CLINICAL FELLOWSHIP

Supported by an independent educational grant from **Merck HealthcareKGaA**, Darmstadt, Germany

EXECUTIVE REPORT 2019-20 INTAKE

"I would highly recommend the ESPE Clinical Fellowship to the young enthusiastic endocrinologist as it provides not only the in depth knowledge of paediatric endocrine disorders but also empowers fellows in counselling, multi-disciplinary clinic processes and paper writing." – Chetankumar Dave, Regency Center for Diabetes, Endocrinology and Research, India

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Introduction

Established in 1993 the Clinical Fellowship aims to promote the development of patient care, clinical management and clinical research in paediatric endocrinology through a training opportunity in a reputable European clinical centre selected for being a centre of excellence in paediatric endocrinology. The Clinical Fellowship helps to overcome significant disparities in the provision of high quality paediatric endocrine clinical care in different parts of Europe and to date 240 clinicians have benefitted from this specialist training. The Fellowship is open to applicants who are fully trained in Paediatrics and/or have started training in Paediatric Endocrinology. The Clinical Fellowship is kindly supported by an educational grant from Merck.

The 2019-20 intake was unfortunately disrupted by the COVID-19 pandemic. This saw only thirteen of the fifteen selected fellowships complete. A number completed their allocated three month visits virtually and some at centres not originally designated due to continuing travel restrictions. Only two fellows were unable to conduct their fellowship. Managing this intake was undoubtedly the most challenging year for the Clinical Fellowship Committee, who persisted through one unpredictable development after another to ensure as many fellows as possible were given the chance to experience this invaluable training opportunity, ensuring that one of ESPE's most important activities was maintained throughout the pandemic. Despite these efforts ESPE was still unable to run the programme for a 2020-21 intake, and instead held the ESPE Clinical Fellowship Spring Initiative in April 2021, in which past, current and prospective fellows were invited to attend to learn from tutors and successful past fellows' experiences on the programme. The content from this event is now online for all to view.

SECTION 1 - DEMOGRAPHICS

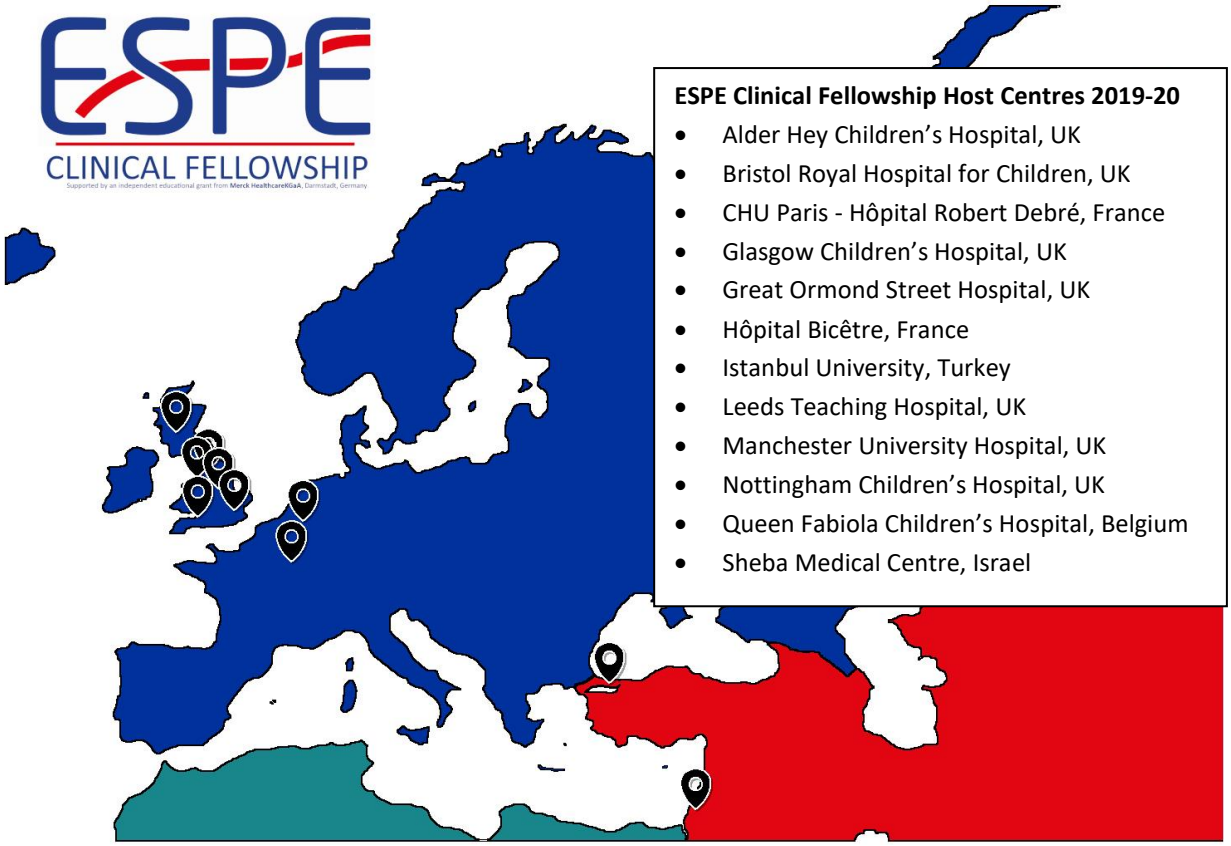
1.1 Clinical Fellow home countries

Fellows are selected from countries lacking opportunities for training in specific skills or specific sub-specialty experience. With the globalization both of ESPE as a society, and of paediatric endocrinology as a recognised paediatric sub-specialty, the need for specialised training is increasing and getting more sophisticated. Therefore, the Clinical Fellowship programme welcomes applicants not only from Europe, but also from Africa, China, the Indian sub-continent, South America and the Middle East.

