Institution: University of St Andrews

Unit of Assessment: A1

a. Overview

Medical research is newly re-established in St Andrews and our overarching strategy is to foster innovative collaborative studies that delivers new knowledge in basic science, evaluates it in the field and prompts new investigations questions in an iterative cycle. This strategy has been focused on areas where we believe we can make an impact. Thus, we work on two broad areas: Molecular Medicine, based in the laboratory, and Health and Behaviour, with its roots in the community. Molecular Medicine has two broad themes; Infection and Genomics, and Translational Cell Biology. Health and Behaviour encompasses health psychology, violence reduction and adolescent health research. In support of this we have forged translational research links with health service partners in hospital and community, and have launched the Global Health Implementation Initiative that will apply our innovations in the context of the developing world.

Since the formation of the new Medical School the university has invested £45m including a major grant from the Wolfson Foundation to provide a state of the art medical photonics research facility further enhanced by £18m from the Wellcome Trust and University to build an annexe to the adjacent Biomedical Science Research Centre. A large private donation has facilitated the Global Health Initiative supporting our research in sub-Saharan Africa. The School of Medicine has been designated as a Collaborating Centre in International Child and Adolescent Health Policy by the World Health Organization (WHO). Critical staff appointments, acquisition of state-of-the art equipment, and development of research networks and patient cohorts allow us to achieve our strategic goals and set a challenging future agenda. The success of this investment is illustrated by a three-fold increase in research funding during this REF cycle.

b. Research strategy

The School of Medicine has, and continues to, invest in research leading to successful and rapid growth. In the last five years, strategic appointments have strengthened existing groups and opened new research areas. The success of our investment strategy is demonstrated by a 100% increase in the number of research active Principal Investigators and a threefold increase in research income in the last five years. Our strategy is to develop an understanding of the biological, psychological and social determinants of human health and disease and to apply that knowledge in the field to the diagnosis, treatment of individual patients and at a population level (MRC Strategic Aim 2). Our goal will be achieved through interdisciplinary working and through investment in people and facilities that together generate new knowledge for action and technology for practice. We aim to create health gain locally and internationally through our NHS and global health implementation initiative (MRC Strategic Aim 3 and MRC Research Priority Theme 2 “Living a long and healthy life.”) We have developed our recruitment and support strategy in personal and infrastructure to provide a world-class research environment in the areas where we work (MRC Strategic Aim 4).

Our underpinning philosophy is ***from academia to the field and back again***; investing in basic science, exploring applicability in practice and then reposing new biological questions amenable to further research. This allows tractable research questions to be tested in our patient populations and is designed to maximise the real world impact of our work and minimise discovery to practice delay. We have ambitious, sustainable, clearly articulated and fully funded plans for further expansion. To achieve this ambitious growth target we have invested in equipment and facilities to support genomics and pathogen/gene discovery, as well as our capacity for functional as well as descriptive characterisation of cells and tissues that informs the application of systems biology techniques to pathology and cancer. Through externally peer-reviewed funding and university support we have increased the number of PhD students significantly (see below) and aim to quadruple the student number within five years.

Molecular medicine

Infection and Genomics. Infection research is a critical focus of UK research councils and charities. It is a way of achieving the Millennium Goals and the internationally agreed targets on poverty eradication and quality of life. We have invested in this area through new appointments. **Gillespie** (appointed 2010) is chief investigator for the ground breaking phase III REMoxTB clinical trial (EDCTP €32m) the first regulatory trial of a treatment shortening regimen for tuberculosis. This work underpins a pan-European grant (PreDiCT-TB IMI 1.2m€) to study the implementation of molecular biomarkers and innovative mathematical models of tuberculosis treatment response developed through interdisciplinary collaboration between the Schools of Physics and of Applied Mathematics. **Cox-Singh** (appointed 2012) identified the role of *P knowlsei* as a zoonotic and is developing it as a model system for studying severe malaria collaborating with colleagues from the Sanger Institute. **Paracchini** has joined the school to investigate the genetic basis of dyslexia and laterality and has established a unique sample collection through collaborations in the UK and overseas and made ground breaking discoveries. We will develop our research in this area further by critical appointments in infectious diseases jointly with the NHS locally, notably **Holden** Reader in Infection Bioinformatics recruited from the Wellcome Trust Sanger Institute.

