Virtual reality, a new therapeutic tool for neurological care

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Disclosure

Part-time employee at MindMaze SA (Lausanne)

Virtual reality, a new therapeutic tool for neurological care

Outline

- What is virtual reality based rehabilitation?
- Examples of treatments using virtual reality
- Is virtual reality effective for (stroke) rehabilitation?
- How to integrate VR-based treatment into standard of care?
- Conclusion, added value of VR-based rehabilitation

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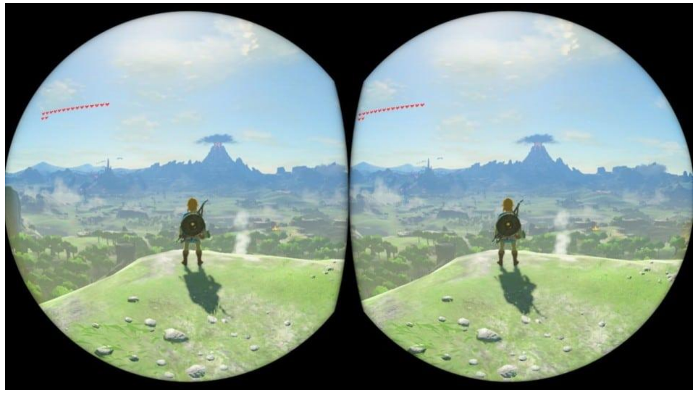
What is virtual reality based rehabilitation?

VR technology in rehabilitation

- Immersive virtual reality (VR): complete immersion in a simulated experience that can be similar to or completely different from the real world



www.realite-virtuelle.com/ zelda-vr-images-details/

www.fun-simulations.fr

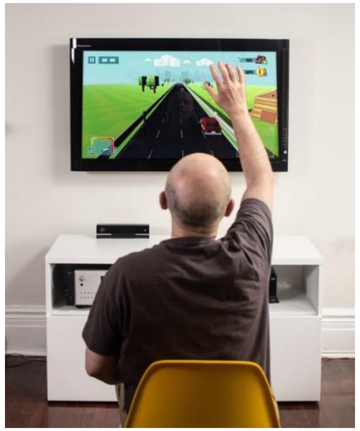
- Augmented reality (AR): adds digital elements to a live (real) view

https://www.fi.edu/difference-between-ar-vr-and-mr

- Mixed reality (MR): combines elements of both immersive VR and AR, use head mounted display

https://www.tom.travel/2020/02/21/quest-ce-que-la-realite-mixte/

- 2D screen-based digital environment



What is virtual reality based rehabilitation?

Non immersive VR

2D environment displayed on a screen, hand controllers, trackers on limbs

Immersive VR

3D environment, head mounted display, hand controllers, trackers on limbs

Cogniplus
www.schuhfried.com/cogniplus/trainings/

Computer Assisted Rehabilitation Environment (CAREN) Laboratory, Bethesda USA

Brandin-De la Cruz et al., Rev Neurol., 2020
San Jorge University, Spain

Tyromotion
www.tyromotion.com
DIEGO Arm robot therapy

All of these set-ups can be used in VR based rehabilitation

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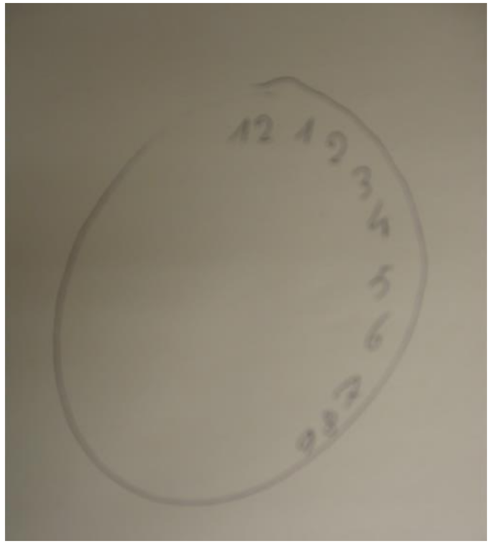
Motor deficits

Cognitive deficits



Virtual reality and motor rehabilitation

With VR:
increase frequency
and intensity

(a) Rodriguez, J. et al. MDPI, 2020 (b)

MindMotion Go
www.mindmaze.ch

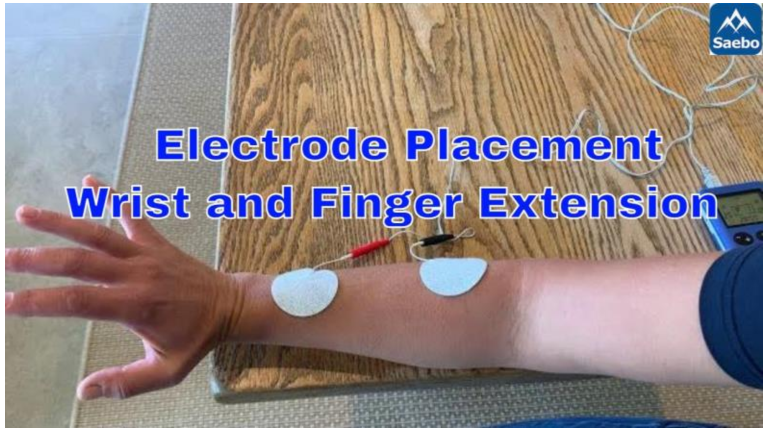
Smart Glove
www. neofect.com

Virtual reality and motor rehabilitation

quality of movements

With VR:
increase frequency
and intensity

Functional electrical stimulation



Bitensky et al., Stroke engine, 2010

Smart Glove
www. neofect.com

Virtual reality and motor rehabilitation

C-Mill virtual reality treadmill
https://agapephysicaltherapy.com/services/c-mill-virtual-reality-treadmill

https://www.physiotherapyglobal.org/blogs/vr-virtual-reality-in-physical-therapy-rehabilitation-with-a-restorative-approach-by-prakash-pandey/

