Association for
Clinical Cytogenetics

NHS Array Service

ACC Audit 2009

Kim Smith

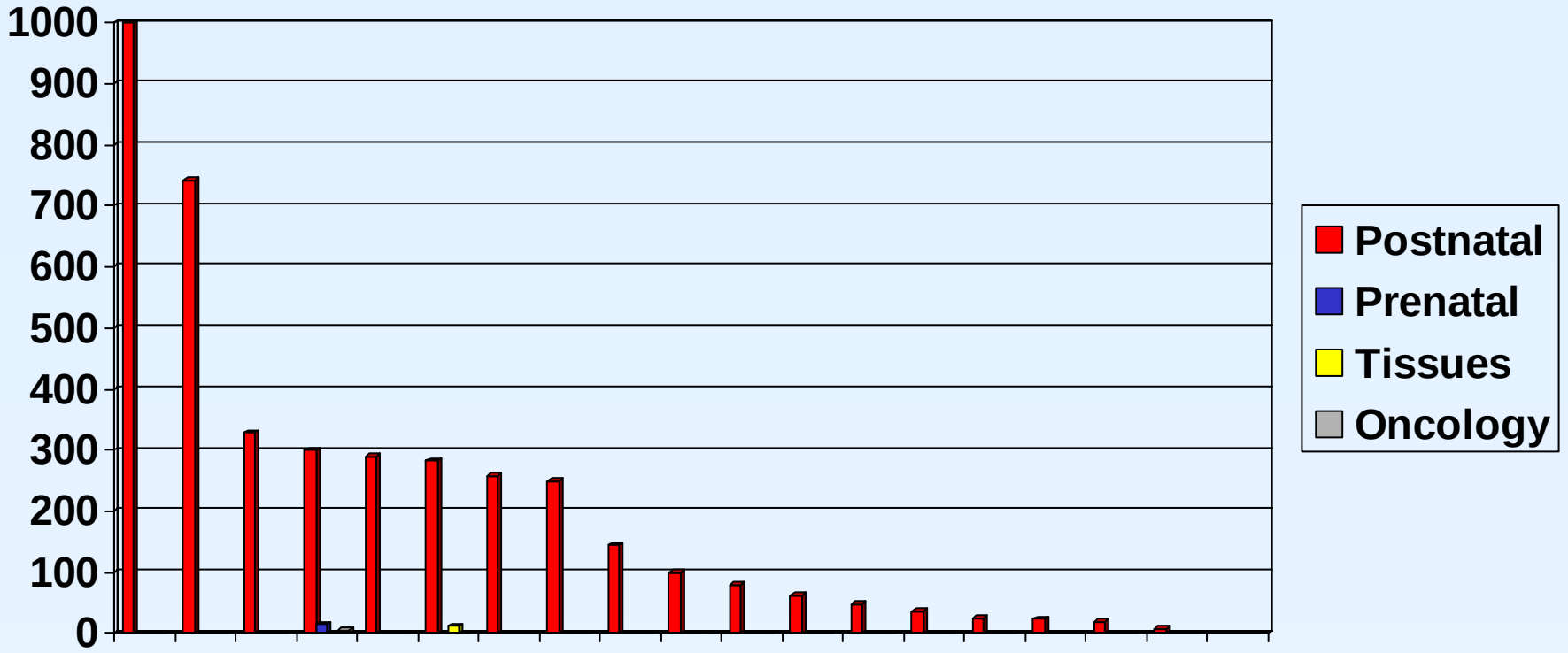
ACC Audit of arrays in diagnostics

- NHS Diagnostic Laboratories
- 2008 audit
  - Regional Genetic Centres (24 centres)
  - Specialist Haematological Cytogenetics Laboratories (7 centres)
    - *Research use only*
- 2009 Audit
  - Regional Genetic Centres only – 22 responses (one joint response from two laboratories)

