

# Development of a new diagnostic tool for rapid detection of bloodstream infections in patients on home parenteral nutrition using '*droplet digital PCR*' (ddPCR)

Drs. Yannick Wouters, PhD-student

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Radboudumc, Nijmegen, The Netherlands

June 22, 2019

# No disclosures

# Diagnosis of bloodstream infections

- **Bloodstream infections:**
  - 1 episode every 1–5 years
- **Diagnosis with blood cultures ('gold standard'):**
  - Slow (1-2 days bacteria, 1-5 days fungi)
  - False-negative results (antibiotics)



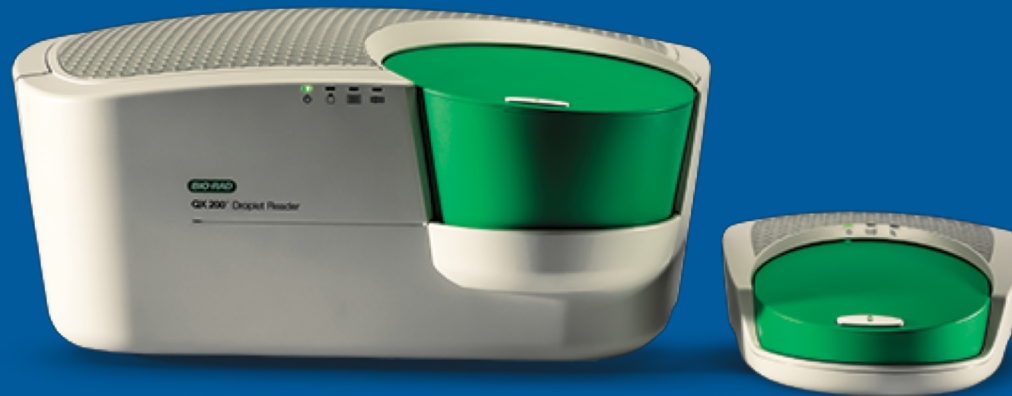
# Molecular techniques

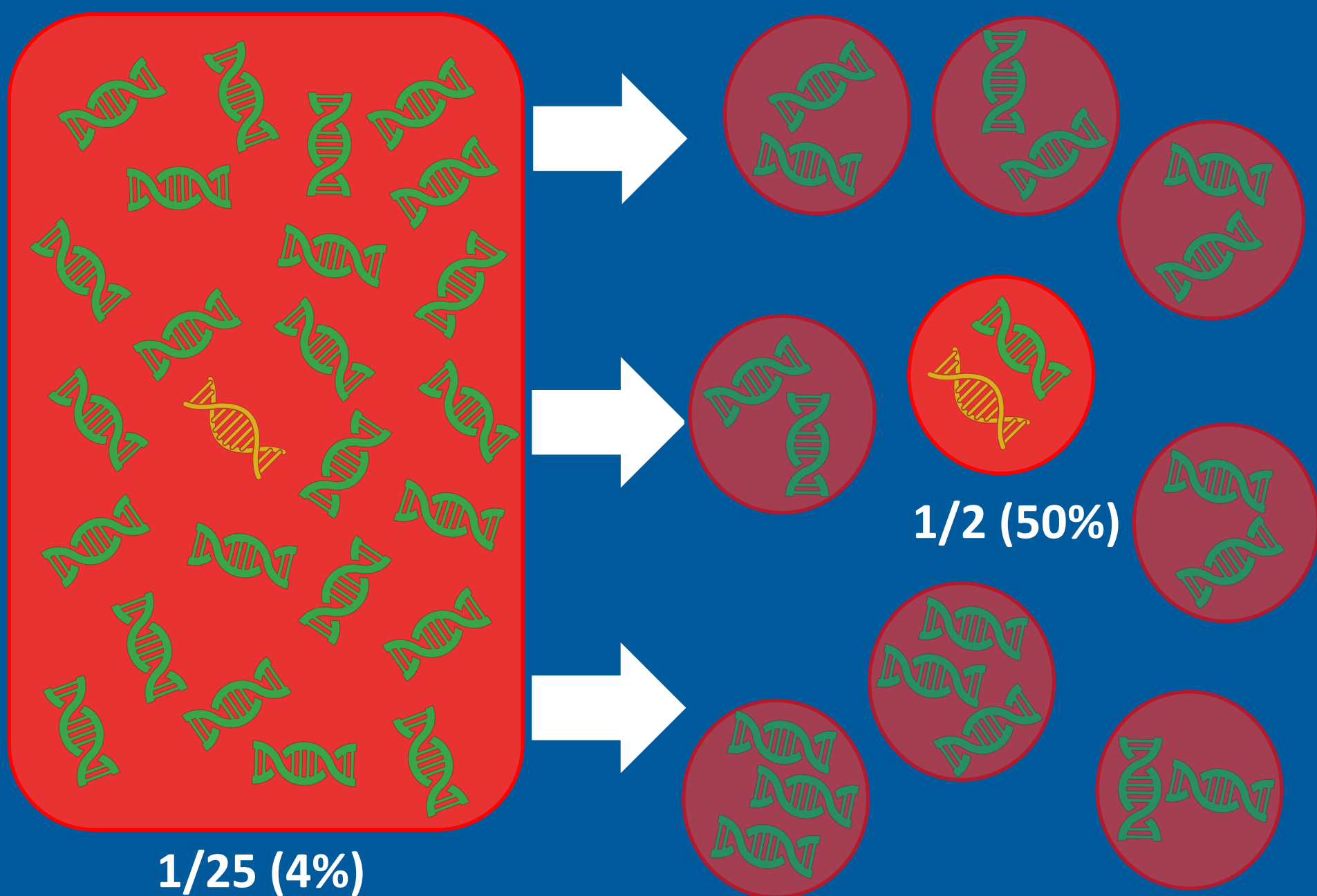
- **Advantages:**
  - Culture-independent
    - Detection of pathogen **DNA** (dead or alive)
  - Rapid diagnosis (4-8 hours)
    - Rapid tailoring of treatment
  - Decreased morbidity and mortality
  - Shorter hospital stay
- **Disadvantage:**
  - Moderate sensitivity (65-85%) to detect pathogens



