

Beca Fundació Societat Catalana de Neurologia
MEMÒRIA DEL PROJECTE

DOMICILIARY ALZHEIMER VISITING IN DOWN SYNDROME EXTENSION PROJECT (DAVIS-2)

Principal investigator: María Carmona Iragui

Unitat Alzheimer-Down

Servei de Neurologia del Hospital de la Santa Creu i Sant Pau

Centre Mèdic Down Fundació Catalana Síndrome de Down

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1. Name and surname, address and place of work of the principal investigator and the other researchers.

- Principal investigator:

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Place of work: Alzheimer Down Unit. Neurology Department, Hospital de la Santa Creu i Sant Pau, Barcelona / Centre Mèdic Down, Down Syndrome Catalan Foundation, Barcelona.

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- Other researchers:

Name and surname: Juan Fortea Ormaechea

Place of work: Alzheimer Down Unit. Neurology Department, Hospital de la Santa Creu i Sant Pau, Barcelona / Centre Mèdic Down, Down Syndrome Catalan Foundation, Barcelona.

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Name and surname: Laura Videla Toro

Place of work: Alzheimer Down Unit. Neurology Department, Hospital de la Santa Creu i Sant Pau, Barcelona / Centre Mèdic Down, Down Syndrome Catalan Foundation, Barcelona.

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Name and surname: Bessy Benejam Paul

Place of work: Alzheimer Down Unit. Centre Mèdic Down, Down Syndrome Catalan Foundation, Barcelona.

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Place of work: Alzheimer Down Unit. Neurology Department, Hospital de la Santa Creu i Sant Pau, Barcelona.

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Place of work: Alzheimer Down Unit. Neurology Department, Hospital de la Santa Creu i Sant Pau, Barcelona.

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2. Background and scientific interest of the project

Down Syndrome (DS) is the most frequent cause of intellectual disability in childhood and it is the most frequent form of genetic developmental and intellectual disability, affecting 5-8 million people worldwide (*Ballard, Lancet Neurol 2016*). During the last 5 decades, improved health care has led to dramatic improvements in life expectancy in individuals with DS, and it is now common for adults with DS to reach old age and to live beyond 65 years (*Bittles, Dev Med Child Neurol 2004*). However, ageing with DS creates new challenges for families, caregivers and professionals, as new problems associated with the aging of people with DS have emerged. These are predominantly neurological conditions such as dementia due to Alzheimer's disease (AD) and adult-onset epilepsy (*Hithersay, J Neurodev Disord 2020*).

DS is considered a genetically determined form of AD (*Dubois, Lancet Neurol 2014*) and all people with DS develop neuropathological findings compatible with AD by the age of 40 (*Wisniewski, Ann Neurol 1985*). Not all individuals with DS develop clinical symptoms of AD, but the lifetime risk of Alzheimer's disease in people with DS is now more than 90% and AD is the leading cause of death in this population (*McCarron, J Intellect Disabil Res 2017*). Therefore, AD in adults with DS poses a significant challenge for the medical profession and for society.

Early diagnosis of cognitive impairment in a population with intellectual disability presents several unique challenges because of the between-patient variability of the cognitive deficits related to their intellectual disabilities. In addition, establishing the diagnosis requires specialized training and adapted and validated diagnostic tools for people with intellectual disability. Providing care for people with DS and AD is also challenging, as they are usually a vulnerable population. The median age at expected symptom of AD in DS is 50,2 years old (*Fortea, Lancet 2020*), thus, the main caregivers, usually parents, are elderly people who may have their own age-related comorbidities, including potential cognitive impairment. In addition, general practitioners and institutions are not prepared to deal with this problem and there are no specialized care centers for people with DS and AD, leaving the caregivers uninformed and unprepared to deal with the situation (https://www.sindromedown.net/wp-content/uploads/2014/09/160L_las.pdf). This problem highlights the need of a comprehensive health care approach to enable an early diagnosis and an individualized follow up and support.

The Fundació Catalana Down Syndrome (FCSD) is a private, non-profit organization that was established in March 1984. It was born as an initiative of a group of parents and professionals with the aim of deepening understanding of DS through research and practical experience through an interdisciplinary approach encompassing pedagogy, psychology, medicine and the social care. The technical team is composed by professionals with training in psychology, pedagogy and medicine and a group of scientific advisers who supervise clinical and research works. One of the main aims of FCSD is to serve as a catalyst and framework for the development of a personalized preventive medical care plan for individuals with DS. This preventative medical care plan is generated by a coordinated group of generalists and specialists dedicated to the diagnosis, systematic assessment, prevention and treatment of people with Down syndrome. The FCSD medical center database currently contains clinical data on over 2500 individuals with DS, of who more than 1,500 are over the age of 18. The FCSD is one of the world's largest specialist medical centers for DS.

