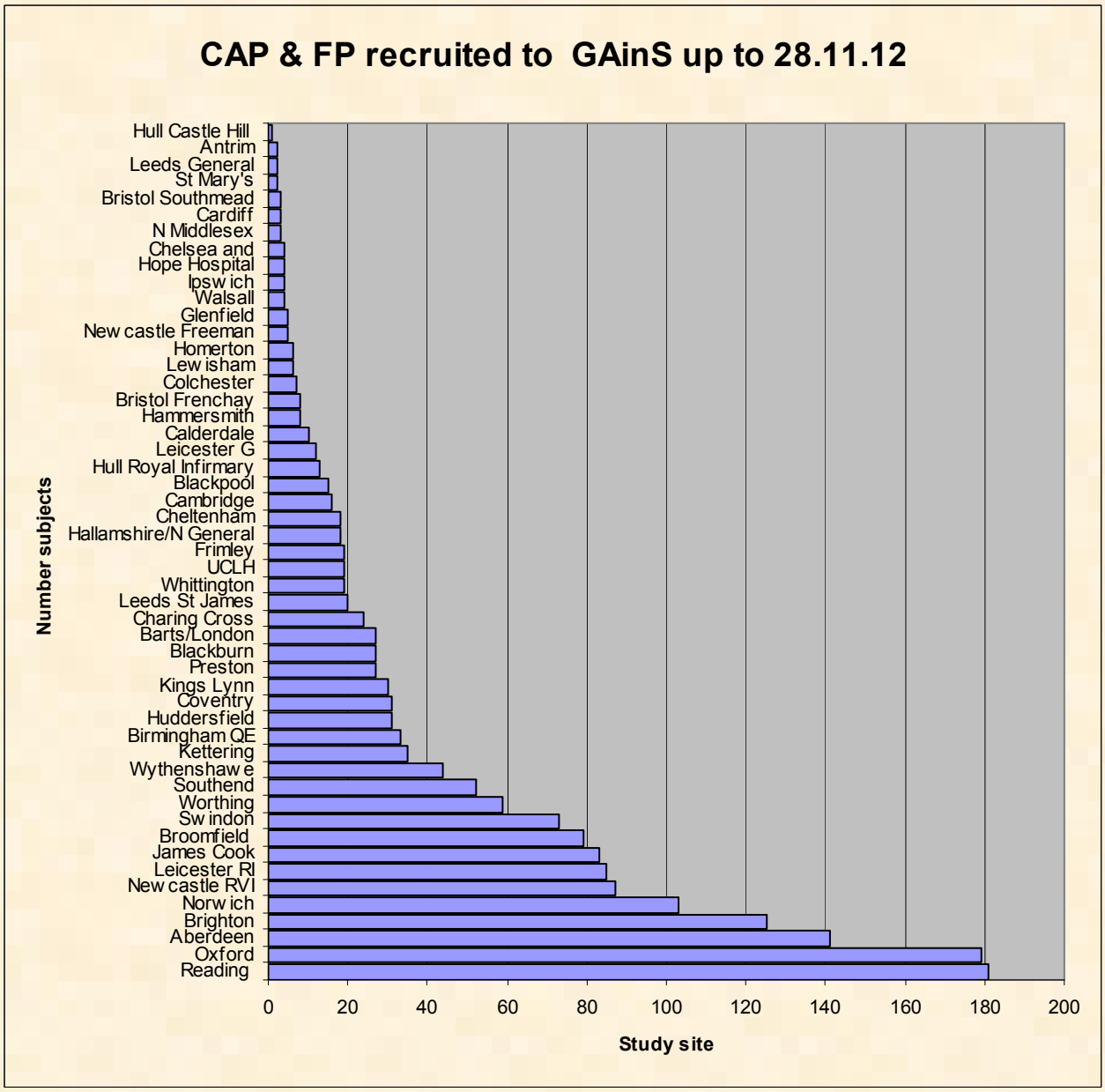
GAinS

Newsletter Nov 2012 No. 10

3631 patients recruited to GAinS/GenOSept!!



