



Critical errors 2014-2016 with polls

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Concept of critical error (CE)

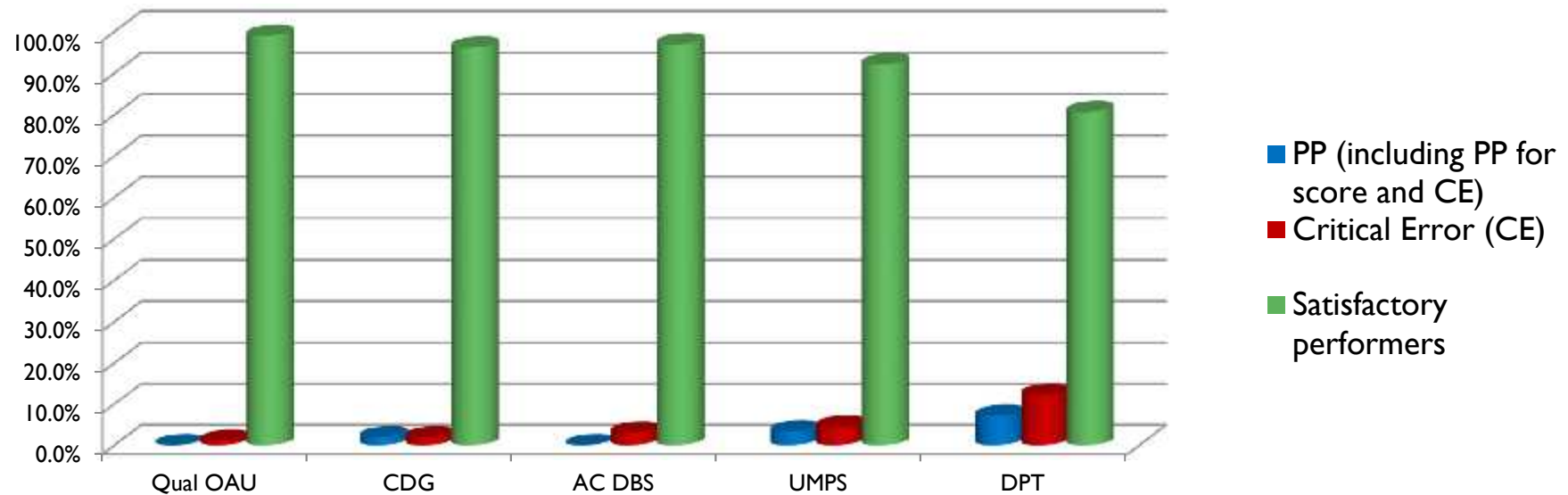
- ▶ In 2014, the SAB introduced the concept of CE for all qualitative schemes
- ▶ A CE is an error that would be unacceptable to the majority of labs and would have a serious adverse effect on patient management
- ▶ The EQA material provides (urine, dried blood spot) must be sufficient to establish diagnosis according to current standards of biochemical genetic testing
- ▶ The guidelines principles to identify a CE are
 - ▶ Failure to perform a relevant test (DPT only)
 - ▶ Failure to identify a relevant metabolite(s)
 - ▶ Failure to establish a diagnosis when proficiency is high (e.g,>95%)

Concept of critical error (CE)

- ▶ So far, samples with no IEM cannot result in CE
- ▶ The procedure to establish a CE has been defined
 - ▶ The Scientific Advisors (SA) identify possible CE after completion of the survey
 - ▶ These proposals are discussed within the Scientific Advisory Board (SAB) during the Autumn meeting
 - ▶ Based upon discussion, CE are either confirmed or rejected
- ▶ A confirmed CE overrules scores and results in “failure to achieve satisfactory performance”
- ▶ The SA issues a performance support letter
- ▶ The participant can appeal via the ERNDIM Administrative Office

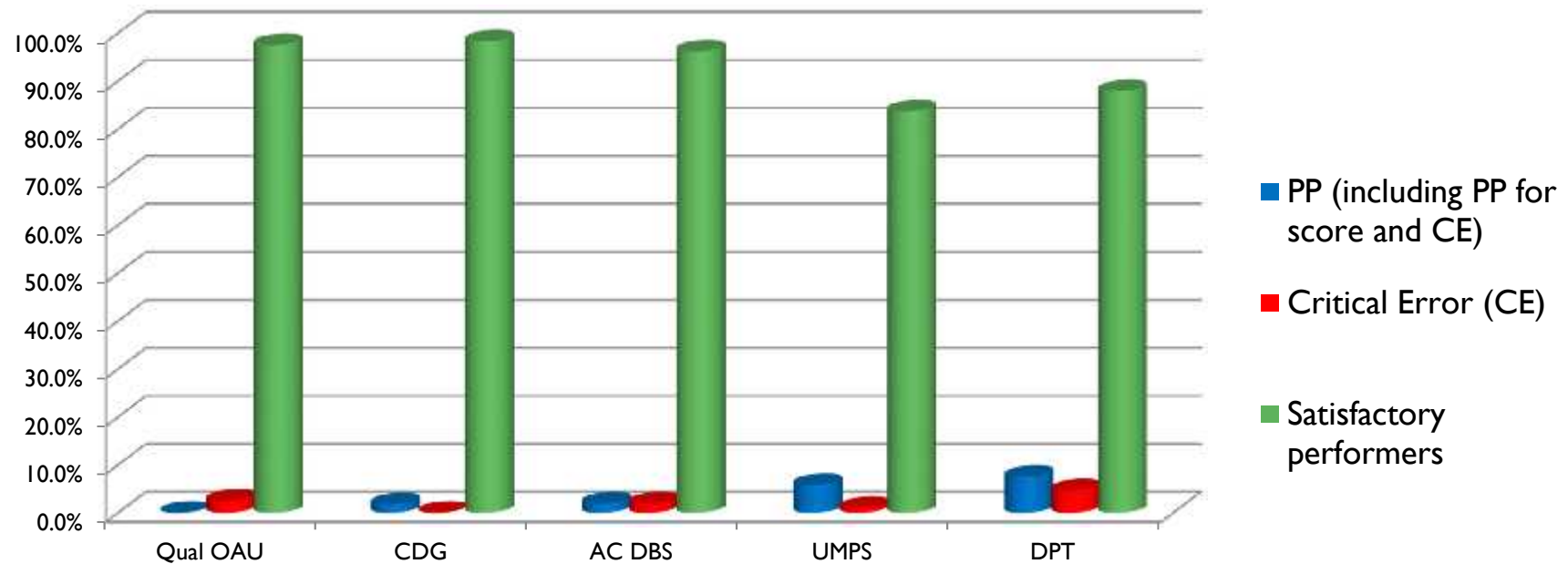
Critical errors 2014

	Qual OAU	CDG	AC DBS	UMPS	DPT
Participating labs	192	52	98	89	98
PP (including PP for score and CE)	0,0%	1,9%	0,0%	3,4%	7,1%
Critical Error (CE)	1,0%	1,9%	3,1%	4,5%	12,2%
Satisfactory performers	99,0%	96,2%	96,9%	92,1%	80,6%