The Memory Unit of the Hospital de la Santa Creu i Sant Pau (HSP) focused in the diagnosis and treatment of patients with cognitive impairment and in applied and translational research in the field of AD and related disorders. At present, the unit is integrated by 10 neurologists, 7 neuropsychologists, 6 basic researchers, 4 laboratory technicians, 2 research nurses, one

neuroradiologist, 3 engineers and one data manager. The Memory Unit is a reference leader in translational research in Alzheimer's disease, both in Spain and internationally. The lines of research include: research in plasma and CSF biomarkers, genetic research, molecular biology research, clinical trials, and neuroimaging research in the field of AD and related. The group has among the highest research indicators in Spain and Europe with more than 100 articles in the last two years (with more than 100 points of impact factor per year). It is a member and coordinator of the program group 1 of CIBERNED.

In December 2014, both institutions (FCSD and HSP) signed an agreement for assistance and collaboration. Under this agreement, the HSP became a referral centre for neuropathology associated with DS in Catalonia, where any person with DS aged 18 or older, diagnosed with any neurological pathology, can attend the HSP, even if they do not live within the HSP catchment area. This gives all individuals attending the FCSD access to professionals specialized in DS based in the HSP.

Also in 2014, the close collaboration of these institutions led to the creation of the Alzheimer Down Unit (ADU), in order to develop and establish a pioneering population-based health plan for adults with Down syndrome in Catalonia. The ADU is formed by a multidisciplinary team and counts with the expertise from 5 neurologists with a wide experience in the diagnosis and treatment of individuals with cognitive disturbances, both in DS and in the general population; 3 neuropsychologists, all of them with a strong background in the study of cognitive impairment in DS, clinical neuropsychology and AD; one postdoctoral researcher with extensive experience in biochemistry, molecular biology and biomarker determination in DS and AD body fluids, one social worker and one research nurse. Its main objective is to offer adults with DS annual medical and neuropsychological assessments in order to prevent and detect medical pathology and, if necessary, to coordinate with the public health system to offer individualized follow-up care, clinical support and social counseling.

Within this population-based health plan, medical pathology, with a special emphasis on AD and neurological diseases and aging-associated comorbidities, is assessed. The health plan includes two components: a comprehensive screen for medical illnesses and the assessment of cognitive status and onward referral where necessary. The screening consists of an integrated medical, neurological and neuropsychological assessment, blood test, and EEG. Screening is carried out annually and, if pathology is detected, every six months. The second component of the health plan consists of onward referral to a local tertiary hospital (or the HSP in case of neurological disease) for further specialist assessment and treatment when medical or neurological problems are detected.

In the setting of this population-based health plan, the Down Alzheimer Barcelona Neuroimaging Initiative (DABNI) project is also offered to every adult with DS in Catalonia. DABNI is a translational research plan to study AD biomarkers in DS and has already led to several studies published in high-impact scientific journals.

Every year we attend more than 300 people within the health plan, however, approximately 60 are not able to attend physically to the ADU Unit. The main causes are logistical difficulties, medical problems, institutionalization, the absence of caregiver to accompany them to the assessment or because they live far away from Barcelona. The exclusion of those candidates reflects, not only disparities in health care of the most vulnerable subgroup, but also a selection bias when analyzing epidemiological variables. In order to bring the health plan closer to all people deprived of the specialized attention and at risk of exclusion, the "Domiciliary Alzheimer Visiting in Down syndrome" (DAVIS) pilot project was implemented in October 2018, thanks to a GBHI/Alzheimer's Association grant awarded to Dr. María Carmona

Iragui. Within this cross-sectional DAVIS pilot project, we contact occupational centers /residences which include users with DS and we organize the visit of a neurologist and a neuropsychologist from our team to the center. Candidates and their caregivers are informed about the health plan and those who accept to participate are assessed. The visit consists of a comprehensive medical, neurological and neuropsychological assessment which screens each participant for cognitive impairment. After this first assessment, an in-person follow-up at the ADU or a telephonic follow-up visit is offered, together with the option of our staff to coordinate with Primary Care or Tertiary Medicine. The participation in the DABNI research project is also proposed.