# Droplet digital PCR

- Novel molecular technique
- Innovative
- Developed to increase sensitivity





# Two studies in one

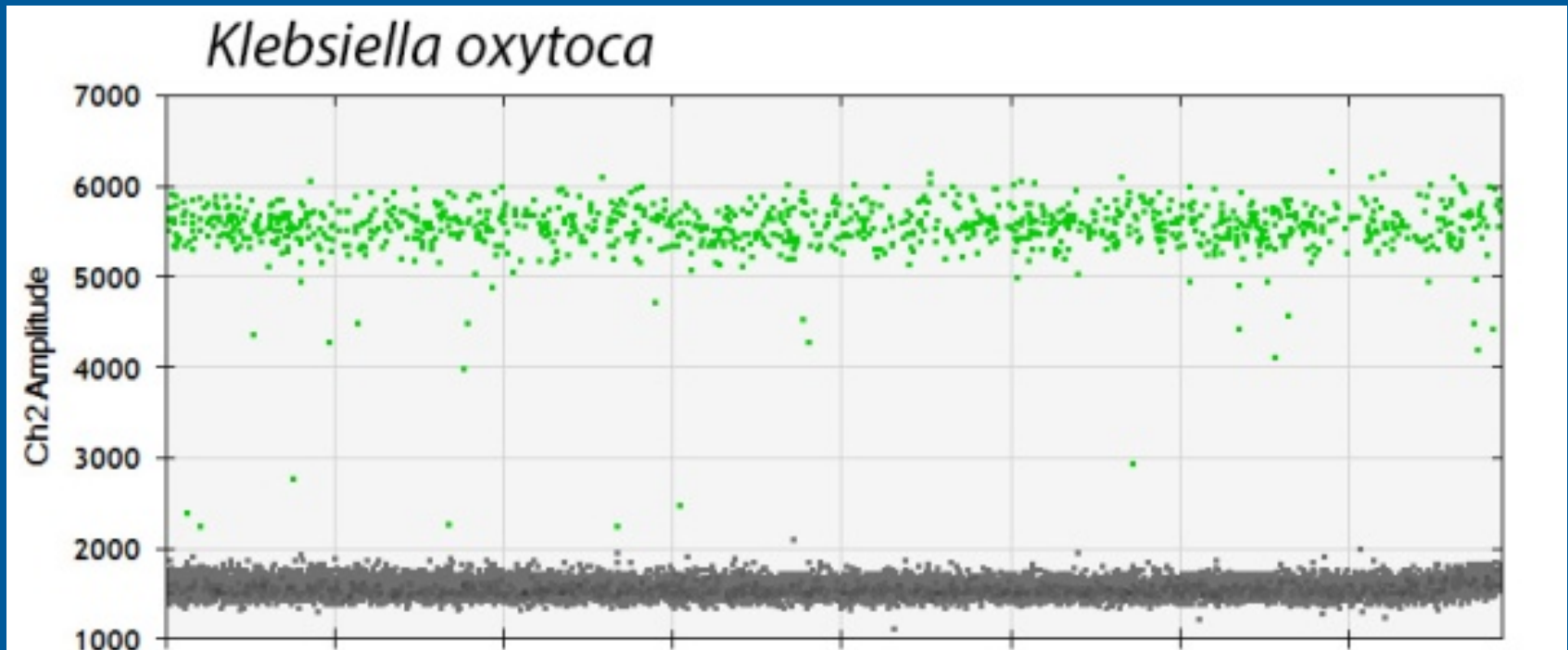
- Feasibility study (does it work?)
- Diagnostic accuracy study (sensitivity?)

# Feasibility of ddPCR

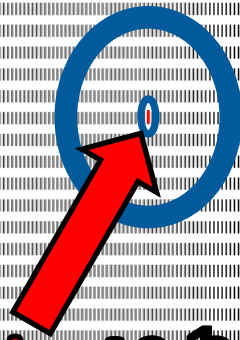
- Can we detect pathogen DNA with ddPCR?
- What is the 'detection limit' of the ddPCR?
- How fast can we detect pathogen DNA?

