

EAS FHSC NEWSLETTER

Issue 2, December 2016

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THE EAS FHSC NETWORK



Global approach

The global approach has led to the expansion of the EAS FHSC consortium and now 71 lead investigators from 60 countries have committed formally to be the part of EAS FHSC. The FHSC [web page](#) at the EAS web has been updated with the interactive map and [lead investigators](#). The [EAS FHSC methods paper](#) and protocol is now available online.

EAS FHSC Meeting

The EAS FHSC is organizing the next meeting where all FHSC lead investigators are invited. Following the success of the previous meetings, we expect this one to be a great occasion for all lead investigators to get first-hand information and updates on the progress of the project and have the chance to meet and network with others. The meeting will be conducted on April 26, 2017, in Prague, Czech Republic, just after the conclusion of the EAS Congress 2017. [Please click here for the preliminary programme details.](#)

News around the globe

EAS-FHSC Newsletter is intended to be a channel through which the investigators of FH global consortium may promote their great work around FH and highlight the research and initiatives that are transpiring in their respective countries. Each issue of this newsletter acquaint you with new stories from the FH experts. Welcome to the second edition of the newsletter. We are delighted to bring you news and updates from around the world.

HoFH International Clinical Collaboration



By Dr. M.L. Hartgers and Prof. G.K. Hovingh, Prof. F. J. Raal, Prof. D. Blom, and Prof. M. Cuchel.

In recent years, a paradigm shift has taken place in our understanding of the prevalence homozygous familial hypercholesterolemia (HoFH). Whereas HoFH was previously considered to occur one in a million, we now have strong evidence that the actual prevalence is in the order of 1:400 000. These numbers are, however, based on regional surveys conducted in Europe, and thus might not be correct for other geographical regions. Due to local founder effects the prevalence of HoFH is much higher in certain geographic locations and can be as high as 1:40 000.

Given the relative rarity of HoFH our current understanding of the clinical course of HoFH is rather limited and management is mainly based on an “expert opinion” level of evidence. Multinational and multicenter collaborations are pivotal to fully leverage knowledge about rare dyslipidemias, most notably about HoFH. A number of initiatives have been initiated that support the creation of regional registries to overcome this lack of data. The recently launched HoFH International Clinical Collaboration (HICC) registry aims to create a formal international network of healthcare providers who manage HoFH patients that transcends the regional natures of current efforts.

The HICC registry will collect de-identified clinical, genetic and treatment information from participating centers. The data collected includes basic demographic information, relevant medical history, lipid levels, treatment prescribed, response to treatment, cardiovascular outcomes and genetic diagnoses where available. These data will be captured electronically in a web-based

database.

Because one of the intentions of the registry is to capture the phenotypic and genetic diversity seen in HoFH all patients with a diagnosis of HoFH, however made, are eligible. The diagnosis of HoFH could thus be based either on clinical or genetic criteria. Patients with discordant clinical and genetic diagnoses, e.g. clinical HoFH but genetic investigations do not confirm HoFH remain eligible. Including such patients will help to better define the phenotypic and genotypic spectrum of HoFH.

The ultimate goal is to enrol more than 500 HoFH patients. This goal can only be achieved by active and enthusiastic participation of all clinicians treating patients with HoFH, whether cardiologists, internist, endocrinologist or lipidologists. Please email to coordinator@eas-hicc.org if you would like to learn more about HICC or would like to participate in this initiative!

Vietnam

Familial Hypercholesterolemia among Individuals with Premature Coronary Heart Diseases. By Ngoc Thanh Kim¹, Trung Thanh Tran², Duc Huy Tran², Hong An Le³, Thanh Huong Truong^{1,2} (1. Vietnam National Heart Institute, 2. Hanoi Medical University, 3. School of Medicine and Pharmacy, Vietnam National University).



This is the first study on the prevalence of familial hypercholesterolemia (FH) among patients with premature coronary heart disease (PCHD) in Vietnam. FH is a genetic disease that occurs on an autosomal dominant gene and is characterised by the rising of plasma LDL-C levels. It leads to early development of atherosclerosis, what ultimately can cause coronary heart disease events among young patients. In Vietnam the awareness and knowledge of FH is limited. The present study was performed with the aim of: (i) to determine the proportion of FH patients among those with PCHD in Vietnam, and (ii) to describe the clinical and non-clinical characteristics of these patients.