The cross-sectional DAVIS pilot project was implemented in October 2018 and its completion, due to the finalization of the specific funding, is expected on April 2021. Until January 2020, the project has been presented in a total of 14 centers in different regions from all over Catalonia (figure 1), we assessed a total of 94 participants (mean age 42.6, 48.9% males), from which 21,3% of them had symptoms of cognitive decline or even established AD dementia. More detailed preliminary results are shown on the viability section of this application (point #4).

So far, this cross-sectional pilot project has demonstrated the feasibility of the DAVIS project and has evidenced successful preliminary results. The main conclusions have been:

- The DAVIS project is feasible and enables the outreach of our health plan for adults with DS in Catalonia.
- We provide specialized clinical care to regions in Catalonia without the resources to perform adequate clinical and cognitive evaluations in people with intellectual disabilities.
- Its clinical application allows the identification of new cases of symptomatic AD.
- The DAVIS pilot project emphasizes the need of specific social and health care improvements and plans for adults with DS.
- An extension of the DAVIS project would provide solid evidence that could have an impact on the local health system, on health authorities and, lastly, on health policy.

For all mentioned above, we believe that the DAVIS-2, an extension of the DAVIS pilot project, would allow to:

- Continue with bringing closer of the health plan to adults with Down syndrome who are particularly vulnerable due to several reasons (i.e: a more severe impairment, geographical disparities, absence of an available caregiver...).
- Minimize the selection bias of our population-based clinical cohort which is evident if we only consider for numbers those adults with DS who come to our site.
- Provide longitudinal assessments of those participants in the DAVIS pilot project who were diagnosed with AD and are still not able to come to the follow-up visit.

Altogether, DAVIS pilot project and DAVIS-2 will provide not only benefits in health care of the population with DS in Catalonia, but also will approach the possibility of research to this population and will minimize the selection bias when obtaining epidemiological measures. In brief, DAVIS-2 will generate robust data that could inform health policy, generate epidemiological data and have an impact on improving the quality of life of people with DS and their caregivers. In brief, DAVIS-2 aims to have a three-fold impact on health care, biomedical research and health policy.

3. Hypotheses and objectives

Hypotheses:

1. Medical pathology in adults with Down syndrome, particularly cognitive impairment associated with Alzheimer's disease, is often unnoticed, underdetected and usually diagnosed at advanced stages (*Strydom et al. 2007*). Active screening as part of a DS-specific, personalized health offers earlier detection and better management of aging pathology in DS. However, in our current model, some individuals with DS, particularly those with advanced disease, are unable to access an annual assessment health plan, due to difficulties attending the assessment center.
2. The cognitive profile of adults with DS with and without symptoms of AD may be different from that in the general population and has been insufficiently studied.
3. Exclusion of adults with DS who are unable to attend the ADU unit from research leads to an evident selection bias.
4. Present models of care do not sufficiently address medical and social needs of people with DS and AD. Caregivers, who are already vulnerable, are uninformed and do not feel prepared to deal AD in individuals with DS.

Objectives:

- To detect those adults with DS who are not able to reach our site and (for several reasons such as age, comorbidities, social factors, geographical disparities, etc) and bring them our health plan which includes a comprehensive assessment to screen for medical comorbidities and research opportunities.
- To provide a longitudinal assessment to those adults with DS already diagnosed with AD who are not able to reach our site.
- To minimize the selection bias intrinsic of only considering adults with DS assessed t our site within the DABNI project.
- To obtain robust data able to orientate the families, the medical community and, finally to change health policies.

4. Material and methods, including the approximate duration of the study.

The main objective of DAVIS-2 is to continue bringing closer the health plan to every adult with DS around Catalonia- in spite of not having the appropriate resources to reach our site- through domiciliary visits providing to the most vulnerables an improvement on health care and an approach to research projects.

3.1 Type of study: Observational cross-sectional and longitudinal study in adults with DS who are unable to attend the ADU.

3.2 Study period: 12 months.

3.3 Study setting: All adults with DS living in Catalonia who are not able to physically attend to the ADU in Barcelona.

3.4 Selection of the population:

- Population of reference: The ADU acts as the referral center for DS in Catalonia, reflecting the population with DS. The health plan cohort is a population-based sample.