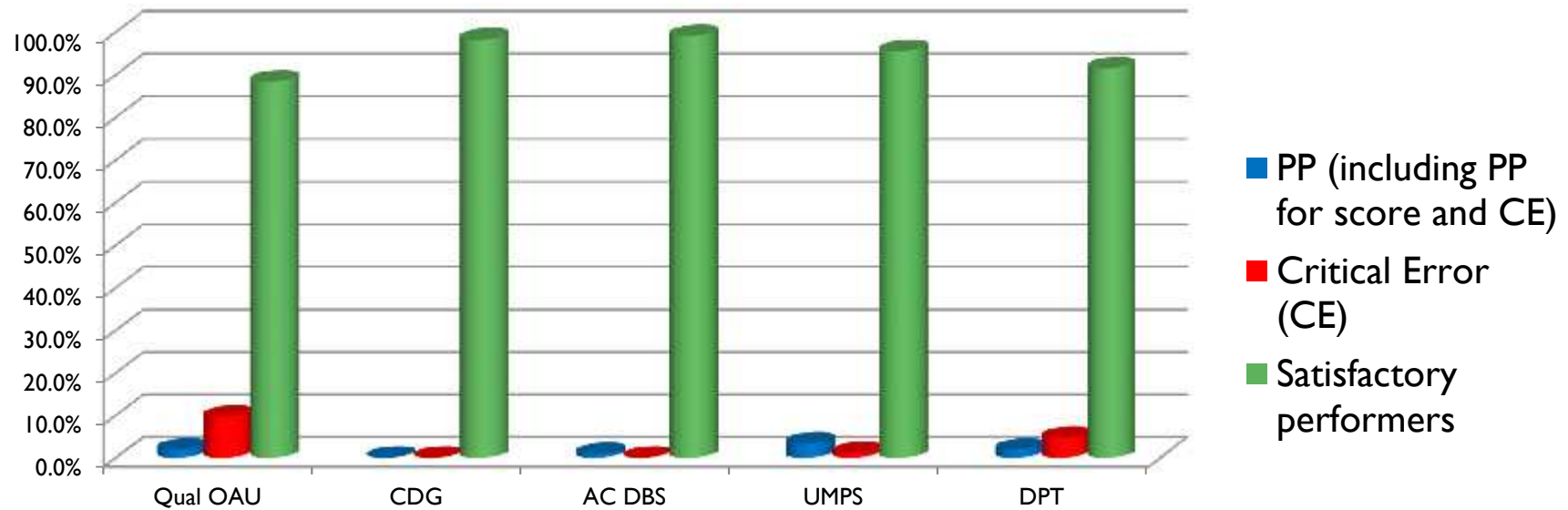
Critical errors 2015

	Qual OAU	CDG	AC DBS	UMPS	DPT
Participating labs	192	52	98	89	98
PP (including PP for score and CE)	0,0%	1,8%	1,9%	5,8%	7,5%
Critical Error (CE)	2,5%	0,0%	1,9%	1,0%	4,7%
Satisfactory performers	97,5%	98,2%	96,2%	83,7%	87,9%



Critical errors 2016

	Qual OAU	CDG	AC DBS	UMPS	DPT
Participating labs	192	52	98	89	98
PP (including PP for score and CE)	1,9%	0,0%	0,9%	3,4%	1,9%
Critical Error (CE)	9,7%	0,0%	0,0%	1,1%	4,7%
Satisfactory performers	88,4%	98,3%	99,1%	95,5%	91,5%

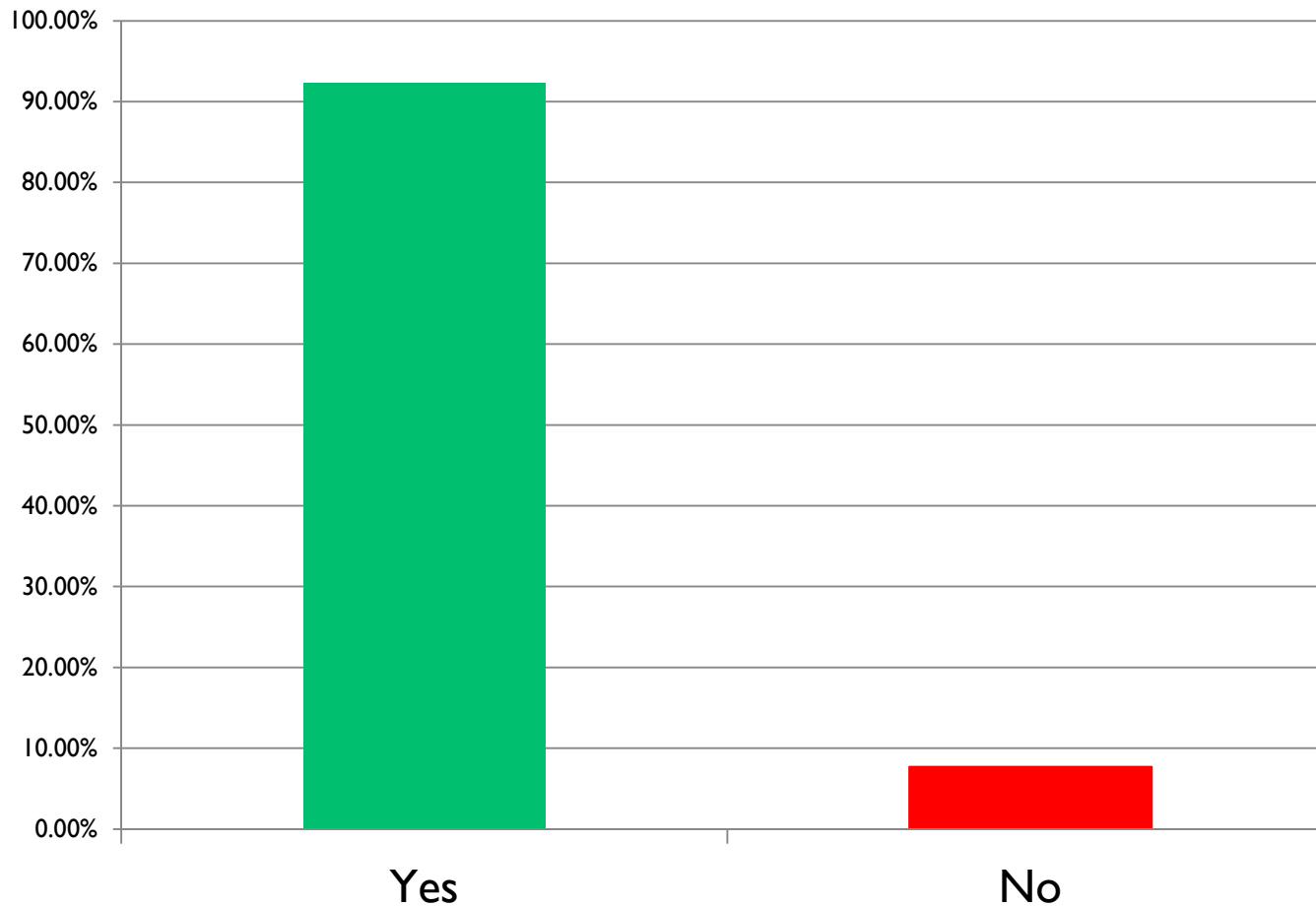


Questionnaire

- ▶ In July 2017, a questionnaire has been sent to all participants to qualitative schemes