# Can we detect pathogen DNA with ddPCR?

- Both bacteria and fungi



# Detection limit of ddPCR



**1 pathogen DNA strand in 40,000 human DNA strands**

# How fast can we detect pathogen DNA?

Detection time: **4 hours**

Collecting blood  Detection pathogen DNA



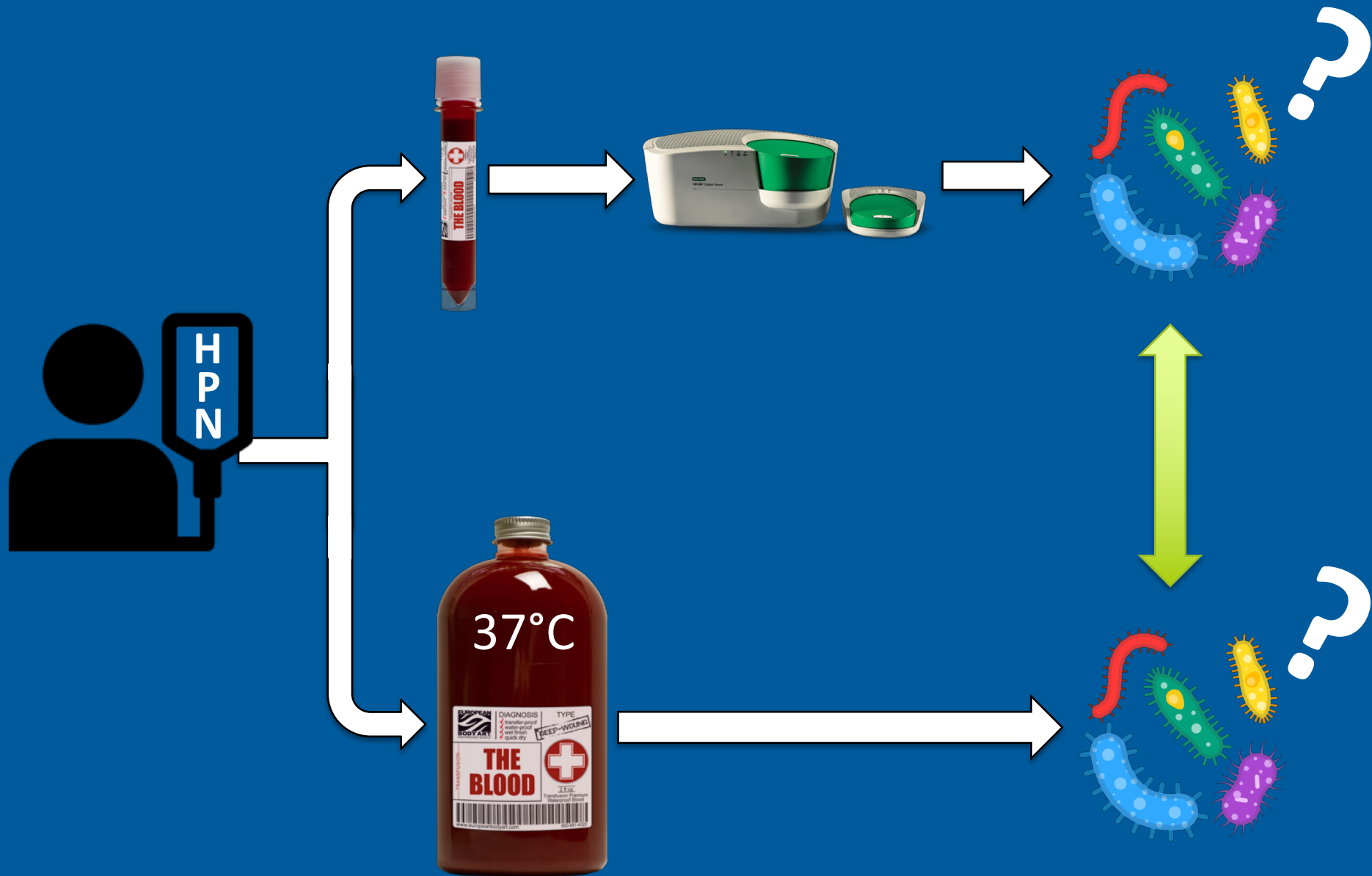
# Diagnostic accuracy of ddPCR

- Retrospective cohort of adult intestinal failure patients
- Suspicion of a bloodstream infection
- Admitted to the Radboudumc between 2008-2010

Nijmegen, The Netherlands




# Design diagnostic accuracy study



# Results diagnostic accuracy study

- 45 patients suspected of a bloodstream infection:
  - 15 had **positive** blood cultures

		Blood cultures
		Positive
ddPCR	Positive	12
	Negative	3
	Total:	15



**12/15 correct:  
Sensitivity = 80%**

# Discussion and conclusions

- Novel diagnostic tool for pathogen DNA detection
- Detection of pathogen DNA is possible within 4 hours
- Extremely low detection limit (1 in 40.000)
- Acceptable sensitivity (80%):
  - Further optimization is required
  - Larger (prospective) studies is needed