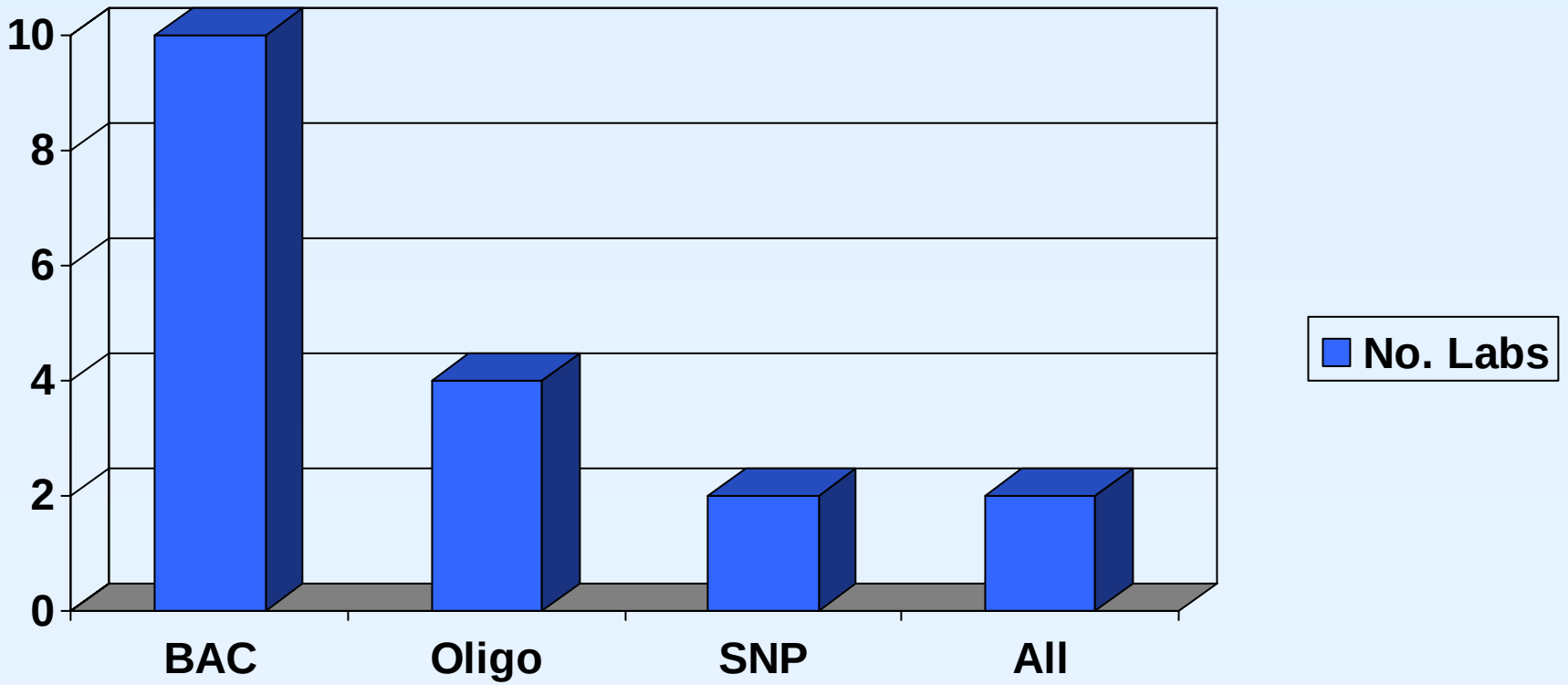
Location of service

- 23 laboratories offer array service
  - 19 laboratories own service
    - 1 laboratory undertakes BAC & oligo in-house but outsources SNP processing outside NHS (but undertakes analysis & reporting)
    - 2 laboratories offer a joint service (single dataset)
      - *[Equates to 18 responses on current service data]*
  - 3 laboratories outsource within NHS whilst validating platform/new service
      - *[2 labs provided data on funding & policy - equates to 20 responses]*
  - 1 laboratory (small) outsources within region
- 2 non-responders
  - *(2008 – outsource within NHS)*

Number of Cases (April 2008 – March 2009)