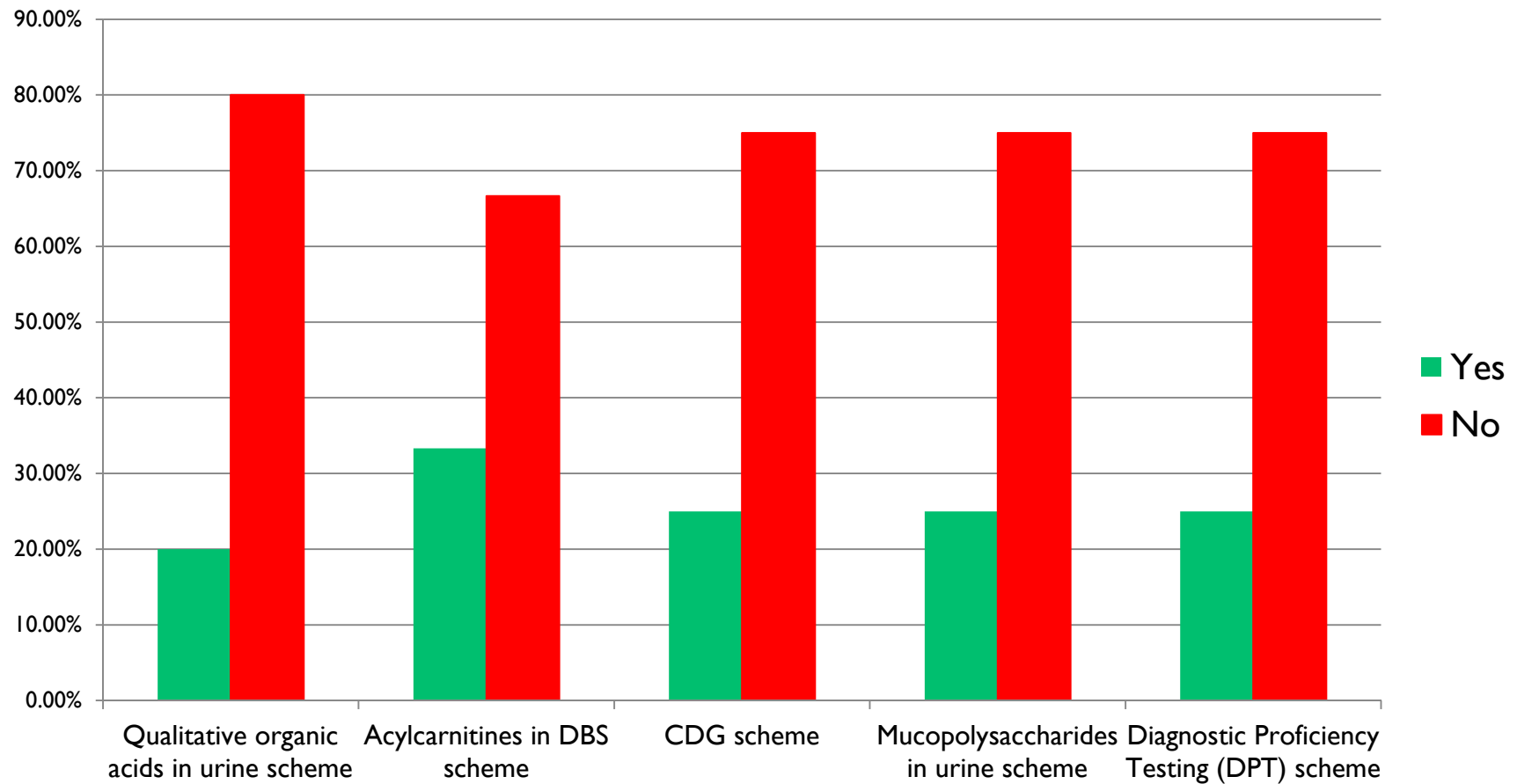
Question 1: Do you agree with the concept of critical error for all qualitative schemes?

117 answers



Q2: If you answered no to Q1, would you agree with the concept of critical error for only some schemes?

6 answers

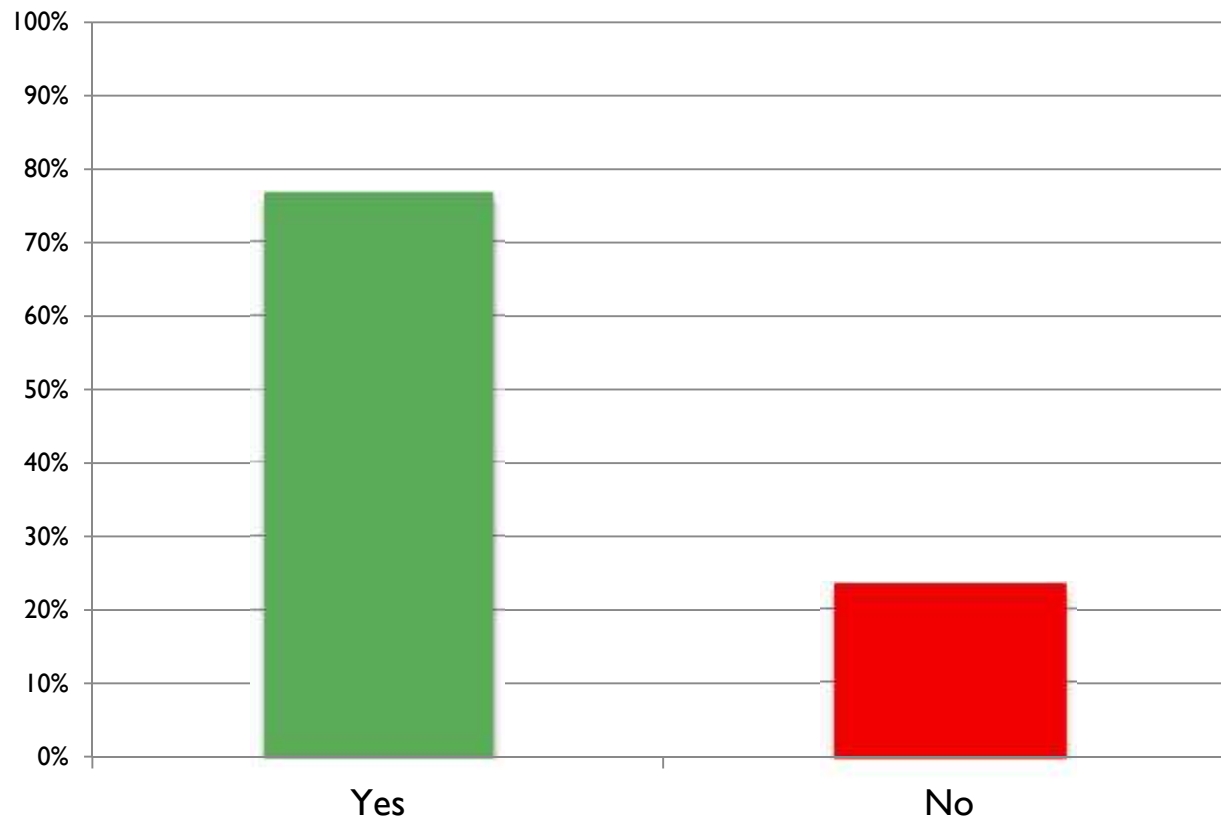


Q3: If you answered no to Q1, please explain why you think critical error should not apply to all the qualitative schemes

- ▶ **Only 2 answers**
 - ▶ Sample quality
 - ▶ We are a lab not a clinician so we do not provide diagnosis. We give out an abnormal report and tell the doctor to refer to a clinician with sufficient expertise