**More information: Breakout Session 3**  
**Sunday 4:20 PM - 5:05 PM**

# Questions?

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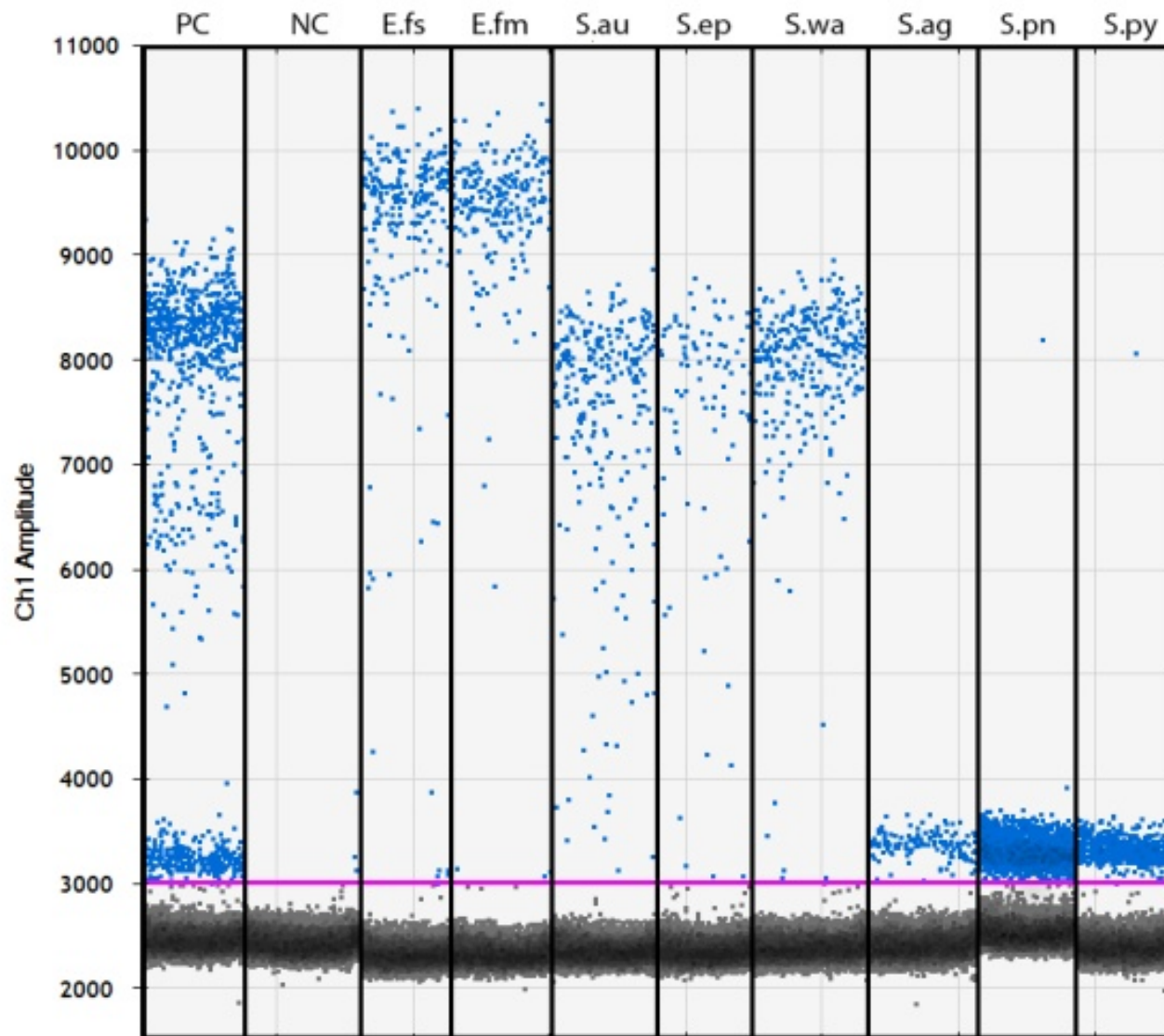
# Results diagnostic accuracy study