Translational Cell Biology: Combining functional characterisation of cell behaviour alongside phenotypic description and application of systems approaches to data integration and modelling, increases understanding of disease and supports rationally designed, personalised medicine and companion biomarkers. **Harrison** leads one of the clinical hubs of the CRUK Stratified Medicine Programme and has established Molecular Pathology in NHS Lothian. He led the MATLOC trial that led to FDA recognition of a new prognostic biomarker tests for prostate cancer, and he is co-PI of a Scottish-wide registry of renal cancer patients and tissues. Studies conducted after establishment of the Scottish Breakthrough Breast Cancer Research Unit (£4.9M; 2008-2012) led to the first working computational models of combinatorial therapy in breast cancer. These clinical studies complement a fully equipped cell biology and imaging laboratory. **Harrison** chairs the Steering Committee of the EU-funded Concerted Action for Systems Medicine Implementation in Europe (CASyM, €2.9M) that draws together all the St Andrews work into a larger, holistic framework. We have further invested in cell biology by the appointment of two new lecturers **Andrews** (neuronal injury) and **Tello** (neuro-endocrinology) and recruited a Royal Society of Edinburgh Fellow **Pitt**.

In the next five years we will develop molecular medicine research alongside Health and Behaviours research (see below) in concert with the Global Health Implementation Initiative (GHII) made possible by donations (£1.7m) given in order to facilitate translational research though our historical links with the College of Medicine Malawi and other worldwide collaborative networks noted above.

Health and Behaviour Directed by **Currie,** the Child and Adolescent Health Research Unit (CAHRU), moved to St Andrews in 2011. The Unit is the International Coordinating Centre of the Health Behaviour in School-Aged Children (HBSC) World Health Organisation Collaborative Cross-national Study, involving 43 countries worldwide now in its 30th year. CAHRU delivers the Scottish element supported by more than £2m funding from Scottish Government and NIHR. The Family Affluence Scale (FAS) is a key tool developed by this group and is now used internationally and is the most cited paper in Social Science and Medicine since 2008. The Medical School has now become a WHO Collaborating Centre (**Currie, Donnelly & Humphris**). We aim to expand the HBSC programme to the Middle and Far East and to Africa through the GHII. The ORION and TRIP projects led by **Humphris** supported from EU Directorate of Justice and Criminality (€0.8m) over the past 5 years has delivered: a toolkit (ORION) to reduce overdose risk in drug users. The tool which is downloadable (http://orion-euproject.com/), has attracted wide interest from many EU states, and was presented to a recent EMCDDA expert meeting in Lisbon (November 2012). The Scottish Government now recommends all Alcohol and Drug Services to use the

Figure 1. Front cover of HBSC Global Report led by St Andrews

ORION tool (June 2013). Violence, often associated with either excess alcohol usage or the illicit drug trade, is a critical area of health and social policy of international importance and our initiatives, led by **Donnelly** include the evaluation of a major gang member rehabilitation and violence reduction initiative (http://www.actiononviolence.com/content/cirv-second-year-report), the findings of which have informed Government policy both within Scotland and in England. His group is also nearing completion of a major five year study conducted in partnership with the World Health Organisation on violence policy in South Africa, Jamaica and Lithuania. **Burr** leads a collaborative multidisciplinary programme of research involving an ophthalmic research network across the UK, Europe, US and in East Asia receiving £2m in funding from NIHR/MRC. The group has developed a robust evidence base to inform policy decisions on effective and efficient models for identifying those at risk of loss of sight. These finding have been included in NICE clinical guidelines for glaucoma.

Building on success we will explore new areas of research and develop new talent. This is achieved by "seed money" from the school for equipment and studentships that allow researchers to compete for grant support from research councils. Researchers in cognate groups work closely together, proposing developments to research facilities and support networks. The school organises work-in-progress talks for graduate students and PIs as well as seminars by national and international research figures. Increasingly we are moving towards providing study days attracting international researchers to speak on a key research topics (e.g., Malaria and Pathogen Genomics http://medicine.st-andrews.ac.uk/documents/seminar-2013-06-14.pdf). Dissemination of research results is achieved beyond the conventional academic paradigm by embracing the web (http://medicine.st-andrews.ac.uk/research/), social media (Twitter), web based scholar communities (e.g., Research Gate), influencing opinion forms (e.g., parliamentarians) and advocacy with national and international groups (e.g. EMCDDA, Throat Cancer Foundation, The Cochrane Collaboration. APPGs and the Violence Prevention Alliance/World Health Organisation). Our future plan is to innovate to communicate to an even wider audience.