- Study Population and Eligibility Criteria: Adults with DS living in Catalonia who are not attending to the visits in the Alzheimer-Down Unit. Written informed consent, approved by the ethics committee, will be obtained.

Inclusion criteria: Participants of both sexes with ages over 18 who understand and accept the study procedures and sign the informed consent (legal representative and/or participant), accompanied by a caregiver (in contact, at least, 10 hours per week).

Exclusion criteria: Not meeting the inclusion criteria, impossibility for being contacted, those who have moved away from Catalonia.

- Sample size: Based on the experience and the numbers of candidates to health plan who are not able to reach our site that we identify each year and the delay on assessments caused by the COVID-19 pandemic, we will include 80 new subjects. In addition, we estimate the inclusion of 40 more adults with DS already diagnosed with AD in the longitudinal follow-up study.

3.5 Information recollection:

First of all, the principal investigator, Dr. Maria Carmona Iragui, will contact centers in Catalonia who attend people with Down syndrome (residences, special work centers, etc) to present and offer the DAVIS-2 project. She will ask for potential candidates interested in being assessed and she will determine if they fulfill the inclusion criteria.

When centers and candidates will be selected, the dates of assessments will be planned according to the number of available candidates in each center. The informed consent and informative leaflets (annex 1) will be sent to the center. A team formed by a neurologist and a neuropsychologist from the ADU will transfer to the centers in the corresponding dates and, on the first day, before starting the assessments, they will give a presentation talk to explain the aims of this project and the protocol to all families and professionals interested in the health plan. Every question will be answered. The number of families or caregivers, who refuse domiciliary attention and their reasons, if provided, will be also recorded. The assessment will then take place and will be divided in two parts:

- **Medical and neurological evaluation:** it will be carried out by the neurologist. In this personal interview, the candidate and her/his legal representative will sign the informed consent. The purpose of this evaluation is to detect medical pathology, with special emphasis on cognitive impairment. The assessment will review the clinical and neurological history of the patient, demographic data, history of current illness (if any), personal, pathological and family history and pharmacological treatment. A general

and neurological physical examination will be performed. If there is a suspicion of non-neurological disease, the neurologist will liaise with the local primary and tertiary medical facilities for further evaluation and treatment. This visit is carried out annually in case of no pathology and, every six months if there is cognitive impairment. Screening for social vulnerability will be carried out, and individuals of concern will be referred on to local social services.

- A neuropsychological assessment will be carried out by a specialized neuropsychologist employed by the ADU. This includes cognitive screening in which the degree of intellectual disability of the person is determined and a brief memory test is given to assess whether or not further evaluation is required. When possible, an interview is carried out with the patient's family or the patient's primary caregiver, to collect data about the patient's daily life, occupation, level of autonomy and level of functionality, mood, cognitive status, social relations, behavior, etc. In addition, 4 scales are administered to capture all this information quantitatively. Subsequently, the cognitive functioning of the person with DS is evaluated, evaluating all cognitive areas: language, memory, attention, orientation (person, time and space), executive functions, praxis, gnosis, and speed of information processing.
- Social work assessment. All participants for whom there is concern around their social circumstances will be offered to a –physically present or telematic- meeting with the FCSD social worker. The social worker makes an individualized assessment of each case, determines their needs and coordinates with local social work services to provide necessary supports. In addition, when AD diagnosis has been established in a person with DS, caregivers are offered an advisory visit with a specialized neuropsychologist and the FCSD social worker. This visit is offered as a space for family support where they can express their doubts about the disease; they receive guidance in the guidelines and procedures to follow in case they require assistance from social services. In cases that cannot attend the ADU unit for assessment with the social worker or for the advisory visit, a telematic visit and the coordination with local social services will be offered. If there is a serious concern but family/caregiver refuses to meet the social worker from FCSD, we will call social services from Generalitat de Catalunya to take care of the situation.
- Satisfaction Survey: A structured questionnaire has been designed to evaluate how useful has the visit been for the patient and family/caregivers, what did they like the most, what things they think we could improve and what their experience was of the home visit.

3.6 Statistical analysis:

Statistical analysis will be performed with SPSS. A descriptive study of the variables will be carried out, using the indexes of central tendency and dispersion as well as corresponding frequency measures.

