	Koch m.fl. 2009	Gläser m.fl. 2010	Gläser m.fl. 2013
	Reference values for cardiopulmonary exercise testing in healthy volunteers: the SHIP study	**Influence of age, sex, body size, smoking, and Beta blockade on key gas exchange exercise parameters in an adult population**	**Referenzwerte für die Spiroergometrie - Ergebnisse der Study of Health in Pomerania (SHIP)**
Författare	Koch, Schäper, Ittermann, Spielhagen, Dörr, Völzke, Opitz, Ewert, Gläser.	Gläser, Koch, Ittermann, Schäper Dörr, Felix, Völzke, Ewert, Hansen	Gläser, Ittermann, Schäper, Obst, Dörr, Spielhagen, Felix, Völzke, Bollmann, Opitz, Warnke, Koch, Ewert.
Referens	*Eur Respir J. 2009; 33: 389-397.*	*Eur J Cardiovasc Prev Rehab. 2010; 17: 469-476.* *(Numera: Eur J Prev Cardiology)*	*Pneumologie 2013; 67: 58-63.*
Journal Impact factor	8.3	3.4	- (länk)
Referee-granskning	Ja	Ja	Ja
Indexerad I PubMed	Ja	Ja	Ja
Antal citeringar	73	30	6
Syfte	The aim of the present study was to acquire a comprehensive set of reference values on gas exchange and exercise capacity in cardiopulmonary exercise in a representative, healthy population. To minimise selection bias for the study population, a standardised progressive incremental exercise protocol on a cycle ergometer was performed by healthy subjects recruited from a large-scale, cross-sectional, population-based cohort in north-east Germany.	The aim of this study was to acquire a comprehensive set of CPET reference values for key gas exchange variables in a large-scale, cross-sectional, population-based, healthy cohort over a wide range of body sizes and ages. The impact of smoking and b blockers could also be assessed.	Ziel dieser Arbeit ist es, alltagstaugliche Referenzwerte fur spiroergometrische Parameter darzustellen, die sowohl fur normgewichtige als auch fur adipöse Personen Anwendung finden können. Somit wird bewusst auf den Ausschluss adipöser Probanden als auch auf die Einrichtung von Altersdekaden als Auswertemodalität - wenn auch von statistischer Attraktivität - verzichtet.
Individer frivilliga till CPET (män/kvinnor)	**1708** (834/874)		**1706** (833/873)
Exkluderar steg 1	• past myocardial infarction • signs of ischaemia/infarction • RBBB or LBBB or WPW-syndrome in the ECG	• past myocardial infarction • signs of ischemia/infarction • right or left bundle branch block	• **aktive Raucher** (n=358) • FEV1/FVC < 0,7) (n = 40) • Myokardinfarkt (n=49)

	• the presence of a cardiac pacemaker • stenosis or insufficiency of the cardiac valves • systolic and diastolic failures or a cardiac shunt vitium found in the echo-cardiography • pulmonary diseases; - bronchial asthma - chronic obstructive bronchitis (FEV1/FVC <0,70) and FEV1<80% of pred - emphysema (intrathoracic gas volume being >140% pred.), RV/TLC >140% pred - or patients' self report • neuromuscular or musculoskeletal disorders based on neurological examination • anaemia • **(with the exception of b-blockers)** the use of drugs with influence on cardiopulmonary function • patients with a breathing reserve (VE/ MVV) >0.8	• pacemaker • stenosis or insufficiency of any cardiac valve • systolic or diastolic dysfunction by echocardiography • abnormal spirometry or plethysmography • self-reported pulmonary disease, including asthma or chronic bronchitis • evidence of neuromuscular or musculoskeletal disorders • anaemia • the use of corticosteroids or antihistamines • drugs suspected of influencing cardiovascular or pulmonary function **(B-blocker usage was allowed)**	• Herzchirurgische Operationen (n=31) • anamnestische Hinweise auf Asthma (n=43) • chronische Bronchitis (n=74) • sonstige Lungenerkrankungen (n=59) • fractional shortening <14% bei Männern und <16% bei Frauen (n=4) • Schrittmacherträger (n=7) • Ischämiezeichen im EKG (n=326) • Bloclbilder im EKG (n=49) • neuromuskulären oder aktiven malignen Erkrankungen befinden sich nicht in der Studien-population. **Läkemedel exkluderande:** • Antiarrhytmika (n=82) • **Betablocker** (n=375) • Kalziumantagonisten (n=14) • Bronchospasmolytika, Xanthine und Steroide (n=116) • RER < 1 am Ende der Belastung
Exkluderar steg 2 (utöver sjuka)	• **Nuvarande rökare** • **BMI > 30 kg/m^2**	X (inga)	
Antal personer (män/kvinnor)	**534** (253/281)	**1203** (577/626)	**616** (283/333) Blodgasanalys: **325** (201/124) - selektionsbias?

