

**A meta-analysis of the effects of feed  
additives on ruminal pH and A/P ratio  
:a potential for reducing the risk of  
subacute ruminal acidosis (SARA)**

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# Subacute ruminal acidosis (SARA)

- 주로 농후사료를 과다 급여하는 반추동물에게 흔하게 나타나는 질병  
(Calsamiglia et al., 2012)
- 고능력우의 20-40%가 SARA를 겪고 있음(Kleen, 2004)
- 미국의 경우, SARA로 유량의 감소, 조기도태, 2차 질병 증가 등으로 인한 손실은  
1.12 \$/day/cow 정도도 예상됨(Stone, 1999)

Calsamiglia, S., M. Blanch, A. Ferret, and D. Moya. 2012. Is subacute ruminal acidosis a pH related problem? Causes and tools for its control. *Anim. Feed Sci. Technol.* 172:42–50.

Kleen, J.L., 2004. PhD Thesis: prevalence of subacute ruminal acidosis in Dutch dairy herds – a field study. Tierärztliche Hochschule Hannover, Germany.

Stone, W.C., 1999. The effect of subclinical rumen acidosis on milk components. In: Proceedings of the Cornell Nutrition Conference of Feed Manufacturers, Syracuse, N.Y. Cornell University, Ithaca, NY, USA, pp. 40–46.



# Subacute ruminal acidosis (SARA)

## 주요증상

- 섭취량/사료효율/유지방 감소
- 제염염(laminitis)
- 간농양(liver abscesses)
- 분내 알곡 발견/설사
- 심한 경우 사망까지 이를 수 있음

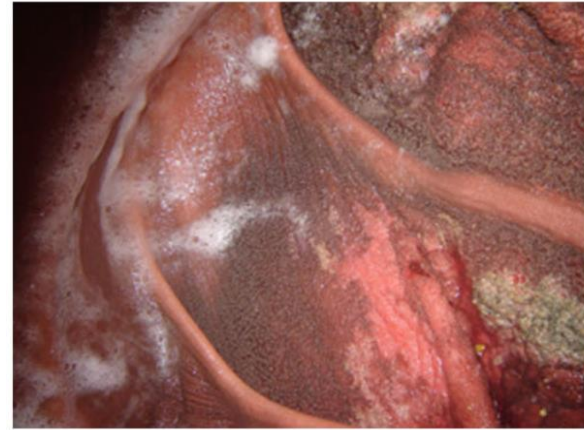


Photo credit: Dr. Greg Penner

# Subacute ruminal acidosis (SARA)

## 주요원인

- 농후사료의 과다 급여

*“We propose that SARA should be redefined as a “**high-concentrate syndrome**” because it includes both the changes in pH and the effect of type of diet” (Calsamiglia et al., 2012)*

- 이유/질병/분만 이후 사료의 급격한 변화

- 전환기/비유초기의 잘못된 사양관리

Calsamiglia, S., M. Blanch, A. Ferret, and D. Moya. 2012. Is subacute ruminal acidosis a pH related problem? Causes and tools for its control. Anim. Feed Sci. Technol. 172:42–50.

↑ Intake of starch and fermentable carbohydrates

↑ VFA production

↓ pH and ↑ osmolarity

pH < 6.0

↓ Fiber digestion and microbial growth

pH < 5.8

↑ *S. Bovis* and lactic acid

↑ Death of the protozoa

pH < 5.5

**SARA**

Glucose accumulation

↑ D-lactate

Death of bacteria

Release of endotoxins

pH < 5.0

**Acute acidosis**

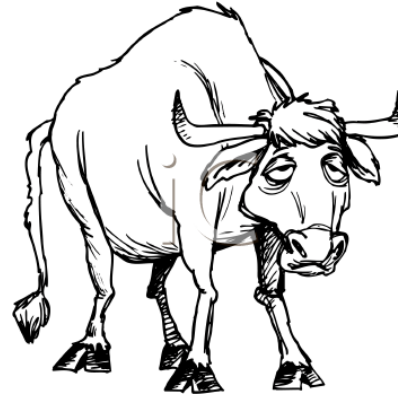
Valente, Tiago Neves Pereira, Cláudia Batista Sampaio, Erico da Silva Lima, Bruno Borges Deminiciis, Andréia Santos Cezário, and Wallacy Barbacena Rosa dos Santos. "Aspects of Acidosis in Ruminants with a Focus on Nutrition: A Review." *Journal of Agricultural Science* 9, no. 3

# Subacute ruminal acidosis (SARA)

## 어떻게 해야 하나?

- 일반적으로 반추위 pH를 높이는 것이 중요하다고 생각
- 하지만 반추위 pH가 5.5보다 높아도 SARA가 발생할 수 있음  
또한 낮다고 100% 발생하는 것도 아님
- 따라서 1) 반추위 pH 조절과 함께 2) 반추위 미생물 컨트롤을  
모두 고려한 접근이 필요함

# PARADOX



**Productivity vs. Health & welfare**



**두마리 토끼를 다 잡을 순 없을까?**



# Subacute ruminal acidosis (SARA)

## 예방 및 치료

- Effective fiber를 충분히 급여
- Ionophores 급여
- ~~항생제~~ 급여
- 완충제 급여 (e.g. bicarbonate)
- 효모제/생균제 급여
- 사료급여 횟수 증가

# Meta-analysis

## 메타분석

- 동일한 주제에 대한 **다양한** 연구결과를  
체계적이고 **계량적**으로 분석하는 분석 방법
- 특정한 한 연구의 결과에만 의존해서 결론을 내릴 경우 -> 잘못된 결정의 위험 ↑
- 연구결과는 연구마다 상충되거나 다를 수 있음

# Meta-analysis

## 메타분석의 단계

1. 연구 주제 선정/질문 제기
2. 문헌검색
3. 데이터 추출 및 코딩
4. 데이터 분석: 효과크기 계산/동질성 검증/출판편향 검증
5. 결과 보고서 작성

# Materials and methods

## 연구 목적

- 각종 첨가제(bicarbonate, yeast culture, essential oil 및 organic acid)가 반추위 발효 안정화를 위해 쓰이나 각각의 효과의 크기에 대한 종합적이고 계량적인 연구가 없음
- 따라서 본 연구에서는 meta-analysis를 통해 각종 사료 첨가제가 반추위 pH 및 A/P ratio에 미치는 영향을 조사하고, 이를 통해 SARA를 예방 및 치료할 수 있는 가능성을 알아보고자 함

# Materials and methods

## 문헌 검색

- Google scholar 및 Science direct를 이용
- Peer-review가 수행된 연구 자료만 수집
- Keywords: sodium bicarbonate; sodium sesquicarbonate; yeast culture; essential oil; malic acid
- Target response: rumen pH 및 acetate to propionate ratio
- 총 41개의 연구 84개의 데이터셋이 사용됨