3.7 Ethical aspects:

The study will rigorously follow international ethical recommendations for medical research in humans. Researchers will be responsible for ensuring that the study is conducted in accordance with the standards set out in the Helsinki Declaration and in Spanish legislation. The Ethics Committee of the HSP has approved the study protocol, the information given to the subject (annex 2) and the Model of informed consent that is used. The CEIC will be informed of any subsequent amendments to the protocol and its opinion should be requested if a reassessment of the ethical aspects of the study is necessary. It is the responsibility of the investigator to obtain the informed consent of each patient, after explaining the objectives, methods and potential risks of the study. All patients will be informed orally and in writing that these procedures are part of their routine evaluation and are also of interest for research. The

participation in this health plan does not imply risks. Regarding the confidentiality of the data of the study will follow the established in the Organic Law 15/1999 of "Protection of Data of Personal Character."The data will be collected in a separate encoded and protected file.

3.7 Timeline

The objective of the application for this grant is to extend de initial DAVIS project in order to increase the scope of the health plan and reach all people with Down syndrome in Catalonia. The DAVIS-2 working plan will proceed as follows:

- Month 1 (November 2020): Contact (phone calls and emails) with new and participant centers in order to: a) identify new candidates and b) organize the follow-up visit of those previously assessed candidates diagnosed with AD who cannot attend to our site.
- Months 2-6 (December 2020-April 2021): Follow-up domiciliary visits to adults with DS who were diagnosed with AD in a previous assessment and are not able to reach our site.
- Months 7-10 (May 2021-August 2021): Domiciliary visits to new candidates (adults with DS who are not able to reach our site without a previous assessment).
- Months 11-12 (September 2021-October 2021): Data analysis. Project results. Communications in scientific congresses and publications. Redaction of the final report.

5. Analysis of the viability of the project, detailing the necessary means and availability

As explained in the introduction, the cross-sectional DAVIS pilot project started in October 2018 thanks to a GBHI/Alzheimer’s Association grant awarded to Maria Carmona Iragui. Therefore, a preliminary analysis of the results obtained so far demonstrates its feasibility, success and viability.

Between October 2018 and January 2020, the project was presented in a total of 14 centers in different regions from all over Catalonia [Fig. 1], we assessed a total of 94 participants (mean age 42.6, 48.9% males), classified as asymptomatic DS- aDS (78.7%), prodromal AD- pDS (4.3%) or AD dementia- dDS (17%) (figures 2 and 3). Thus, a 21.3% of the participants assessed presented symptoms of cognitive decline or even established AD dementia.

Of the recruited participants, the 71.3% accepted to continue with in-person follow up visits and a 24.5% accepted a telephonic follow-up instead (figure 4).

Finally, a 12.8% of the participants agreed to collaborate on research projects (figure 5).

Figure 1. Distribution of centers reached by the cross-sectional DAVIS pilot project.

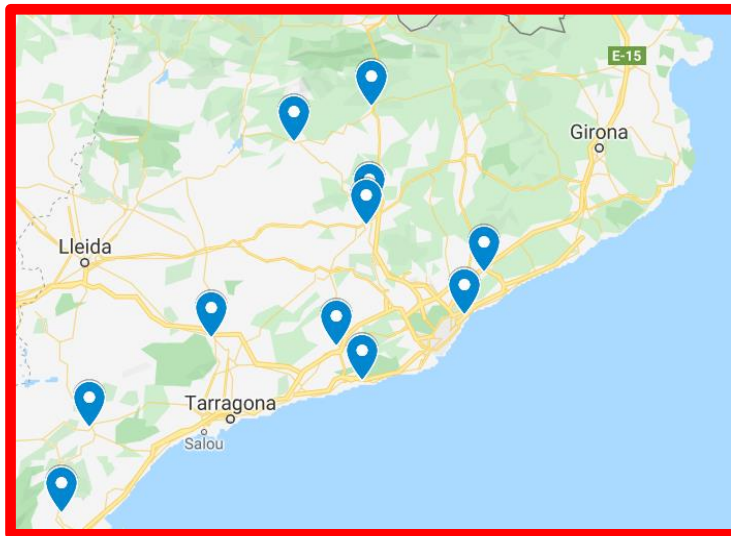


Figure 2. Diagnostic distribution of the participants included in the cross-sectional DAVIS pilot project.