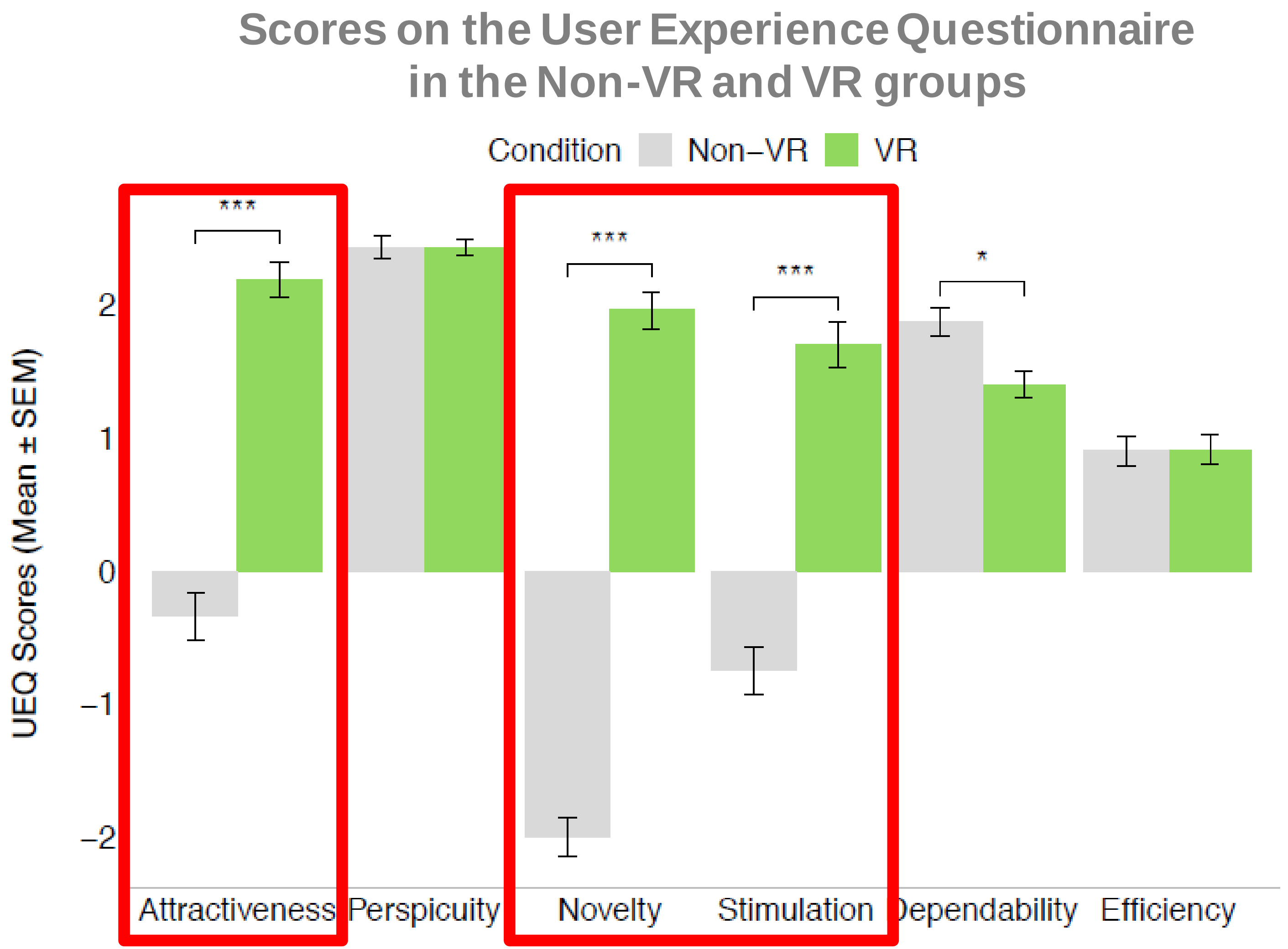
Virtual reality and motor rehabilitation

Gamification of gait training

Kern et al. IEEE Conference on Virtual Reality and 3D User Interfaces (VR). 2019

Virtual reality and motor rehabilitation

With VR: increase motivation and attractiveness of the therapy



Kern et al. IEEE Conference on Virtual Reality and 3D User Interfaces (VR). 2019

Virtual reality and cognitive rehabilitation

Standard cognitive rehabilitation of visual neglect deficits

Virtual reality and cognitive rehabilitation

Our pilot study

New VR-based rehabilitation of visual neglect deficits

mindmaze

Virtual reality and cognitive rehabilitation

Our pilot study

New VR-based rehabilitation of visual neglect deficits

mindmaze

Is VR a useful therapeutic tool?

Is VR-based rehabilitation effective?

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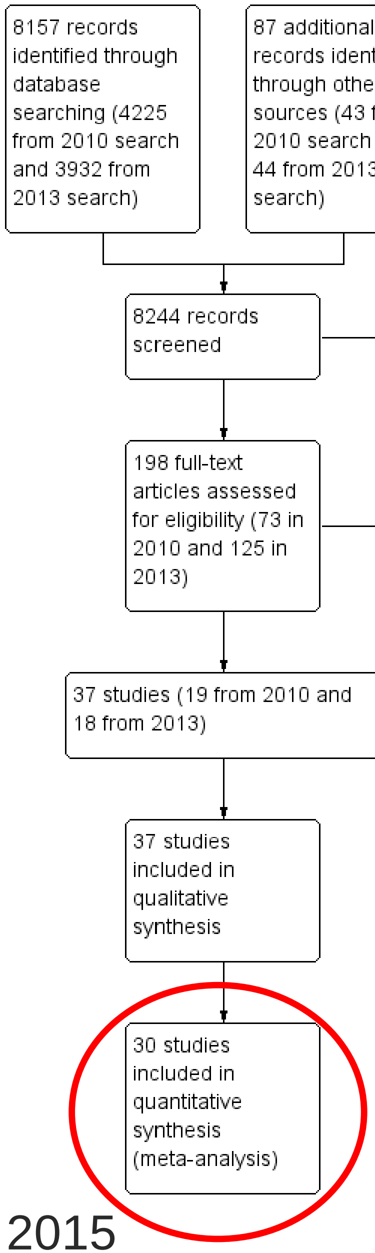
Is virtual reality effective for (stroke) neurorehabilitation?