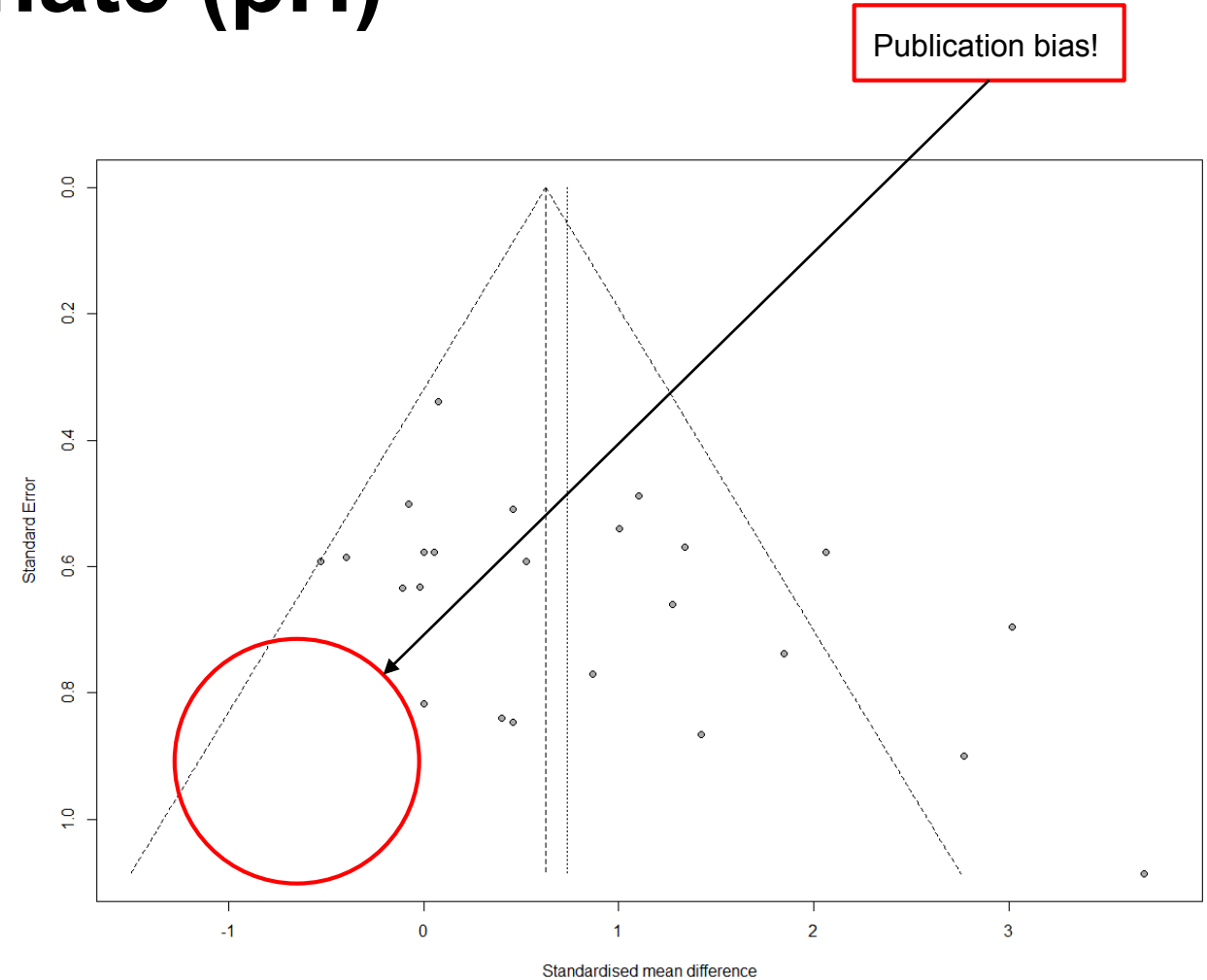
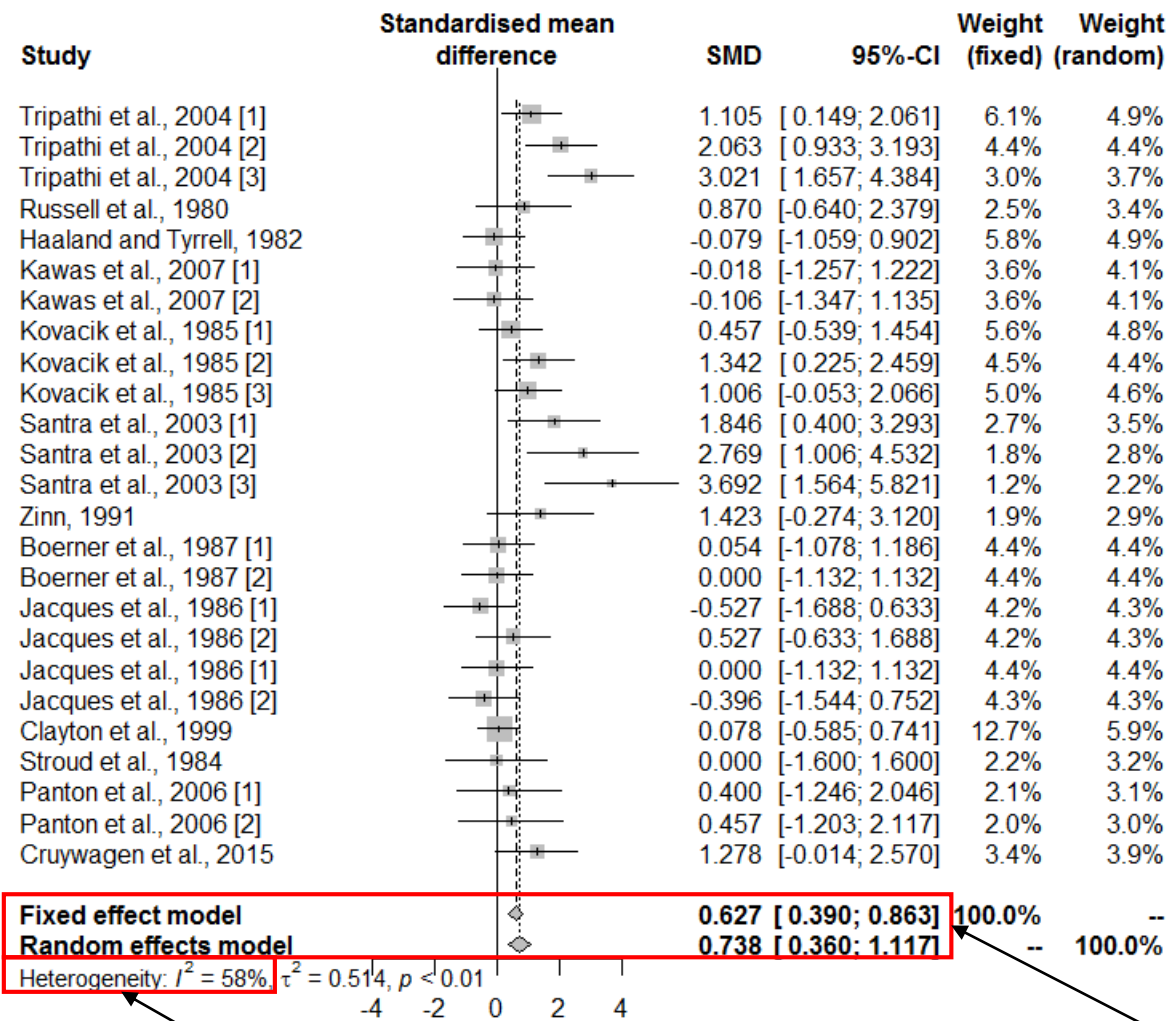


# Materials and methods

## 통계 분석

- 통계분석은 R software (version 3.4.0)의 Meta package를 이용하여 분석
- Standardized mean difference (SMD; a.k.a Effect size)를 계산
- SMD의 이질성(heterogeneity)은 tau square ( $T^2$ ) 및 I square ( $I^2$ )를 이용하여 계산
- 이질성이 높을 경우 meta-regression 및 Meta-ANOVA 분석을 수행
- 출판편향(publication bias) 분석을 위해 funnel plot test를 수행

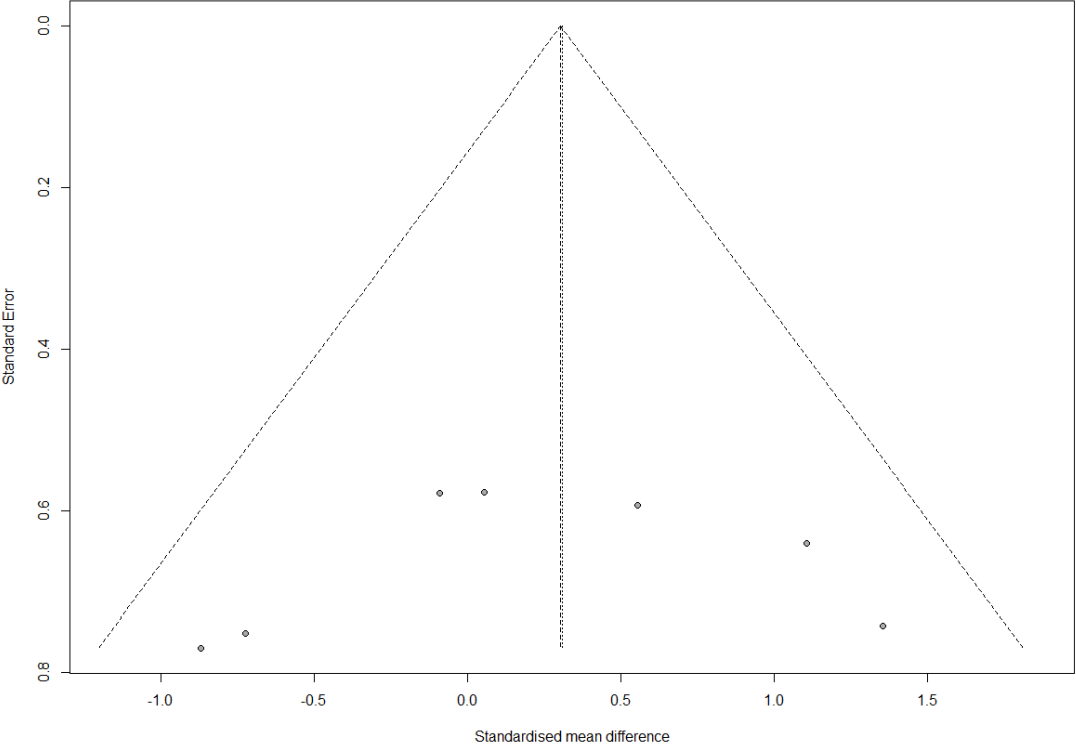
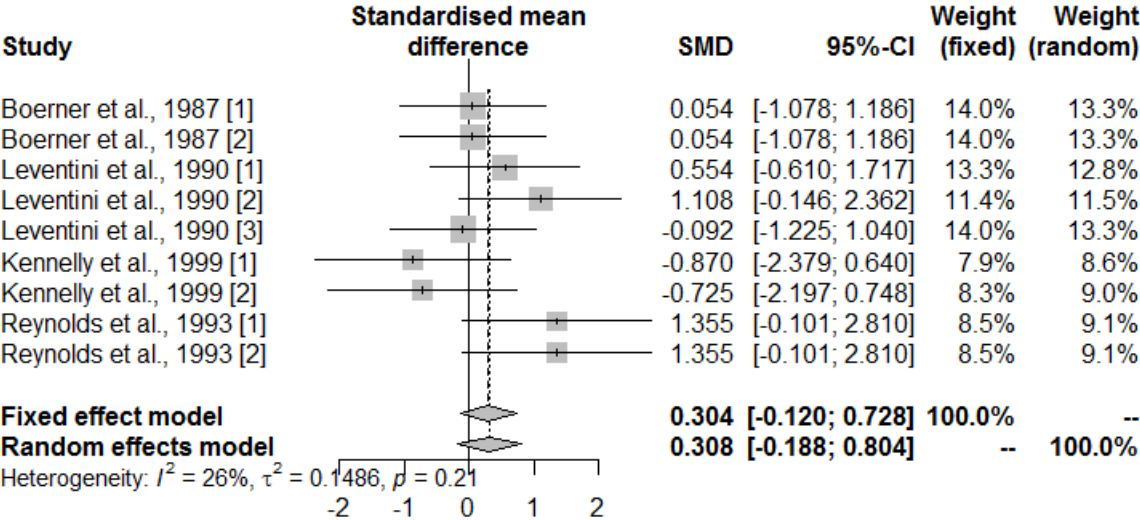
# Results: sodium bicarbonate (pH)