This was a descriptive study including clinical records of 677 individuals with PCHD collected from 2014-2015 in Vietnam National Heart Institute. Screening of patients with PCHD was based on the following selection criteria: male <55 years old or female <60 years old with evidence of coronary lesions on multi-slice computer tomography or percutaneous coronary intervention. FH patients were diagnosed using the Dutch criteria modified with Vietnamese 95 percentile LDL-C. Patients with kidney failure, hypothyroidism and diabetes were excluded from the study.

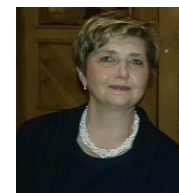
Results showed that 18 (2.7%) patients with PCHD suffered from FH (FH-PCHD). Among those with FH-PCHD, males had higher prevalence with 2.6 times higher rate than females. The average concentration of LDL-C in plasma was 4.73 ± 1.15 mmol/l (minimum 3.64 mmol/l, maximum 8.1 mmol/l). 77.8% patients had narrowed coronary arteries $\geq 70\%$ with at least one branch affected; 34.5% patients had three major coronary arteries narrowed. 12 individuals had stent insertion and 2 had coronary artery bypass grafting.

Before getting discharged, all patients were started on statin, with the following daily doses: 27.8%, 11.1%, and 5.6% patients were prescribed with atorvastatin 10 mg, 20 mg and 40 mg, respectively; 44.4% and 11.1% patients were given rosuvastatin 10 mg and 20 mg respectively. According to the European Atherosclerosis

Society's (EAS) recommendations, the treatment goals for FH-PCHD patients should be to achieve a LDL-C < 1.8 mmol/L or a reduction of at least 50% if the baseline is between 1.8 and 3.5 mmol/L. Therefore, to meet the goal, high intensity statin is recommended. However, this study revealed that only 16.7% patients were treated based on the EAS recommendation (11.1% patients using rosuvastatin 20 mg once a day, 5.6% patients using atorvastatin 40 mg once a day).

In conclusion, the prevalence of FH patients among those with PCHD in Vietnam was 2.7%. Only 16.7% of FH-PCHD patients received recommended statin intensity therapy, showing there is a large lack of appropriate treatment of FH-PCHD in Vietnam.

Bosnia and Herzegovina



By Prof. Dr. B. Pojskić: FH is almost an unknown illness in our country. Screening for FH began as ScreenPro FH program and has been started in Cantonal hospital Zenica, which covers a region of about 150000 inhabitants. Our first set of activities included approval from the local ethics committee, development of the medical consent form for the patients and notifying the Ministry of Health about starting the screening process. Participation in the projects until now are on voluntary basis, therefore, we requested and received support from Medical Council for extra CME credits for participating in the project. We are under the auspices of the Association of Cardiologists in Bosnia and Herzegovina – Working Group on Atherosclerosis, and update information around FH educational programmes, our activities, as well as information about our meetings (e.g. in Gothenburg, Warsaw and Prague) on the web page of the Society.

We started with lectures for doctors who are more likely to meet FH patients, such as GPs, paediatricians, internists, ophthalmologists, or

dermatologists. We had lectures at the Congress of Cardiologist in BiH; translated a book on FH by Richard Ceska into Bosnian language; shared written basic instructions about FH with doctors; and owing to an ophthalmologist we identified the first index case in an FH family.

We have created Excel spreadsheets based on the form received from the EAS FHSC Coordinating Centre led by Prof. K. Ray. We have started to collect data using the cut off LDL-C > 5 mmol/l and the Dutch Lipid Clinic Network Score (DLCNS) for FH. In the last three months 4 medical institutions from different parts of the country joined us and it looks like the starting of the network of FH project in our country.

There are approximately 1000 people in the database with 3 definite and more than 5 probable FH families. We acknowledge there are several obstacles including: how to persuade doctors for cooperation; problems with cascade screening and people migrating; no medical health system supporting laboratory tests for "healthy" family members and specially screening lipids in children; genetic testing is not available; statins are prescribed in inadequate doses; there are often avoidance or interruption of therapy due to the limited drug costs covered from the health insurance; ezetimibe is not available as well as PCSK9 inhibitors or lipid apheresis; there is no patient organization; and on top of that, there is lack of time and funding. However, we think we have had a successful start owing to our great enthusiasm and willingness, and are very positive for the future development of this project and cooperation with the global network.