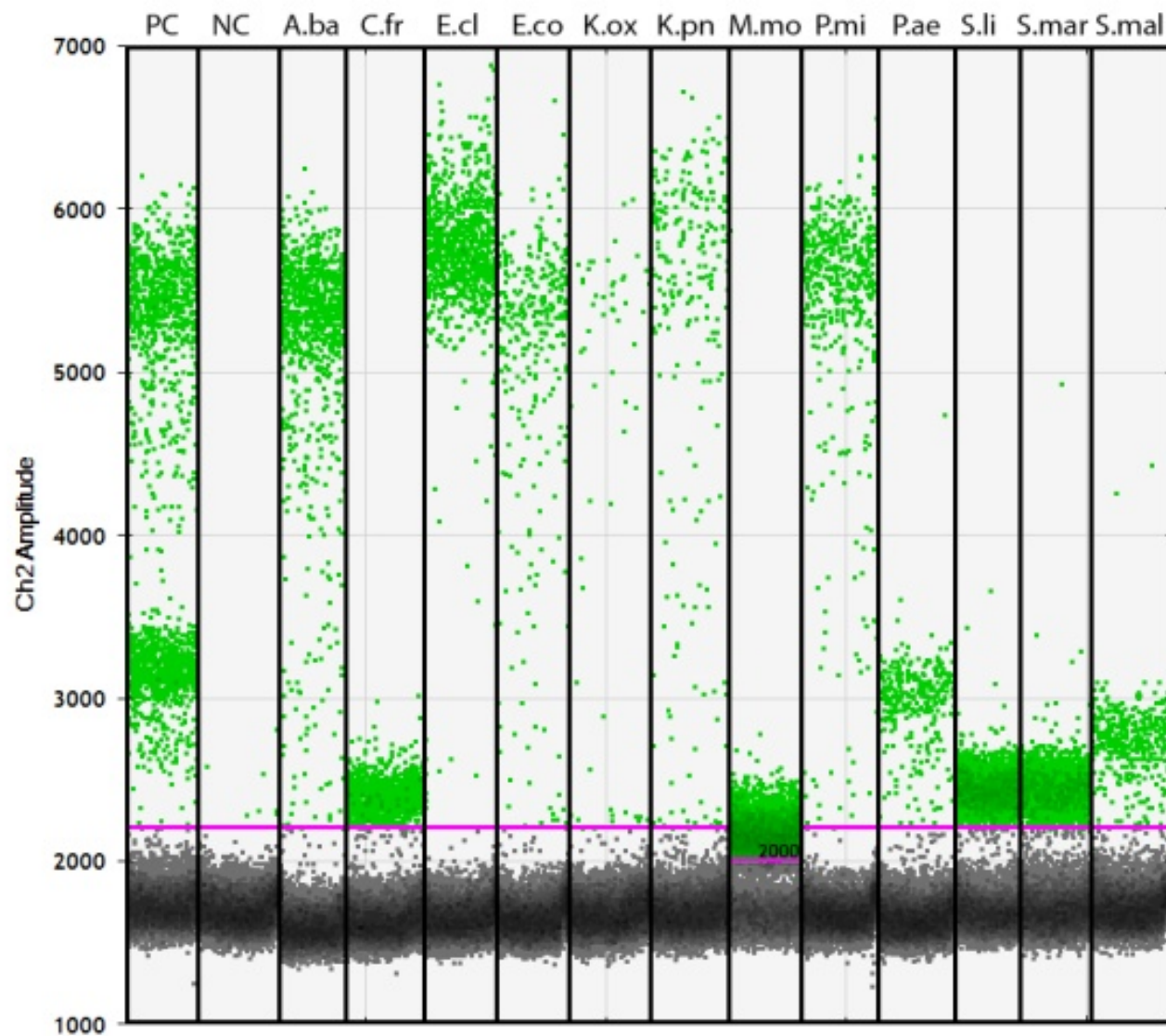
- 45 patients suspected of a bloodstream infection:
  - 15 had **positive** blood cultures
  - 30 had **negative** blood cultures