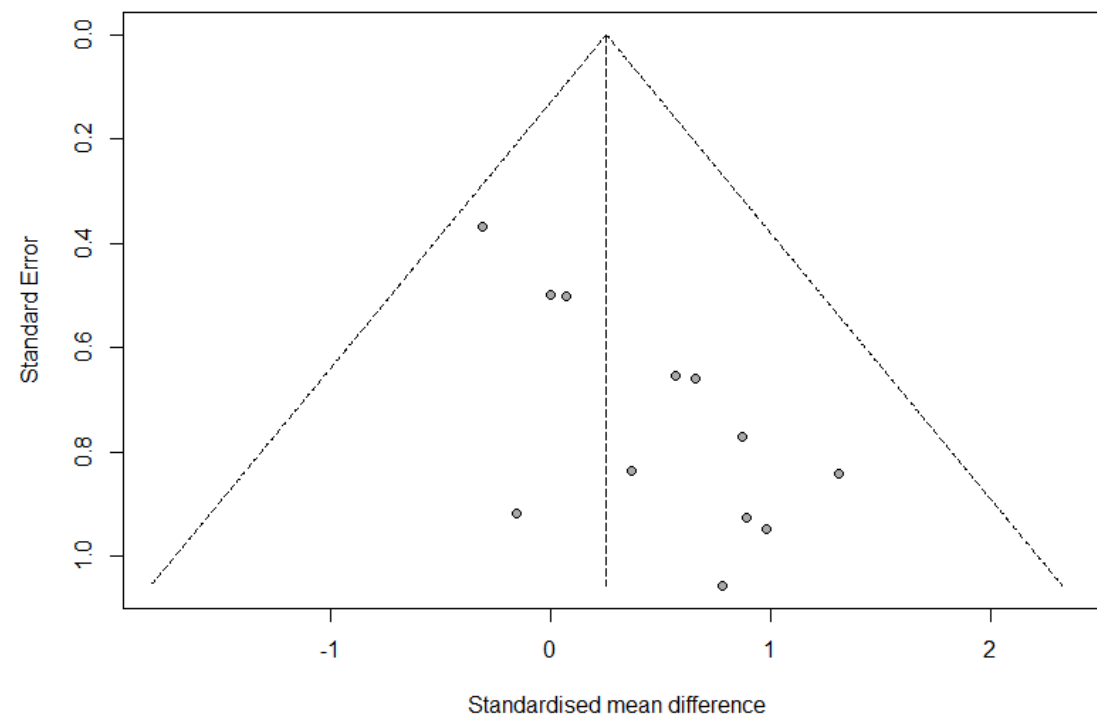
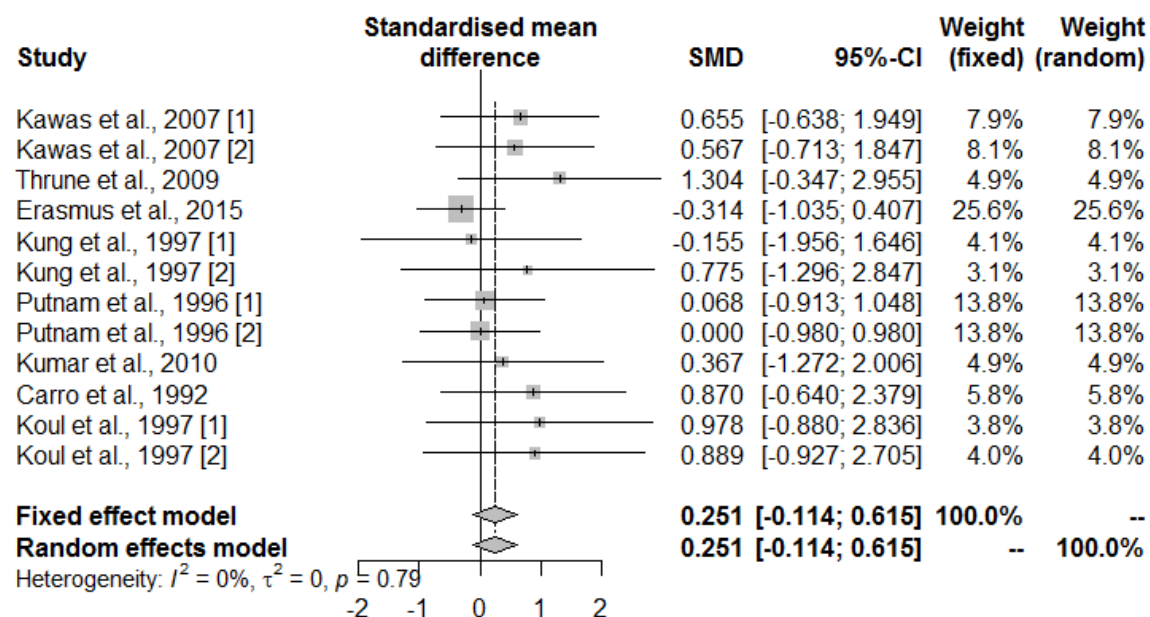
An  $I^2$  value less than 25% indicated low heterogeneity, whereas values between 35 to 50% denoted moderate heterogeneity and those above 50% denoted high heterogeneity (Higgins et al., 2003).

Standardized mean difference values of  $< 0.2$ ,  $> 0.2$  and  $< 0.7$ , or  $> 0.8$  were considered small, moderate, or large effects, respectively (Cohen, 1988).

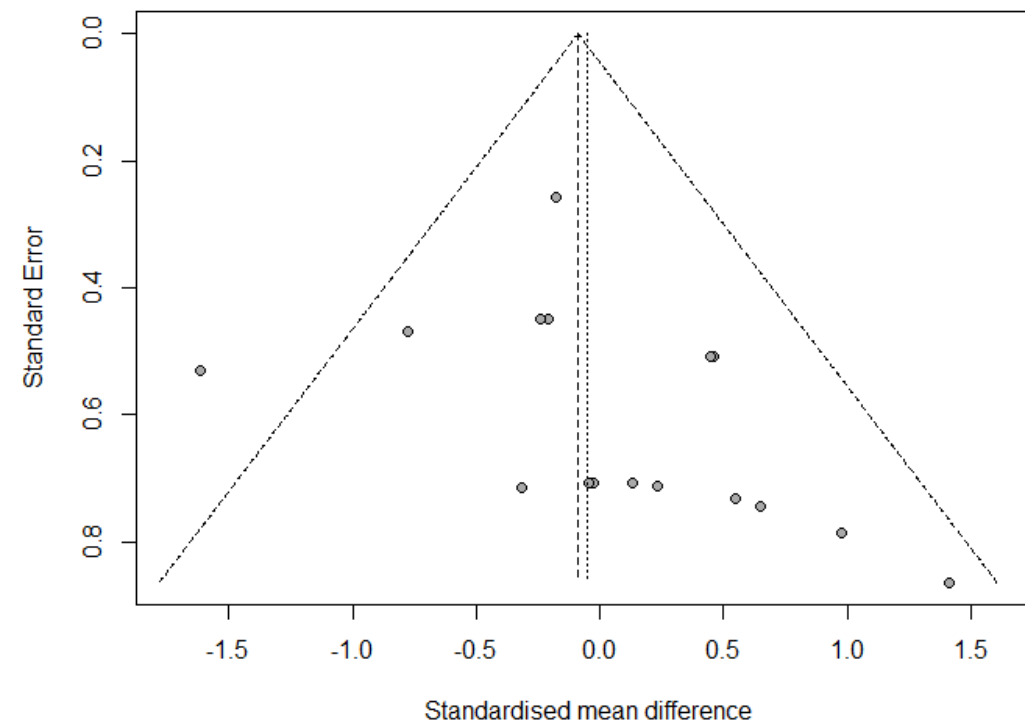
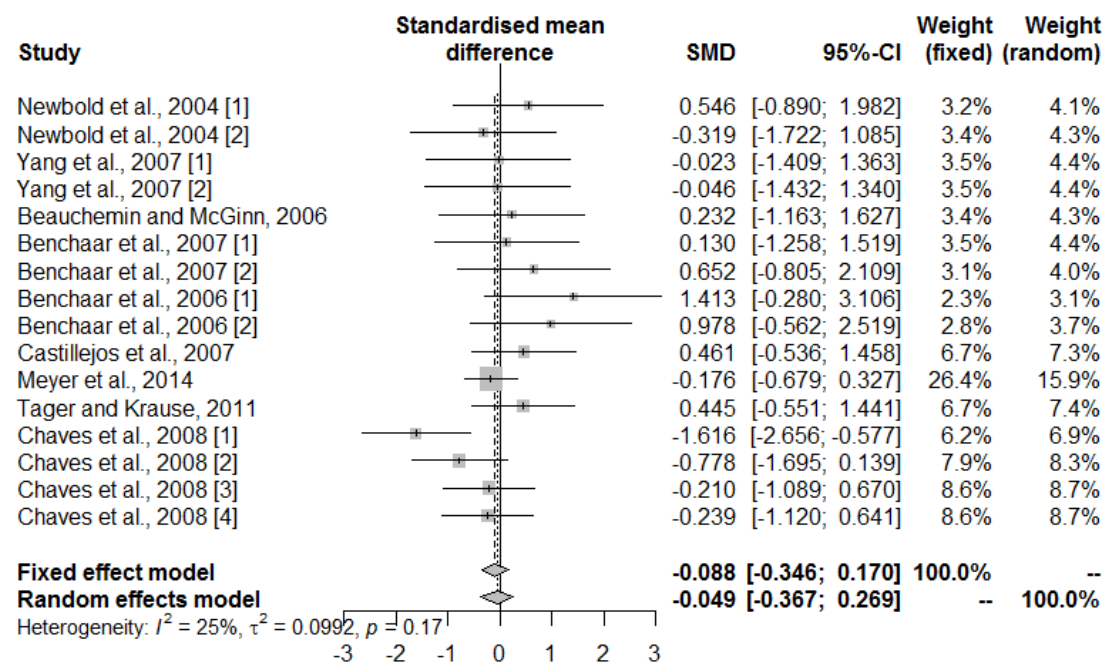
# Results: sodium sesquicarbonate (pH)