1.2 Clinical Fellowship Host Centres

Fellowships are carried out at European Centres with a highly recognised reputation in clinical paediatric endocrinology. Host centres are selected by the fellowship committee. Applicants are expected to both to understand and speak fluently the language of the population of the selected host centre country. The application, confirming the candidate's training needs, readiness to use newly acquired knowledge, skills and experience, and a declaration to support the candidate's future career in paediatric endocrinology upon successful completion of the Clinical Fellowship is a vital part of this selection process. It is expected that the fellows will return to their home country at the end of the fellowship to promote paediatric endocrinology in their home centre/country.

The below graphic shows the host centres in the 2019-20 intake. It should be noted that the spread of centres was limited due to the border restrictions and pandemic status throughout 2021.



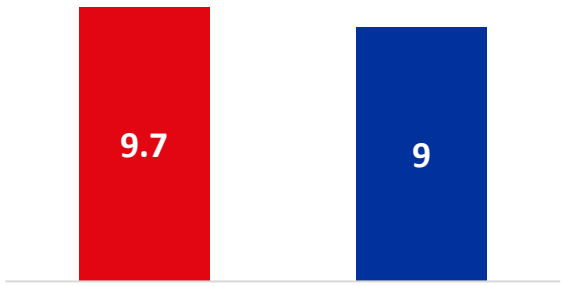
Unfortunately there were difficulties in securing a placement for one fellow from Armenia who was due to attend their fellowship in Zurich, Switzerland under the tutelage of Professor Daniel Konrad. Despite multiple attempts through 2020 and 2021 it proved impossible to financially, and logistically arrange the three month visit due to restrictions surrounding visa applications and quarantine rules (extra cost to fellows). The fellow's mentor from the Clinical Fellowship Committee eventually found a suitable placement in Tel Aviv, Israel, under Prof. Orit Hamiel, beginning in late 2021. Although not in a European centre, this still provided the valuable opportunity to learn in a centre of paediatric endocrine excellence. Another fellow was unable to secure a placement in Southampton, UK, under Professor Justin Davies, due to the local institutional rules of not taking any placements, however they were later successful in being accepted to Bristol, UK, under the supervision of Dr Dinesh Giri. Only two fellows were completely unable to secure a placement in this intake, and this was due to being denied a visa to work in France in November 2021, and due to late UK travel restrictions imposed in December 2021. The fellows were unable to apply for a visa in time to attend any other European centre as the Clinical Fellowship Committee agreed that any delayed fellowships must start before the deadline of 30th November 2021.

SECTION 2 – DETAILS OF TRAINING AND CONDITIONS SEEN ON THE CLINICAL FELLOWSHIP

2.1 Overall experience

Thirteen fellows successfully completed their visits of the fifteen that were selected. The data below outlines the feedback from the thirteen fellows. Fellows are asked to rate the overall experience of their clinical training on a scale of 1 to 10 (1 being extremely negative and 10 being extremely positive. *Figure 1* demonstrates the average responses over the past two intakes.

Fig1. **Average overall experience of the clinical training received on fellowships**



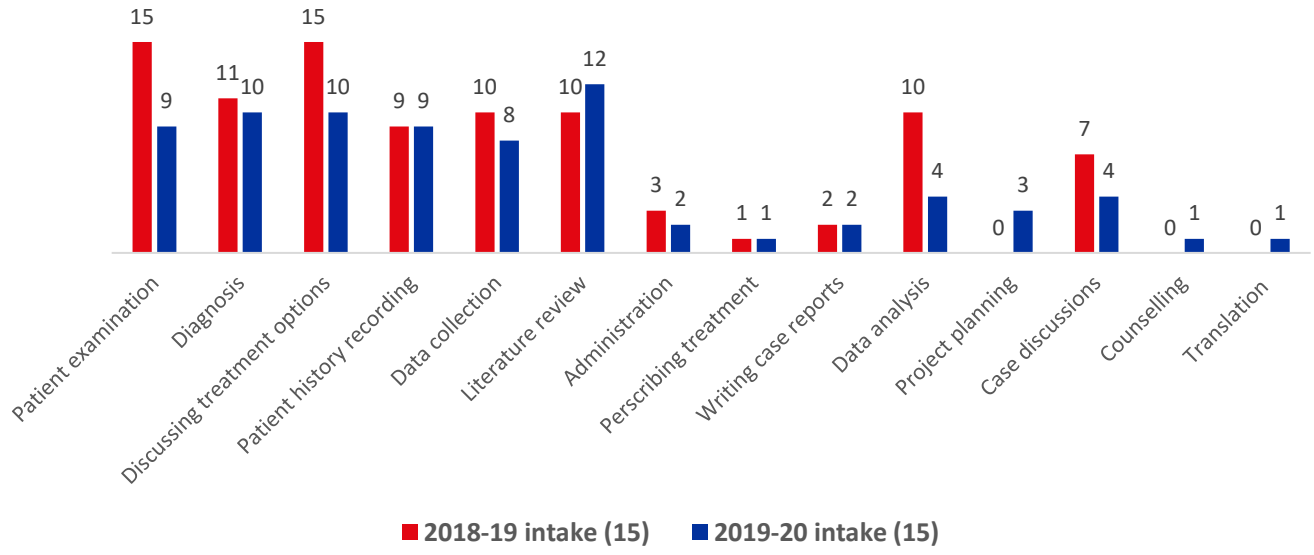
The lower average point score in the current intake can be attributed to the fact that a number of the fellows' visits were disrupted by COVID-19 and they were forced to complete the training virtually. Although they were happy to receive any form of training during the lockdown, it is understandable that this is not a format deemed as valuable as face-to-face learning. Another one of the fellows was disrupted on their visit, but managed to secure another placement later on in 2020 once restrictions had eased. She had rated the training as extremely positive and was grateful to be able to complete it in person. The fellows whose visits were delayed significantly (early 2022) all rated the experience as extremely positive.

