbridge, **Bangor**, Wansford	Daiichi Sankyo Europe, GmbH, a Daiichi Sankyo Company
Research Study Investigating How Well NDec Works in People With Sickle Cell Disease	Manchester	London, Manchester, **Cardiff**	Novo Nordisk A/S
Avatrombopag for the Treatment of Thrombocytopenia in Pediatric Subjects With Immune Thrombocytopenia for ≥6 Months	Liverpool	Birmingham, Liverpool, London, Manchester, Sheffield, **Cardiff**	Sobi, Inc.
Enroll -HD: A Prospective Registry Study in a Global Huntington's Disease Cohort	Liverpool	Poole, Sheffield, Reading, Southampton, Liverpool, Manchester, London, Dundee, **Cardiff**, Exeter, Larbert, Narborough, Bristol, Kirkcaldy, **Wrexham**, Aberdeen, Birmingham, Cambridge, Edinburgh, Glasgow, Kilmarnock, Leeds, Newcastle, Northampton, Oxford, Plymouth, Stoke-on-Trent, Swindon	CHDI Foundation, Inc.

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