# Results: yeast culture (pH)

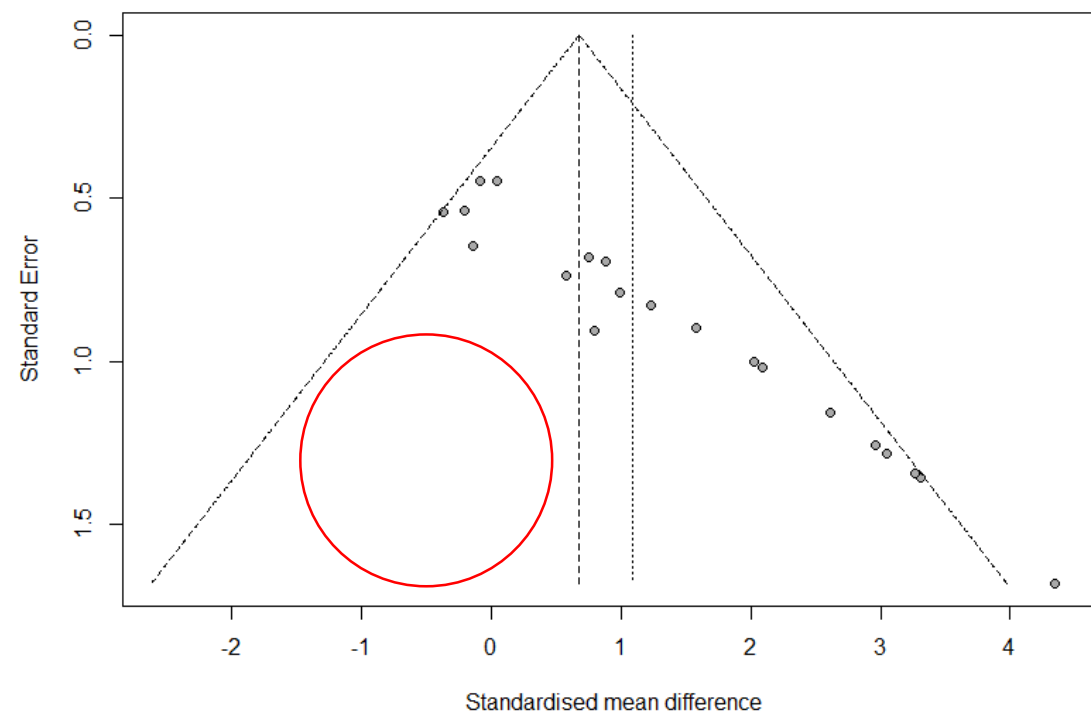
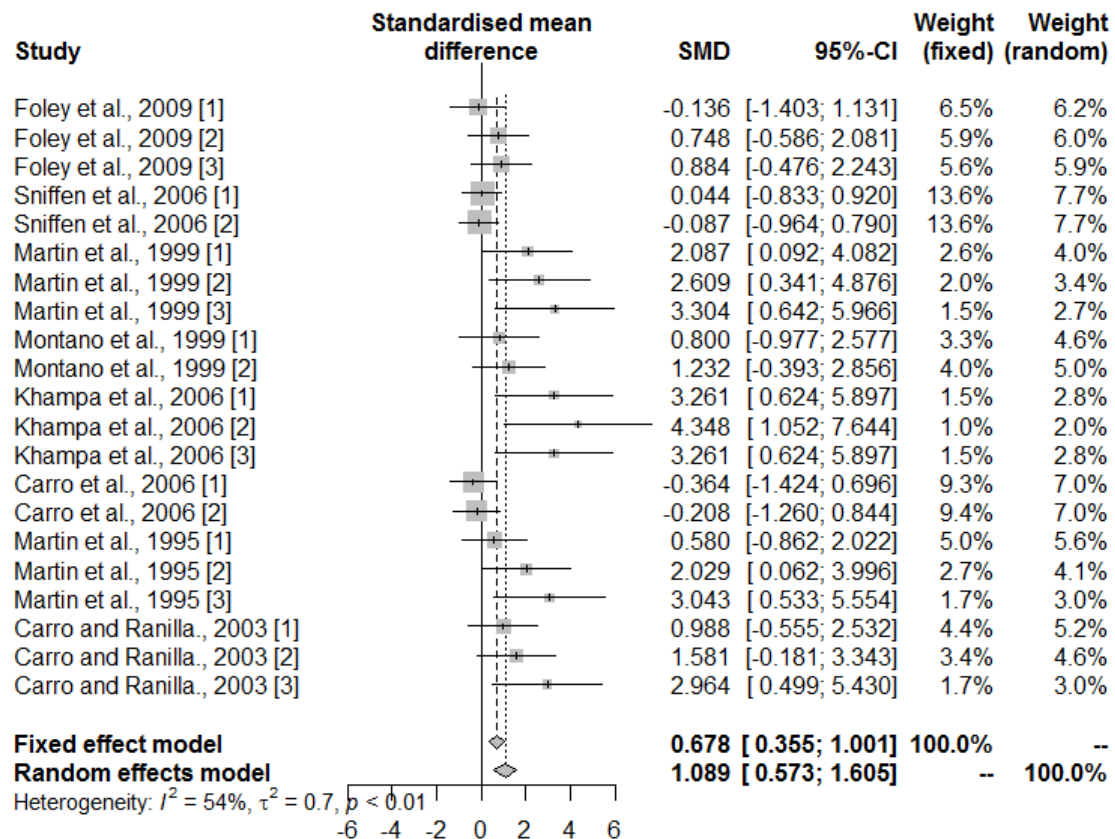