Antal <35 år (män/kvinnor)	**92** (?/?)	**169** (79/90)	**???**
Antal >65 år (män/kvinnor)	**62** (?/?)	**184** (99/85)	**65** (39/26)
Antal >75 år (män/kvinnor)	**7** (?/?)	**30** (21/9)	?
Metod	• electromagnetically braked cycle ergometer (Ergoselect 100; Ergoline, Germany) • protocol: 3 min rest, 1 min unloaded cycling, 1 min increases in work load of 16 W/min, 5 min recovery • symptom-limited or terminated by the physician because of chest pain or ECG abnormalities • Before the test, patients were encouraged to reach maximal exhaustion; during exercise no further motivation was used. • Gas exchange and ventilatory variables were analysed breath-by-breath using a VIASYS HEALTHCARE system (Oxycon Pro, Rudolph's mask, JAEGER/VIASYS Healthcare system; Hoechberg, Germany) • VE, V_T, VO_2 and VCO_2 were acquired on a breath-by-breath basis and averaged over 10-s intervals. VO_2peak was defined as the highest 10-s average of VO_2 in late exercise or early recovery. The AT was determined according to Wasserman et al., V-slope-method. The VE/VCO_2@AT was averaged over a 30-s period and the VE versus VCO_2 slope was calculated up to the ventilator compensation point		
Watt			Ja
PeakVO_2 (ml/min)	Ja	Ja	Ja
PeakVO_2 (ml/kg/min)	Ja		
VO_2@AT (ml/min)	Ja	Ja	Ja
VO_2@AT (ml/kg/min)	Ja		
Syrepuls (ml/slag)	Ja	Ja	Ja
VE/VCO_2-slope	Ja	Ja	Ja
VE/VCO_2@AT	Ja	Ja	Ja
Övriga variabler, max	HF, AF, VE, VE/MVV%		RER, HF, SystBT, DiastBT, $SatO_2$, VE, AF, Vt, Vd/Vt, P(a'-et)CO_2, P(a'-et)O_2, $AaDO_2$, Pa'O_2, Pa'CO_2

Övriga variabler, submax	$PetCO_2$		$PetCO_2$@AT
Övriga variabler, vila	VE/VCO_2, $PetCO_2$		VO_2, $SatO_2$, VE/VCO_2, $Pa'O_2$, $Pa'CO_2$, $AaDO_2$, $P(a'-et)O_2$, $P(a'-et)CO_2$, Vd/Vt, $PetCO_2$
Formel tar hänsyn till	Kön, Ålder (kvintiler), BMI (><25)	Kön, Ålder, Längd, Vikt, Rökning (hos män)	Kön, Ålder, Längd, Vikt
Lägesmått VO_{2peak}	Median	Medel	Median
Spridningsmått	5 + 95 percentil	5 + 10 percentil	5 + 10 percentil

Detaljerad jämförelse exklusion/inklusion i de tre SHIP-publikationerna

Gläser 2010 (G2010) vs Gläser 2013 (G2013)

From the sample of 3300 individuals, ages 25–85 years, **1708 individuals** (834 men, 874 women) volunteered for cycle ergometer CPET with gas exchange measurements. **(52% accepterar att delta)**
Ytterligare 2 exkluderas efter "kvalitetskontroll" i G2013.