Figure 1. Study flow diagram.



Laver et al., 2015

Upper limb function and activity

Cochrane Library

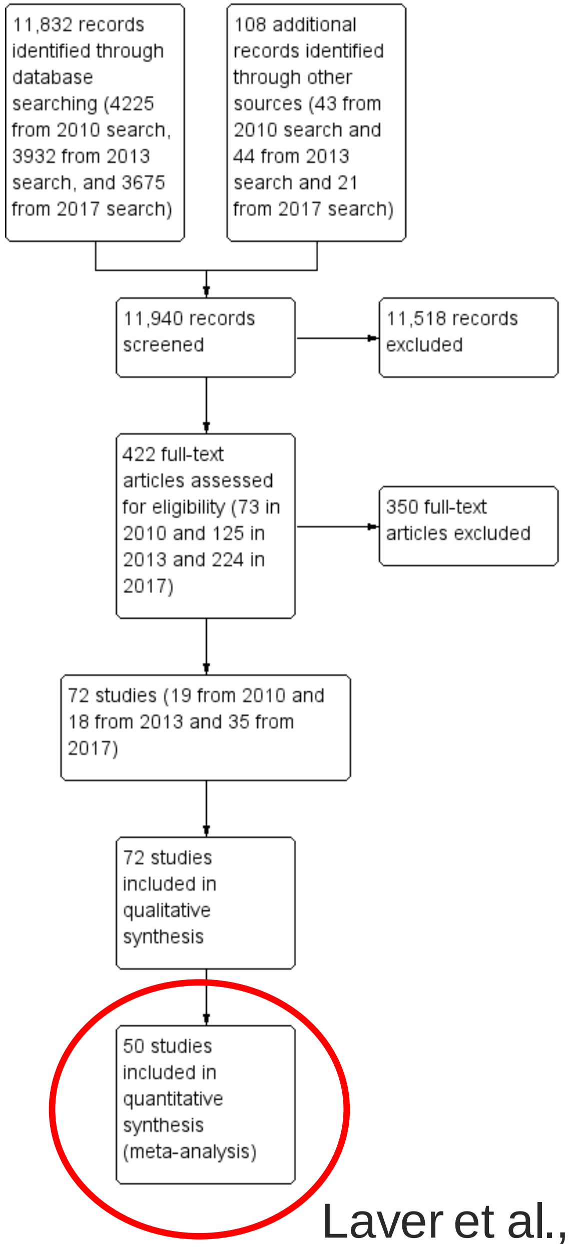
Cochrane Database of Systematic Reviews

Virtual reality for stroke rehabilitation (Review)

Laver KE, Lange B, George S, Deutsch JE, Saposnik G, Crotty M

Number of studies increased of more than 50%

Figure 1. Study flow diagram



Laver et al., 2017

Is virtual reality effective for (stroke) neurorehabilitation?

VR therapy versus Conventional therapy

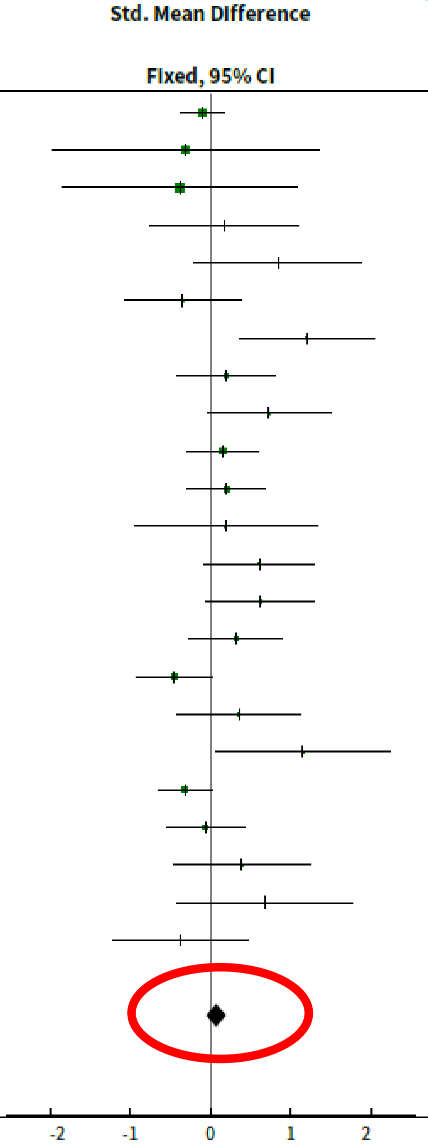
VR only versus OT only

Comparison 1.1: Upper limb function and activity

Twenty-two studies presented outcomes for upper limb function and activity in a form suitable for inclusion in the meta-analysis (1038 participants) (Adie 2017; Byl 2013; Crosbie 2008; da Silva Cameirao 2011; da Silva Ribeiro 2015; Galvao 2015; Givon 2016; Housman 2009; Kiper 2011; Kong 2014; Levin 2012; Piron 2007; Piron 2009; Piron 2010; Prange 2015; Reinkensmeyer 2012; Saposnik 2010; Saposnik 2016; Subramanian 2013; Sucar 2009; Thielbar 2014; Zucconi 2012). The impact of virtual reality on upper limb function was not significant: standardised mean difference (SMD) 0.07, 95% confidence interval (CI) -0.05 to 0.20, low-quality evidence (Analysis 1.1). Statistical heterogeneity was moderate (I^2 = 43%).