# Results: essential oil (pH)

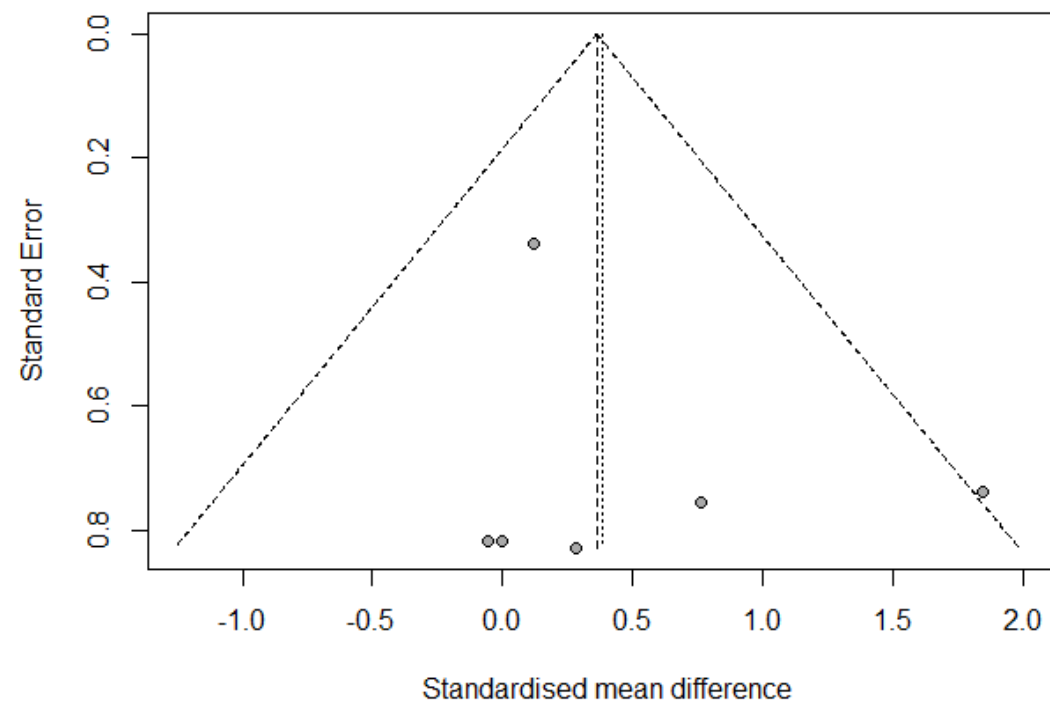
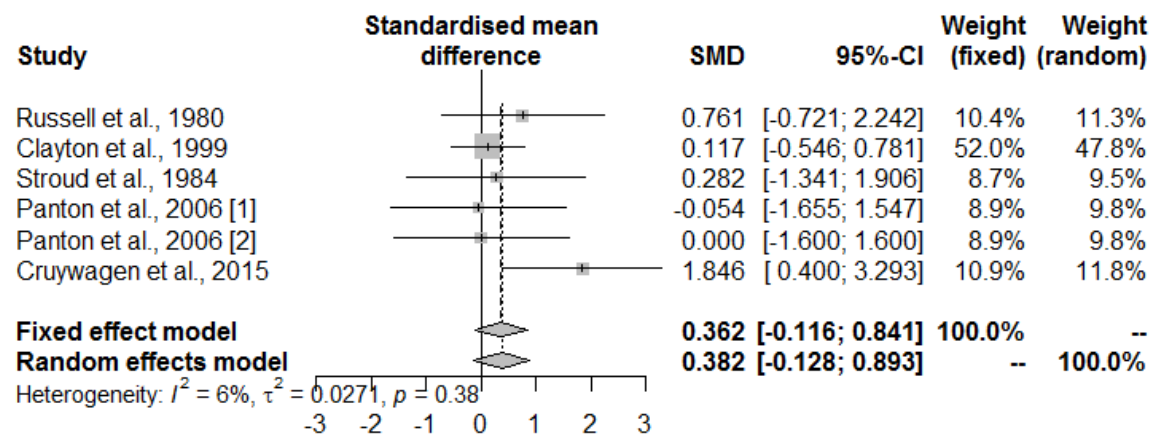




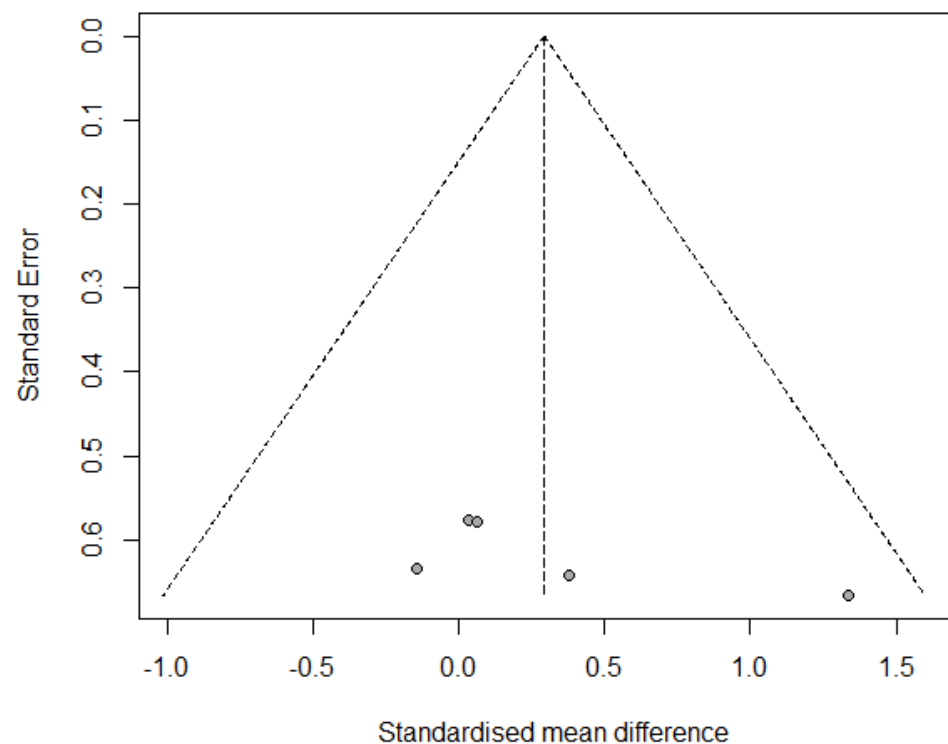
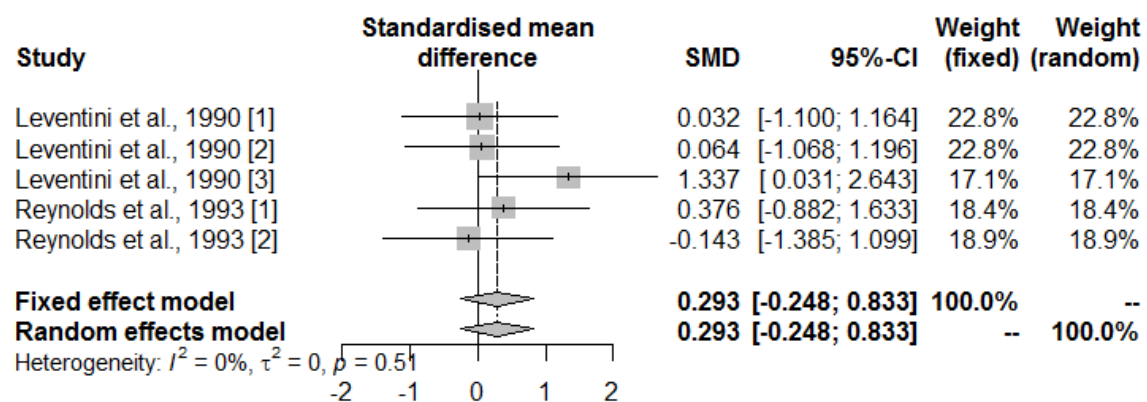
# Results: malic acid (pH)



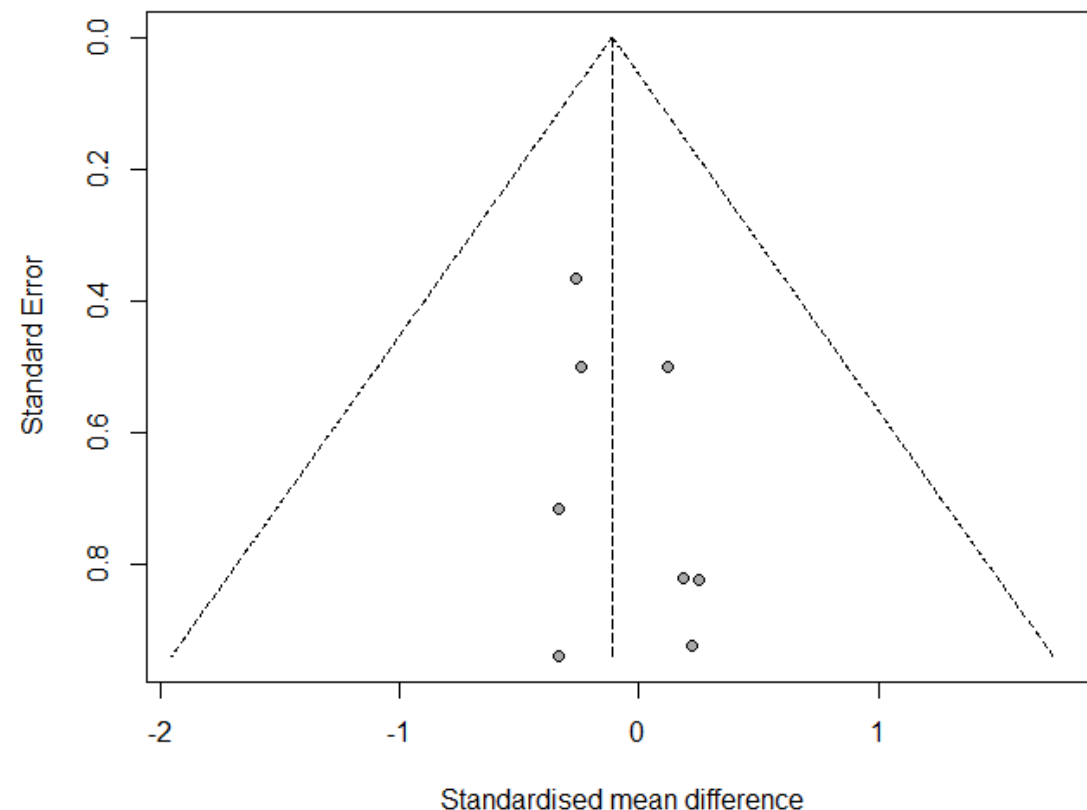
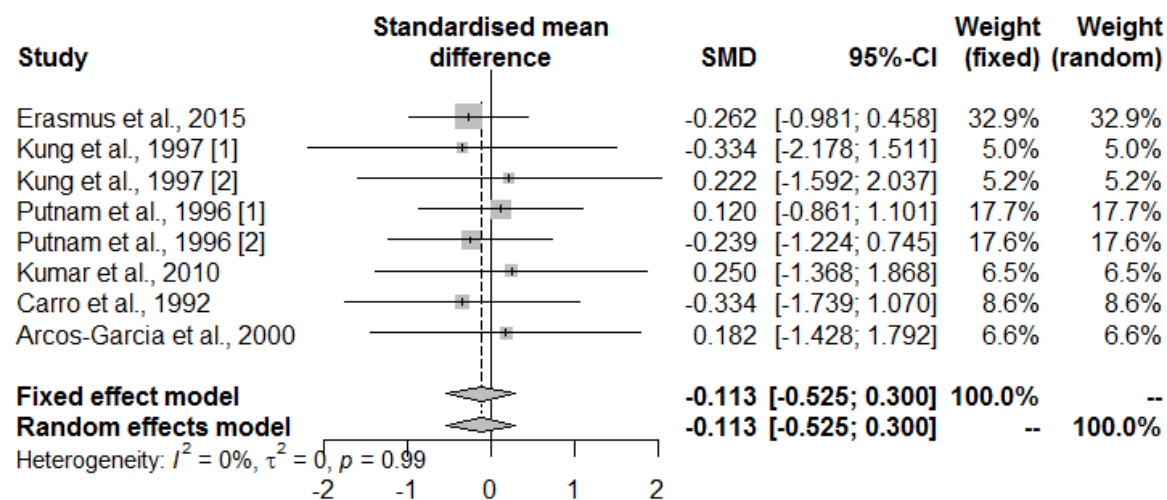
# Results: sodium bicarbonate (A/P ratio)