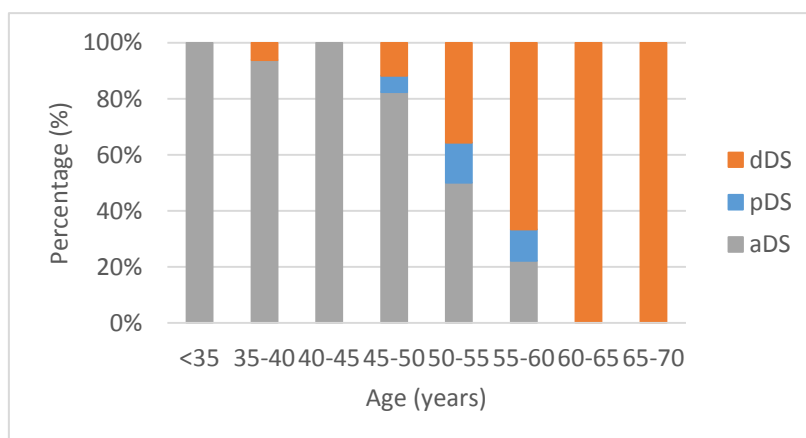
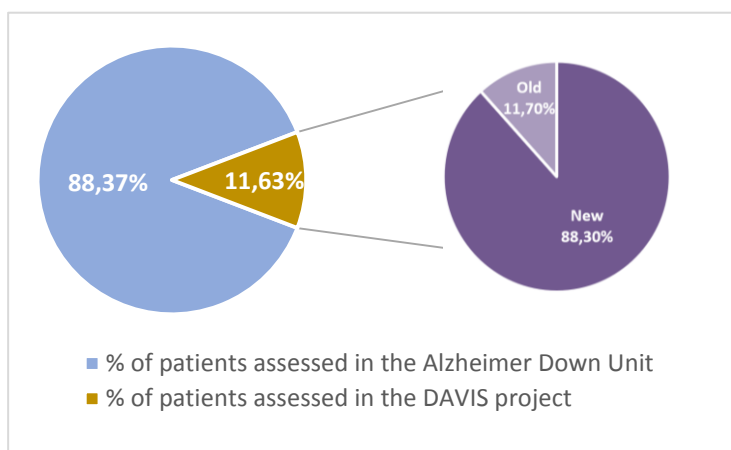
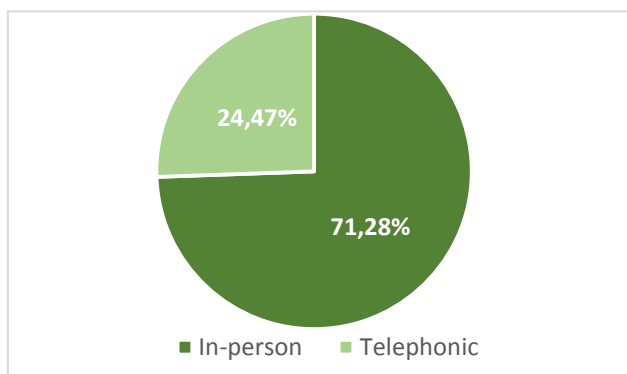


Figure 3. The total of the participants assessed within the cross-sectional DAVIS pilot project.



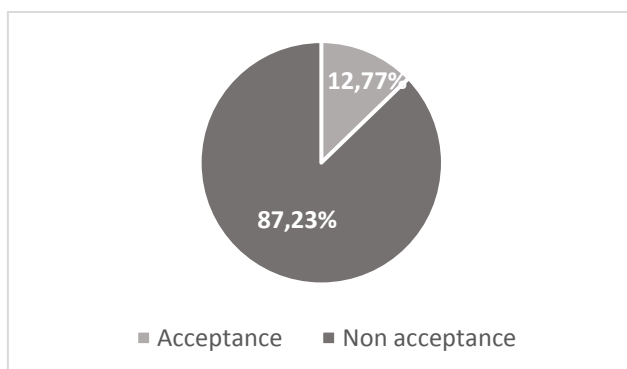
The participants recruited in the cross-sectional DAVIS pilot project represent an 11,6% of our total cohort in the Alzheimer Down Unit (ADU). From them, a 11,7% had already been visited in the ADU before and had stopped coming for diverse reasons.

Figure 4. Acceptance to attend to the UAD for the follow up visits.



The preferred follow up was in-person, at the Alzheimer Down Unit in Barcelona.

Figure 5. Acceptance of participation in research projects



Almost a 13% of the participants recruited in the DAVIS project were willing to participate in research projects.

These preliminary results demonstrate that the DAVIS project is feasible, viable and possible, considering that the project is carried out by professionals who normally work in a clinical setting.