Analysis 1.1. Comparison 1 Virtual reality versus conventional therapy: effect on upper limb function post intervention, Outcome 1 Upper limb function post intervention (composite measure).

Study or subgroup	Virtual reality		Conventional therapy		Weight	Std. Mean Difference
	N	Mean(SD)	N	Mean(SD)		Fixed, 95% CI
Adie 2017	101	47.6 (14.2)	108	49 (13.6)	20.73%	-0.1[-0.37,0.17]
Byl 2013	5	27.8 (7.9)	2	30.6 (6.9)	0.56%	-0.31[-1.96,1.35]
Byl 2013	5	28.2 (4.6)	3	30.6 (6.9)	0.72%	-0.38[-1.84,1.07]
Crosbie 2008	9	52.8 (6.9)	9	50.2 (18.9)	1.78%	0.17[-0.75,1.1]
da Silva Cameirao 2011	8	60.4 (7.6)	8	53.4 (8.1)	1.42%	0.84[-0.19,1.88]
da Silva Ribeiro 2015	15	38.7 (19.6)	15	44.7 (14.2)	2.93%	-0.34[-1.06,0.38]
Galvao 2015	18	120.9 (13.7)	10	101.7 (18.5)	2.14%	1.2[0.36,2.04]
Givon 2016	20	28.4 (23.1)	21	23.7 (24)	4.05%	0.2[-0.42,0.81]
Housman 2009	14	24.9 (7.4)	14	19.6 (6.7)	2.58%	0.73[-0.04,1.5]
Kiper 2011	40	48.9 (15.2)	40	46.4 (17.1)	7.93%	0.15[-0.29,0.59]
Kong 2014	33	32.8 (18.2)	34	29.2 (17.5)	6.63%	0.2[-0.28,0.68]
Levin 2012	6	47.3 (11.9)	6	44.9 (11.7)	1.19%	0.19[-0.95,1.32]
Piron 2007	25	51.4 (9.8)	13	45.4 (9.3)	3.25%	0.61[-0.08,1.3]
Piron 2009	18	53.6 (7.7)	18	49.5 (4.8)	3.39%	0.62[-0.05,1.3]
Piron 2010	27	49.7 (10.1)	20	46.5 (9.7)	4.51%	0.32[-0.27,0.9]
Prange 2015	35	29.6 (17.2)	33	37.4 (17.3)	6.58%	-0.45[-0.93,0.03]
Reinkensmeyer 2012	13	27.4 (11.4)	13	23.8 (8)	2.54%	0.35[-0.42,1.13]
Saposnik 2010	9	-19.8 (3.4)	7	-27.4 (8.7)	1.29%	1.15[0.06,2.24]
Saposnik 2016	71	-64.1 (104)	70	-39.8 (35.5)	13.85%	-0.31[-0.64,0.02]
Subramanian 2013	32	43 (15.2)	32	43.9 (14.7)	6.36%	-0.06[-0.55,0.43]
Sucar 2009	11	30 (12.4)	11	26.4 (2.3)	2.14%	0.39[-0.45,1.24]
Thielbar 2014	7	50.4 (10.4)	7	43.6 (8.1)	1.29%	0.68[-0.41,1.77]
Zucconi 2012	11	45.2 (20.3)	11	51.8 (13.1)	2.14%	-0.37[-1.22,0.47]
Total ***	**533**		**505**		**100%**	**0.07[-0.05,0.2]**



Heterogeneity: Tau^2=0; Chi^2=38.37, df=22(P=0.02); I^2=42.67%

Test for overall effect: Z=1.14(P=0.25)

Favours conventional | Favours virtual reality

Laver et al., 2017

Is virtual reality effective for (stroke) neurorehabilitation?

Effect on the Fugl Meyer UE scale

VR only versus OT only

Comparison 1.2: Upper limb function (Fugl Meyer Upper Extremity Scale)

Sixteen of the trials (with 599 participants) used the Fugl Meyer Upper Extremity (UE) Scale as an outcome measure (Byl 2013; da Silva Cameirao 2011; da Silva Ribeiro 2015; Galvao 2015; Housman 2009; Kiper 2011; Kong 2014; Levin 2012; Piron 2007; Piron 2009; Piron 2010; Prange 2015; Reinkensmeyer 2012; Subramanian 2013; Sucar 2009; Zucconi 2012). The impact of virtual reality as measured by the Fugl Meyer UE Scale showed a small significant effect: mean difference (MD) 2.85, 95% CI 1.06 to 4.65 (Analysis 1.2).

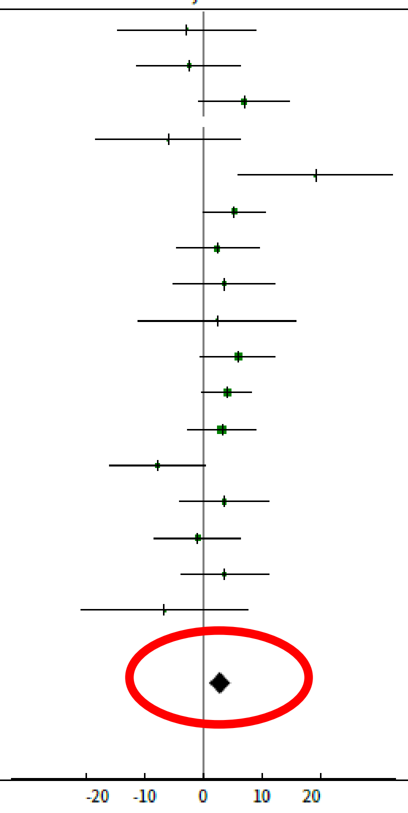
"….virtual reality and interactive video gaming was **more beneficial on the Fugl Meyer score** than conventional therapy approaches in improving upper limb function…"

Analysis 1.2. Comparison 1 Virtual reality versus conventional therapy: effect on upper limb function post intervention, Outcome 2 Upper limb function post intervention (Fugl Meyer).