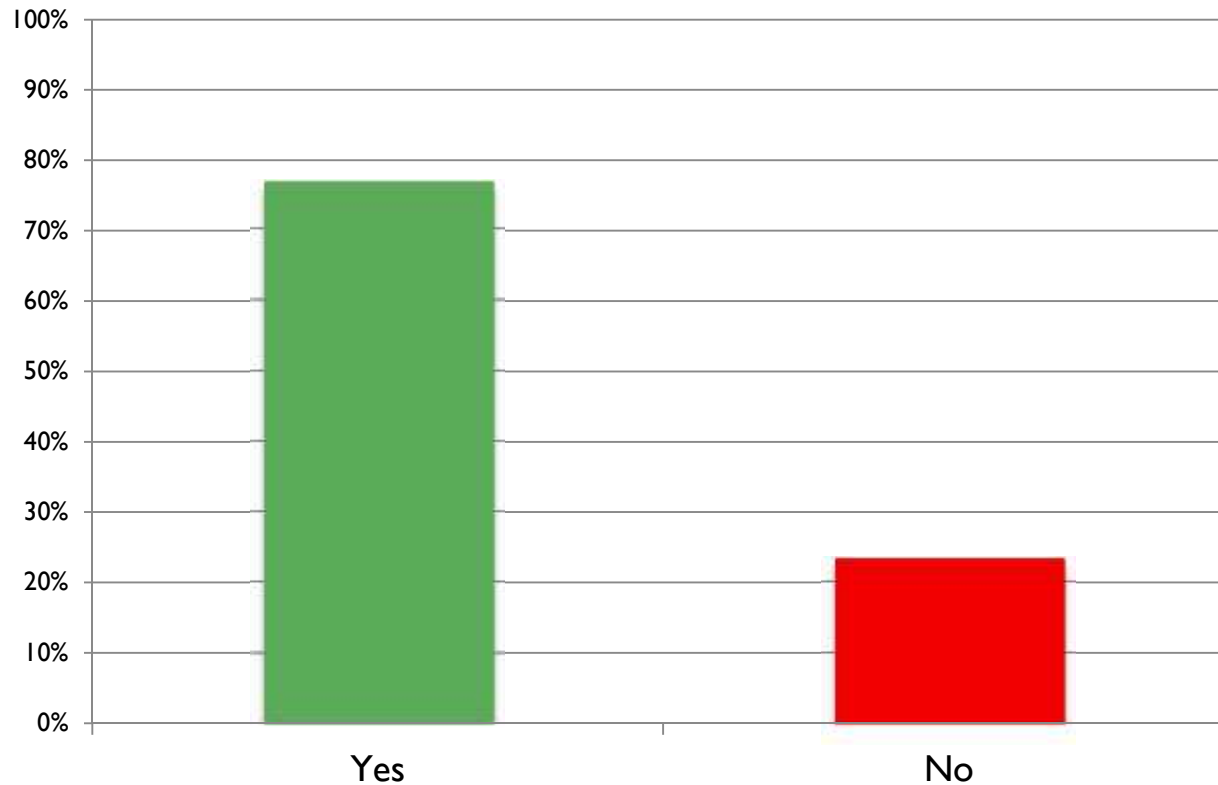
Q4: Which definition(s) of critical error do you agree with?

- ▶ Missing a treatable disorder when diagnostic metabolites are excreted in significant amounts (91 answers)



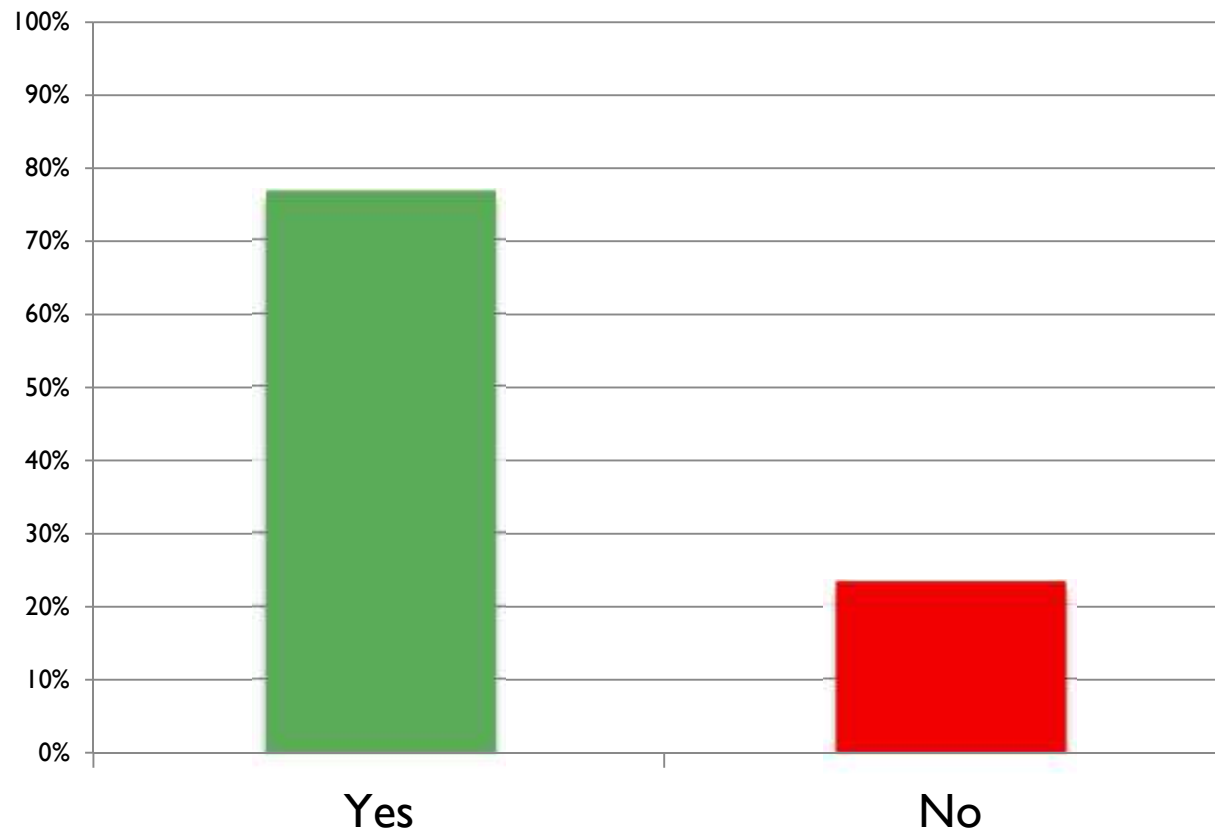
Q4: Which definition(s) of critical error do you agree with?

- ▶ Missing a treatable disorder when diagnostic metabolites are excreted in low amounts but identified by more than 80% of participants (91 answers)



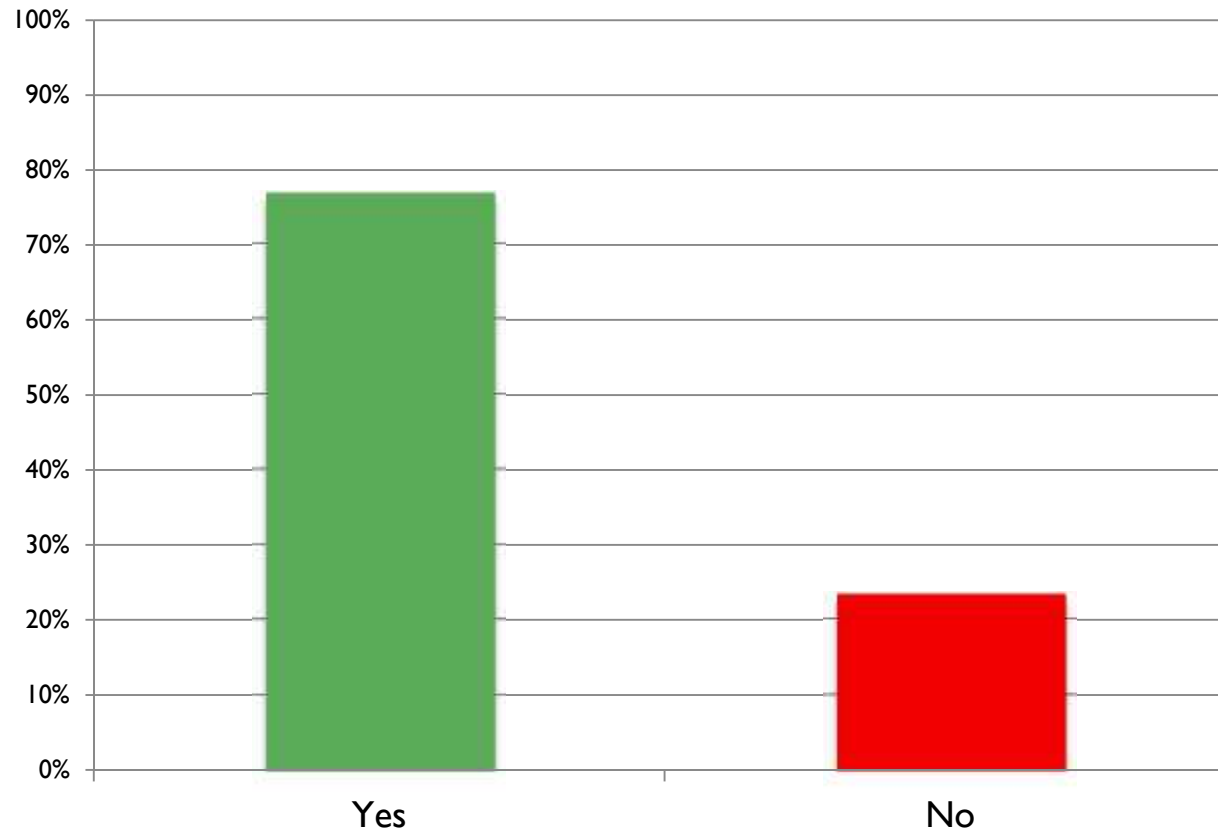
Q4: Which definition(s) of critical error do you agree with?