Individuals with the following criteria were excluded **(n=505, 30%, n=590, 35%)** from analyses:

- signs of ischemia/infarction; **326**
- the use of corticosteroids or antihistamines **(116)** or drugs suspected of influencing cardiovascular or pulmonary function (**96** antiarytmika + Ca2+-ant). **b blocker usage was allowed. (375 m β-block exkl i G2013)**
- self-reported pulmonary disease, including asthma or chronic bronchitis; **176**
- past myocardial infarction; **49** (+**31**, tid hjärtoperation)
- right or left bundle branch block; **49** ("block-bild")
- abnormal spirometry or plethysmography; **40**
- pacemaker; **7**
- systolic (**4**) or diastolic dysfunction **(diastolic HF ingår ej som exkl-krit i G2013)** by echocardiography;
- evidence of neuromuscular or musculoskeletal disorders; **0**
- stenosis or insufficiency of any cardiac valve; **(ingår ej som exkl-krit i G2013)**
- anaemia; **(ingår ej som exkl-krit i G2013)**

Således exkluderas enligt ovan 85 fler individer i G2013, vilket får förmodas bero på personer med β-block som isolerat exklusionskriterium.

Härutöver exkluderas i G2013:

- Rökare: **358**
- RER < 1, **okänt antal.**

KVAR: **1203 individer**, (G2010) **(kvar 616 i G2013)** varav (i G2010):

- **BMI > 30 kg/m^2**: n = 284 (16.6 % av 1708, **23.6 % av 1203**)
- **Nuv. rökare:** n = 320 (18.7% av 1708, **26.6 % av 1203**)
- **β-block:** n = 67 (3.9% av 1708, **5.6% av 1203**)

Det är oklart varför 587 personer fler inkluderas i G2013, när antalet individer som röker och/eller har beta-blockare endast är (som högst) 425 (358+67).

Koch 2009 (K2009) vs Gläser 2013 (G2013)

The sample (without migrated, deceased or nonresponding people) **then comprised 3,300 subjects** (1,589 males and 1,711 females) aged 25–85 yrs. Of those, **1,708 individuals** (834 males and 874 females) volunteered for a standardised progressive incremental exercise test on a cycle ergometer. (52% accepterar att delta)
Ytterligare 2 exkluderas efter "kvalitetskontroll" i G2013.

Individuals with the following criteria were excluded **(n=632, 37%, n=590, 35%)** from analyses:

- current smokers and current obese smokers, n=317 i Koch 2009; **358 i G2013**
- signs of ischemia/infarction; **326**
- obese non-smokers, BMI >30, n=225
- the use of drugs with influence on cardiopulmonary function (**with the exception of β-block**); (corticosteroids or antihistamines **(116 + 96 antiarytmika + Ca2+-ant).**
- pulmonary diseases, bronchial asthma, chronic obstructive bronchitis (ratio of forced expiratory volume over one second (FEV1) to forced vital capacity being <0.7 and the FEV1 being <80% predicted or emphysema (intrathoracic gas volume being >140% predicted, residual volume percentage of total lung capacity being >140% predicted), all defined by spirometric/body-plethysmographic criteria **(40)** and/or patients' self report **(176)**
- past myocardial infarction; **49 (+31, tid hjärtoperation)**
- right or left bundle branch block or WPW-syndrome in the ECG; **49 ("block-bild")**
- pacemaker; **7**
- systolic (**4**) or diastolic failures **(diastolic HF anges ej som exkl-krit i G2013)** or a cardiac shunt vitium **(shunt anges ej som exkl-krit i G2013)** found in the echocardiography;
- neuromuscular or musculoskeletal disorders based on neurological examination; **0**
- stenosis or insufficiency of the cardiac valves; **(anges ej som exkl-krit i G2013)**
- anaemia**; (anges ej som exkl-krit i G2013)**
- Patients with a breathing reserve (VE/maximum voluntary ventilation (MVV)) >0.8% were also excluded from the study **(anges ej som exkl-krit i G2013)**
  Vad menar man eg här? Är det andningsreserv <20% eller >80%? Formeln är ju inte för andningsreserven (skulle lyda MVV-VE/MVV i så fall).

Härutöver exkluderas i G2013:

- **375** m β-block exkl i G2013
- RER < 1, **okänt antal**.

KVAR: **534 individer**, (K2009) **(kvar 616 i G2013)** varav (i K2009):

- **β-block:** n = 67 (3.9% av 1708, **5.6% av 1203**)

I K2009 exkluderas alltså 225 fler individer överviktiga, men 67 färre med β-block och 41 färre nuv rökare (av oklar anledning). Skillnaden blir enligt detta (225 – 67 – 41) = 117 individer färre i K2009, medan det i praktiken endast är (616 – 534) = 82 individer färre i K2009.