Study or subgroup	Virtual reality N	Virtual reality Mean(SD)	Control N	Control Mean(SD)	Weight	Mean Difference Fixed, 95% CI
Byl 2013	5	27.8 (7.9)	2	30.6 (6.9)	2.29%	-2.8[-14.64,9.04]
Byl 2013	5	28.2 (4.6)	3	30.6 (6.9)	4.14%	-2.4[-11.21,6.41]
da Silva Cameirao 2011	8	60.4 (7.6)	8	53.4 (8.1)	5.42%	7[-0.7,14.7]
da Silva Ribeiro 2015	15	38.7 (19.6)	15	44.7 (14.2)	2.14%	-6[-18.25,6.25]
Galvao 2015	18	120.9 (13.7)	10	101.7 (18.5)	1.87%	19.22[6.1,32.34]
Housman 2009	14	24.9 (7.4)	14	19.6 (6.7)	11.75%	5.3[0.07,10.53]
Kiper 2011	40	48.9 (15.2)	40	46.4 (17.1)	6.39%	2.5[-4.59,9.59]
Kong 2014	33	32.8 (18.2)	34	29.2 (17.5)	4.39%	3.6[-4.95,12.15]
Levin 2012	6	47.3 (11.9)	6	44.9 (11.7)	1.8%	2.4[-10.95,15.75]
Piron 2007	25	51.4 (9.8)	13	45.4 (9.3)	7.97%	6[-0.35,12.35]
Piron 2009	18	53.6 (7.7)	18	49.5 (4.8)	18.28%	4.1[-0.09,8.29]
Piron 2010	27	49.7 (10.1)	20	46.5 (9.7)	9.86%	3.2[-2.51,8.91]
Prange 2015	35	29.6 (17.2)	33	37.4 (17.3)	4.77%	-7.8[-16,0.4]
Reinkensmeyer 2012	13	27.4 (11.4)	13	23.8 (8)	5.6%	3.6[-3.97,11.17]
Subramanian 2013	32	43 (15.2)	32	43.9 (14.7)	5.98%	-0.9[-8.23,6.43]
Sucar 2009	11	30 (12.4)	11	26.4 (2.3)	5.78%	3.64[-3.82,11.1]
Zucconi 2012	11	45.2 (20.3)	11	51.8 (13.1)	1.58%	-6.6[-20.88,7.68]
Total ***	**316**		**283**		**100%**	**2.85[1.06,4.65]**

Heterogeneity: Tau^2=0; Chi^2=22.78, df=16(P=0.12); I^2=29.76%

Test for overall effect: Z=3.12(P=0)



Is virtual reality effective for (stroke) neurorehabilitation?

Increase dosage thanks to VR interventions

OT+VR versus OT only

Comparison 3.1: Upper limb function

Ten studies with a total of 210 participants presented outcomes for upper limb function (Cho 2012; Coupar 2012; Jang 2005; Kim 2011a; Kwon 2012; Manlapaz 2010; Shin 2014; Sin 2013; Standen 2011; Yavuzer 2008). There was a moderate significant effect that demonstrated that virtual reality intervention was more effective than no intervention: SMD 0.49, 95% CI 0.21 to 0.77, low-quality evidence (Analysis 3.1). There was no statistical heterogeneity.

“Virtual reality may be beneficial …. when used as an **adjunct to usual care** (to increase overall therapy time).”

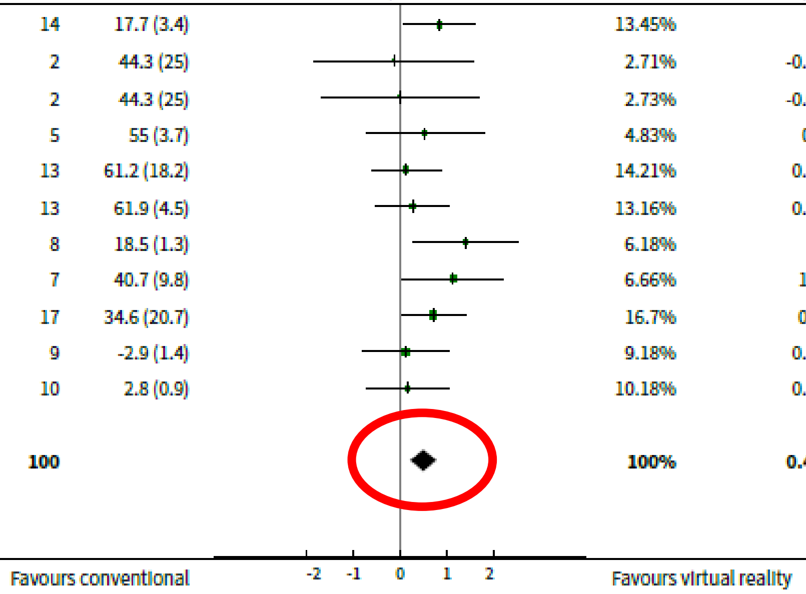
Comparison 3. Additional virtual reality intervention: effect on upper limb function post intervention

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Upper limb function (composite measure)	10	210	Std. Mean Difference (IV, Fixed, 95% CI)	0.49 [0.21, 0.77]