c. People, including:

Staffing strategy and staff development

As a small school we have made strategic appointments at all academic levels to develop internationally competitive research that supports the outstanding teaching and to ensure sustainability, resilience and a supportive environment for younger scientists. Appointments are made in line with the research strategy described above and in areas related to teaching medical students in their early years. There is a strong commitment to staff development. At a junior level the medical school has appointed a number of University Fellows: e.g., **Inchley**, **Currie**, **Zhou**, **Williams** and the latter has progressed to appointment to a lectureship. Other significant progress includes **Paracchini** appointed Royal Society Fellow, and **Pitt** Royal Society of Edinburgh Fellow.

St Andrews University values its Post graduate research students (PGR) and research staff as key cohorts in its research community. The University meets all the key principles of the *Concordat* regarding the recruitment, selection and retention of researchers; the recognition of the value of researchers to the institution; the development of generic and flexible skills; the promotion of personal and career development, the promotion of diversity and equality practices; and the regular review of progress. The success of St Andrews in this area has recently been acknowledged by an Athena Swan Bronze Award and a European Commission HR Excellence in Research Award. **Paracchini** leads our submission for a bronze award within the School. It also actively promotes our Stonewall membership and LGBT Charter Mark, and supports Women in Science networking events as a means of ensuring equality across all our practices.

Alongside the School level skills training for graduate students and staff; training is augmented via an award-winning generic skills training programme (GRADskills) which is run the by University's Centre for Academic, Professional and Organisational Development (CAPOD). GRADskills aims to develop and support the acquisition of generic transferrable skills with a view to increasing research effectiveness and widening the potential employability opportunities of young researchers. Many research staff engage with a university-wide mentoring scheme (run jointly with the University of Dundee) where research staff can choose to be mentored by an

experienced member of staff from either institution.

Career development support The allocation of lecturing and administrative loads takes account of the need to grow research activity and support career development. Much core teaching and administration is undertaken by teaching fellows, thus protecting research time of new lecturers. Newly appointed research staff have a reduced teaching load for up to three years and can be granted research leave of one semester in eight. The School has a Discretionary Strategic Innovation Fund to support new developments such as pilot experiments for new interdisciplinary research, support the development of external research collaborations, and facilitate key external collaborations to engender.

Research students

The School holds a Wellcome Trust INSPIRE award **Harrison** promoting research amongst medical students. The School has prioritised growth in post-graduate student numbers as a key strand in its strategy. Many projects are multidisciplinary jointly supervised with Applied Maths, Biology, Chemistry Geography, Physics and Psychology, providing PGR students at the School with a wealth of opportunities for innovative research. The number of graduate research students has more than doubled in the last five years and will be expanded through the 600th anniversary scholarship programme. We are a partner in a number of University-wide funding schemes e.g. the MRC virology DTG and a donation of £0.6m is facilitating further development in MD studentships and PhD students from sub-Saharan Africa. At St Andrews, postgraduate research (PGR) students are inducted into St Leonard's College and are able to take advantage of generic skills training provided by the University through a highly commended programme (CAPOD and GRADskills http://www.st-andrews.ac.uk/capod/students/pgresearch/ and specialist mathematics support.

Students learn presentation skills and other transferable skills by participating in the annual Research Symposium organised by the School of Medicine, as well as weekly Work in Progress (WiP) meetings and Seminar speaker events. Postgraduate students are formally assessed by their thesis review committee (2 academic staff) at regular intervals during their studies; twice in their first year and then annually. Progression after the first year is contingent on a satisfactory 10 month report, a successful viva, review of written work and transferable skills training of each student. Each student is interviewed yearly to identify additional training requirements or support. (http://www.st-andrews.ac.uk/staff/policy/tlac/postgraduate/research/)

d. Income, infrastructure and facilities

The ability of the Medical School to achieve our research objectives has been transformed by the £45M investment in the new Medical School building, the £18M Wellcome Trust and University investment Biomedical Science Research Centre extension and strategic appointments. As well as state of the art laboratory facilities, the building has been designed to optimise support for PhD students by co-location with post-doctoral researchers and principle investigators. Co-location on the North Haugh with the Science schools has driven cross-disciplinary innovation harnessing developments in physics and chemistry for application to biomedical problems. The Global Health Implementation Initiative has opened new collaborations with Geography, International Health and the Business School. We have also appointed a Professor of obstetrics and gynaecology (**Stones**) and a Senior Lecturer in paediatrics (**O'Hare**) who will be located in Malawi associated with the College of Medicine in Blantyre.