"After coming back to India, due to the COVID-19 crisis, I would attend weekly online teaching sessions and multidisciplinary virtual clinics." Chetankumar Dave, Regency Center for Diabetes, Endocrinology and Research, India

2.2 Training activities undertaken

The fellows reported undertaking daily clinical training in the form clinics (in person and virtual), ward rounds, case presentations, team meetings and seminars. *Figure 2* displays the number of fellows in the intake who undertook the different types training activities reported in the past two intakes.

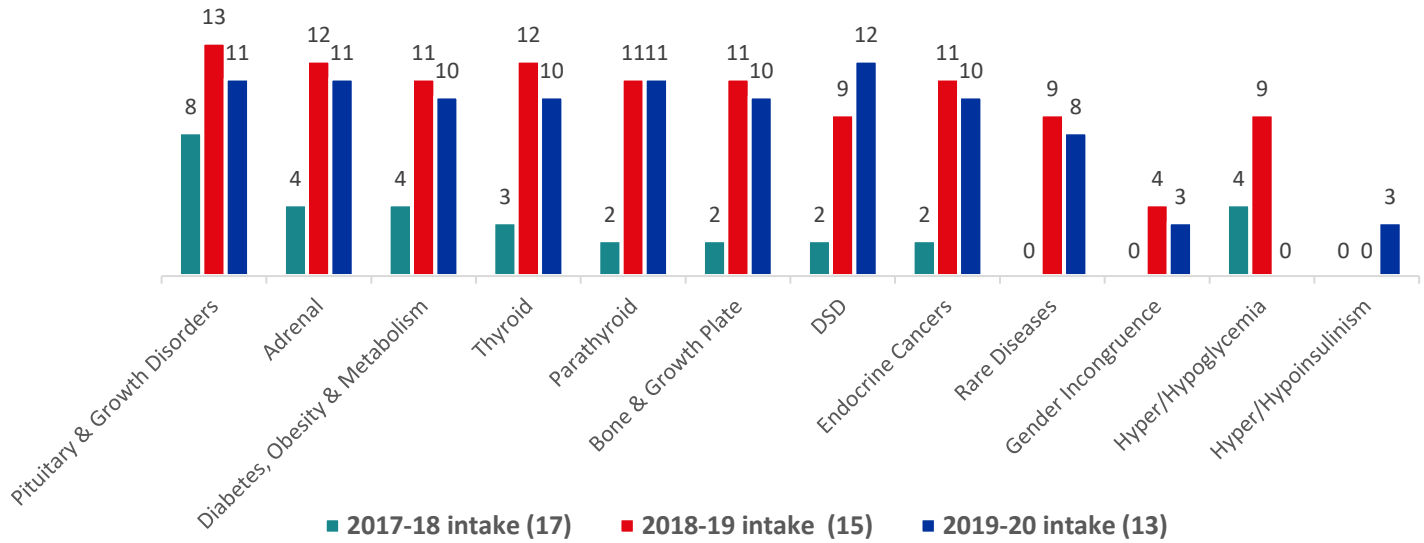
Fig 2. **Number of fellows undertaking specific training activities on their Clinical Fellowship**



2.3 Conditions seen on the fellowships

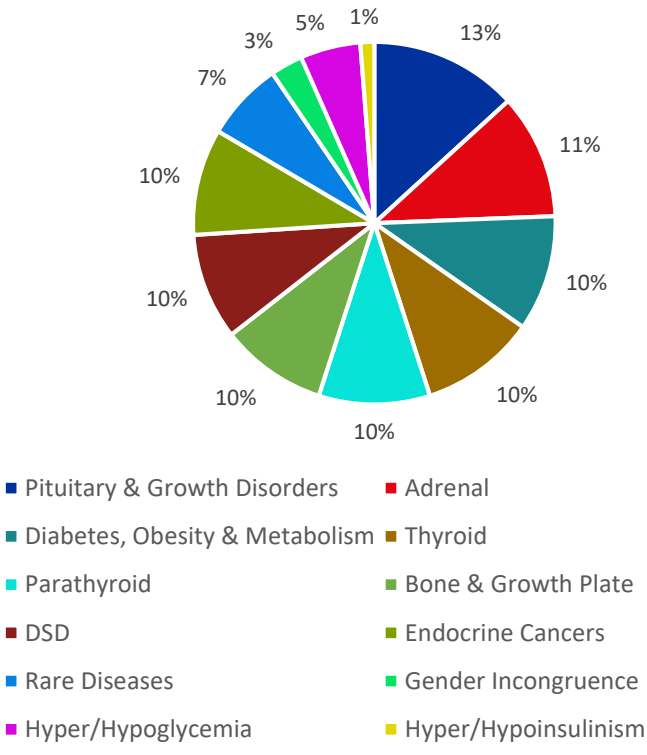
The fellows are asked to report on the conditions encountered during their visits. For the previous two intakes pituitary and growth disorders were the most common endocrine conditions witnessed, but in this intake it was DSD. *Figure 3* displays the number of fellows in each intake who encountered a specific condition. The conditions listed are those reported by the fellows themselves.

