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HEALTH SERVICES RESEARCH

ORPHANET TRANSLATION: ACTIVITY REPORT (2018-2019)

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SUMMARY

Orphanet is a European database providing information on rare diseases and orphan drugs, aimed at both healthcare personnel and patients. The information is freely accessible and is published on a website (http://www.orpha.net/). Orphanet contains an inventory, classification and encyclopaedia of rare diseases, information on laboratories, research projects, clinical studies and patient organisations, and a collection of guidelines and reports. This information is curated in English and afterwards translated in different languages.

Within the framework of the Orphanet-project, Sciensano is responsible for the translation of both the structural webpages and the scientific content (medical terms such as names and synonyms of diseases, and textual summaries of diseases) of Orphanet from English to Dutch, thus making the content of Orphanet also available in the third Belgian national language, besides French and German, for Dutch-speaking healthcare professionals, researchers and patients. In addition, Sciensano is also responsible for validating the terminology translated to Dutch, in collaboration with Erfocentrum in the Netherlands. The translation of Orphanet is a continuous process, carried out by Sciensano at the pace and according to the procedures determined by the coordinator of Orphanet (INSERM). Currently (December 2019), over 30,000 medical terms and over 3,000 summaries of rare diseases are available in Dutch.

This work is also important for the Dutch part of the Belgian version of SNOMED CT®, which is currently being developed by the Terminology centre of the Federal Public Service of Health, Food Chain Safety and Environment (FOD-VVVL), with the goal of implementing a standardized and validated Dutch terminology for rare diseases in the Belgian healthcare information systems. To facilitate this collaboration on translation and validation of terms, both Sciensano and the Terminology centre use the XTM translation software. This already resulted in the incorporation of about 3,000 disease terms in the first release of the Dutch Belgian version of SNOMED CT®.

To inform different target groups about the work of Sciensano and Orphanet, as well as the different activities concerning rare diseases, Sciensano manages several publically accessible websites, including the national Orphanet website for Belgium, available in French and Dutch, and a separate website of Sciensano dedicated to rare diseases with specifications about the Central Registry for Rare Diseases, among other things.

ABBREVIATIONS

FOD-VVVL	Federal Public Service Health, Food Chain Safety and Environment
INSERM	Institut National de Santé et de Recherche Médicale
LUMC	Leids University Medical Centre
SNOMED CT®	Systemized Nomenclature of Medicine Clinical Terms®
FTE	Full-time equivalent

FIGURES AND TABLES

INTRODUCTION

Orphanet is a European database that offers information on rare diseases and orphan drugs, aimed at both healthcare personnel and patients. The information is freely accessible and published on a website (http://www.orpha.net/). Orphanet contains an inventory, classification and encyclopaedia of rare diseases, information on laboratories, research projects, clinical studies and patient organisations, and a collection of guidelines and reports. Each rare disease in Orphanet is described using a preferred term, possible synonyms, a definition and a textual summary subdivided in different sections describing different aspects of the disease, namely epidemiology, clinical description, etiology, diagnosis, differential diagnosis, prenatal diagnosis, genetic counselling, treatment, and prognosis. All this information is available in English and is currently being translated in French, Spanish, Italian, Portuguese, German, Polish and Dutch. Part of the database content is currently also available in Greek, Slovenian, Finnish and Russian.

Within the framework of the Orphanet-project, Sciensano is responsible for the translation of both the structural webpages (Figure 1) and the scientific content (medical terms such as names and synonyms of diseases, and textual summaries of diseases) (Figure 2, Figure 3) of Orphanet from English to Dutch.