Research cohorts

We have growing research links with the NHS (Harrison is Director of Laboratory Medicine, NHS Lothian) and we hold regular meetings with NHS Fife and Tayside research groups with multiple joint grants. Having established our laboratory and office based research within St Andrews we will promote target finding and product evaluation in community settings locally and internationally. We have developed important community cohorts through the research clinics we have established and our network of GPs who facilitate recruitment of patients with diabetes, inflammatory airways and cardiovascular disease. Accessing the Scottish Health Informatics databases facilitates this growing initiative. Through NHS Fife, Lothian and Tayside we have access to extensive bio-

repositories of clinically annotated diseased samples. The PanACEA consortium (EDCTP €27m) http://panacea-tb.net/, and (PANBIOME EDCTP 1.2m€) together these studies bring together 30 clinical trial sites in Africa, Asia and the Americas and provide unrivalled access to specimen sets and the capacity to test clinical and diagnostic methodologies that will form the basis of future trials. To support pathogen discovery patient cohorts have been recruited in collaboration groups in with UK, France Africa and South East Asia.

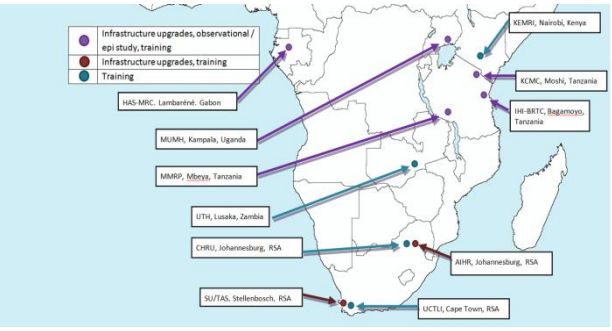

Figure 2. Distribution of African collaborators in the PanACEA consortium

Molecular medicine

Infection and Genomics we have developed improved sequencing and bioinformatics facilities with funding from the Wellcome Trust and we have enhanced infrastructure and appointed an infectious diseases bio-informatician at Reader level. This development has created novel collaborations across the university creating a bioinformatics critical mass within St Andrews. There has been extensive investment in facilities for research in molecular medicine focussed in four areas: Medical Photonics and Engineering**,** Genomics and bio-informatics, imaging, and cell biology. The new Medical School Building and BMS annexe provide comprehensive state of the art laboratories providing facilities for next generation sequencing and bioinformatics facilities with category 3 containment.

Medical photonics as a world-leading focus for inter disciplinary research in St Andrews was initiated by a grant from the Wolfson Foundation. The programme links Medicine with the School of Physics supported by collaborative grants (CRUK/EPSRC/MRC/NIHR £1.36m**,** PreDiCT-TB €1.2m) and built on the initial funding provided for the Interdisciplinary Centre for Medical Photonics. Of note is our dedicated photonics suite with five interlocked laser suites, a tissue culture laboratory, a robot for surgical device testing, including two haptic controllers. Optimal Raman spectroscopy facilities are applied to the diagnosis of malignant cells and dormant cell states in mycobacteria. Medical rapid prototyping is now available to develop medical devices at affordable cost linking to the Global Health Implementation initiative. Innovative diagnostic imaging and source design are used for cardiac screening (Scottish Enterprise £450K), and photodynamic therapy.

Translational Cell biology the School has invested heavily to establish a multi-user cell biology facility. This provides a suite of tissue culture rooms, including a hypoxia work-station and the facility to grow cells lines and primary tissues in three dimensions. Proteomics includes automated, quantitative, multichannel immunofluorescence microscopy, reverse phase protein array technology and LiCor Odyssey reader with Vigene software. A Celigo^{TM} cytometer allows sequential semi-automated measurement of cell growth in two or three dimensions over time and tracking of fluorescent-labelled cells. All of these technologies generate high quality, reproducible data that is used for computational systems modelling. Slide scanning and web based access facilitate secure transfer of image data, and use of Definiens Developer image analysis software allows quantitation of biomarkers in situ and measurement of other parameters to facilitate modelling. We have new imaging facilities including the recent acquisition of SIM super-resolution capability combined with ground breaking laser poration and RAMAN imaging for diagnostics, EM-based quantitative wide-scale morphomics providing protein and lipid based mapping integrated with unbiased 3D quantitation of structures and an Arcturus Laser Capture Microscope.