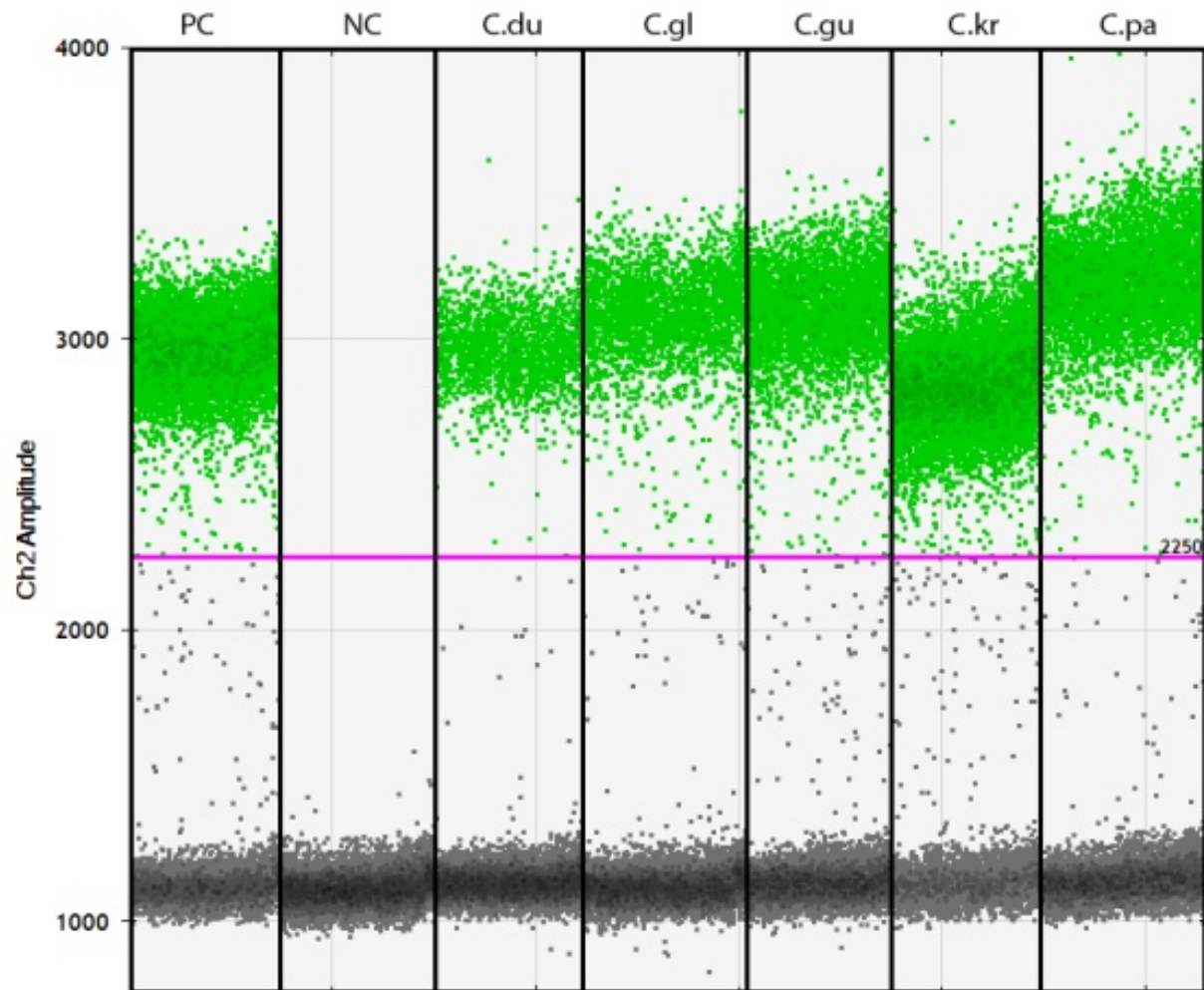
		Blood cultures	
		Positive	Negative
ddPCR	Positive	12	4
	Negative	3	26
	Total	15	30