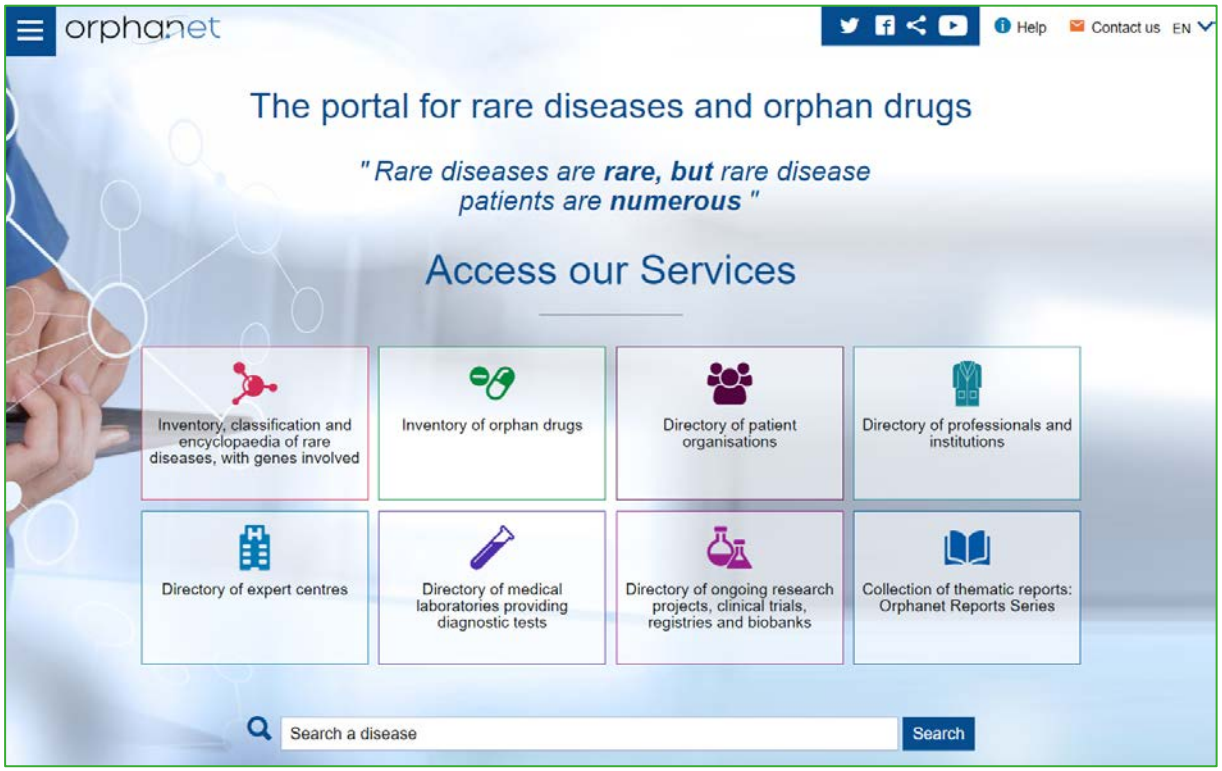


***Figure 1**: **Structural webpages of the Orphanet website.** The structural webpages of the Orphanet website were previously translated to Dutch and are available online. Orphanet regularly adapts existing pages or adds new pages, and these changes are subsequently translated to Dutch by the Belgian Orphanet team.*