Japan

By Dr. D. Masuda: The committee member of Public Relations, Japanese Atherosclerosis Society (JAS): In Japan, the incidence of heterozygous FH is estimated to be 1/200-500 and that of homozygous FH 1/1,000,000, which signifies that, with a population of 127 million, between 250,000 to 630,000 people may suffer from FH in Japan. The majority of people in Japan receive the annual health check-up and those who have dyslipidaemia

are encouraged to receive a secondary screening.

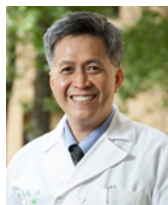
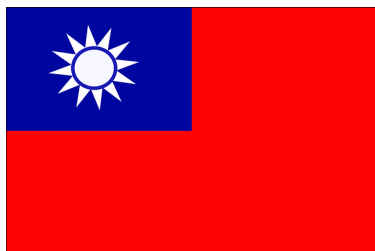
Patients with hypercholesterolaemia are often diagnosed following the criteria established by the JAS guidelines on the Diagnosis and Prevention of Atherosclerotic Cardiovascular Diseases in Japan (2012) and receive lipid lowering treatment accordingly. Based on the results of different epidemiological studies, the diagnostic criteria for HeFH in Japan have been established and included in these guidelines: An individual is considered to have HeFH if possessing two or more of the following criteria: 1) LDL-cholesterol ≥ 180 mg/dL, 2) tendon/skin xanthoma(s), and 3) family history of FH or premature CAD within second degree relatives for adults. The diagnosis and treatment of hypercholesterolemia are adequately performed, unlike that for FH. Only 20 % or less individuals with FH in Japan are identified; therefore, most patients with FH still remain at high-risk for atherosclerotic cardiovascular disease.

In order to support the EAS-FH awareness week in Japan, the JAS and the EAS Familial Hypercholesterolemia Studies Collaboration (EAS-FHSC) national lead Professor Shizuya Yamashita (President of JAS) with Dr. Mariko Harada-Shiba (also EAS FHSC national lead investigator for Japan) and colleagues organized a meeting on September 25th, 2016 at the JP Tower Hall and Conference in Tokyo that included a lecture for general physician, a public lecture for citizens and a seminar for mass media to promote better understanding of FH. The lecture for general physician was about a frontline of FH and the public lecture was focused on the clinical features,



pathology and diet therapy of hypercholesterolemia and FH. Over one hundred physicians and more than three hundred citizens participated in these meetings which might have facilitated better understandings of FH among them. Subsequently, a seminar for mass media was held, where the JAS answered the queries on FH. JAS believes that these kind of meetings will improve the understanding of FH leading to higher diagnostic rate and better care for FH patients in Japan.

Taiwan



By Dr. Ta-Chen Su, Dept. of Internal Medicine and Cardiovascular Center, National Taiwan University Hospital.

Setting up the registry: We have organized a FH registry group and a FH consortium under the Taiwan Society of Lipids and Atherosclerosis.

Setting up the rapid screening platform for FH: With the support from Prof. Min-Ji Charng, a cardiologist of Taipei Veterans General Hospital, Taipei (an expert in Molecular Biology and Cell Biology in FH), we plan to set up a rapid screening protocol by establishing a genetic screening algorithm for FH diagnosis, which includes a method of single strand conformation polymorphism by DHPLC (Denaturing high performance liquid chromatography) and then using MassARRAY iPLEX assay for single nucleotide polymorphism detection. For unidentified patients, we plan to set up a next-generation sequencing (NGS)-based genetic test platform in National Taiwan University Hospital in 2017.

Setting up the lipid guideline: We will announce the 2017 Taiwan Lipid Guidelines for High Risk Patients on December 25, 2016.

Setting up a patient group for FH: We have reached a consensus to promote and set up a patient group for FH in early 2017 under the support from the Taiwan Society of Lipids and Atherosclerosis, and Taiwan Society of Cardiology on Nov. 25, 2016.

Setting up a special session for FH: For providing education on awareness and management of FH, we plan to set up a scientific session on FH in the annual meeting of the Taiwan Society of Lipids and Atherosclerosis.

Setting up a special column in mass media for FH: For the awareness and education, early diagnosis, and early treatment of FH patients, we plan to set up a special column in mass media.