Project title: Domiciliary Alzheimer Visiting in Down syndrome extensión Project (DAVIS-2)
Principal investigator: María Carmona Iragui

5. Curriculum vitae of the researchers and previous experience on the subject.

See attached documents.

Annexes

Annex 1: Informative leaflet

Qui conforma l'equip del pla DAVIS?

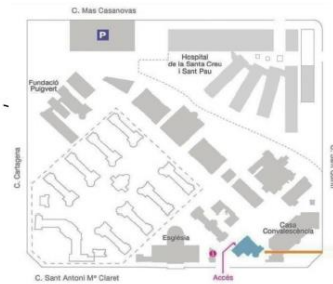
L'equip multidisciplinari altament especialitzat està format per:

- Neuròlegs especialistes en trastorns cognitius
- Neuropsicòlogues amb experiència en el síndrome de Down i en trastorns cognitius

- *Infermera per a l'atenció al pacient neurològic*

Com treballem a la Unitat Alzheimer-Down?

- Proporcionant una medicina centrada en la persona: atenció individualitzada i humanista
- De forma multidisciplinària i transversal
- Basant-nos en la més recent evidència científica
- En coordinació amb altres professionals de l'entorn de la persona amb síndrome de Down: personal de residència, metge d'atenció primària o especialistes, referents tutelars, etc.

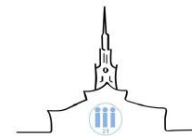


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Visites domiciliàries en el Síndrome de Down, pla DAVIS
(DAVIS: Domiciliary Alzheimer Visiting in Down Syndrome)

DETECCIÓ PRECOÇ DE MALALTIES NEUROLÒGIQUES



Unitat Alzheimer-Down
Fundació Catalana Síndrome de Down
Hospital de la Santa Creu i Sant Pau

Gràcies a l'esforç, persistència i optimisme de les persones amb síndrome de Down, els seus familiars

i els avenços socio-sanitaris experimentats, la seva esperança de vida ha augmentat considerablement.

Això justifica que l'envelliment en el síndrome de Down sigui una etapa vital amb interès creixent. És un repte socioeconòmic, emocional, així com de salut.

En l'actualitat existeix evidència sobre que les persones amb trisomia 21 presenten un envelliment més precoç que la resta de la població. Això els predisposa a patir certs problemes mèdics, associats a l'edat com la malaltia d'Alzheimer, a una edat més primerenca.

- En ells els primers símptomes de la malaltia d'Alzheimer poden aparèixer a partir dels 40 anys i afectar a més del 80% dels majors de 60 anys.
- Existeix una necessitat d'atenció integral i individualitzada per un equip especialitzat per establir un diagnòstic precoç i un abordatge específic.

Per donar resposta a aquesta problemàtica, el **Centre Mèdic Barcelona Down de la Fundació Catalana Síndrome de Down i el Servei de Neurologia de l'Hospital de la Santa Creu i Sant Pau** van unir els seus esforços i coneixement per crear la **UNITAT ALZHEIMER-DOWN**, activa des de l'any 2014 i afavorida per la Generalitat de Catalunya.

En què consisteix el pla DAVIS?

El projecte neix amb l'objectiu de fer extensible l'accés a aquest recurs a totes les persones majors d'edat amb Síndrome de Down, presentin o no símptomes de deteriorament cognitiu o sospita de Malaltia d'Alzheimer, que no puguin desplaçar-se a la consulta.

Un equip format per un neuròleg i un neuropsicòleg es traslladarà al seu domicili o institució per oferir-li una valoració individualitzada.

La valoració que oferim és la següent:

- Visita de **neurologia** que consta de la recollida de història mèdica, exploració física, diagnòstic i recomanacions incloent ajust de tractament si procedeix.
- Exploració **neuropsicològica** que inclou l'avaluació de les funcions cognitives superiors mitjançant tests adaptats (memòria, atenció, orientació, etc.).

Per facilitar la seva participació en aquest pla, amb dues valoracions tindran lloc el mateix dia i de manera simultània, amb una duració estimada de 1.5-2 hores.

Al finalitzar se li proposarà completar un qüestionari de satisfacció sobre l'atenció rebuda.

Comuniquem que el pla DAVIS té finalitat tant assistencial com investigadora. Vostè serà informat

dels resultats que tinguin repercussió en la seva salut.

Quins són els beneficis de la participació?