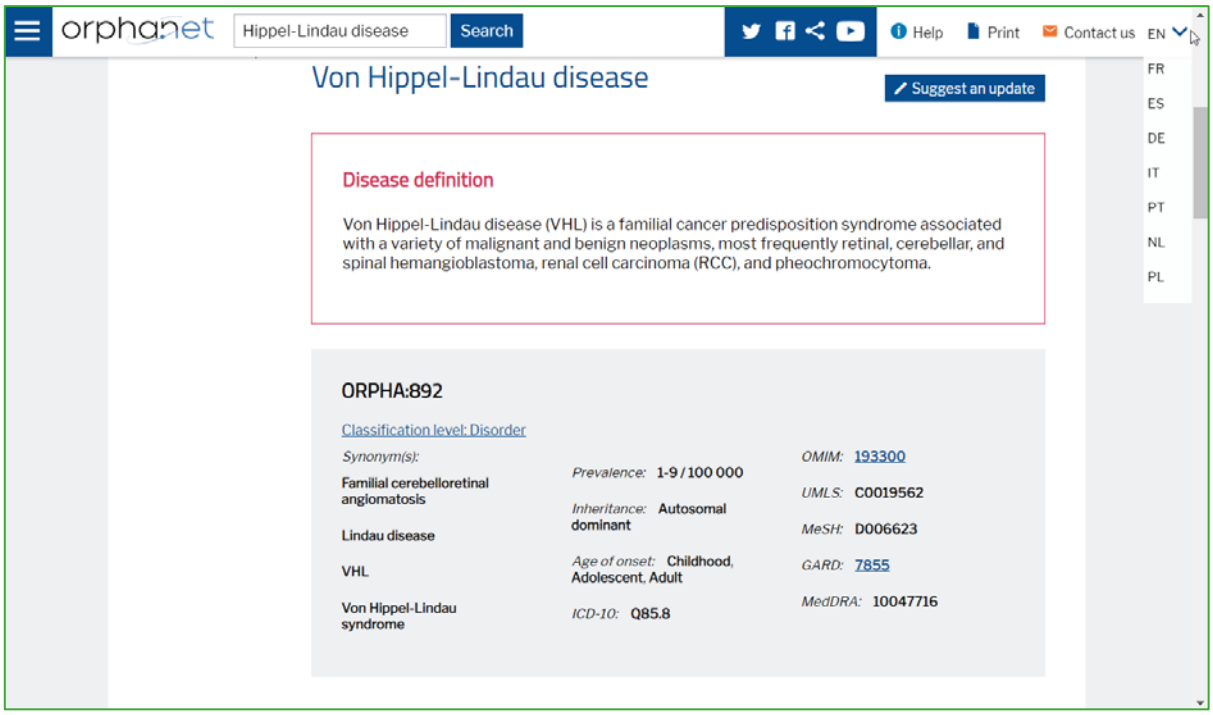
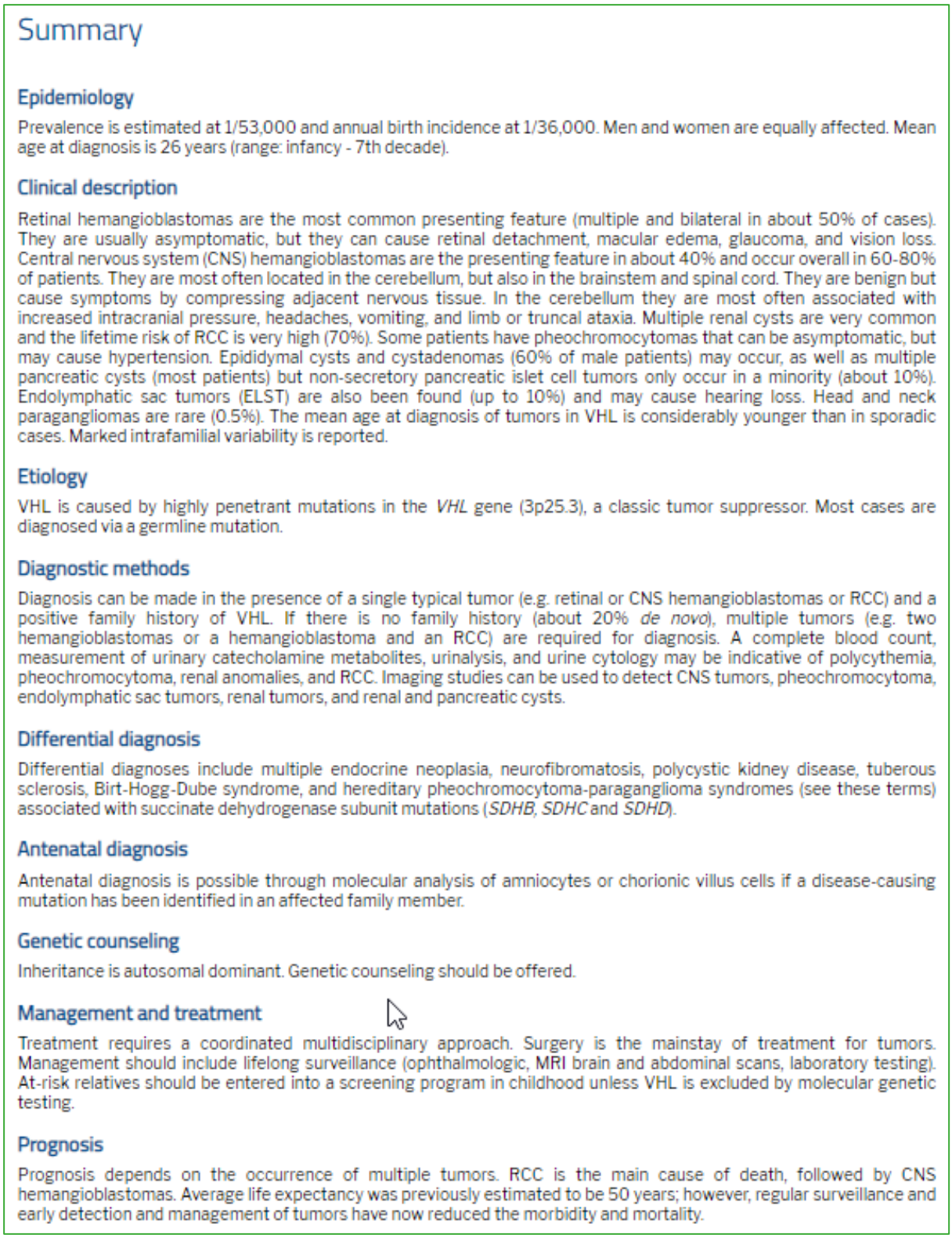