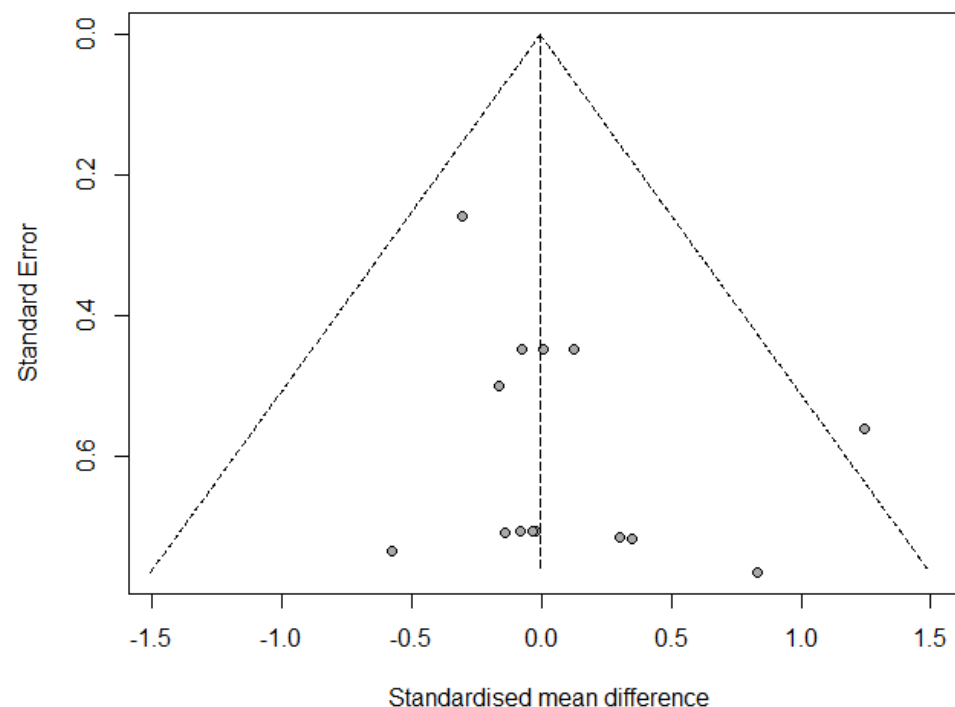
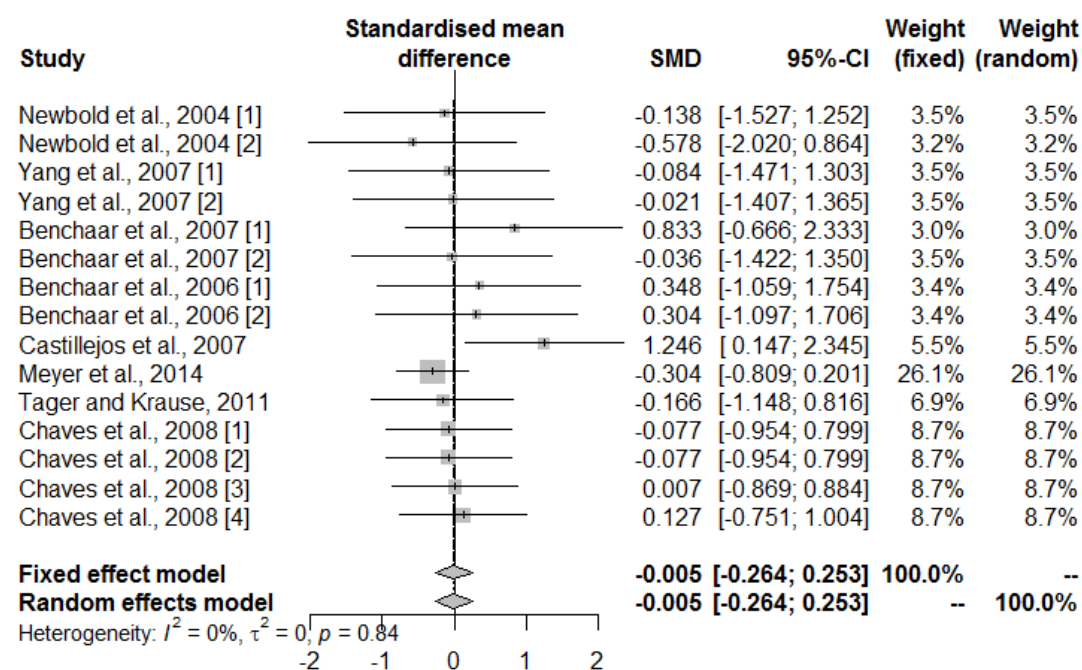
# Results: sodium sesquicarbonate (A/P ratio)



# Results: yeast culture (A/P ratio)

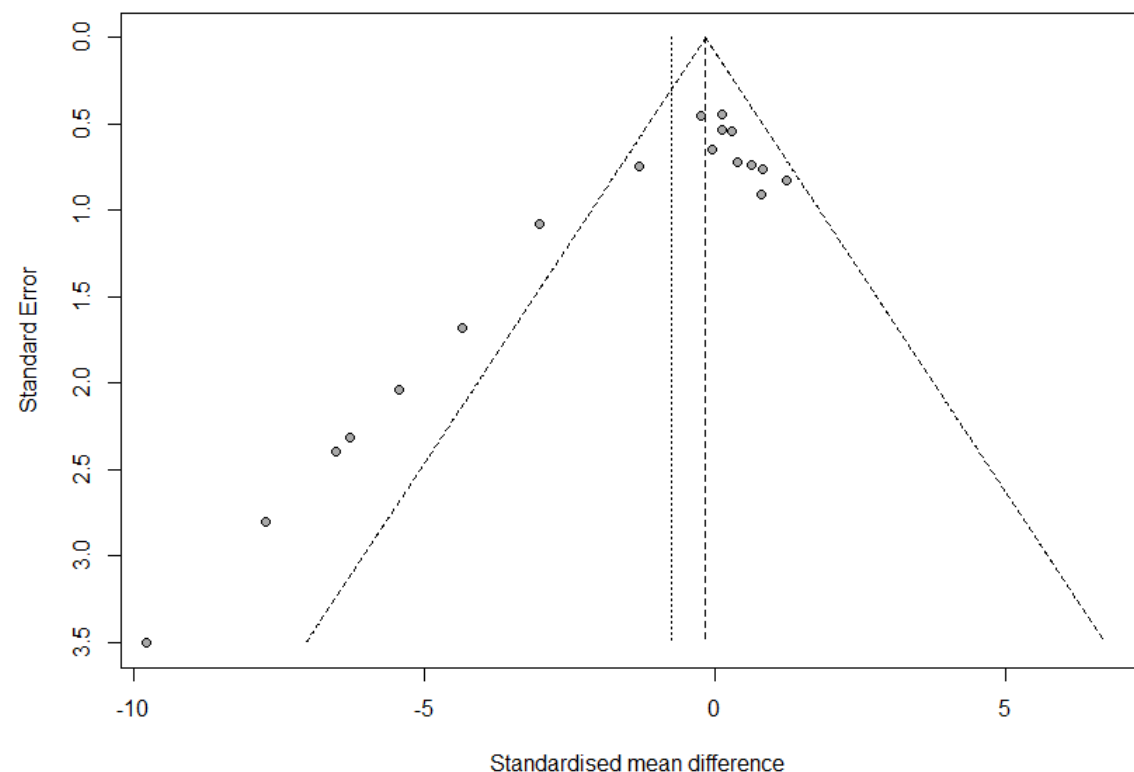
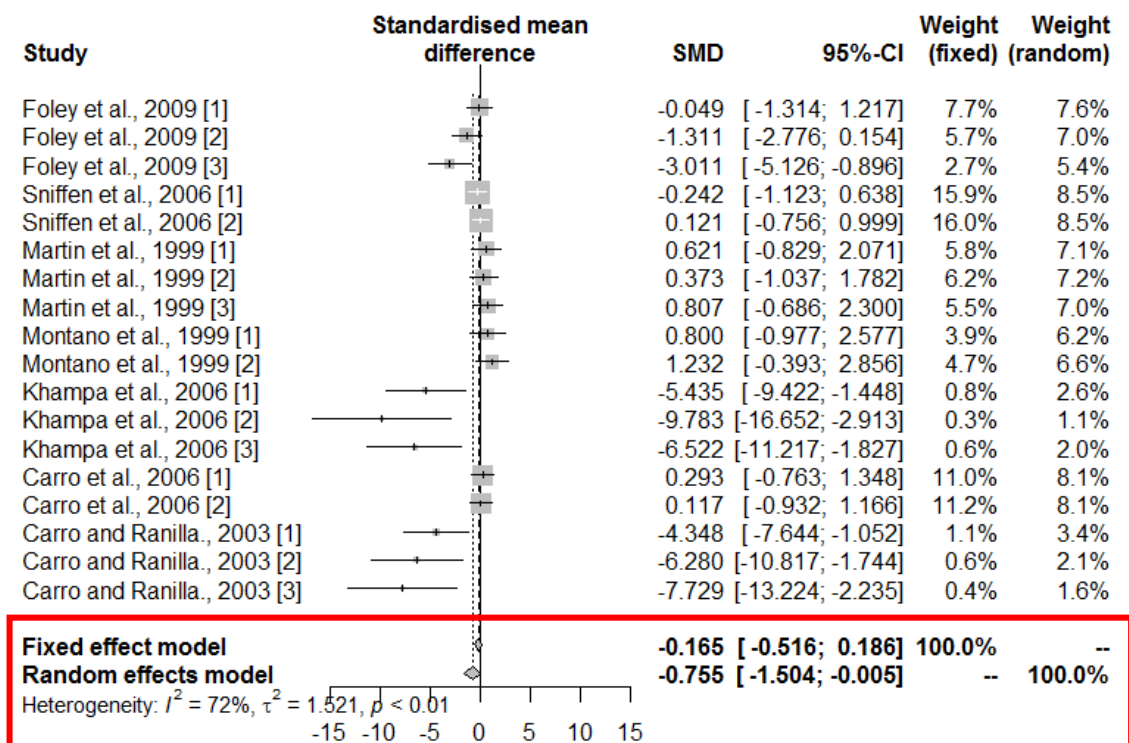