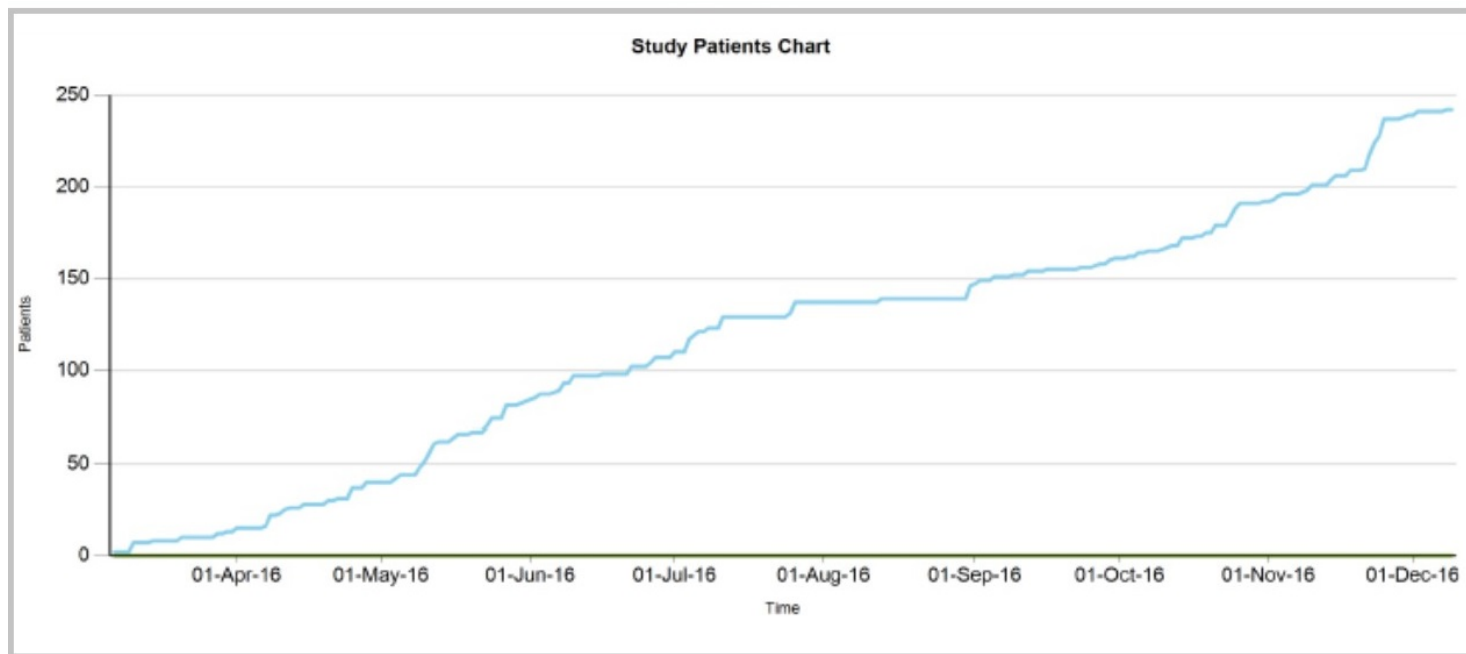
Special lecture of patient education for FH: Dr. Ta-Chen Su gave a special lecture on awareness and management of FH on Nov. 24, 2016 held in National Taiwan University Hospital. Over 300 FH patients attended the lecture.

Publications: Some important findings in FH diagnosis and management have been published by Taiwan and the Ten-country Study. Please refer to the publication section of the newsletter. Under the international collaboration with Gerald F Watts (Australia), there has been a publication "Translational research for improving the care of familial hypercholesterolemia: The "Ten Countries Study" and beyond". Moreover, international cooperation by joining the EAS FH Studies Collaboration also help us to expand the vision and achieve the consensus of FH diagnosis and treatment. An important call for action letter was announced in an article: Familial hypercholesterolaemia: A global call to arms.

In conclusion, we see a great advancement after integrating the expertise of lipid specialists in Taiwan. We are also making efforts to establish a FH consortium and national registry in Taiwan. We will organize a patient group and plan to deliver more FH education for general practitioners and patients in the next year. As well as, Participating in more international collaboration and call for action in Taiwan.

Greece: The Hellas FH Registry

By Dr E. Liberopoulos: The Hellas Familial Hypercholesterolemia Registry is sponsored by the Hellenic Atherosclerosis Society (HAS). Almost 250 FH patients have been registered in 8 sites since it was launched in April 2016 (see figure). Moreover, 3 more sites will be active in 2017.