Figure 2: The Orphanet encyclopaedia. *The Orphanet encyclopaedia (with medical terms, including names and synonyms of rare diseases, classifications and keywords, and with textual summaries including a definition) is currently being translated form English to Dutch, among other languages; the different languages in which Orphanet is available, can be selected by the user (top right).*

Hence, besides French and German, the content of Orphanet is progressively becoming accessible in the third Belgian national language for Dutch-speaking healthcare professionals, researchers and patients. In addition this effort is important in the context of the Dutch part of the national terminology policy of the Federal Public Service of Health, Food Chain Safety and Environment (FOD-VVVL) (see Methodology).

The translation of Orphanet is a continuous process, since regularly new diseases are defined, medical terms are changed, new summaries are added and existing summaries are updated or corrected (every year new, updated or corrected summaries are released by the Orphanet coordinator, via the so-called translation reports), and structural webpages are modified. The structural webpages were translated and validated a first time in 2012. In 2013 translation of the complete list of 30,640 (at that time) medical terms (including names and synonyms of the nearly 6,000 rare diseases in Orphanet, the classification system, symptoms and keywords) was initiated. These translated terms remain to be validated. In addition (until December 2017) 1,499 summaries were translated, 681 of which were published on the Orphanet website, and 705 summaries were updated or corrected (Table 1).



Summary

Epidemiology

Prevalence is estimated at 1/53,000 and annual birth incidence at 1/36,000. Men and women are equally affected. Mean age at diagnosis is 26 years (range: infancy - 7th decade).