# Results: essential oil (A/P ratio)



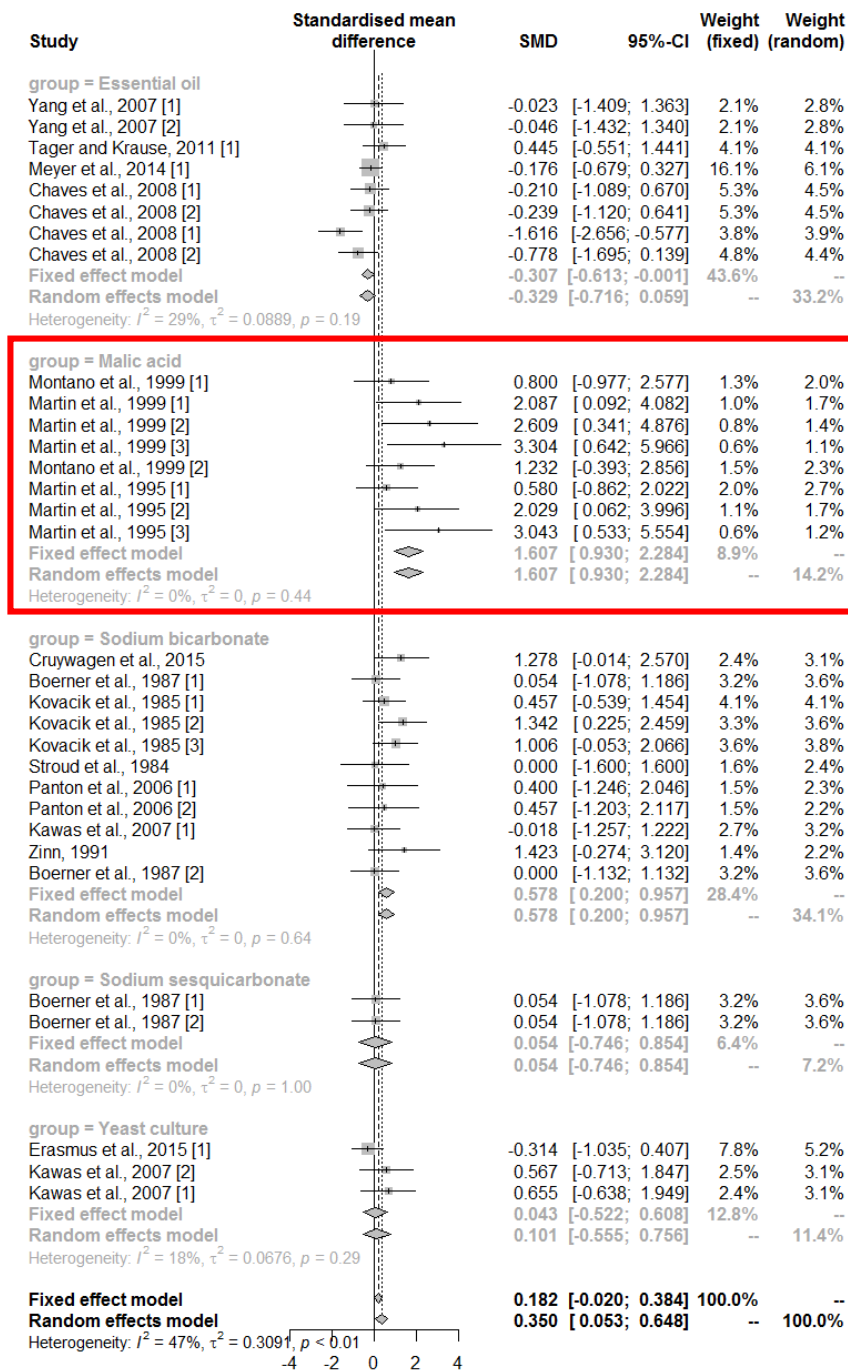


# Results: malic acid (A/P ratio)

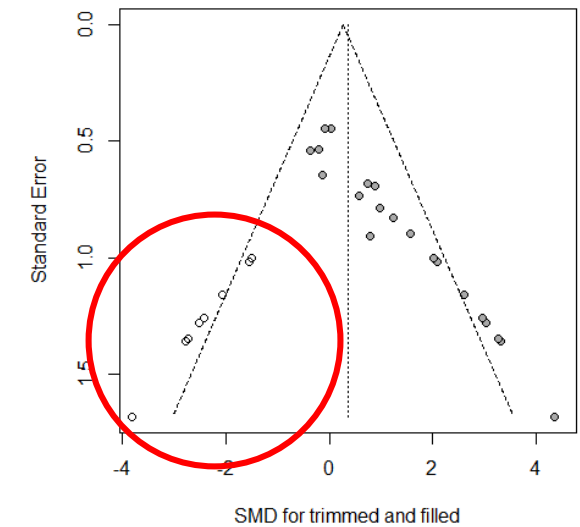
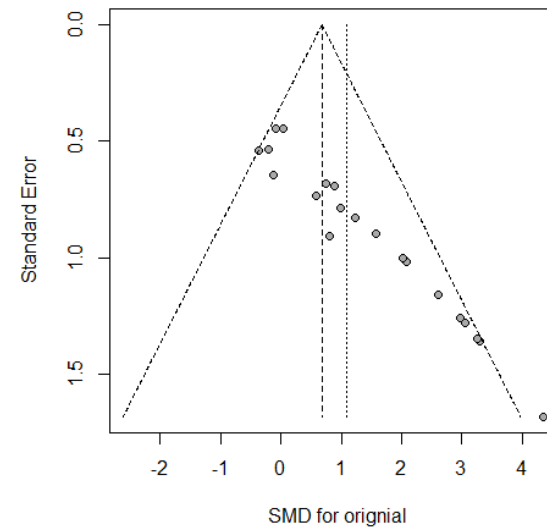
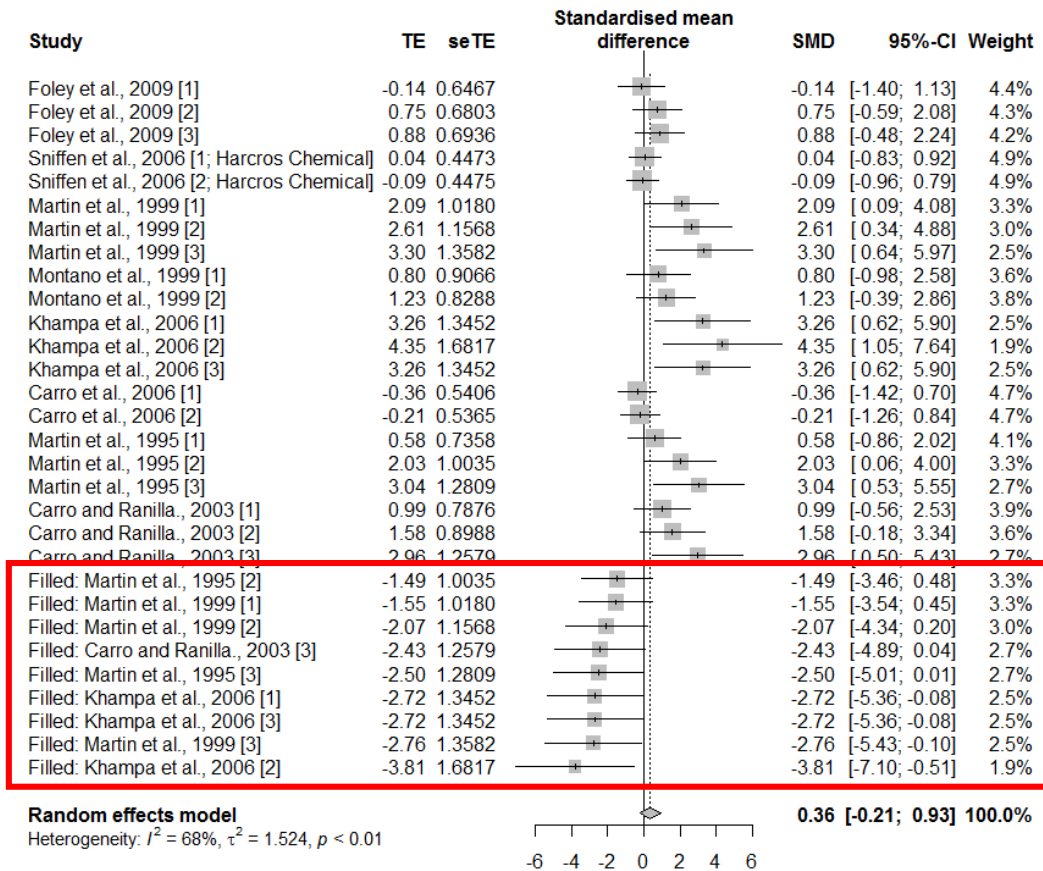