Study or subgroup	Virtual reality N	Virtual reality Mean(SD)	No intervention N	No intervention Mean(SD)	Weight	Std. Mean Difference Fixed, 95% CI
Cho 2012	15	21.6 (5.4)	14	17.7 (3.4)	13.45%	0.83[0.07,1.6]
Coupar 2012	4	40.8 (17.2)	2	44.3 (25)	2.71%	-0.14[-1.85,1.56]
Coupar 2012	4	44 (16)	2	44.3 (25)	2.73%	-0.01[-1.71,1.69]
Jang 2005	5	58 (6.2)	5	55 (3.7)	4.83%	0.53[-0.75,1.8]
Kim 2011a	15	64 (26.7)	13	61.2 (18.2)	14.21%	0.12[-0.63,0.86]
Kwon 2012	13	62.9 (3.5)	13	61.9 (4.5)	13.16%	0.26[-0.52,1.03]
Manlapaz 2010	8	21 (2)	8	18.5 (1.3)	6.18%	1.4[0.27,2.53]
Shin 2014	9	51.1 (7.8)	7	40.7 (9.8)	6.66%	1.13[0.04,2.21]
Sin 2013	18	47.7 (15.3)	17	34.6 (20.7)	16.7%	0.71[0.02,1.39]
Standen 2011	9	-2.7 (1.6)	9	-2.9 (1.4)	9.18%	0.11[-0.81,1.04]
Yavuzer 2008	10	3 (1.5)	10	2.8 (0.9)	10.18%	0.15[-0.72,1.03]
Total ***	**110**		**100**		**100%**	**0.49[0.21,0.77]**

Heterogeneity: Tau^2=0; Chi^2=[illegible], df=10(P=0.59); I^2=0%

Test for overall effect: Z=3.43(P=0)

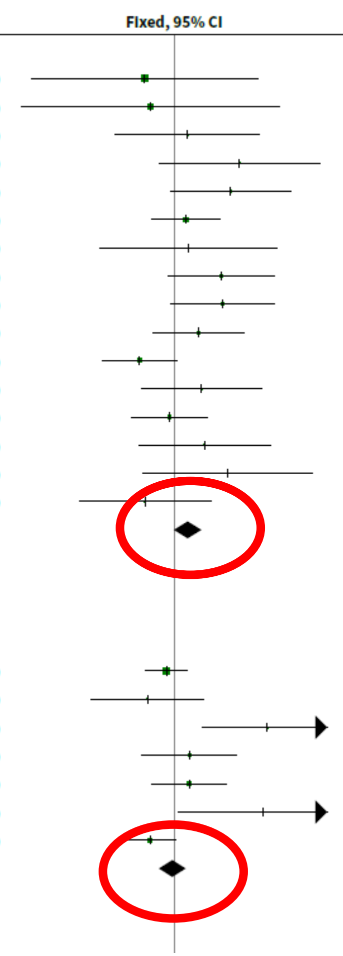


Is virtual reality effective for (stroke) neurorehabilitation?

Specialized VR system versus "off the shelf" system

Comparison 2.3: Specialised virtual reality system or commercial gaming console

Studies utilising virtual reality programs specifically designed for rehabilitation settings demonstrated statistically significant benefits over alternative intervention (SMD 0.17, 95% CI 0.00 to 0.35). In contrast those involving off-the-shelf gaming programs were not found to be significant (SMD -0.02, 95% CI -0.20 to 0.15)



Analysis 2.3. Comparison 2 Virtual reality versus conventional therapy: upper limb function: subgroup analyses, Outcome 3 Specialised or gaming.

Study or subgroup	Virtual reality N	Virtual reality Mean(SD)	Comparison treatment N	Comparison treatment Mean(SD)	Weight	Std. Mean Difference Fixed, 95% CI
2.3.1 Specialised						
Byl 2013	5	28.2 (4.6)	3	30.6 (6.9)	0.72%	-0.38[-1.84,1.07]
Byl 2013	5	27.8 (7.9)	2	30.6 (6.9)	0.56%	-0.31[-1.96,1.35]
Crosbie 2008	9	52.8 (6.9)	9	50.2 (18.9)	1.78%	0.17[-0.75,1.1]
da Silva Cameirao 2011	8	60.4 (7.6)	8	53.4 (8.1)	1.42%	0.84[-0.19,1.88]
Housman 2009	14	24.9 (7.4)	14	19.6 (6.7)	2.58%	0.73[-0.04,1.5]
Kiper 2011	40	48.9 (15.2)	40	46.4 (17.1)	7.93%	0.15[-0.29,0.59]
Levin 2012	6	47.3 (11.9)	6	44.9 (11.7)	1.19%	0.19[-0.95,1.32]
Piron 2007	25	51.4 (9.8)	13	45.4 (9.3)	3.25%	0.61[-0.08,1.3]
Piron 2009	18	53.6 (7.7)	18	49.5 (4.8)	3.39%	0.62[-0.05,1.3]
Piron 2010	27	49.7 (10.1)	20	46.5 (9.7)	4.51%	0.32[-0.27,0.9]
Prange 2015	35	29.6 (17.2)	33	37.4 (17.3)	6.58%	-0.45[-0.93,0.03]
Reinkensmeyer 2012	13	27.4 (11.4)	13	23.8 (8)	2.54%	0.35[-0.42,1.13]
Subramanian 2013	32	43 (15.2)	32	43.9 (14.7)	6.36%	-0.06[-0.55,0.43]
Sucar 2009	11	30 (12.4)	11	26.4 (2.3)	2.14%	0.39[-0.45,1.24]
Thielbar 2014	7	50.4 (10.4)	7	43.6 (8.1)	1.29%	0.68[-0.41,1.77]
Zucconi 2012	11	45.2 (20.3)	11	51.8 (13.1)	2.14%	-0.37[-1.22,0.47]
Subtotal ***	**266**		**240**		**48.38%**	**0.17[-0,0.35]**
Heterogeneity: Tau²=0; Chi²=18.16, df=15(P=0.25); I²=17.42%						
Test for overall effect: Z=1.92(P=0.06)						
2.3.2 Gaming						
Adie 2017	101	47.6 (14.2)	108	49 (13.6)	20.73%	-0.1[-0.37,0.17]
da Silva Ribeiro 2015	15	38.7 (19.6)	15	44.7 (14.2)	2.93%	-0.34[-1.06,0.38]
Galvao 2015	18	120.9 (13.7)	10	101.7 (18.5)	2.14%	1.2[0.36,2.04]
Givon 2016	20	28.4 (23.1)	21	23.7 (24)	4.05%	0.2[-0.42,0.81]
Kong 2014	33	32.8 (18.2)	34	29.2 (17.5)	6.63%	0.2[-0.28,0.68]
Saposnik 2010	9	-19.8 (3.4)	7	-27.4 (8.7)	1.29%	1.15[0.06,2.24]
Saposnik 2016	71	-64.1 (104)	70	-39.8 (35.5)	13.85%	-0.31[-0.64,0.02]
Subtotal ***	**267**		**265**		**51.62%**	**-0.02[-0.2,0.15]**
Heterogeneity: Tau²=0; Chi²=17.76, df=6(P=0.01); I²=66.22%						
Test for overall effect: Z=0.27(P=0.79)						

Is virtual reality effective for (stroke) neurorehabilitation?