Clinical description

Retinal hemangioblastomas are the most common presenting feature (multiple and bilateral in about 50% of cases). They are usually asymptomatic, but they can cause retinal detachment, macular edema, glaucoma, and vision loss. Central nervous system (CNS) hemangioblastomas are the presenting feature in about 40% and occur overall in 60-80% of patients. They are most often located in the cerebellum, but also in the brainstem and spinal cord. They are benign but cause symptoms by compressing adjacent nervous tissue. In the cerebellum they are most often associated with increased intracranial pressure, headaches, vomiting, and limb or truncal ataxia. Multiple renal cysts are very common and the lifetime risk of RCC is very high (70%). Some patients have pheochromocytomas that can be asymptomatic, but may cause hypertension. Epididymal cysts and cystadenomas (60% of male patients) may occur, as well as multiple pancreatic cysts (most patients) but non-secretory pancreatic islet cell tumors only occur in a minority (about 10%). Endolymphatic sac tumors (ELST) are also been found (up to 10%) and may cause hearing loss. Head and neck paragangliomas are rare (0.5%). The mean age at diagnosis of tumors in VHL is considerably younger than in sporadic cases. Marked intrafamilial variability is reported.

Etiology

VHL is caused by highly penetrant mutations in the *VHL* gene (3p25.3), a classic tumor suppressor. Most cases are diagnosed via a germline mutation.

Diagnostic methods

Diagnosis can be made in the presence of a single typical tumor (e.g. retinal or CNS hemangioblastomas or RCC) and a positive family history of VHL. If there is no family history (about 20% *de novo*), multiple tumors (e.g. two hemangioblastomas or a hemangioblastoma and an RCC) are required for diagnosis. A complete blood count, measurement of urinary catecholamine metabolites, urinalysis, and urine cytology may be indicative of polycythemia, pheochromocytoma, renal anomalies, and RCC. Imaging studies can be used to detect CNS tumors, pheochromocytoma, endolymphatic sac tumors, renal tumors, and renal and pancreatic cysts.

Differential diagnosis

Differential diagnoses include multiple endocrine neoplasia, neurofibromatosis, polycystic kidney disease, tuberous sclerosis, Birt-Hogg-Dube syndrome, and hereditary pheochromocytoma-paraganglioma syndromes (see these terms) associated with succinate dehydrogenase subunit mutations (*SDHB*, *SDHC* and *SDHD*).

Antenatal diagnosis

Antenatal diagnosis is possible through molecular analysis of amniocytes or chorionic villus cells if a disease-causing mutation has been identified in an affected family member.

Genetic counseling

Inheritance is autosomal dominant. Genetic counseling should be offered.

Management and treatment

Treatment requires a coordinated multidisciplinary approach. Surgery is the mainstay of treatment for tumors. Management should include lifelong surveillance (ophthalmologic, MRI brain and abdominal scans, laboratory testing). At-risk relatives should be entered into a screening program in childhood unless VHL is excluded by molecular genetic testing.

Prognosis

Prognosis depends on the occurrence of multiple tumors. RCC is the main cause of death, followed by CNS hemangioblastomas. Average life expectancy was previously estimated to be 50 years; however, regular surveillance and early detection and management of tumors have now reduced the morbidity and mortality.

Figure 3: Textual summaries of rare diseases. *The summaries of rare diseases in Orphanet are currently being translated to different languages, including Dutch. These summaries are subdivided in different sections: definition (Figure 2), epidemiology, clinical description, etiology, diagnostic methods, differential diagnosis, prenatal diagnosis, genetic counselling, management and treatment, and prognosis.*

Each country of the Orphanet network maintains a national Orphanet website that acts as a national access point to the Orphanet website and provides information on national activities regarding rare diseases and Orphanet in the corresponding national language(s). Belgium has a Dutch (http://www.orpha.net/national/BE-NL/) and a French (http://www.orpha.net/national/BE-FR/) website. In 2015 Sciensano also released a website dedicated to rare diseases (https://rarediseases.sciensano.be/). This website also provides some background information on Orphanet and a direct link to the Orphanet website and the Belgian national Orphanet websites.