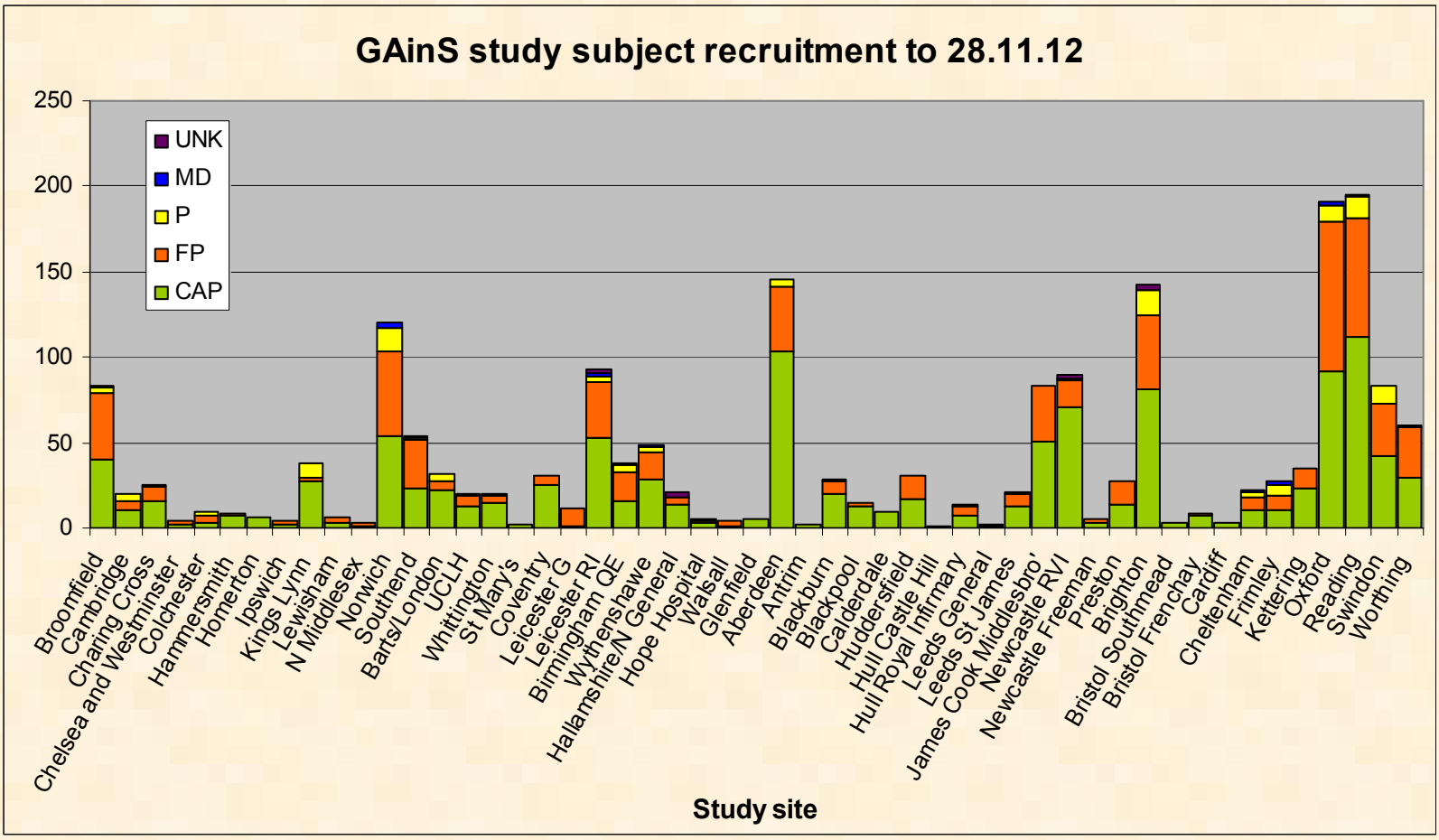
A fantastic effort from all the centres and our thanks to all investigators and research nurses for your continued commitment to the project!

