

Quality Assurance (QA) of the Biostatistical Workflow in Forensic Genetic Casework

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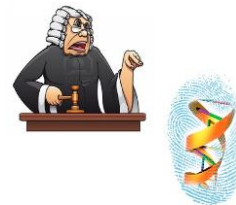
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Aim with this talk

- QA aspects of (bio)statistical workflow
 - How to define a workflow?
 - How to validate a workflow?
 - Competence of the staff?
- Our experiences
 - Revised definition/strategy of such a workflow
 - Paternity/maternity testing (approx. 3000-5000/year).
 - Complex kinship testing (approx. 300/year).
 - Missing person identifications (approx. 100/year).
- Goal
 - Increase quality
 - Increase competence

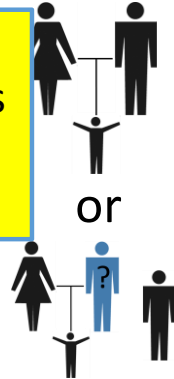


Introduction: Use of DNA in forensic genetics

- Link a suspect to a crime scene

- Kinship
- More distant relationships, missing person identification

All applications involve complex interpretations that need to be properly addressed.



- Phenotyping testing
 - Eye, hair color
- Cell type identification

(A)	Hair	Dark brown	Light brown	Dark brown	Light brown	Dark brown	Light brown
(A)	Eye	Blue	Green	Blue	Green	Blue	Green
(B)	Hair	Dark brown	Light brown	Dark brown	Light brown	Dark brown	Light brown
(B)	Eye	Blue	Green	Blue	Green	Blue	Green
(C)	Hair	Dark brown	Light brown	Dark brown	Light brown	Dark brown	Light brown
(C)	Eye	Blue	Green	Blue	Green	Blue	Green
(D)	Hair	Dark brown	Light brown	Dark brown	Light brown	Dark brown	Light brown
(D)	Eye	Blue	Green	Blue	Green	Blue	Green

Walsh et al., 2014

DNA investigation, 2 parts

1. Lab workflow
Sample -> DNA profile(s)

2. Interpretation/Statistical workflow
DNA-profiles -> Weight of evidence/conclusion

Relationship testing:
"There was a general agreement in how the weight of evidence was calculated in routine genetic constellations, but there was a large variation in the biostatistical calculations in case of rare events such as rare alleles, silent alleles and genetic inconsistencies"
Thomsen et al., 2009, Forensic Sci Int Genet.

Mixed profiles:
"Despite the improvements ... mixture interpretation is still all over the place...Some of this is a consequence of using a statistical approach that is inappropriate for complex mixture interpretation"
Mike Coble, ISFG-meeting Krakow, 2015

-Case ques
-Sample(s)



$$\begin{aligned}
 &Pr(d_1, \dots, d_L, s_1, \dots, s_L, v_1, f_1, \dots, f_{L+1}, \dots, f_L, g_{-L+1}, \dots, g_L) \\
 &Pr(d_i | v_i, f_i, g_i) Pr(v_i | g_i) \\
 &\sum_{v_1=f_1, g_1} \dots \sum_{v_L=f_L, g_L} [Pr(d_1, \dots, d_{L-1}, s_1, \dots, s_{L-1}, v_{L-1}, \\
 &f_{L-1}, \dots, f_{L-1}, g_{L-1}, \dots, g_{L-1}) Pr(f_L | f_{L-1}, \dots, f_{L-1}) \\
 &Pr(g_L | g_{L-1}, \dots, g_{L-1}) Pr(v_L | v_{L-1})]
 \end{aligned}$$

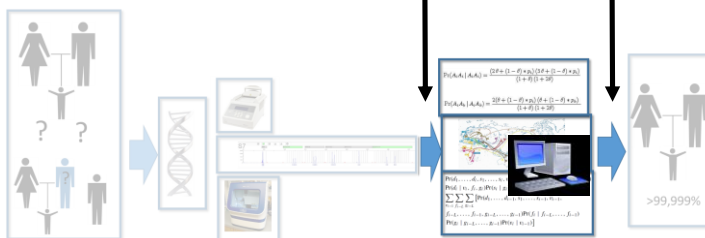
Weight of evidence / Conclusion

Quality assurance (QA)

- Quality assurance is a key element in an accredited forensic laboratory.
- Quality involves several components such as:
 - Validation of methods, instruments, and software;
 - Documented maintenance.
 - Secured chain of custody.
 - Documented operating procedures.
 - Traceability.
 - Proven competence of the staff.
 - Proficiency testing
- The general goal is to produce test reports of forensic investigations with legal certainty.