METHODOLOGY

1. TRANSLATION OF MEDICAL TERMS AND SUMMARIES OF RARE DISEASES

The Orphanet coordinator (INSERM) releases translation reports (bimonthly reports with new, updated or corrected English medical terms and textual summaries of rare diseases) for the national teams responsible for the translation. The summary of a disease can be limited to a definition, or can contain additional sections describing different aspects of the disease. The summaries are subsequently translated, updated or corrected by a collaborator of Sciensano, and afterwards inserted in the Orphanet database and published on the website. Since 2017 translation and editing of terms and summaries are performed using the XTM translation software (see below).

2. VALIDATION OF MEDICAL TERMS

A portion of the translated medical terms are validated by the National Information Centre Heredity (Erfocentrum) in the Netherlands. Sciensano supplies a list of terms for validation (via the Orphanet team for the Netherlands at the Leids University Medical Centre (LUMC)). After validation in the Netherlands, the edits and remarks are evaluated by a collaborator of Sciensano and applied using the XTM translation software, including curation of the necessary documentation specifying what editing was done and why. The Belgian Orphanet team will also contact other medical experts for validation of translated terms.

In addition, some terms can also be validated in collaboration with the Federal Public Service of Health, Food Chain Safety and Environment (FOD-VVVL) (in the context of codification of rare diseases for the European Rare Diseases Joint Action), where the Terminology centre is developing a Belgian version (in Dutch and French) of the SNOMED CT® (Systemized Nomenclature of Medicine Clinical Terms®) terminology. On the one hand Dutch Orphanet terms can be integrated in the Belgian version of SNOMED CT®. On the other hand the concepts in the Belgian SNOMED CT® release, which are validated by the FOD-VVVL, can be used for validation of translated Orphanet terms.

3. AD HOC TRANSLATIONS

Orphanet regularly requests specific translations, from single words, concepts and sentences to whole texts for the structural webpages of the Orphanet website, guidelines and reports. These requests are made using a separate e-mail address that is accessible to the translation teams in the different countries. A collaborator of Sciensano addresses the translation and delivers it to Orphanet using the same e-mail address.

4. MANAGEMENT OF WEBSITES

The Belgian national Orphanet websites and the Sciensano website on rare diseases are being managed by a collaborator of Sciensano using the corresponding administrative webpages.

PROGRESS

From January 2018 to May 2019 0.7 FTEs of the Belgian Orphanet team at Sciensano were attributed to the Orphanet translation project. The progress that has since been made for each part of the project is described below.

1. TRANSLATION OF MEDICAL TERMS AND SUMMARIES OF RARE DISEASES

Until December 2017 the summaries of 1,499 rare diseases had been translated, 681 of which were published on the Orphanet website. Since then an additional 1,530 summaries were translated, and all the summaries translated to Dutch were published on the Orphanet-website. As a result, 3,029 Dutch summaries are currently available on the website, an increase of 2,348 summaries since the previous report (Figure 4, Table 1). Also, 91 summaries that had been previously translated and put online were updated or corrected (Table 1).

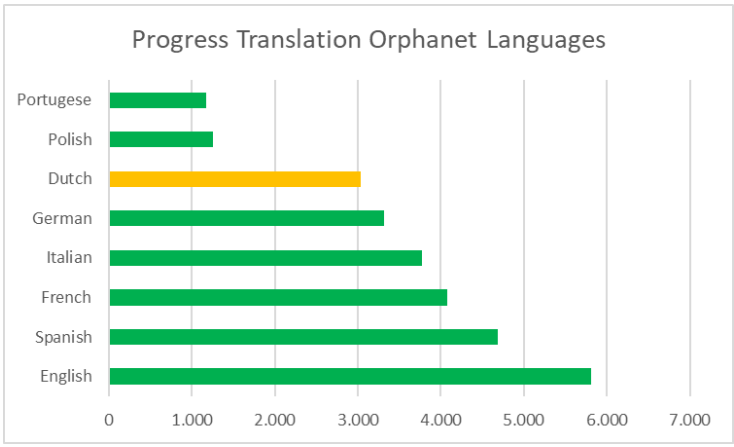
Translation of the complete list of 30,640 medical terms was already initiated in 2013. However, bimonthly additions and/or adjustments are released in the translation reports. From January 2018 until December 2019, 1,114 new terms (preferred terms, synonyms and keywords) for 576 rare diseases were translated, and terms (preferred terms, synonyms and keywords) of 1,399 other rare diseases were updated, corrected or deleted.