- ▶ Missing a disorder for which metabolites are excreted in great amounts even if it is not treatable (91 answers)

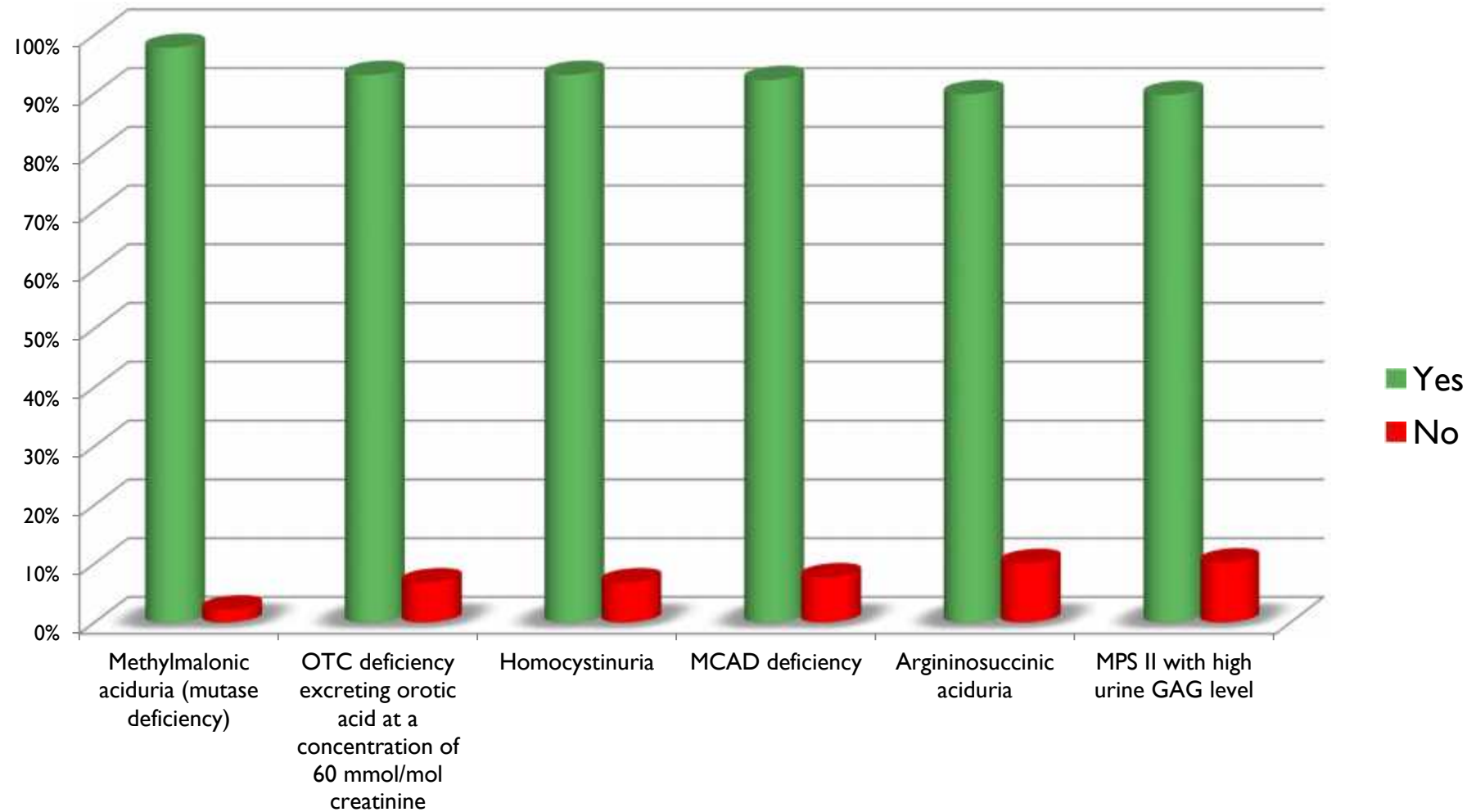


Q4: Which definition(s) of critical error do you agree with?

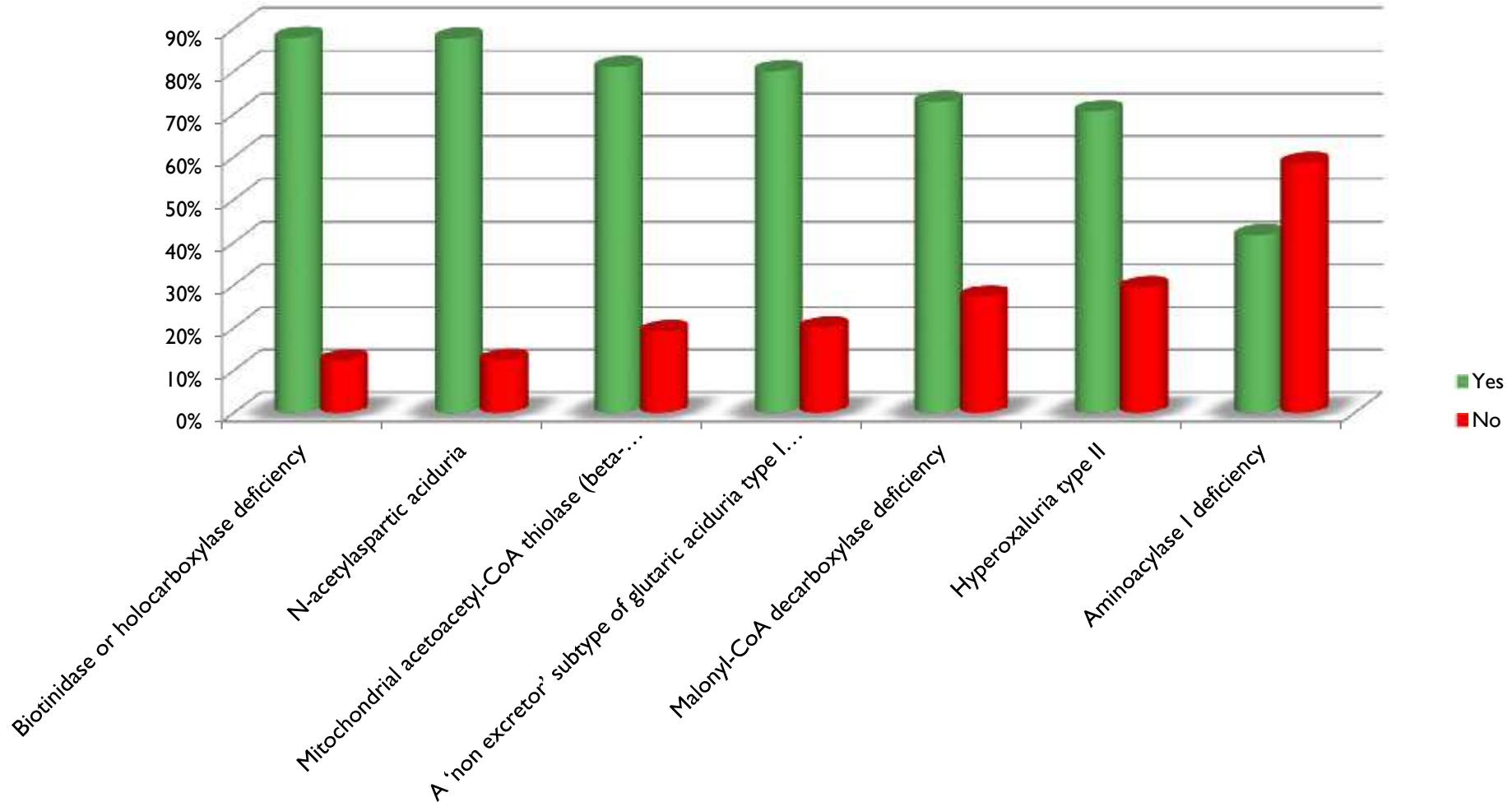
- ▶ Misdiagnosing a non-treatable disorder as a treatable disorder : e.g. proposing the diagnosis of multiple acyl-CoA dehydrogenase deficiency for a patient affected with GMI gangliosidosis (91 answers)