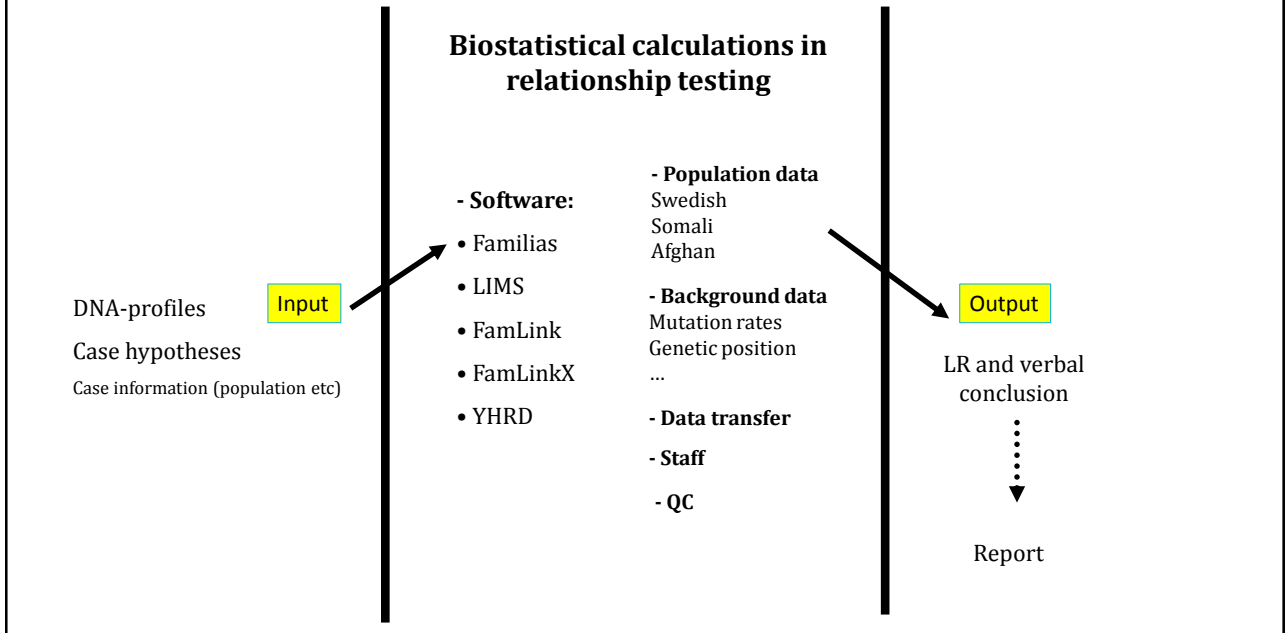


Define your workflow, input/output



- It is not only the software!
- This is what you need to validate and the focus of QA.
- May depend on
 - Lab's processing design
 - Case types
 - Competence of staff
 - ...

Relationship testing – Biostatistical workflow



QA and validation, some aspects

- Define your strategies, principles and models

- LR principle?
- Ho
- Ho

- Adjust for the needs in your lab.

- Software - High work efforts at beginning, then decreasing.

- Background - Increase in competence!

- Population data
 - Population?
 - Allele freq?
 - Silent alleles?
 - Co-ancestry?
- Background marker data
 - Mutation rates?
 - Genetic position?
 - Dropin/drop out rates?

- Reporting strategy

- LR
- Verbal – thresholds?
- Scale – thresholds?

ENFSI, Guideline for Evaluative Reporting in Forensic Science, 2015

- Staff

- Level of competence?
- Maintain competence?

Gjertson et al, ISFG: Recommendations on biostatistics in paternity testing, Forensic Sci. Int. Genetics, 2007

Gill et al, DNA commission of the International Society for Forensic Genetics, 2006

Recommendations on the use of Y-STRs in forensic analysis, Forensic Sci. Int. 157, 187-97 (Gusmao et al. 2006)

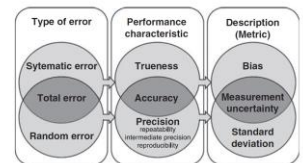
ISFG: an update on the use of Y-STRs in forensic analysis, Forensic Sci. Int. 157, 187-97 (Gusmao et al. 2006)

Validation parameters, examples

- Software
 - Verify traceability to version, background data etc.
 - How to implement new versions.
 - Secure software parameter settings (e g iterations).
- Databases/reference data
 - Make sure that appropriate reference data are to be used.
- Accuracy
 - Verify that the output from the wf is valid.
 - Ensure guidelines (SOPs) for when and how to use the software.
- Transfer of data
 - Secure that data are safely transferred (LIMS->software->LIMS->report).

Validation parameters, example (cont)

- Identify possible sources of errors
- Estimate risks for "false" outputs
 - false positives/negatives, under –/over-estimations of the evidential weight
- Backup routines
- **Think about the extent of your validation!**
- Continuous validation
 - Should the wf undergo continuous validations/tests



Competence of the staff

- In my view, a key component (apart from software).
- Not always a “recipe” to follow the workflow.
- Be able to make decisions based on case specific information.
- Hard to get “trained” staff direct from university.
- In house education/training.
- Training, training, training.



<http://coders-view.blogspot.se/>

Competence requirement of the staff at our lab (case reporting geneticist)

Previously

- A number of general requirements.
- Many “should”.

Now

- We implemented sub-workflows.
- Specified theory and practical test cases, followed by an “exam”.
- Every year (continuous requirements):
 - Must have completed at least 10 real cases within each sub-workflow.
 - Must have completed 5 test cases (“exam”).



Summary

- More than just the software.
- Increase quality.
- Increase competence.
- Learn from other fields (clinical molecular genetic testing etc).
- Produce results of forensic investigations with legal certainty.
 - The rule of law.
 - Confidence, for forensic inv, in the society.