

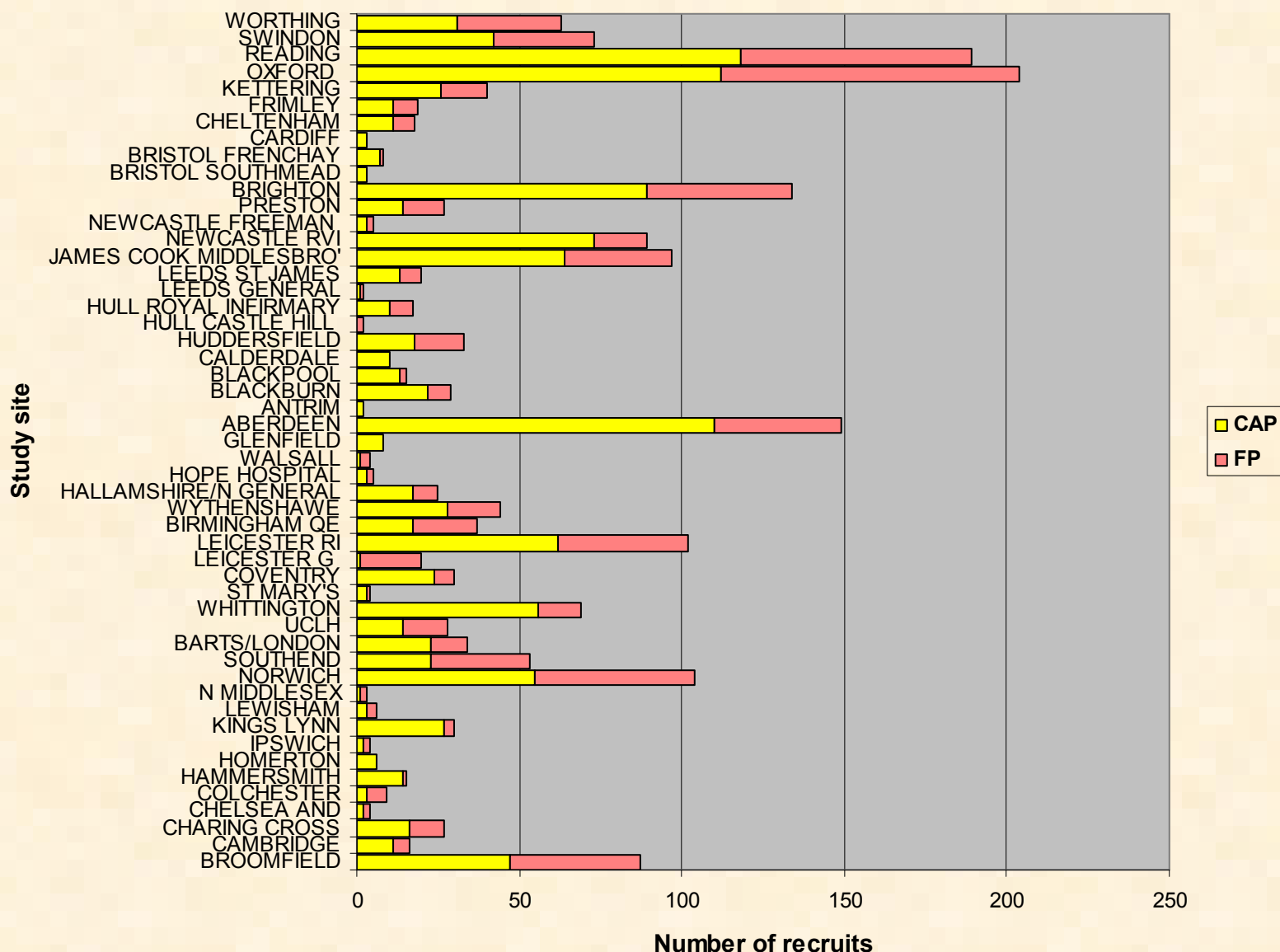


G A i n S

Newsletter Dec 2013 No. 11



Subjects recruited to GAinS to 05.12.13



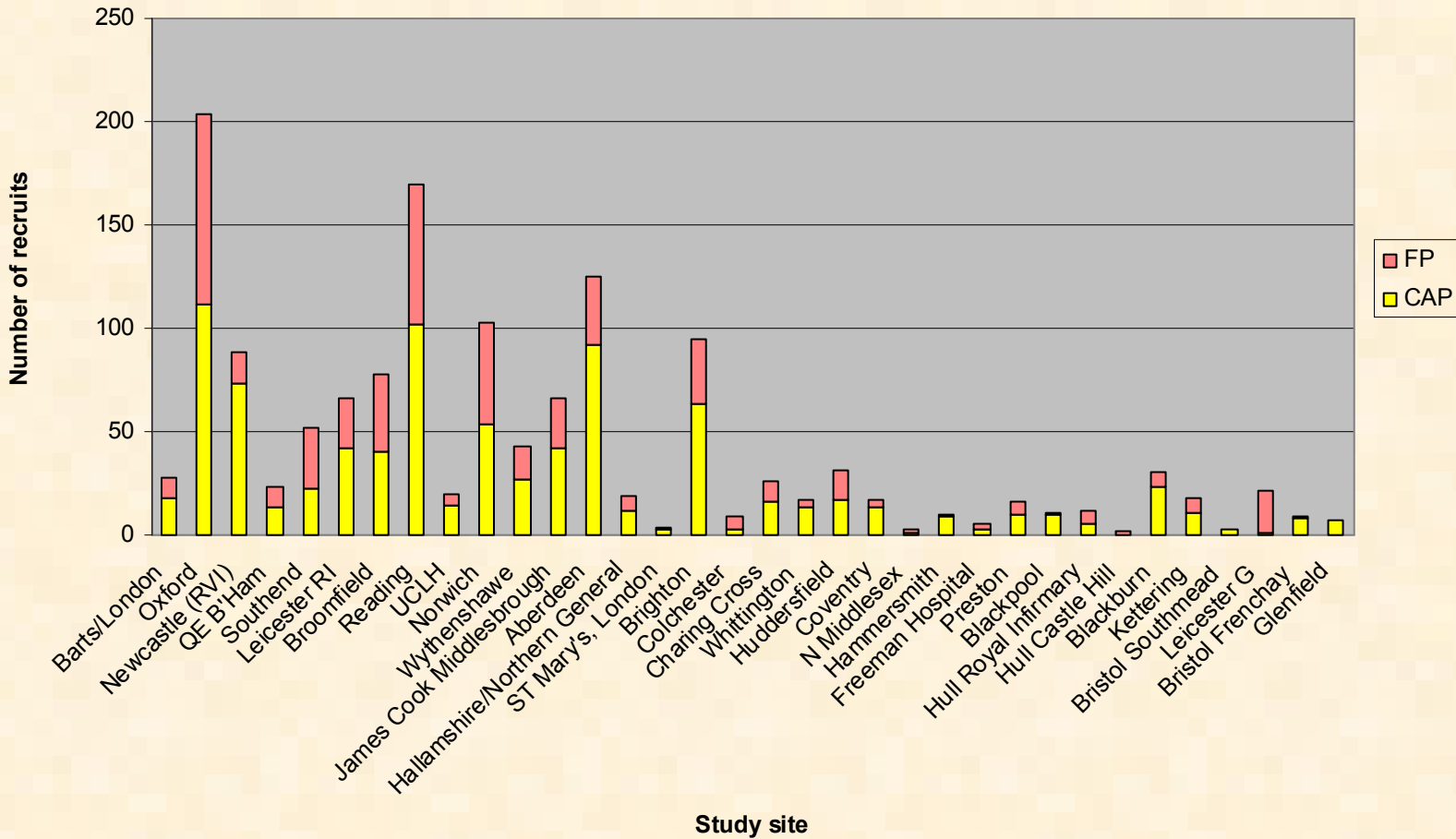
Thanks to all investigators and research nurses for your commitment to the project!

Serial Sampling



Although GAINs has been scaled down and stopped at a number of study centres we are still recruiting some patients with CAP or FP for serial sampling in a limited number of sites. For sites that have ended GAINs; If anyone still has any serial samples or supplies at their study sites please do let us know so that we can arrange for their collection.

Serial sample patients in GAINs to 05.12.13



Excellent progress, we still have 7 sites collecting serial samples for the gene expression element of the GAINs study.

1033 patients have been recruited and 1690 sets of samples have been obtained. These patients are all included in the portfolio accrual figures. Don't forget we need to have your serial sample logs at the end of each month in order to upload the accrual figures – this is absolutely vital as it is the process by which your CLRN will be able to assess your research activity and determine future funding.

Serial sample supplies

When you are down to your last 3 filters please send an email to ICUGeneticresearch@orh.nhs.uk to request more serial sampling supplies.