- Rebrà atenció mèdica i neuropsicològica especialitzada gratuïta a domicili. Gràcies a això es podrà:
 - Detectar la presència del deteriorament cognitiu i establir el seu grau.
 - Establir un pla de tractament i seguiment socio-sanitari individualitzat.
- També contribuirà a avançar en el coneixement:
 - De l'evolució de les malalties degeneratives que ocasionen pèrdua de memòria.
 - Contribuint així en el desenvolupament de millors tractaments per curar o prevenir aquestes malalties.
- Recordem que la participació en aquest pla no comporta riscos.

Annex 2: Informed consent approved by the local IRB.



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DICTAMEN DEL COMITÉ ÉTICO DE INVESTIGACIÓN CLÍNICA

Doña Milagros Alonso Martínez, Secretaria del Comité Ético de Investigación Clínica de la Fundació de Gestió Sanitària del Hospital de la Santa Creu i Sant Pau de Barcelona,

CERTIFICA

Que este Comité ha evaluado la propuesta del promotor, para que se realice el estudio observacional:

TITULO: Domiciliary Alzheimer Visiting in Down syndrome. Visitas domiciliarias de Alzheimer en el síndrome de Down			
PROMOTOR: INSTITUT DE RECERCA HSCSP			
CÓDIGO	Nº EudraCT	VERSION	Ref. HSCSP
HBSP-DAV-2017-95	NO PROCEDE	2 de fecha 28/02/2018	18/019 (OBS)
Hoja de información al participante y consentimiento informado, versión: 2 de fecha 28/02/2018			

Y considera que:

- Se cumplen los requisitos necesarios de idoneidad del protocolo en relación con los objetivos del estudio y están justificados los riesgos y molestias previsibles para el sujeto, teniendo en cuenta los beneficios esperados.
- La capacidad de los investigadores y las instalaciones y los medios disponibles son apropiados para llevar a cabo el estudio.
- Son adecuados tanto el procedimiento para obtener el consentimiento informado como el plan de reclutamiento de los sujetos.
- El alcance de las compensaciones económicas previstas no interfiere con el respeto a los postulados éticos.

Por tanto este CEIC acepta que dicho estudio observacional sea realizado en el Hospital de la Santa Creu i Sant Pau (Barcelona) por el investigador principal **DRA. M. CARMONA IRAGUI**.

Lo que firmo en Barcelona, a 14 de marzo de 2018.


 FUNDACIÓ DE GESTIÓ SANITÀRIA DE
L'HOSPITAL DE LA SANTA CREU I SANT PAU
COMITÉ ÈTIC D'INVESTIGACIÓ CLÍNICA

Dña. Milagros Alonso Martínez

Annex 3: Budget distribution

The global health plan, that includes the longitudinal medical, neurological and neuropsychological assessments, is funded for every adult with Down syndrome in Catalonia who attends to our site. The offices in where patients are assessed, the expert personnel – neurologists, neuropsychologists, a social worker, and a nurse -, part-time administrative personnel, four computers that include the informatics logistics for executing a common dataset where data of every subject are collected, is already available. For the Pilot Project we acquired two tablets, one router and one wifi connection which can be used for this DAVIS-2 project.

The transfer of the personnel (a neurologist and a neuropsychologist) to the facilities of these subjects will allow performing their clinical and cognitive assessment.

The requested budget is broken down as follows:

A) Personnel costs:

- Salaries & wages: 6000€

These costs are justified to cover the administrative tasks that are derived from the development of this project. The amount has been calculated following the established salaries from our institution to cover a 8 h-week journey during the year of duration of the project.

B) Non-personnel costs:

- Equipment: 789 €

This amount derives from the acquisition of one tablet (575€), so each team will have one available tablet, containing the hardware that supports the database used for the evaluation and data collection from the assessed patients. In addition, it will include the acquisition of one wireless router (150€) and wifi connection for 1 year (89€).

This equipment will allow the assessment of those subjects at home in the same conditions as those who reach our site and data will be directly introduced into our database. The use of this equipment will be strict for this extension project implementation.

- Transfers: 1800€

This point refers to the expenses that cover the transfer of the neurologist and neuropsychologist to the subjects' facilities. The amount has been calculated based on the amount expended for this same purpose during 2019.

- Publication costs: 500€

This section derives from the current system of publication in high impact journals.

C) Indirect costs (10%): Overheads for the local institution. Subtotal=9089€ x 0,1= 908,9 €.

TOTAL: 9997,9 €