***Fig 3.* Number of fellows encountering specific conditions during their Clinical Fellowship**



It should be noted that the 2017-18 intake displays lower values due to the fact that the completion reports were updated in 2019 in order to capture more information from the fellows. It is expected that once the remaining reports are returned from the 2019-20 intake the number of reported conditions will be in line with the trend seen in the 2018-19 intake. On average fellows from each intake report seeing between 50-60 patients per week. *Figure 4* displays the percentage of conditions seen over the course of the past three fellowships which shows pituitary and growth disorders being the most common condition encountered, followed closely by adrenal and thyroid conditions.

***Fig 4.* Conditions seen since 2017**



"During my training in Glasgow, I had the opportunity to be exposed to and gain further clinical experience in the management of the vast majority of paediatric endocrine conditions. Interestingly, the attendance of Clinics designed for the follow-up of patients with specific endocrine conditions, such as DSD, hyperinsulinism, Prader-Willi syndrome, genetic endocrine tumors, complex bone diseases and gender dysphoria, was really helpful to me." Ioannis Kyrgios, Papageorgiou General Hospital, Greece

In 7% of the cases seen, patients were suffering from rare endocrine diseases. The invaluable experience and knowledge transferred by the hosts to the fellows in these instances highlight the importance of the Clinical Fellowship programme to the fellows, the patients and the society. The fellows will have likely not encountered some of these rare diseases and are therefore unlikely to have the support, resources and experience of treating these disorders in their home institutions. The fellows will take home this newly acquired knowledge, from the centre of excellence, and improve the rare disease treatment in their home countries. This is also in line with ESPE's strategy to develop activities in the rare disease area, which is lead by the newly established ESPE Rare Disease Advisory Group.

"I have encountered various uncommon syndromes also during my fellowship. These included Lipodystrophy, Noonan Syndrome, Russell Silver syndrome, Prader Willi Syndrome, McCune Albright syndrome, Klinefelter syndrome, Albright's Hereditary Osteodystrophy." - Nikhil Lohiya, Jehangir Hospital, India

2.4 New techniques/treatment modalities/screening methods learnt on the fellowship (including the development of screening programmes)

The Clinical Fellowship enables the learning of new techniques and treatment modalities that are otherwise inaccessible in fellow's home countries. This helps to improve patient care and general practice of paediatric endocrinology globally. Below are listed the new diagnostic techniques and modalities acquired in this intake:

- Growth hormone treatment, dose adjustment and device usage
- Communicating with patients
- Genetic laboratory testing – NGS, Sanger sequencing, real time PCR.
- Radiological testing – for skeletal dysplasia and pituitary disorders
- Screening – Thyroid, pituitary, adrenal
- Communicating with patients – disclosing diagnoses, discussion investigations and management, obesity counselling and related psychological disorders.
- Patient follow-ups in new therapeutic drug treatments
- Insulin pump management
- Glucose monitoring systems
- DSD gene panel testing
- Specific autoantibodies in Addison disease detection
- Arginine stimulation testing for GH deficiency
- Insulin tolerance test
- Growth hormone suppression test
- Thyroid screening – TRAb antibody assessment
- Pituitary screening – tumour screening, post oncology therapy
- Adrenal screening – synacthen stimulation test for patients on prolonged steroid treatment
- New diagnostic approaches – genetics for congenital hyperinsulinism, salivary cortisol assessment

"*Multidisciplinary clinics (MDTs) were state of the art. I was lucky enough to attend two of them. DSD (Disorders of sexual differentiation) MDT was associated with holistic care with the involvement of endocrinologist, geneticist, surgeon and psychologist. Obesity MDT had involvement of endocrinologist, psychologist, nurse and dietician. I am planning to establish a similar concept in my clinic in India.*" – Chetankumar Dave, Regency Center for Diabetes, Endocrinology and Research, India