In order to increase awareness of the disease we have created an [info-graphic](#) to be posted in cardiology and lipid clinics all over the country. During our recent annual conference (1-3 December 2016) we held a 2-hrs course for FH, which was attended by more than 300 physicians. A study using the data from a large lipid clinic in Greece showed that almost one third of FH patients do not receive intensive lipid-lowering treatment and a high proportion does not achieve LDL-C targets in clinical practice ([Hell J Atheroscl 2016;7:120-30](#)).

The Gulf FH Registry

By Prof. K. Al-Rasadi: The Gulf FH registry is a Multi-Center National Registry in the Middle East to Study the Prevalence, Management, Genetic Characteristics and Outcomes of Patients with FH in 6 Arabian Gulf Countries (Saudi Arabia, Oman, United Arab Emirates, Kuwait, Qatar and Bahrain). Patients will be included in the registry if they have previous clinical or genetic diagnosis of FH. Also, patients will be recruited through other different sources like laboratory data. This registry would be initiated soon.



EAS FHSC Central and Eastern European Symposium on FH



The EAS-FHSC Central and Eastern European Symposium on FH was held on November 25-27 in Warsaw, Poland. This 3-day symposium was attended by physicians, researchers and others involved in the screening, diagnosis and management of patients with familial hypercholesterolaemia. Attendees shared their knowledge and experiences in both scientific and organizational matters at the Central & Eastern European Key Opinion Leader Summit. Additional lectures and workshops were held on topics including epidemiology,

genetics, diagnosis, screening, FH in children, management of FH patients, registries, therapeutic strategies, implementation of guidelines, and severe & Homozygous FH.

The EAS thanks everyone who contributed to the meeting's success for the interesting discussions, and look forward to continuing to work together to reduce the impact of FH and the global burden of the disease.

PUBLICATIONS

Click on the reference to be directed to the publication

- Barkas F, Liberopoulos E, Liamis G, Elis M. Familial hypercholesterolemia is undertreated in clinical practice. *Hell J Atheroscler* 2016, 7:120-130.
- Napier KR, Pang J, Lamont L, Walker CA, Dawkins H, Hunter AA, Bockxmeer F, Watts GF, Bellgard M. A Web-Based Registry for Familial Hypercholesterolaemia. *Heart Lung and Circulation* 2016, 1-5 1443-9506.
- Mehta R, Zubiran R, Martagon A, Vazquez-Cardenas A, Segura-Kato Y, Tusie-Luna MT and Aguilar-Salinas CA et al. The panorama of familial hypercholesterolemia in Latin America: a systematic review. *Journal of Lipid Research* 2016.
- Chiou KR, and Charng MJ, Genetic diagnosis of familial hypercholesterolemia in Han Chinese. *J Clin Lipidol* 2016, 10(3):490-6.
- Watts GF, Ding PY, George P, Hagger MS, Hu M, Lin J, Khoo KL, Marais AD, Miida T, Nawawi HM, Pang J, Park JE, Gonzalez-Santos LB, Su TC, Truong TH, Santos RD, Soran H, Yamashita S, Tomlinson B. Translational research for improving the care of familial hypercholesterolemia: The "Ten Countries Study" and beyond. *J Atheroscl Thromb* 2016, 23(8):891-900.
- The EAS FHSC Investigators. Pooling and expanding registries of familial hypercholesterolaemia to assess gaps in care and improve disease management and outcomes: rationale and design of the global EAS Familial Hypercholesterolaemia Studies Collaboration, *Atherosclerosis Supplements*, 2016, 1567-5688(16)30049-6.
- Lipids: Advanced Training [Lípidos: Formação Avançada]. Risk Factors 2015;38.
- Educational video on FH for raising awareness by FH Portugal.

EVENTS

- ▶ **85th EAS Congress:** The 85th EAS Congress will be held in Prague, Czech Republic, between 23-26 April, 2017.
- ▶ **EAS FH Studies Collaboration meeting:** The EAS-FHSC Lead Investigators meeting will take place next April 26, 2017, at Corinthia Towers Hotel (next to the Congress centre), in Prague, Czech Republic. Organisers: Alberico L. Catapano & Kausik Ray.
- ▶ **Meeting on Management of Paediatric FH:** Satellite meeting on Management of Pediatric FH, April 27, 2017. Venue: Vavruska Congress Centre, Prague, Czech Republic, Time: 09:00 – 16:30. More detailed information on the programme and registration to this event will be available on the EAS 2017 web soon.