2025 in GAINs



By December 5th 2013 2159 patients (752 with faecal peritonitis and 1273 with community-acquired pneumonia), the remainder being Pancreatitis and Meningococcal disease, had been recruited to GAINs and GenOSept.

| STUDY SITE | CAP | FP | P | MD | UNK | TOTALS |
|--------------------------|-----|----|----|----|-----|--------|
| Broomfield | 47 | 40 | 3 | 1 | 0 | 91 |
| Cambridge | 11 | 5 | 4 | 0 | 0 | 20 |
| Charing Cross | 16 | 11 | 0 | 1 | 0 | 28 |
| Chelsea & Westminster | 2 | 2 | 0 | 0 | 0 | 4 |
| Colchester | 3 | 6 | 3 | 0 | 0 | 12 |
| Hammersmith | 14 | 1 | 0 | 0 | 0 | 15 |
| Homerton | 6 | 0 | 0 | 0 | 0 | 6 |
| Ipswich | 2 | 2 | 0 | 0 | 0 | 4 |
| Kings Lynn | 27 | 3 | 8 | 0 | 0 | 38 |
| Lewisham | 3 | 3 | 0 | 0 | 0 | 6 |
| N Middlesex | 1 | 2 | 0 | 0 | 0 | 3 |
| Norwich | 55 | 49 | 14 | 3 | 0 | 121 |
| Southend | 23 | 30 | 1 | 0 | 0 | 54 |
| Barts/London | 23 | 11 | 5 | 0 | 0 | 39 |
| UCLH | 14 | 14 | 1 | 0 | 0 | 29 |
| Whittington | 56 | 13 | 0 | 0 | 0 | 69 |
| St Mary's | 3 | 1 | 0 | 0 | 0 | 4 |
| Coventry | 24 | 6 | 0 | 0 | 0 | 30 |
| Leicester G | 1 | 19 | 0 | 0 | 0 | 20 |
| Leicester RI | 62 | 40 | 4 | 2 | 2 | 110 |
| Birmingham QE | 17 | 20 | 4 | 1 | 0 | 42 |
| Wythenshawe | 28 | 16 | 3 | 1 | 0 | 48 |
| Hallamshire/N General | 17 | 8 | 0 | 0 | 0 | 25 |
| Hope Hospital | 3 | 2 | 0 | 0 | 0 | 5 |
| Walsall | 1 | 3 | 0 | 0 | 0 | 4 |
| Glenfield | 8 | 0 | 0 | 0 | 0 | 8 |
| Aberdeen | 110 | 39 | 5 | 0 | 0 | 154 |
| antrim | 2 | 0 | 0 | 0 | 0 | 2 |
| Blackburn | 22 | 7 | 0 | 0 | 0 | 29 |
| Blackpool | 13 | 2 | 0 | 0 | 0 | 15 |
| Calderdale | 10 | 0 | 0 | 0 | 0 | 10 |
| Huddersfield | 18 | 15 | 0 | 0 | 0 | 33 |
| Hull Castle Hill | 0 | 2 | 0 | 0 | 0 | 2 |
| Hull Royal Infirmary | 10 | 7 | 0 | 0 | 0 | 17 |
| Leeds General | 1 | 1 | 0 | 0 | 0 | 2 |
| Leeds St James | 13 | 7 | 1 | 0 | 0 | 21 |
| James Cook Middlesbrough | 64 | 33 | 0 | 0 | 0 | 97 |
| Newcastle RVI | 73 | 16 | 3 | 0 | 0 | 92 |
| Newcastle Freeman | 3 | 2 | 0 | 0 | 0 | 5 |
| Preston | 14 | 13 | 0 | 0 | 0 | 27 |
| Brighton | 89 | 45 | 14 | 0 | 0 | 148 |
| Bristol Southmead | 3 | 0 | 0 | 0 | 0 | 3 |
| Bristol Frenchay | 7 | 1 | 0 | 0 | 0 | 8 |
| Cardiff | 3 | 0 | 0 | 0 | 0 | 3 |
| Cheltenham | 11 | 7 | 3 | 1 | 0 | 22 |
| Frimley | 11 | 8 | 6 | 2 | 0 | 27 |
| Kettering | 26 | 14 | 0 | 0 | 0 | 40 |
| Oxford | 112 | 92 | 11 | 2 | 0 | 217 |
| Reading | 118 | 71 | 13 | 1 | 0 | 203 |
| Swindon | 42 | 31 | 10 | 0 | 0 | 83 |
| Worthing | 31 | 32 | 1 | 0 | 0 | 64 |