***Table 1**: Progress of the Orphanet translation from January 2018 until December 2019. The table shows the progress of the translation of Orphanet content to Dutch during this reporting period, by comparing the volume translated until December 2017 with the volume translated until December 2019. This shows that significant progress has been made with the translation and actualisation of textual summaries.*

Activity	Situation in December 2017	Situation in December 2019	Realised in 2018-2019[b]
Number of translated summaries[a]	1,499	3,029	**1,530**
Number of updated or corrected summaries	705	796	**91**
Number of translated summaries online	681	3,029	**2,348**

[a] When necessary, the newly translated summaries were also updated or corrected before being published online (according to the translation reports).

[b] Until December 2019.



1. English (5,809)
2. Spanish (4,681)
3. French (4,081)
4. Italian (3,772)
5. German (3,317)
6. Dutch (3,029)
7. Polish (1,259)
8. Portuguese (1,172)
9. Part of the summaries is also available in Greek, Slovenian, Finnish and Russian.

***Figure 4: Number of textual summaries of rare diseases per language (December 2019).** The summaries of rare diseases in Orphanet are produced in English and subsequently translated to different European languages by the national teams.*

2. VALIDATION OF MEDICAL TERMS

Most of the 30,640 translated medical terms still need to be validated. In 2017 Dutch translations of preferred terms and synonyms for 660 rare diseases were validated by Erfocentrum in the Netherlands. This validation was assessed and applied by the Belgian Orphanet team, and the changes and/or corrections were documented.

In 2018 a new list of rare disease terms was delivered to the Orphanet team in the Netherlands for validation, but due to other priorities of Erfocentrum the validation of this list has not yet been initiated. In addition Sciensano contacted a Belgian physician specialised in rheumatologic disorders, with the request to validate medical terms for rheumatologic disorders translated to Dutch for Orphanet. The reply was positive and a list of terms was provided to the physician for validation, which is currently ongoing.

3. AD HOC TRANSLATIONS

Translations of Orphanet-webpages and reports requested by Orphanet were always instantly completed by the Belgian Orphanet team and returned to Orphanet. The most important *ad hoc* translations during the recent reporting period are the satisfaction survey for Orphanet users, new or modified structural webpages of the Orphanet website (https://www.orpha.net/consor/cgi-bin/Disease_HPOTerms.php?lng=NL), and Orphanet Report Series:
https://www.orpha.net/orphacom/cahiers/docs/NL/Prevalentie_van_zeldzame_ziekten_Nummer1.pdf;
https://www.orpha.net/orphacom/cahiers/docs/NL/Prevalentie_van_zeldzame_ziekten_Nummer2.pdf;
https://www.orpha.net/orphacom/cahiers/docs/NL/Zeldzame_ziektenlijst_in_alfabetische_volgorde.pdf.

4. MANAGEMENT OF WEBSITES

The Belgian Orphanet team ensures continuous maintenance and regular actualisation of the national Orphanet websites for Belgium and the Sciensano website on rare diseases.

CONCLUSION

Management of the different websites, *ad hoc* translations at the request of Orphanet, and the translation, actualisation and correction of medical terms and scientific summaries for Orphanet is a continuous process. In 2018-2019 significant progress was made regarding translation and online publishing of textual summaries of rare diseases, and the backlog of translation reports that had accumulated in 2016-2017 has been eliminated. Since the previous report, the number of summaries translated to Dutch has doubled, while the number of Dutch summaries published on the publically accessible Orphanet website has nearly quadrupled.

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MORE INFO

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