Q5: Would you consider it a critical error if any of the following diagnoses were missed?



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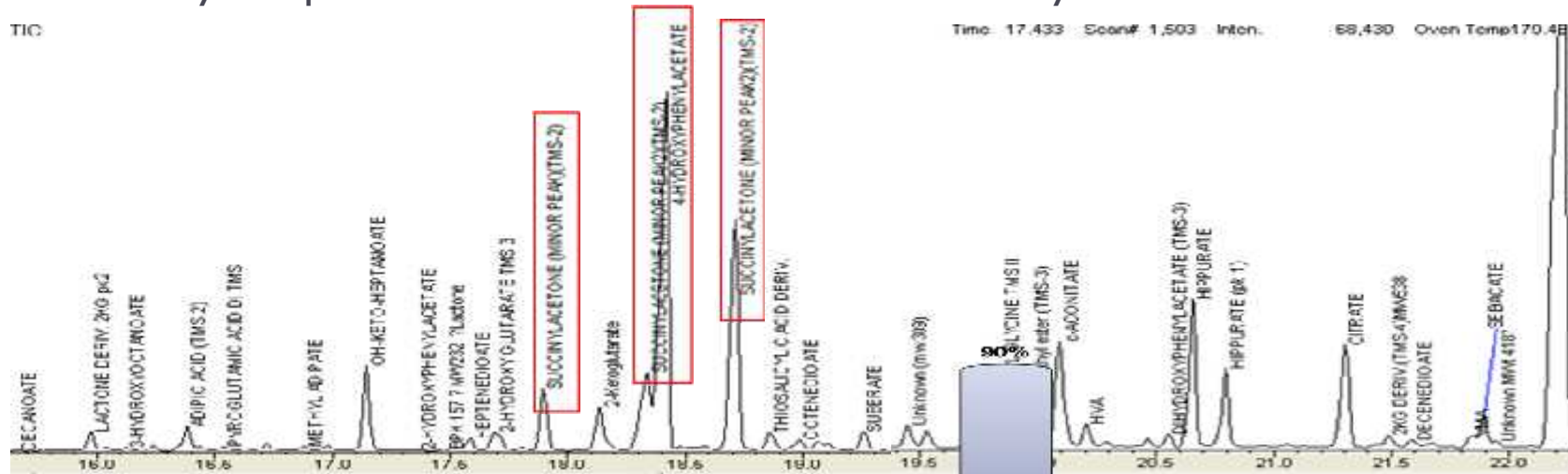


E-Voting

DPT UK 2017- F : tyrosinemia type I

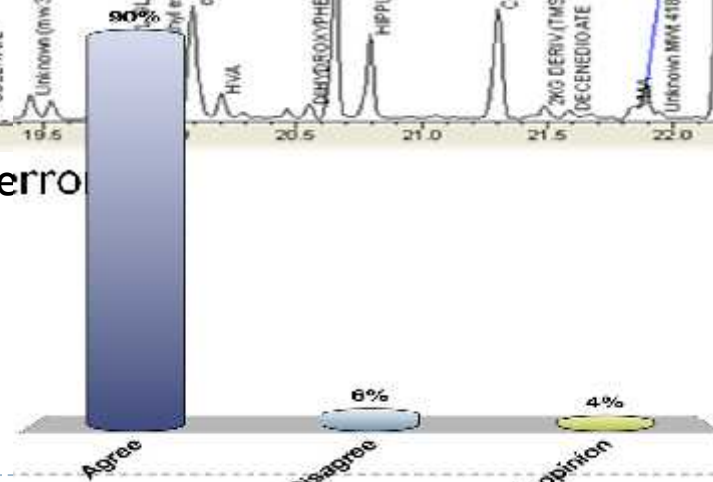
▶ “Presented with jaundice and hepatomegaly. Sample collected while treatment commencing.”

- ▶ Succinylacetone : median = 7.5 mmol/mol creat
- ▶ Analytical performance: 20/22 labs identified succinylacetone



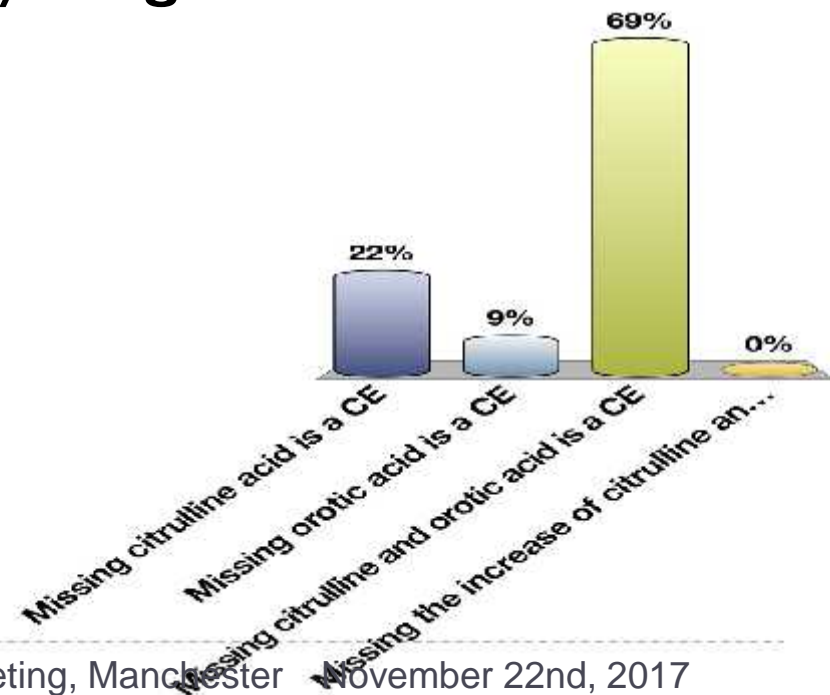
▶ Question: Missing succinylacetone is a critical error