The [FHSC Rational and Methods paper](#) has now been published (see full reference in the publications section). It constitutes an issue of the Atherosclerosis Supplements itself, it includes the FHSC protocol, and the article is available Open Access.

The coordinating Centre at Imperial College London is developing the programme for the EAS FHSC meeting in Prague, Czech Republic, see events section.

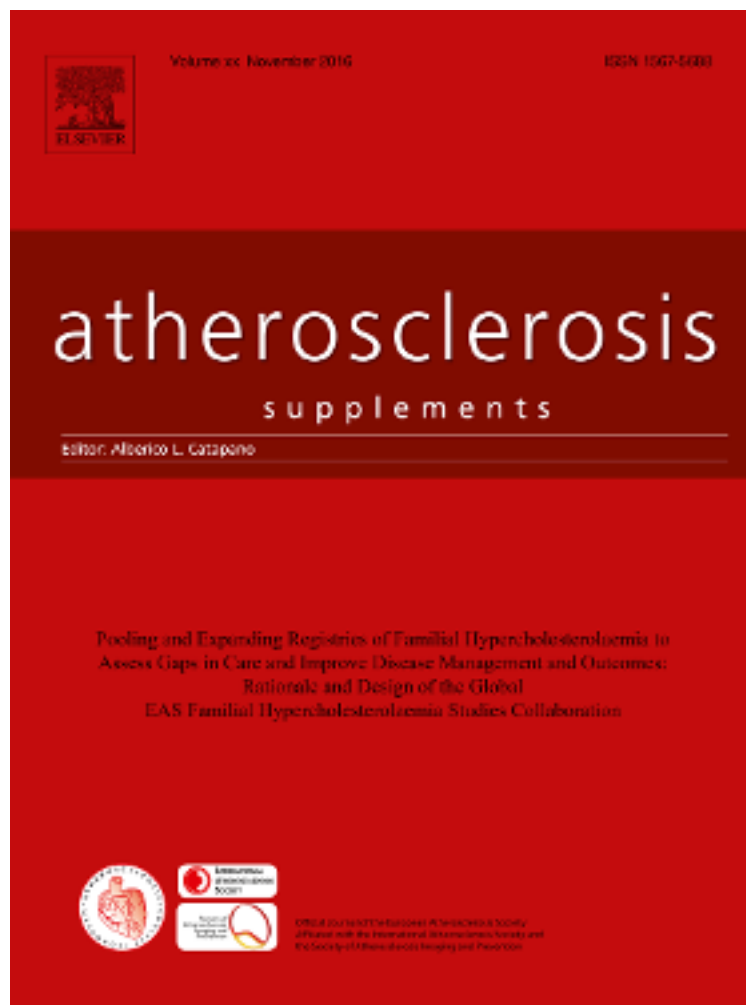
We have already received data from a few countries. These data sets are in the process of cleaning and initial exploratory, descriptive analyses.

Bioinformatics update

The IT team at the Coordinating Centre has progressed in developing the central bespoke data warehouse and data sharing application. It is getting tested and we expect that from the beginning of next year the FHSC lead investigators could register to the website.

FHSC Executive committee meeting

The Quarterly WebEx meeting of the EAS FHSC Executive Committee (EC) met and discussed the progress of the FHSC. There were no issues of governance raised and all in attendance were pleased with the progress and the scope and geographical reach of the FHSC as it stands. The EC commended the Coordinating Centre on its progress. No changes were recommended to the



current protocol and progress will continue to be reviewed quarterly. In addition to the quarterly EC meeting, the coordinating centre will look to host 2 Steering Committee meetings for all lead investigators every 6 months to keep them updated and allow an opportunity to interact via WebEx.

Contact

Let us know about your news, publications, achievements or events around FH and we will include them in the following issues of the EAS FHSC newsletter, so they can be shared with the other colleagues, given publicity and contribute to networking within the EAS FHSC collaboration.

info@eas-fhsc.org.

coordinator@eas-fhsc.org.

We would like to thank very much to those of you contributing to the present newsletter, as well as to those who have sent some texts that we have been finally unable to include now due to restrictions of space; we will include these texts in the next newsletter.

Thank you very much!