Publications

“Patients with community acquired pneumonia admitted to European Intensive Care Units: an epidemiological survey of the GenOSept cohort”. Walden et al and the ESICM/ECCRN GenOSept Investigators—a revised version has been submitted to *Critical Care*

Dalli J, Melendez TM, Norling LV, Yin X, Hinds C, Haskar D, Mayr M, Perretti M. Heterogeneity in neutrophil microparticles reveals distinct proteome and functional properties. *Mol Cell Proteomics* mcp.M113.028589. First Published on May 8, 2013, doi:10.1074/mcp.M113.028589.

Mills TC, Rautanen A, Elliott KS, Parks T, Naranbhai V, Ieven MM, Butler CC, Little P, Verheij T, Garrard CS, Hinds CJ, Goossens H, Chapman S, Hill AVS. IFITM3 and susceptibility to respiratory viral infections in the community. *Journal of Infectious Diseases* 2013 (in press).

Tridente A, Clarke GM, Walden A, McKechnie S, Hutton P, Mills GH, Gordon AC, Holloway PAH, Chiche J-D, Bion J, Stuber F, Garrard C, Hinds C and the GenOSept Investigators. Patients with faecal peritonitis admitted to European Intensive Care Units: An epidemiological survey of the GenOSept cohort. *Intensive Care Medicine* 2013; (in press).

Jesmond Dalli, Lucy V Norling, Trinidad Montero-Melendez, Donata F Canova, Hazem Lashin, Anton M Pavlov, Gleb B Sukhorukov, Charles J Hinds & Mauro Perretti. Microparticle alpha-2-macroglobulin enhances pro-resolving responses and promotes survival in sepsis. *EMBO Molecular Medicine* 2013 (in press).

A manuscript reporting the results of the GenOSept Genome Wide Association Study (GWAS) is in the final stages of preparation for submission to the *New England Journal of Medicine*.

A number of other publications are planned for 2014.



Published abstracts and free paper presentations

Radhakrishnan J, Svoren E, Ellis P, Langford C, Hutton P, Garrard C, Hinds CJ, Knight J and the GAINs Investigators. Evolution of gene expression signatures in septic shock due to community-acquired pneumonia. *Journal of the Intensive Care Society* 2009; 11: 60.

Dalli J, Radhakrishnan J, Yin X, Knight JC, Hinds C, Peretti M and the GAINs Investigators. Neutrophil microparticles and their contents as potential novel biomarkers in sepsis. *Journal of the Intensive Care Society* 2011; 12: 72.

Tridente A, Clarke GM, Walden A, McKechnie SR, Hutton P, Martynoga R, Mills GH, Gordon AC, Stueber F, Garrard C, Hinds C. Epidemiology of faecal peritonitis in the GenOSept cohort. *Intensive Care Medicine* 2011; 37: S199.

Radhakrishnan J, Svoren EM, Ellis P, Langford C, Hutton P, Davenport E, Thorpe A, Garrard C, Knight JC, Hinds CJ and The Genomic Advances in Sepsis (GAINs) Investigators. A functional genomics approach to the identification of biomarkers of survival in severe sepsis due to community acquired pneumonia. *Intensive Care Medicine* 2011; S200.

Knight JC. Altered gene function in sepsis. Invited oral presentation at the Intensive Care Society, State of the Art Meeting London December 2011.

Rautanen A et al. Genome-wide association study of sepsis mortality in Europe, presented at the "Host genetic control of infectious diseases" Conference, Paris September 2011.

Knight JC, Berlanga-Taylor A, Hinds CJ. Vitamin D supplementation in severe sepsis on the intensive care unit. Oral presentation and runner up, 2011 Research Prioritisation Exercise of the Intensive Care Foundation at the Intensive Care Society State of the Art Meeting 2011, London December 2011.

Radhakrishnan J, Svoren E, Ellis P, Langford C, Hutton P, Davenport E, Thorpe A, Garrard C, Hinds CJ, Knight JC and the GAINs Investigators. A functional genomics approach to the identification of biomarkers of survival in severe sepsis due to community-acquired pneumonia. Oral presentation at the Annual Congress of the European Society of Intensive Care Medicine, Berlin Germany October 2011 (winner of International Sepsis Forum Research Award).