1812 in GAinS

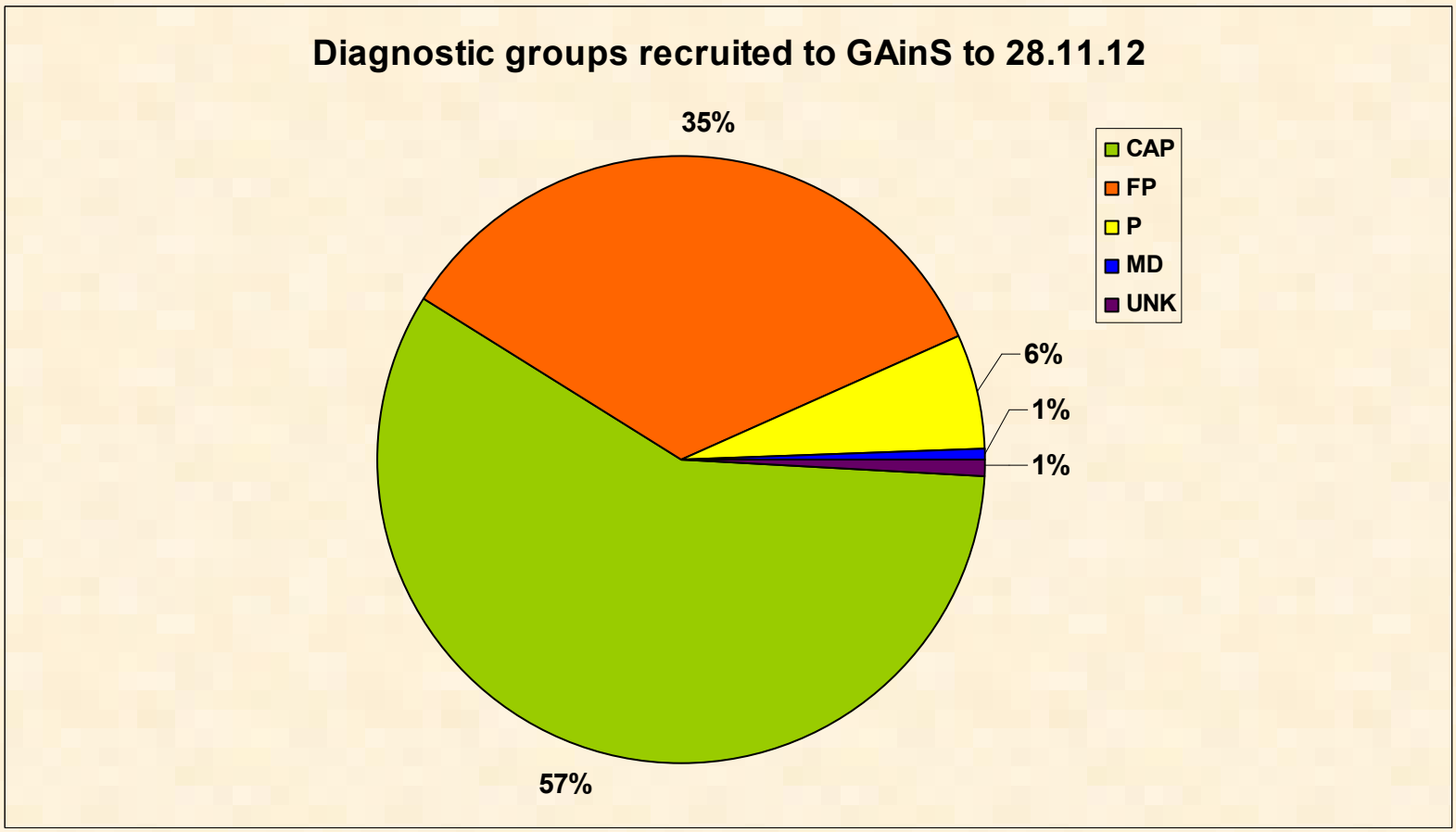
By the end of November 2012 1956 patients (679 with faecal peritonitis and 1133 with community-acquired pneumonia), the remainder being Pancreatitis and Meningococcal disease, had been recruited to GAinS and GenOSept.

Recruitment numbers for GAinS and GenOSept, for individual centres are shown in the table below:

Site	CAP	FP	P	MD	UNK	TOTALS
Reading	112	69	13	1	0	195
Oxford	92	87	10	2	0	191
Aberdeen	103	38	5	0	0	146
Brighton	81	44	14	0	3	142
Norwich	54	49	14	3	0	120
Leicester RI	53	32	4	2	2	93
Newcastle RVI	71	16	1	0	2	90
Swindon	42	31	10	0	0	83
James Cook Middlesbro'	51	32	0	0	0	83
Broomfield	40	39	3	1	0	83
Worthing	30	29	1	0	0	60
Southend	23	29	1	0	1	54
Wythenshawe	28	16	3	1	0	48
Kings Lynn	27	3	8	0	0	38
Birmingham QE	16	17	4	1	0	38
Kettering	23	12	0	0	0	35
Barts/London	22	5	5	0	0	32
Huddersfield	17	14	0	0	0	31
Coventry	25	6	0	0	0	31
Blackburn	20	7	0	0	1	28
Preston	14	13	0	0	0	27
Frimley	11	8	6	2	0	27
Charing Cross	16	8	0	1	0	25
Cheltenham	11	7	3	1	0	22
Leeds St James	13	7	1	0	0	21
Hallamshire/N General	14	4	0	0	3	21
Whittington	15	4	0	0	1	20
UCLH	13	6	1	0	0	20
Cambridge	11	5	4	0	0	20
Blackpool	13	2	0	0	0	15
Hull Royal Infirmary	7	6	0	0	1	14
Leicester G	1	11	0	0	0	12
Colchester	3	4	3	0	0	10
Calderdale	10	0	0	0	0	10
Hammersmith	7	1	0	0	0	8
Bristol Frenchay	7	1	0	0	0	8
Lewisham	3	3	0	0	0	6
Homerton	6	0	0	0	0	6
Newcastle Freeman	3	2	0	0	0	5
Hope Hospital	3	1	1	0	0	5
Glenfield	5	0	0	0	0	5
Walsall	1	3	0	0	0	4
Ipswich	2	2	0	0	0	4
Chelsea and Westminster	2	2	0	0	0	4
N Middlesex	1	2	0	0	0	3
Cardiff	3	0	0	0	0	3
Bristol Southmead	3	0	0	0	0	3
St Mary's	2	0	0	0	0	2
Leeds General	1	1	0	0	0	2
Antrim	2	0	0	0	0	2
Hull Castle Hill	0	1	0	0	0	1



92% of the UK patients have a diagnosis of CAP or FP. The unknown 1% represents those for whom the diagnosis has not yet been confirmed.



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 Clinical Infectious Diseases.

"Patients with faecal peritonitis admitted to European Intensive Care Units: an epidemiological survey". Tridente et al and the ESICM/ECCCRN GenOSept Investigators—in preparation.

"IFITM3 and susceptibility to respiratory viral infections". Mills et al—submitted to Nature as a "Brief communication arising"

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 State of the Art Meeting 2011 Intensive Care Society, 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 2011, 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, October 2012.

Serial sampling

Excellent progress, we have 33 sites collecting serial samples for the gene expression element of the GAinS study.
881 patients have been recruited and 1489 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 beginning 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.

Nearing recruitment target for serial samples and DNA collection!

We have now nearly achieved our proposed sample sizes and are very well powered for the on-going analyses.
We have established one of the largest and most comprehensive patient cohorts assembled to date in the field of sepsis genetics. This is allowing us on behalf of the GAinS and GenOSept Investigators to perform a genome-wide association study (GWAS) of susceptibility and outcome in severe sepsis, including discovery and replication cohorts. We have been able to complement this with a substantive functional genomics analysis to interpret the results of the GWAS and establish mechanisms. This involves the serial samples of leukocyte and plasma samples collected by many of the participating ICUs, using gene expression profiling and genetic mapping to define regulatory genetic variants.
We aim to move into the next phase of GAinS in 2013. 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.

Collection of serial samples

We will be arranging to collect the serial samples ,currently stored in your freezers, in January next year . We will be contacting you to arrange the collection dates and times.

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.

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 prepaid for the smaller, lighter CRFs and the post office are not delivering packages which are 'overweight'.

Investigators Meeting

We are planning to hold an investigators meeting on May 1st 2013. The results of the different analyses will be presented and future plans discussed. We very much hope you will be able to attend this meeting which we plan to hold in Oxford. Further details of the Investigators Meeting and registration details will be sent in January 2013.

Collaborative Research

Do you have any original research questions that could be answered by examining the GenOSept/ GAinS data? If so, you might wish to discuss the possibility of collaborative research with Prof Charles Hinds or Dr Chris Garrard.
Written applications will be reviewed by the UKCCG management committee

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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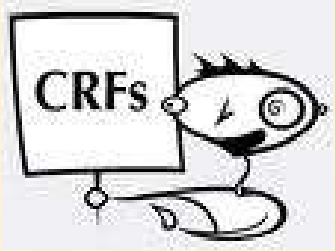

Data Quality

Quality assurance work is still ongoing for both the GAinS and GenOSept data sets. Over 3,630 CRFs have been reviewed by Alex, Penny and Paula in Oxford and more than 16,000 data queries have been created.
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.

Outstanding recruitment!

Well done to Charley Higham , Research Nurse at the RVI in Newcastle who recruited **10** patients in November. This is a massive achievement and we'd like to say a big thank you Charley for all your hard work .

Thank you!

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.