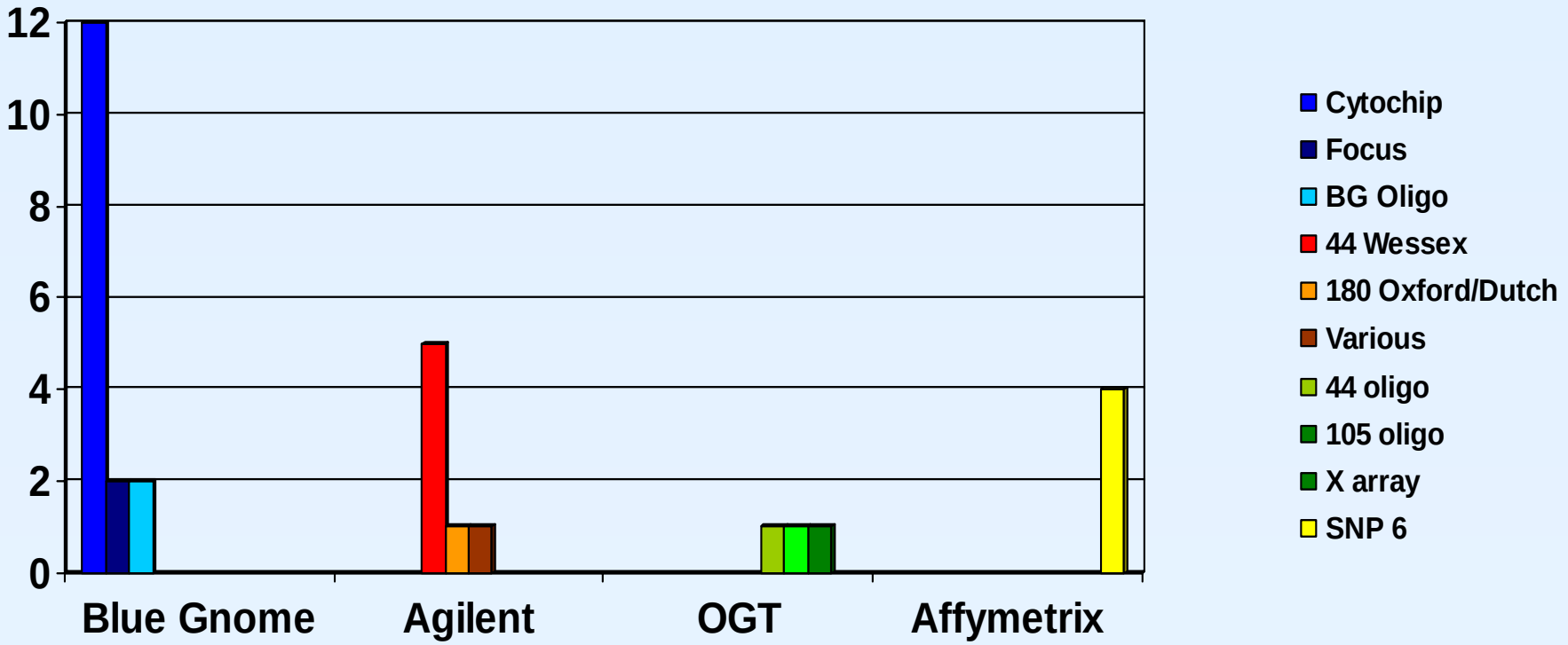
Diagnostic Array platform



Change to Array platform

- BAC only users (10) anticipate changing to another platform in either short or long term
  - oligo platform (8)
  - oligo and/or SNP platforms (2)
- All other users will continue with their existing platform
- One laboratory outsourcing to BAC platform will change to in-house SNP platform

Array design



Consensus array?