- A. Agree
- B. Disagree
- C. No opinion



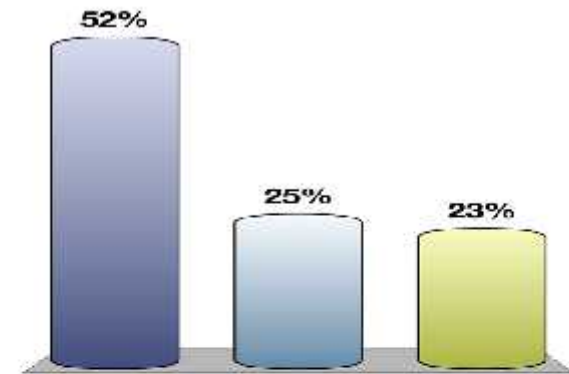
DPT 2017-A : Citrullinemia type I

- ▶ Infant presented at Emergency Department. Febrile, query infection. Sample collected after commencing therapy.”
 - ▶ Citrulline : median = 15 000 mmol/mol creat
 - ▶ Orotic acid : median = 80 mmol/mol creat
- ▶ With which of these proposals do you **agree**?
 - Missing citrulline acid is a CE
 - Missing orotic acid is a CE
 - Missing citrulline **and** orotic acid is a CE
 - Missing the increase of citrulline and orotic is **not** a CE



DPT France 2017-B : MNGIE

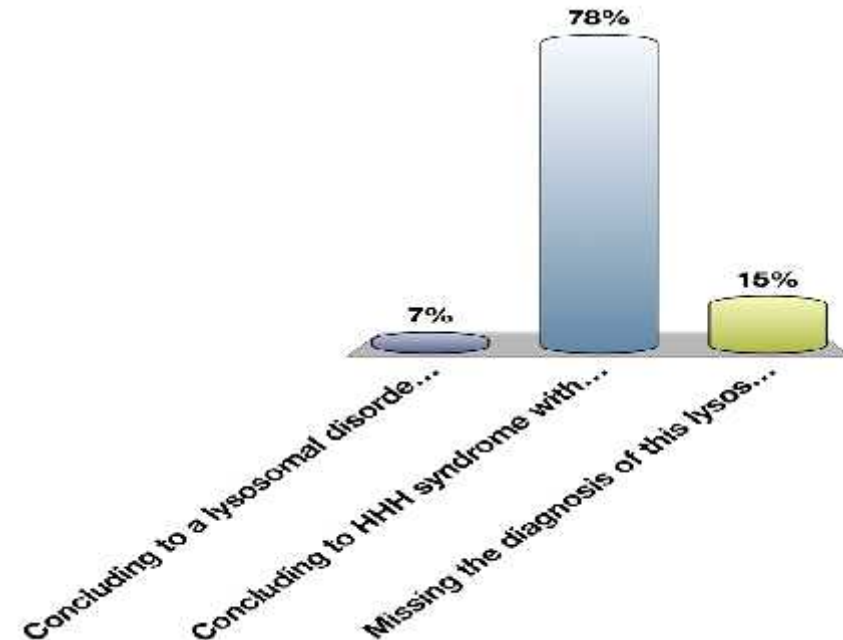
- ▶ “48-year old patient. Investigated because of diabetes and hypothyroidism from the age of 42, diarrhea with anorexia and denutrition from the age of 44.”
 - ▶ Lactic acid : median = 5 800 mmol/mol creat (pH urine = 6.0)
 - ▶ Deoxyuridine : median = 300 mmol/mol creat
 - ▶ Thymidine : median = 250 mmol/mol creat
 - ▶ Uracil : median = 75 mmol/mol creat
 - ▶ Thymine : median = 45 mmol/mol creat
- ▶ With which proposal do you **agree**?
 - A. Missing the increase of at least one of the pyrimidine derivatives is a CE
 - B. Missing the increase of lactic acid is a CE
 - C. Reporting an increase of lactic acid and concluding to GLUT2 defect (Fanconi-Bickel syndrome) is a CE



DPT France 2017-D: GM1 gangliosidosis

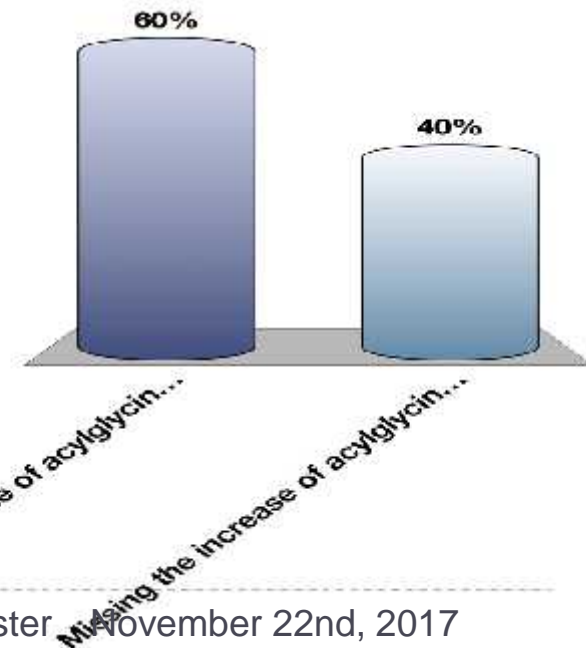
- ▶ “7-month-old girl. Hospitalized from birth because of ascites, dysmorphic features and hepatosplenomegaly.”
 - ▶ Abnormal oligosaccharide profile (all 22/25 labs who performed the analysis)
- ▶ With which proposal do you **agree**?

- A. Concluding to a lysosomal disorder without performing oligosaccharides but advising to perform it is a CE
- B. Concluding to HHH syndrome without performing oligosaccharides (GAGs normal) is a CE
- C. Missing the diagnosis of this lysosomal disorder is not a CE



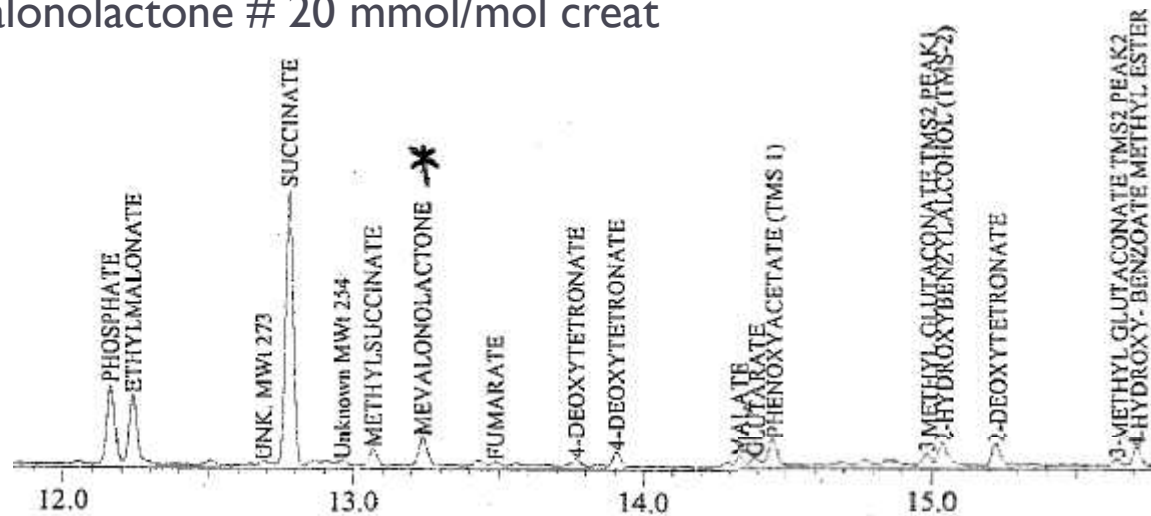
Qual. Organic Acids Sheffield 245: MCAD

- ▶ “Episodes of unresponsive hypoglycaemia, 7 year old”
 - ▶ Hexanoylglycine +
 - ▶ Suberylglycine +
 - ▶ Phenylpropionylglycine +
 - ▶ No increase of dicarboxylic acids
 - ▶ Proficiency 94%
- ▶ With which proposal do you **agree**?
 - A. Missing the increase of acylglycines is a CE
 - B. Missing the increase of acylglycines but asking for acylcarnitine is **not** a CE