SECTION 3 – Output from the Clinical Fellowship 2019-20 intake

3.1 Details of clinical/audit, research projects or presentations resulting from the fellowships

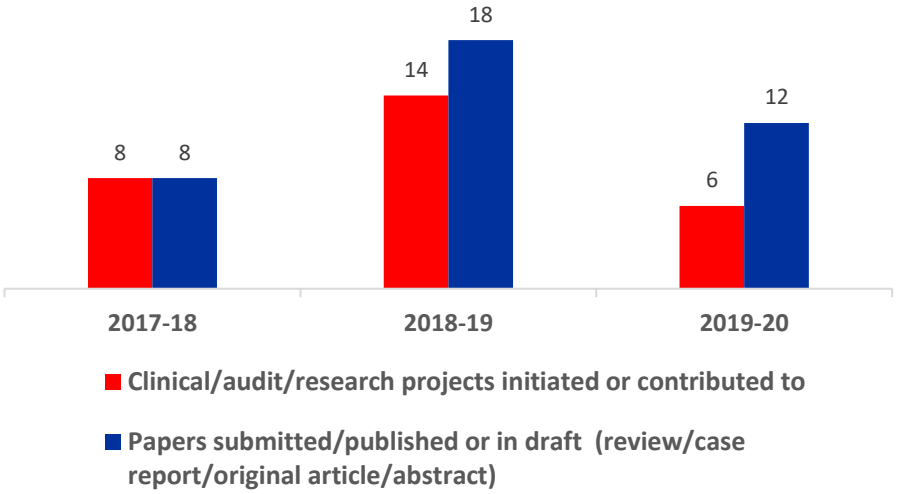
A key aim of the Clinical Fellowship is to facilitate the establishment of long term relationships and collaboration. The fellows are required to report on any clinical/audit/research projects that they partake in whilst conducting their visits. International collaboration is a vital part of progressing the discipline, and opportunities to do so during 2020-21 have been at a premium. The connections made during this difficult time are ever more important due to the strains on endocrine services caused by the pandemic both directly and indirectly. Below are detailed the projects carried out, or established, by fellows in the 2019-20 intake:

I. *Inactivating PTH/PTHrP signaling disorders (iPPSDs): evaluation of the new classification in a multicenter large series of 544 molecularly characterized patients*– D. Ertl (fellow), A. Linglart (host)
II. *DeR Registry/ IPPSD DEtailed Registry for improvement of diagnosis and care* (a cross centre collaboration currently applying for grant funding) – D. Ertl (fellow), A. Linglart (host)
III. *Data collection for a case report on benign intracranial hypertension in obese subjects* (in draft) – C. Dave (fellow), S, Senniappan (host), L. Apperly
IV. *58 patient genetic study on congenital hypothyroidism patients presenting dyshormonogenetic thyroid* (in draft) – D Miclea (fellow), J. Leger (host), N de Roux
V. *A review manuscript on gynaecomastia in patients with DSD* (in draft) – I Kyrgios (fellow)
VI. *Profile of Diazoxide responsive congenital hyperinsulinism children* (Abstract submitted to ESPE 2021) – N. Lohiya (fellow), S. Senniappan (host)
VII. *Hyperinsulinemic Hypoglycemia in a child with Peroxisomal Biogenesis Disorder due to a Novel PEX1 mutation* (Abstract submitted to ESPE 2021) – N. Lohiya (fellow), S. Senniappan (host)
VIII. *Use of Tolvaptan in a child with SIADH post pituitary surgery* – N. Lohiya (fellow), S. Senniappan (host)
IX. *Spectrum of diabetes mellitus in patients with Shwachman-Diamond syndrome: case report and review of the literature* (in draft) – L. Navasardyan (fellow), M. Wabitsch (host)
X. *Severity of acute phase reactions after the first dose of intravenous Zoledronic acid infusion* (in draft) - L. Navasardyan (fellow), M. Wabitsch (host)
XI. *Searching for hidden cases of Maturity Onset Diabetes of the Young in a paediatric diabetes clinic - A clinical review* (in draft) – D Jeevarathnam (fellow), P Sachdev (host)
XII. *Service review of Klinefelter syndrome and variations in the clinical care* (in draft) – D Jeevarathnam (fellow), P Sachdev (host)
XIII. *A case report of siblings with MAMLD mutation is under process* (Abstract submitted to ESPE 2022) – D Jeevarathnam (fellow), P Sachdev (host)
XIV. *Successful use of sulfonylurea in the management of new onset diabetes mellitus after transplantation (NODAT) in an adolescent* (case report in draft) – K Meena (fellow), D Giri (host)

In a number of cases fellows were unable to be fully involved in research projects due to restrictions relating to COVID-19, or due to the in-person fellowship being cut short. In the past fellows who have established research projects, that take longer than the three month fellowship time-frame, have been able to revisit their host centres on their own time and continue the work. This has not been possible this year. More output projects will be added once the remaining fellowships are completed. *Figure 5* shows the number of clinical/audit/research projects and papers submitted/in development that have resulted from the ESPE Clinical Fellowship since 2017. As with the conditions seen, this information was only effectively collected from late 2018 onwards and therefore the 2017-18 intake report lower output. Similarly the 2019-20 intake report lower output due to only thirteen fellows having completed, and the pressures of COVID-19 travel restrictions.