- Yes – 3
- Optimum resolution / screening level – 4
- Optional – 9
- No / not yet - 4

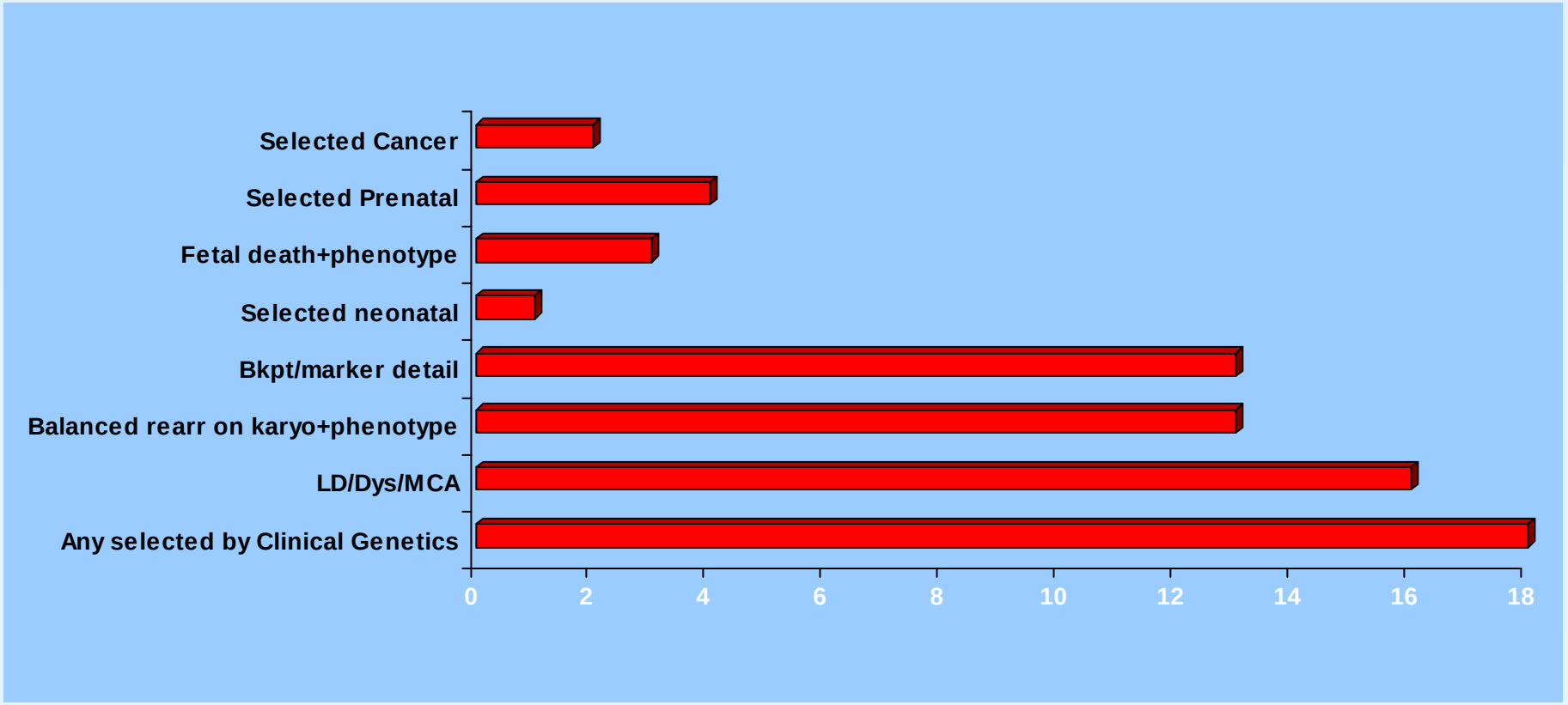
Funding

	Number of Labs
Commissioned	10
Virement from existing budget only	5
Part commission / part virement	3
Part commission / part soft money	1
Part virement / part soft money	1

Cost

£	Pay + non-pay + overheads	Pay + non-pay	Consumables only
200-299	1		
300-399	2	5	2
400-499	1	2	1
500-599			
600-699			
700-799	1		
800-899	2		
900-999	1		

Referrals


Selected Cancer
Selected Prenatal
Fetal death+phenotype
Selected neonatal
Bkpt/marker detail
Balanced rearr on karyo+phenotype
LD/Dys/MCA
Any selected by Clinical Genetics
0
2
4
6
8
10
12
14
16
18