People and populations

Coordinated from the School of Medicine, Health Behaviour of School age Children (HBSC) is a unique international study that has developed new indicators of health and its social determinants among adolescents. Through the GHII we plan to expand this initiative globally. The Health Psychology group have a secure entry coding room to code, analyse and store both audio and video recording of confidential clinical interactions. This is a unique facility that includes sophisticated 'bespoke' coding software (The Observer XT system) supplied by Noldus. The

facility has been enhanced by an eye-tracker system makes this a cutting-edge, internationally recognised research facility. We provide one of three coordinating centres for the Verona CoDES system. The People and Populations group also benefits from linkage into the Social Dimensions of Health Institute, the Scottish Institute for Policing Research and the Scottish Violence Reduction Unit as well as the Violence Prevention Alliance and WHO.

Management and Governance Our research laboratories are working towards Good Laboratory Practice. The School has its own Ethics Committee (SEC) convened by **Humphris** who also convenes the University Teaching and Research Ethics Committee. This enables efficient and secure management of crucial ethical matters. Access to human tissue, including cohorts with detailed clinical history and follow-up, is achieved primarily through a Material Transfer Agreement with NHS Lothian where **Harrison** is Designated Lead for Tissue Governance, and also from NHS Fife. The Director of Research (DoR) is a member of the School Executive and Management Groups integrating the research agenda into all academic business. The strategic direction and allocation of research resources through the Research Management Group chaired by the DoR. A monthly meeting of Principal Investigators manages the research facilities, optimises applications, coordinates outreach and provides support for career development.

e. Collaboration and contribution to the discipline or research base

National and international research leadership. High priority is accorded to leading and partaking in large scale, international research collaborations and networks for each of the focussed areas of science that shape research direction, policy development and contribute new knowledge. **Currie** coordinates a 32 Country World Health Organisation Collaborative Cross-national Group for Health Behaviour in School-Aged Children (HBSC), in adolescent health research. **Cox-Singh** leads a 14 partner international consortium addressing *Plasmodium knowlsei* pathogenesis. **Donnelly** helps lead several important international collaborations on violence prevention, for example The Violence Prevention Alliance. **Gillespie** leads the PanACEA consortium (3 European 13 African collaborators) and he is a co-leader of the PreDiCT-TB consortium (22 European partners) and Predicting Antibiotic Resistance (PAR), a consortium of 11 EU partners. **Harrison,** chairs the steering group of the 20 partner Co-ordinating Action for Systems Medicine (CASyM https://www.casym.eu) and as vice-Chair of the Gene Therapy Advisory Committee chaired the group that delivered the first roadmap for clinical trials using stem cells. **Humphris** leads 8 EU partners in the ORION Drug Addiction Research Programme. **MacDougall** serves on the Board for Academic Medicine.

Wider influence:

Guideline development: **Burr** and **Gillespie** contribute to Scottish Intercollegiate Guidelines Network (SIGN) (Burr, glaucoma; Gillespie on Council). **Currie** is on the WHO ARIA guidelines committee. **Harrison** contributed to Scottish Government policy development on the use of human tissue for research and **MacDougall** serves on the MHRA/CSM advisory committee on the Safety of Medicines.

NHS and professional leadership: **Donnelly** is a member of NHS Scotland Leadership Board. **Gillespie** is Council and Executive Member Royal College of Pathologists and Chair Scottish Regional Council, formerly Chair of Microbiology Specialty Committee and Joint Committee in Infection and Tropical Medicine. **Harrison** is deputy-Chair Committee on Toxicity and Director of Laboratory Medicine in NHS Lothian comprising 19 laboratories in all disciplines.

Translational implementation and service development: **Harrison** has introduced molecular pathology and consolidated molecular diagnostics in NHS Lothian. **Gillespie** and **Harrison** are leading implementation of molecular microbiology testing with robust delivery models.