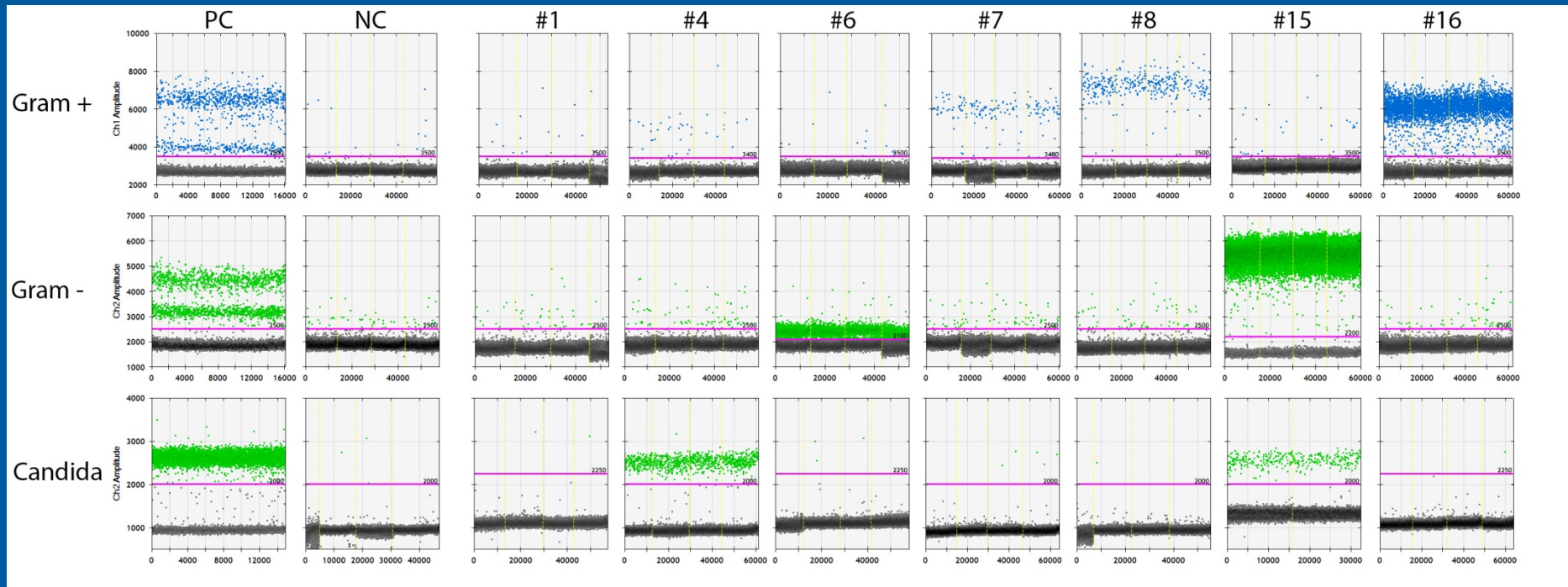


**12/15 correct:  
Sensitivity = 80%**









	Bloodstream infection	Bacteria	Gram-positive bacteria	Gram-negative bacteria	Fungi
<b>Sensitivity (95%CI)</b>	80 (52–96)	83 (52–98)	71 (29–96)	67 (22–96)	60 (15–95)
<b>Specificity (95%CI)</b>	87 (69–96)	82 (65–93)	89 (75–97)	92 (79–98)	100 (91–100)
<b>LR+ (95%CI)</b>	6.00 (2.33–15.46)	4.58 (2.13–9.87)	6.79 (2.40–19.17)	8.67 (2.54–29.52)	NA
<b>LR– (95%CI)</b>	0.23 (0.08–0.64)	0.20 (0.06–0.73)	0.32 (0.10–1.04)	0.36 (0.12–1.12)	0.40 (0.14–1.17)
<b>PPV (95%CI)</b>	75 (54–89)	63 (44–78)	56 (31–78)	57 (28–82)	NA
<b>NPV (95%CI)</b>	90 (76–96)	93 (79–98)	94 (84–98)	95 (85–98)	95 (85–99)