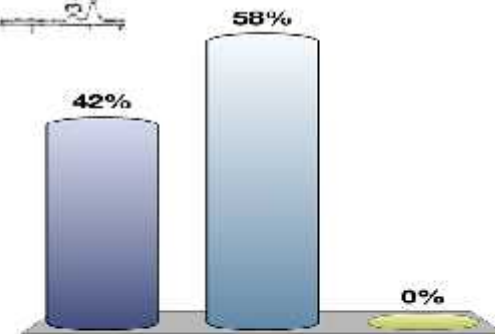
Qual. Organic Acids Sheffield 249: MK

- ▶ “3 years old – Fever (sample taken at time of fever)”
 - ▶ Mevalonolactone # 20 mmol/mol creat



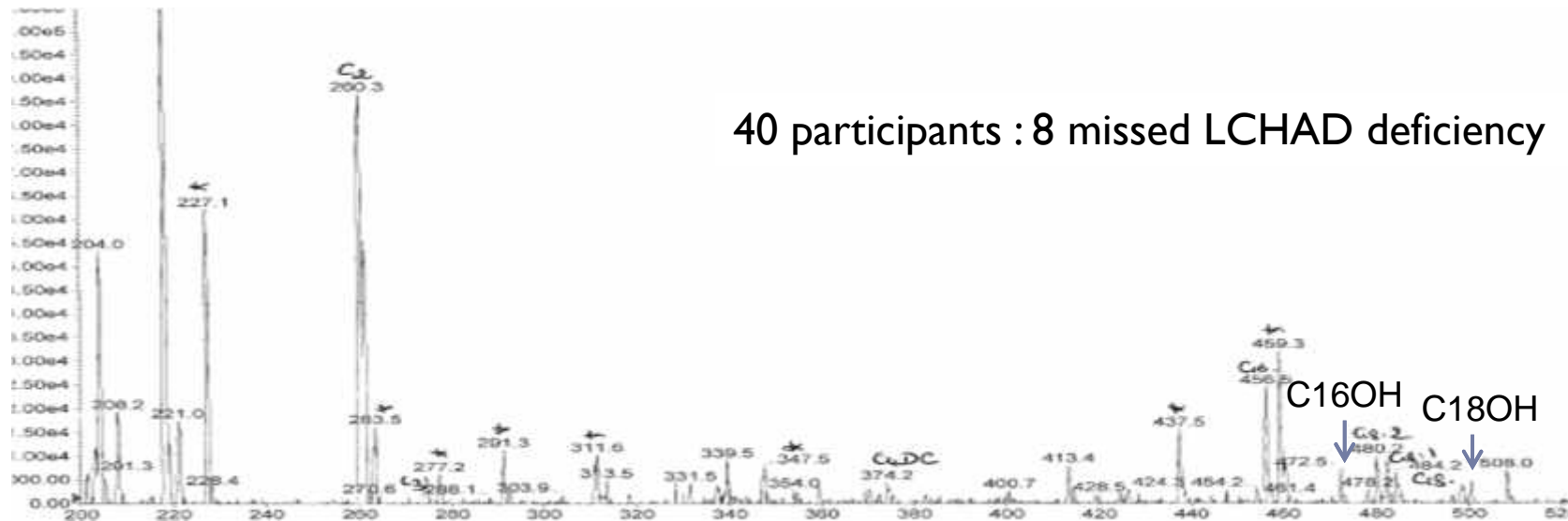
With which proposal do you **agree**?

- A. Missing the increase of mevalonolactone is a CE
- B. Missing the increase of mevalonolactone and advising to measure mevalonolactone using stable isotope dilution is **not** a CE
- C. Missing the increase of mevalonolactone and advising to measure IgD is **not** a CE



Acylcarnitines in DBS H2017-03: LCHAD

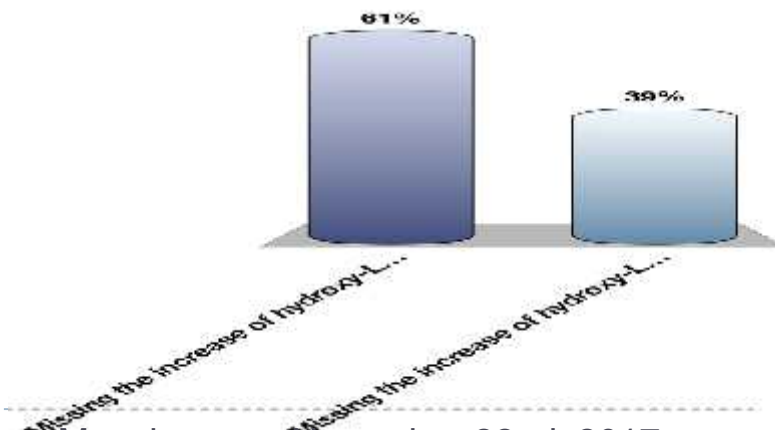
- ▶ “3-year old girl with recurring rhabdomyolysis”



40 participants : 8 missed LCHAD deficiency

With which proposal do you **agree**?

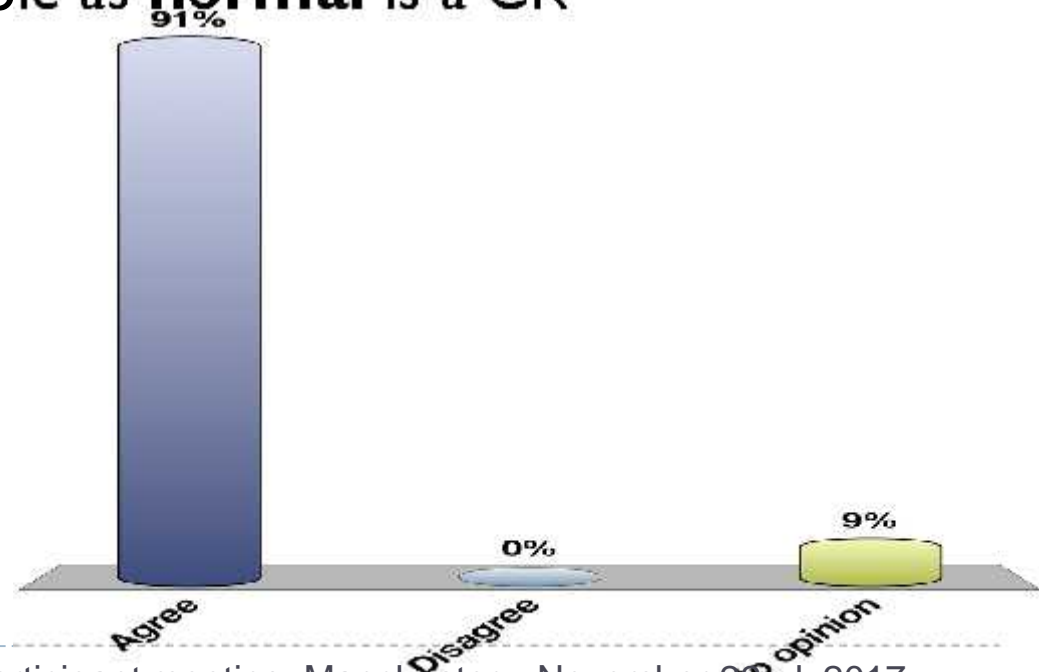
- A. Missing the increase of hydroxy-LC-acylcarnitines is a CE
- B. Missing the increase of hydroxy-LC-acylcarnitines but asking to repeat acylcarnitine profile during an episode of rhabdomyolysis is **not** a CE



Urine MPS 2017-6 : MPS VI

- ▶ Reminder: no clinical data
- ▶ GAG's quantification : increased (99% labs)
- ▶ GAG's fractionation : increase of dermatane sulfate (98% labs)
- ▶ Reporting this urine sample as **normal** is a CR

- A. Agree
- B. Disagree
- C. No opinion



Thank you for your participation!