Radhakrishnan J, Svoren E, Davenport E, Ellis P, Langford C, Garrard C, Hinds CJ, Knight JC and the GAINs Investigators. Functional genomics of severe sepsis in patients with community acquired pneumonia and faecal peritonitis. Oral presentation for Gold Medal (Radhakrishnan, finalist) Intensive Care Society State of the Art Meeting London December 2012.

Mills T et al. "Genome-wide association study for susceptibility to sepsis in Europe—methodology" presented at the "Infectious disease genomics and global health" Conference, London October 2012.

Emma E. Davenport, Jayachandran Radhakrishnan, Peter Humburg, Tara C. Mills, Paula Hutton, Chris Garrard, Charles Hinds, Julian C. Knight and The GAINs Investigators Mapping expression of quantitative trait loci in a clinical setting: insights from sepsis The Genomics of Common Diseases Conference, Keble College, Oxford September 2013,

Emma E. Davenport, Jayachandran Radhakrishnan, Peter Humburg, Tara Mills, Paula Hutton, Chris Garrard, Charles Hinds, Julian C. Knight and The GAINs Investigators Resolving regulatory genetic variants in severe sepsis due to community acquired pneumonia by mapping context specific expression quantitative trait loci. American Society of Human Genetics, , Boston, USA October 2013

A.Ndungu, K.S. Elliott, T. Mills, P. Hutton, C. Garrard, J.A. Scott, A. Gordon, C.J. Hinds, A.V.S. Hill, S.J. Chapman and the GenOSept Investigators Exome sequencing reveals a novel putative risk mutation for meningococcal disease. American Society of Human Genetics, , Boston, USA October 2013

Tara C. Mills, Anna Rautanen, Emma Davenport, Paula Hutton, Julian C. Knight, Thomas Meitinger, Chris Garrard, Frank Stueber, Charles Hinds, Adrian V. S. Hill, and the GenOSept Investigators Genome-wide imputation in multiple cohorts to study susceptibility to sepsis in Europe. American Society of Human Genetics, , Boston, USA October 2013

(Three poster presentations will be displayed at the SOA December 2013 meeting)



Future of GAINs!

We have established one of the largest and most comprehensive patient cohorts assembled to date in the field of sepsis genetics.

We aim to move into the next phase of GAINs in 2014. We plan to study how genes and the environment interact based on epigenetics. It is likely this work will involve much more complex laboratory processes and is therefore likely to be performed in a smaller number of centres initially.

Plans for this next stage of GAINs are now underway.

Collaborative Research

Do you have any original research questions that could be answered by examining the GenOSept/GAINs data and sample collection?

If so, you might wish to discuss the possibility of collaborative research with Prof Charles Hinds.

Written applications will be reviewed by the UKCCG management committee

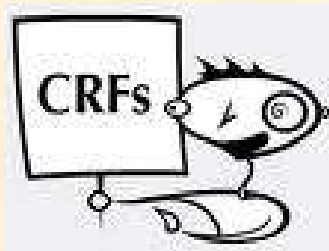


Patient Recruitment Packs

When you are down to your last 3 patient recruitment packs (containing the paper CRFs, 10ml EDTA blood tubes and blue postage containers etc), please send an email to Charles Mein c.a.mein@qmul.ac.uk at the Genome Centre in London to request more. If you are taking serial samples please ensure that you also request bar codes for serial sampling at the same time.

Postage of paper CRFs:

Please only use the A5 size paper CRFs to send to us in Oxford. This is because postage is pre-paid for the smaller, lighter CRFs and the post office are not delivering packages which are 'overweight'.



Data Quality

Quality assurance work is still ongoing for both the GAInS and GenOSept data sets. Over 3,790 CRFs have been reviewed by Alex, Penny and Paula in Oxford and more than 17,600 data queries have been created.

We are working through the eCRFs as quickly as we can.

Please remember to review all your patients in the eCRF at least weekly to look for any DQs that may have been created (follow the red icons!) and please answer them as soon as possible.

Clearly it is essential that phenotypic datasets are complete if patients are to be included in the various analyses.

CRF questions

CRF questions and answers can be found on the UKCCG website:

<http://www.ukccg-gains.org/>

select 'technical information'.

Of course you are welcome to contact us at any time by phone or email with any questions you may have about the studies. Please see contact details below.

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Merry 
Christmas 

Thank you and wishing you a very Merry Christmas and a prosperous New Year!

We would like to **thank you all** for the extraordinary support that you have given the GAInS project, enabling the establishment of one of the largest and most comprehensive patient cohorts assembled to date in the field of sepsis genetics.