Referring clinicians

Current service referrers	No. of labs (total 18 + 2 outsource)
Clinical Genetics only	14
Paediatrics directly	1
Clinical Genetics plus occasional referrals from •Paediatricians •Obstetricians •Fetal pathologists	5

Investigation

- Validation of imbalance by:
  - FISH – 18 labs
  - MLPA – 8 labs
  - QPCR – 3 labs
  - Array – 7 labs
- Minimum Size cut-off
  - No – 15 labs (depends on content)
  - Yes – 3 labs (50kb, ~100kb, depends on content)
- Pathogenic abnormality rate decreased over time (retrospective case effect) – Yes = 3, No = 11
- Smallest size of confirmed imbalance
  - 1-2Mb (1 BAC)
  - 600kb, 450kb, 320kb, 300kb, 180kb, 100kb, 87kb, 13kb, 9kb

Abnormality rate

	%												
Pathogenic	14	14	15	0	8	7	10	13	17	11	25	4	19
Non-pathogenic or inherited & normal parental phenotype	10	8	15	6	8	-	14	5	-	7	-	8	-
Imbalance awaiting parental studies	10	4	15	14	11	16	10	11	9	14	-	15	-

First line investigations?

- Do you think we are at a stage where arrays should be first line investigations?
  - Yes = 13
    - Any current referrer / Any against referral guidelines = 7
    - Clinical Geneticists & Paediatricians = 3
    - Clinical Geneticists only = 3
  - No = 6 (clinical understanding of result, patient understanding of result, volume of follow-up investigations, knowledge to support interpretation)
- And for what referral reason?
  - LD/MCA/Dysmorphism – 10*
  - Postnatal with abnormal phenotype / all paediatric / exclude DNA copy number change – 3*
    - **Note – 2 comments - **not** common trisomies*
  - *PD - Abnormal scan with hard markers – 1/19*

First line investigations?

- Able to start first line testing?
  - Now = 2, Within 1 year = 11, Within 2 years = 5
- Lab needs
  - Commissioning – array service PLUS follow-up investigations
  - Referral guidelines & good clinical information from referrers
  - Trained staff, equipment, IT, bioinformaticians
  - Laboratory Guidelines (reporting what & how, follow-up)
  - Good reference databases, dissemination/sharing of data on CNVs
- Anticipated number of cases (reflect size of lab & perception of “front line” testing)?
  - 8 = <500
  - 3 = 500 – 1000
  - 2 =1000 – 1500
  - 3 = 1500 – 2000
  - 2 = >2000

First line investigations?

What other requirements?

- Agreement of *modus operandi*
- Bioinformatics training
- Education of clinical users
- Commissioning – labs plus clinical genetics
- Patient information
- Clinical follow-up strategies responsive to gene content

Prenatal Diagnosis?

- Use arrays for prenatal cases with abnormal scans?
  - Yes = 8
  - Some/possibly = 10
  - Not yet = 2
- Array format?
  - Targeted = 9
  - Whole genome = 5
  - Combination targeted & genome = 2

Where?

- All regional labs = 18
  - “Core service”, “service in place”
- Few supra-regional labs = 1
- Postnatal regional, prenatal supra-regional = 1

Data Sharing

- Optimise sharing of information – pathogenic and local non-pathogenic CNV data
- DECIPHER – create NHS superuser group – lab data accessible to all UK NHS registered laboratories
- ALL respondents = Yes – support
- Database issues
  - Easier/quicker uploading
  - Agreement on what categories uploaded

Acknowledgements

- Aberdeen
- Belfast
- Bristol
- Birmingham
- Cambridge
- Cardiff
- Dundee
- Edinburgh
- Glasgow
- Leeds
- Liverpool
- London – GOS
- London – Guy's
- London – Northwick Park
- London – St George's
- Manchester
- Newcastle
- Norwich
- Oxford
- Nottingham/Leicester
- Salisbury
- Sheffield