# Results: Meta-ANOVA analysis result of feed additives on ruminal pH below 6.0 (SARA induced condition)

- 대조구의 pH가 6.0 이하인 연구(SARA 조건 유도)를 대상으로 Meta-ANOVA 분석을 수행함
- Malic acid의 SMD는 1.61로 매우 높은 효과크기를 보임
- Sodium bicarbonate는 중간 효과크기를 보임
- Sodium sesquicarbonate 및 yeast culture는 작은 효과 크기를 보임
- Essential oil은 pH를 낮추는 경향을 보임(SMD = - 0.307)



# Results: Trim-and-fill analysis (pH; malic acid)

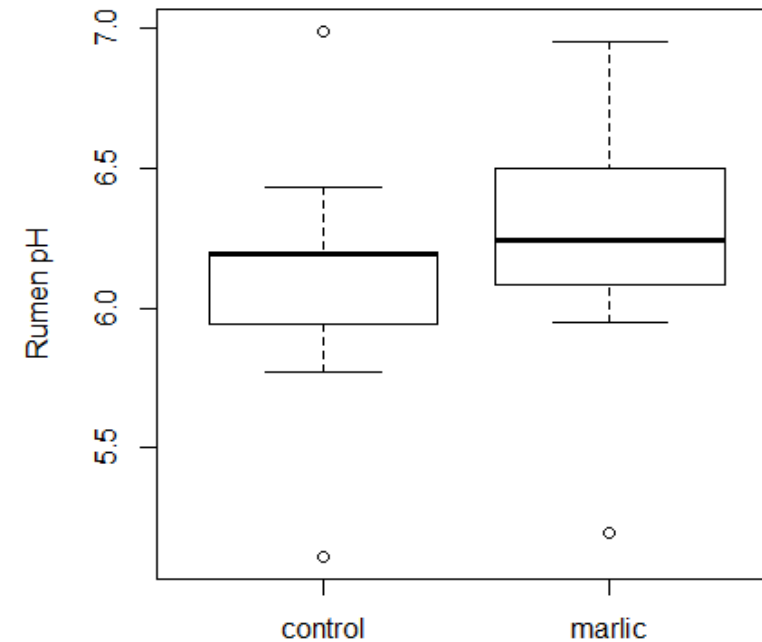


Duval, S., & Tweedie, R. 2000. A nonparametric “trim and fill” method of accounting for publication bias in meta-analysis. *Journal of the American Statistical Association*, 95(449), 89-98.

# Results: Meta-regression analysis (pH; malic acid)

	Value	SE	DF	T value	P value
Intercept	6.125	0.152	32	40.2	<0.001
Treatment	0.140	0.045	32	3.1	0.004

AIC: 5.08; BIC: 15.21; Model, pH = intercept + treatment + random effect (study+animal+dose).



# Mode of action: role of the malic acid in the prevention of ruminal pH changes (Castillo et al., 2004)

C. Castillo et al. / *Animal Feed Science and Technology* 115 (2004) 101–116

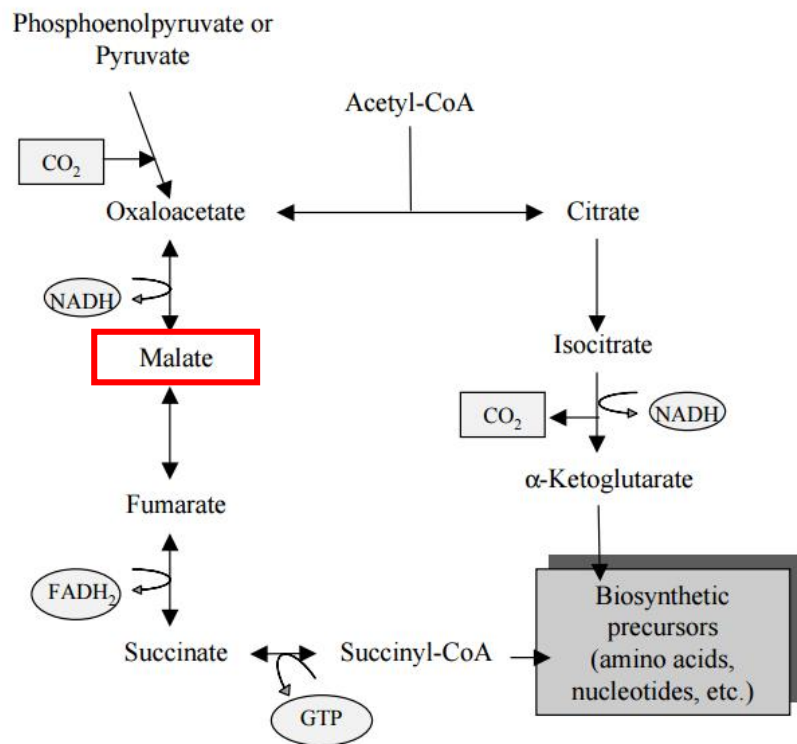


Fig. 1. Biosynthetic precursors produced by an incomplete citric acid cycle in anaerobic bacteria (adapted from Nelson and Cox, 2000).

C. Castillo et al. / *Animal Feed Science and Technology* 115 (2004) 101–116

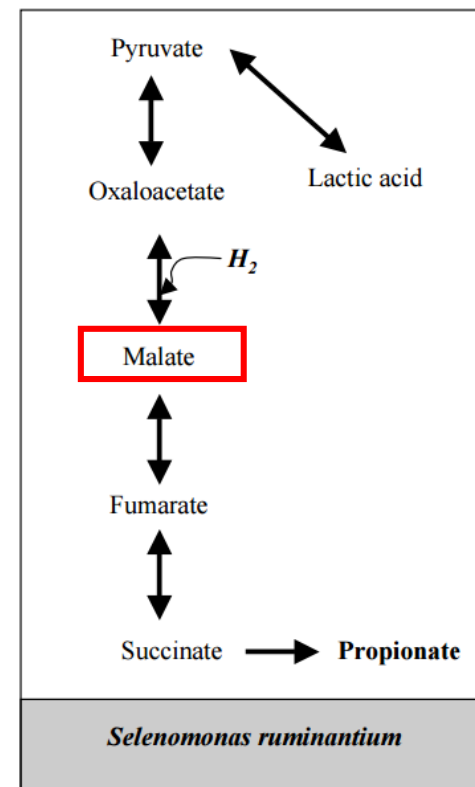


Fig. 2. Effect of malate in a medium that contains lactic acid (Crespo et al., 2002).

Castillo, C., J. L. Benedito, J. Méndez, V. Pereira, M. López-Alonso, M. Miranda, and J. Hernández. 2004. Organic Acids as a Substitute for Monensin in Diets for Beef Cattle. *Animal Feed Science and Technology* 115, no. 1–2: 101–16.



# Conclusion

- 각종 사료첨가제가 반추위 발효에 미치는 영향에 대한 메타분석을 실시하였음
- Malic acid의 첨가급여 시 반추위 pH가 증가(SMD=1.08)하였으며, 특히 SARA induced condition에서 더 높은 효과크기를 보임(SMD=1.61)
- 이유, 분만, 전환기 등의 이유로 동물의 사료 섭취량과 에너지 공급량 등 급격한 변화가 있을 경우 SARA의 위험이 증가할 수 있음
- 이러한 경우, malic acid 와 sodium bicarbonate 등 각종 첨가제의 급여가 SARA의 발병을 예방 및 완화할 수 있을 것으로 보임

# 감사합니다

Thank you!

ありがとうございました

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