"Based on direct contact with patients with bone and mineral disorders, which are of interest to both our research groups, we built the foundations for co-operation on future joint studies. Conducting research in co-operation with other centers of expertise, will insure a greater number of patients and therefore better data quality" – Diana-Alexandra Ertl, University Cl. Paediatrics and Adolescent Medicine, Austria

***Fig 5*. Output during the Clinical Fellowship programme**



3.2 Clinical Course, symposia, scientific conferences attended by 2019-20 fellows

As part of the allowed budget fellows are allowed to attend courses/events that would benefit them in line with the aims of the Clinical Fellowship programme. The opportunity to partake in these types of activity have been considerably limited for this intake, but some fellows have reported attending online courses. These are displayed below:

- ASPAE Annual Conference 2022
- ESPE Clinical Fellowship Spring Initiative 2021
- Diploma in Dysmorphology and Developmental anomalies, Univ Paris Diderot
- Diploma in Reproductive Endocrinology, Univ Paris Sud
- French Exchange Academy, Symposium on XLH
- EuRRECa Webinar and Calcium/Phosphate Working Group Webinar at Endo- ERN General Assembly 09-10/03/2020
- Novo-Nordisk Symposium Interdisciplinary Management in Endocrinology (Livestream am 28.01. – 29.01.2022)
- Endo-ERN 2022 meeting (Livestream on 16.02.2022)
- Interactive online course dedicated to French fellows in pediatric endocrinology (16-18/03-2020):
- 23th Annual Pediatric Endocrinology and Diabetes Congress.

- 86th Pediatric Endocrinology meeting Of Marmara group.
- In hospital meetings with pediatric surgeons for consulting DSD patients.
- I-DSD I-CAH User Group Meeting
- Metabolic/ Bone conference at Alder Hey children's Hospital Liverpool
- EASO COMs Webinar: Obesity Pharmacotherapy
- Childhood Obesity Webinar Series – CoCo Clinic

SECTION 4 – Post Clinical Fellowship outcomes

4.1 How the Clinical Fellowship will affect fellows practice upon returning to their home centres

The seven fellows who have completed their fellowships thus far all state that the experience will strongly shape their careers, and they would recommend it to their colleagues. Fellows are asked how the training received on the fellowships will change the way they practice, below are listed the ways in which they plan to improve paediatric endocrine care in their region:

- Initiated a paediatric and adolescent endocrinology clinic in Rajkot, India – **C. Dave**
- Improving patient/parent communication training with colleagues
- Investigation/project planning process improvement
- Application to a visiting consultant position in local medical college
- Initiated NGS diagnostic tests use, learnt on fellowship, to detect congenital hypothyroidism in Cluj-Napoca, Romania – **D.Miclea**
- Taking part in the national reference center for rare bone diseases and growth disorders
- Playing a key role in the application for full membership to BOND-ERN – **D. Ertl**
- Introducing the current guideline/protocol in the management of patients with endocrine problems from host centre at home centre – **U. Chikani**
- Training Junior doctors in order to arouse their interest in Endocrinology
- Have established links to send blood samples of rare monogenic cases of diabetes and/or obesity – **L Navasardyan**
- Focusing research on pseudo-hypopituitarism and achondroplasia
- Improved diagnosis of rare and difficult to diagnose disease such as iPPSD
- Improving local registries and improving collaboration with international registries, after experience collecting data for EuRRECa
- Organising educational workshops and patient information for rare diseases
- Establishing a therapeutic clinic in Azerbaijan Medical University – **G Jabrayilova**
- Improvement of English language skills for international collaboration
- Improved practice in working in a multi-disciplinary team – **N. Lohiya**
- Hope to establish the endocrine clinic as a separate department in home centre over the next few years – **D. Jeevarathnam**
- Starting a transition of care clinic with adult colleagues
- Working with biochem department for improving the quality of investigations at host centre

"The experience that I have gathered here, regarding how a national reference center provides diagnostics and follow-up to patients with rare diseases and regularly improves the medical care of these patient groups, by undergoing research in the field, will help improve our own medical strategy." – Diana-Alexandra Ertl, University Cl. Paediatrics and Adolescent Medicine, Austria

SECTION 5 – Financial aspects of the Fellowship

5.1 Expenditure breakdown for the 2019-20 intake

The funding for the 2019-20 intake was kindly provided by Merck in the form of an unrestricted grant of €60,000. This allowed the selection of fifteen fellows, to attend three month fellowship on a budget of €4000. Only thirteen of these were able to complete their fellowships. Fellows are given 80% of their allocation at the start of their fellowship, and the remaining 20% is on successful completion. The total amount spent on the fellowship in 2019-20 was **€50,247**. A financial reconciliation can be found in *Appendix 1*. Below is a graphical breakdown of expenditure on the Clinical Fellowship on the 2019-20 intake, and a summary of the expenditure on the programme as a whole since 2017.