Yes! But:

- effects not always captured (e.g. Fugl Meyer but not composite score)

- when used in addition to standard of care, to increase intensity

- when specific VR programs are used (not “off-the-shelf” program)

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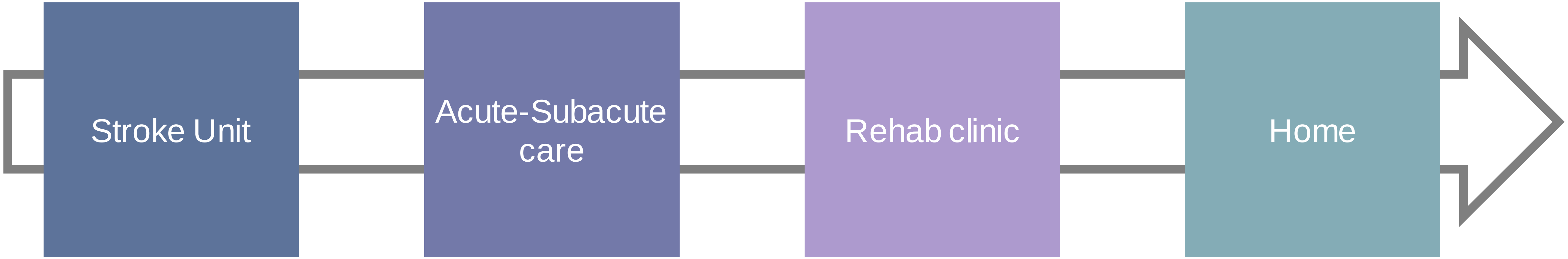
How to integrate VR-based treatment into standard of care?

Current management of stroke patients



~ No rehab

Some rehab
Up to 3 h/day?

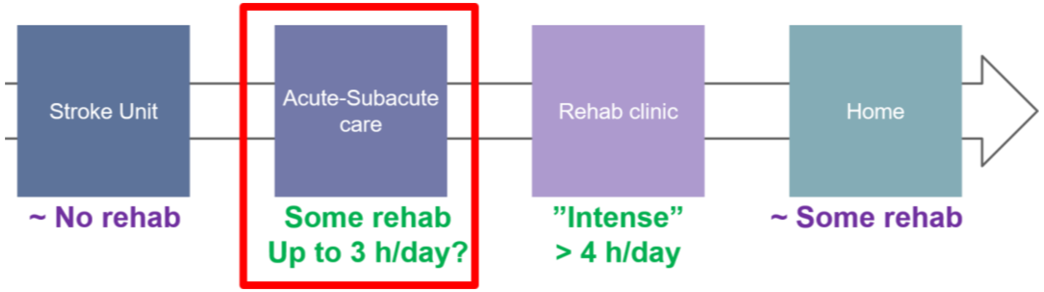
"Intense rehab"
> 4 h/day

~ Some rehab

Where should VR therapy be added?

How to integrate VR-based treatment into standard of care?

Early post acute - In clinic



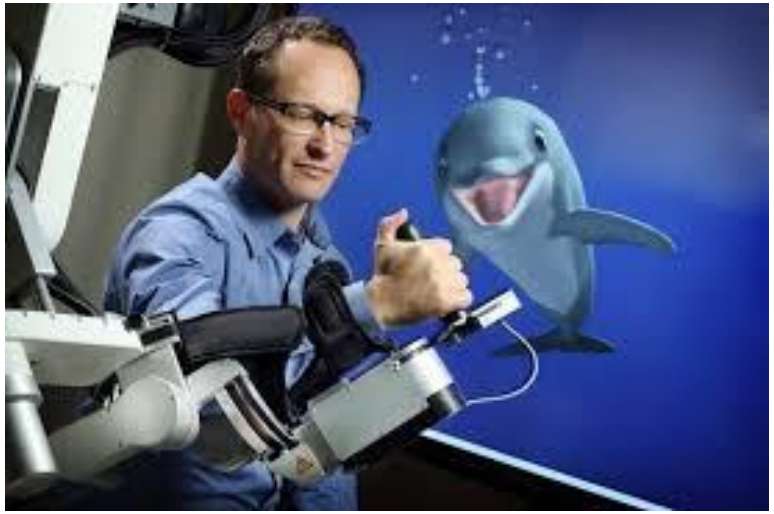
SMART-2 trial

Early post-acute patients (< 6 weeks) - N=24

Groups: VR + OT versus OT + OT

2 hours/day (2x1hour), 5 days/week

3 weeks (30 sessions)



MindPod Dolphin (MindMaze SA) and
Armeo power (Hocoma AG)