Advisory roles: **Currie** is International Advisory Board Member of European Schools for Health Network and Scientific Advisor to EuroHealthNet. **Gillespie** is a member of Wellcome Trust Pathogen Variation SAB and PathoNGenTrace Ltd. **Harrison** is on the SAB of the €50M German Virtual Liver Network, Melville and Cunningham Trusts.

Interaction with industry and the economy: **Harrison** is Director of Innovation for Medtech in the new NHS Scotland Health Innovation Partnership (HIP), a Board Member of the Scottish Lifesciences Association with a portfolio of more than 20 Scottish biotech companies. **Jackson** has received enterprise funding to roll out a point-of-care diagnostic device into the community.

Peer Review:
School of Medicine personnel contribute to peer review leading and contributing to grant giving Boards e.g., **Burr**, NIHR HTA Clinical Evaluation and Trials Board, **Donnelly** Milbank Memorial Fund. **Gillespie**, MRC Infection and Immunity Board (2006-10 and 2012) National Institutes of Health (USA). **Harrison**, Chair, Medical Research Scotland, Chair, Melville Trust; **MacDougall** NIHR Senior Fellowship Selection Panel, **Powis,** Chair Experimental and Translational Medicine Research (Chief Scientist Office Scotland). Our staff review for International funders and are members of journal editorial boards in their respective disciplines.

National and International Meetings organised or chaired include
Cecil; VIVA congress http://www.vivacongress2013.co.uk/ **Currie;** 30th International conference HBSC study: WHO collaborative cross-national study, June 20-21 2013 **Cox-Singh;** Pathogen Genomics and Genetics, **Donnelly;** Safety and Violence Initiative (SAVI) University of Cape Town in South Africa 2011 and WHO Milestones meeting (both co chair), **Gillespie;** Joint Symposium on Antibiotic Resistance (Royal College of Pathologists, Royal College of Physicians of London and Royal College of Veterinary Medicine (www.rcvs.org.uk/news-and-events/past-events/joint-symposium-on-antimicrobial-resistance), **Harrison**, Systems Medicine Workshops in lung, public health and infection, St Andrews, May, 2013. **Humphris**; International Conference for Communication in Healthcare, 2012.

Health Service: Almost uniquely St Andrews is active academically in three health boards, Fife, Lothian and Tayside. All senior academic clinicians hold honorary posts in Fife and **MacDougall** serves on the NHS Fife Health Board. **Gillespie** and **Harrison** also hold consultant positions in NHS Lothian. **Donnelly** chairs the NHS Scotland clinical leadership development program steering board and serves on the Scottish Governments Drug strategy delivery commission. **Harrison** Director Laboratory Medicine in Lothian providing laboratory services to Edinburgh, St Andrews and Strathclyde Universities facilitating rapid translation from academic laboratory to clinic and community. A particular strength has been the collation of patient cohorts, for example 5,000 community based patients with asthma in Fife for genetic studies (**Jackson**), and numerous clinically annotated tissue collections in NHS Lothian which in 2012 released more than 9,000 tissue samples to a wide variety of researchers in UK and more than 1,200 internationally (directed by **Harrison**). **Harrison** directs a molecular pathology laboratory and CRUK Clinical Hub providing NHS service and research support, where the senior NHS consultant holds an honorary position in St Andrews. Enhancing NHS connectivity through developing East of Scotland research nodes in our areas of research interest will be an important goal for the next cycle. **Harrison** was involved in setting up the Scottish NHS Health Innovation Programme (HIP) to bring together industry, NHS and academia; he is currently Director of Innovation for the evolving Medtech HIP.

Honours/Fellowships: **Currie,** 2008, OBE, services to healthcare and Scottish Woman of Influence award, **Carnochan,** 2013, OBE for work on violence reduction; **Paracchini**, 2011, Royal Society University Research Fellowship; **Pitt,** 2013, RSE/Caledonian Research Fund Biomedical Research Fellowship.

Outreach activities: We endeavour to make disseminate research findings to the most appropriate constituencies as quickly as possible through a multiplicity of media, and where possible to support a new users specific needs through expert engagement. The use of web and social media (including a dedicated School site) is used to promote our research findings. The University supports the hosting of international conferences hosting for example, the conference that marked the 30th anniversary of HBSC was held in St Andrews in June 2013.