Fig. 6 **Expenditure breakdown 2019-20 to date**

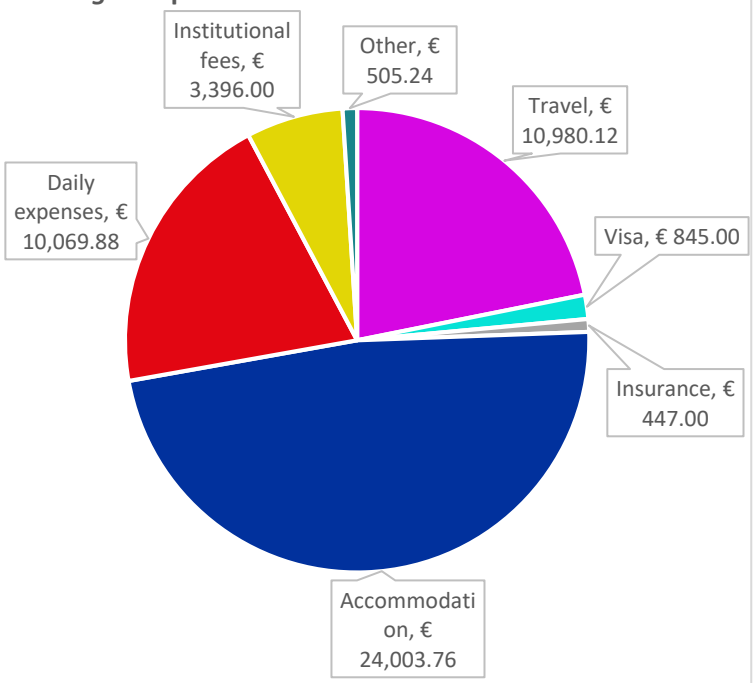


Figure 6 shows that, like in previous intakes, the highest expense is accommodation, with daily expenses and travel costs being the next two highest. It should be noted that in this particular intake travel expenses would likely be higher due to unexpected and emergency flights home, following national lockdowns. Previous expenditures can be compared to the current intake in *Figure 7* and *Figure 8*. *Figure 9 shows to the total percentage spend since 2017 for each category.* Since 2017 Merck has kindly sponsored €140,000 for the programme, with ESPE supporting with €120,000.

Fig 7. **Comparison of expenditure on the Clinical Fellowship programme since 2017**

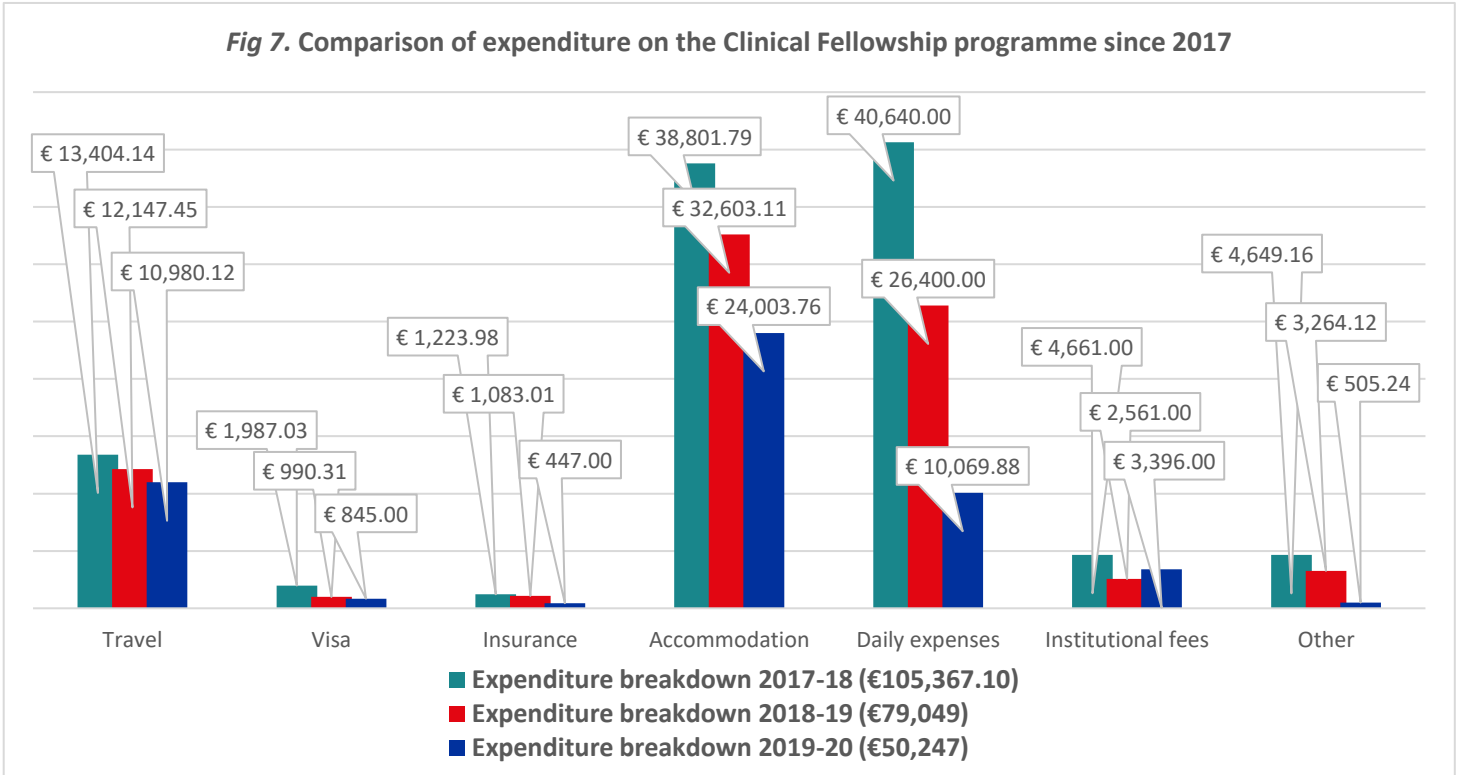


Fig 8. **Detailed breakdown of expenditure on the Clinical Fellowship programme since 2017**

	2017-18 intake	**2018-19 intake**	**2019-20 intake**	**Total**
Amount sponsored by Merck	€ 40,000.00*	€ 40,000.00**	€ 60,000.00***	€ 140,000.00
Amount sponsored by ESPE	€ 65,367.10	€ 39,049.00	€25,123.50	€ 104,416.10
	Expenditure breakdown 2017-18	**Expenditure breakdown 2018-19**	**Expenditure breakdown 2019-20**	**Total expenditure since 2017**
Travel	€ 13,404.14	€ 12,147.45	€ 10,980.12	€36,531.71
Visa	€ 1,987.03	€ 990.31	€ 845	€3,822.34
Insurance	€ 1,223.98	€ 1,083.01	€ 447	€2,753.99
Accommodation	€ 38,801.79	€ 32,603.11	€ 24,003.76	€95,408.66
Daily expenses	€ 40,640.00	€ 26,400.00	€ 10,069.88	€77,109.88
Institutional fees	€ 4,661.00	€ 2,561.00	€ 3396	€10,618.00
Other	€ 4,649.16	€ 3,264.12	€ 505.24	€8,418.52
Total expenditure	**€ 105,367.10**	**€ 79,049.00**	**€ 50,247.00**	**€234,663.10**

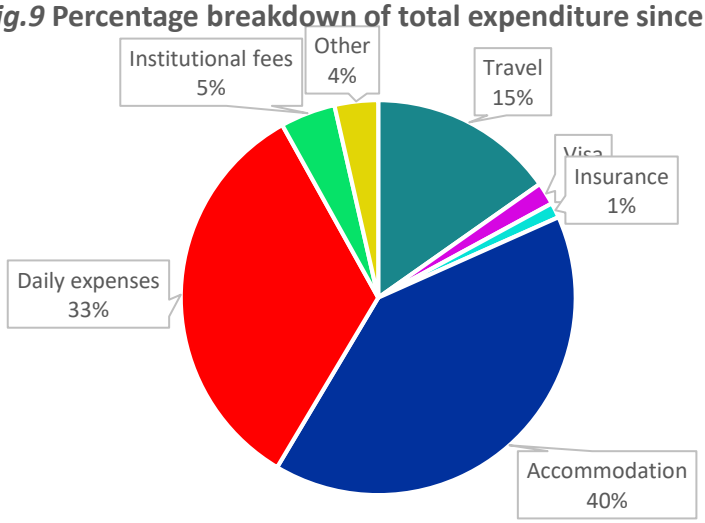
**Effective date August 2018 (applied for funding February 2018)*

***Effective date November 2018 (applied for funding September 2018)*

**** Effective date December 2019 (applied for funding September 2019)*

The Clinical Fellowship Committee decided to select fellows only conducting 3 month fellowships to a budget of €4000, to account for the funding received by Merck. Therefore €60,000 was the total budget for the fellows in this intake. ESPE has agreed, as per the contract, to match what Merck fund for the programme. In this instance, as only €50,247.00 was spent in total, both Merck and ESPE fund this intake for €25,123.50 each. ESPE also financially supports the programme by funding Bioscientifica to provide the invaluable administration support throughout the year, and for 2021 this amounted to ~€4500. ESPE also completely funded the ESPE Clinical Fellowship Spring Initiative to the amount of €7,600 + VAT.

Fig.9 **Percentage breakdown of total expenditure since 2017**



SECTION 6 – Summary

The Clinical Fellowship continues to be one of ESPE's most valued activities, from both the perspective of the membership and the organising committees. Despite the difficulties imposed by COVID-19 throughout 2020 and 2021, the programme was still able to offer an invaluable educational experience to thirteen recipients of the 2019-20 intake, and forge long-lasting relationships for future collaboration and support. Creating and maintaining connections between early-career clinicians and highly experienced, and respected, specialists in paediatric endocrinology is a key strategic aim for ESPE. Creating these bonds with young doctors, in countries that have underdeveloped paediatric endocrinology programmes, multiplies the value of the Clinical Fellowship in terms of ESPE's global strategic reach and impact on healthcare for children.

Unfortunately, due to the restrictions still in place in September 2020, the Clinical Fellowship Committee decided that selecting recipients for the 2020-21 intake would not be possible, and the fellowship took a one year hiatus. These applicants are still awaiting selection once funding is secured. In place of the 2020-21 intake programme, ESPE delivered the first ESPE Clinical Fellowship Spring Initiative to provide an online space to gather over one hundred former and current ESPE clinical fellows, their hosts and tutors as well as the 2020 applicants who missed out on the full activity. The activity was widely regarded as a success and all the content is available online. This activity was supported wholly by ESPE, and did not come under the budget of the usual Clinical Fellowship programme, however Merck was acknowledged as the sponsor of the usual programme.

All fellows who completed the 2019-20 intake stated that the support they receive during their visits was unanimously excellent. This is not only down to the commitment of the ESPE member hosts, who provide the education, but to the Clinical Fellowship mentors Professor Violeta Iotova, Dr Senthil Senniappan, Dr Maria Guemes, Dr Alina German, and Professor Paul van Trotsenburg. Their tireless efforts to find and secure placements for the fellows this year must be commended, especially given the strains imposed on them at their own home centres. The programme would not be possible if it was not for the dedication of this Clinical Fellowship Committee, and the support given by the Education & Training Committee, and ESPE Council.

"*During the course of my fellowship, I had the opportunity to either physically or virtually meet and learn about the work of eminent paediatric endocrinologists in Glasgow as well as around the UK (that were invited by members of the endocrine team in Glasgow to give a lecture). I hope to contact those, who are specialized in specific areas of research, with regards to the management of my future patients who may fall in their field of expertise*." - Ioannis Kyrgios, Papageorgiou General Hospital, Greece