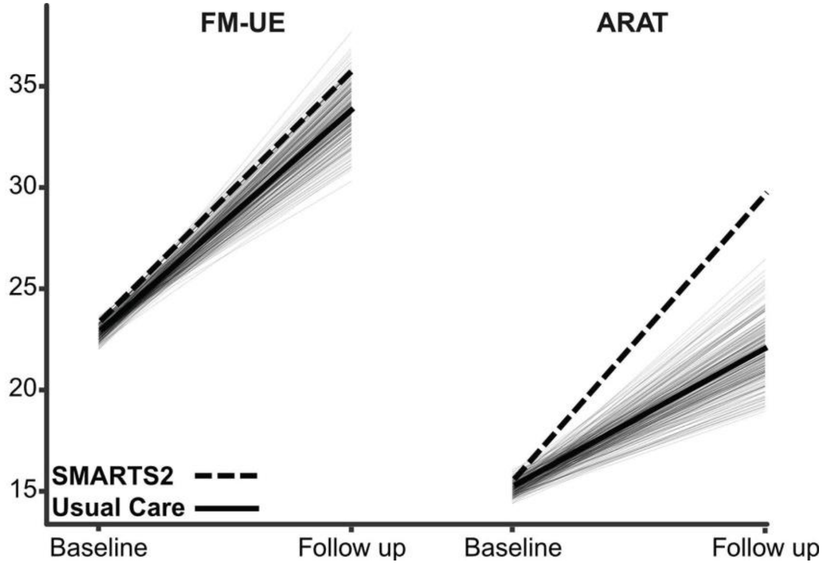
Finding 1:
All outcomes: Improvement
VR+OT group = OT+OT group

Finding 2:
Improvement
VR+OT and OT+OT groups
>
Usual OT care group (retrospective)

SMARTS2 19.0 days post-stroke
IQR 12.0, 33.0

Usual care 14.0 days post-stroke
IQR 12.5, 35.5

Upper limb motricity

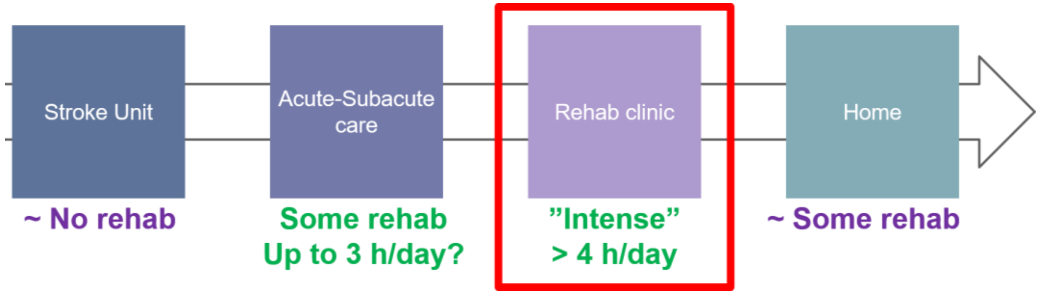


ARAT kit
(action research
arm test)

Krakauer et al., Neurorehabilitation and Neural Repair, 2021

How to integrate VR-based treatment into standard of care?

Chronic - In clinic (ambulatory)



The Queen Square Trial

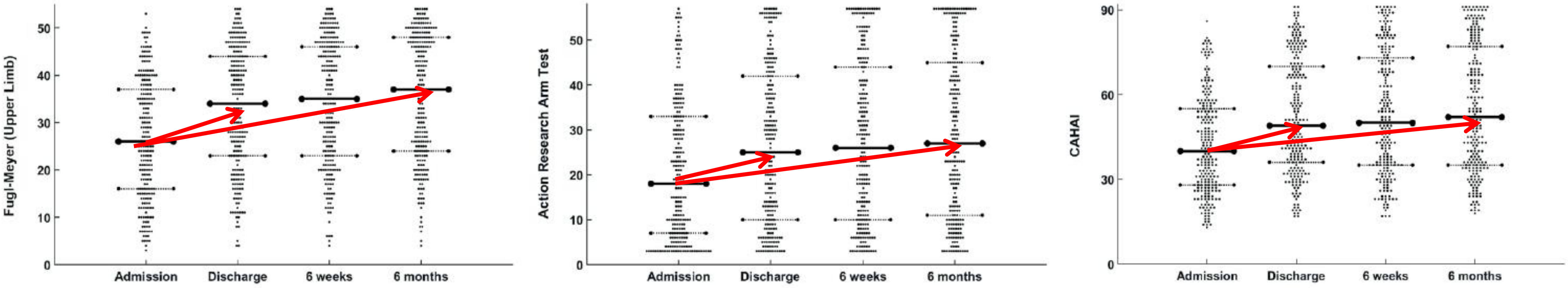
Chronic patients (> 6 months) - N=224 (no control group)

6 hours/day, 5 days/week, 3 weeks (90 sessions)

Motor tasks: passive or active, assisted or unassisted (robot), functional or nonfunctional (PT + OT)

Finding 1:
Improvement between scores at admission and discharge

Finding 2:
Improvement continued after discharge



Ward et al., JNNP, 2019

How to integrate VR-based treatment into standard of care?

Chronic

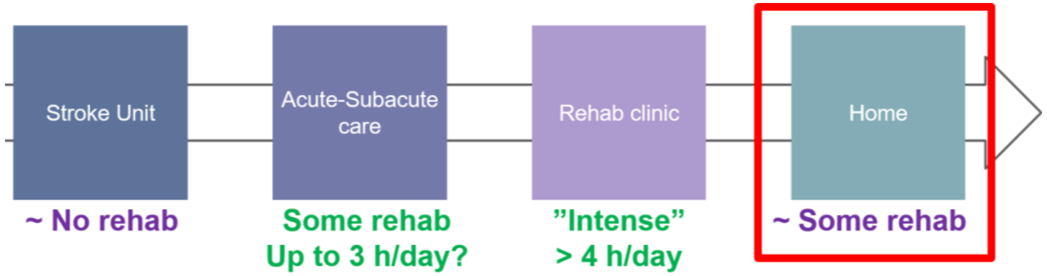
Home telerehabilitation vs In-clinic

Chronic patients (4-36 weeks post-stroke) - N=124

70 min/day (~1 session/day), 6-8 weeks

36 sessions (18 supervised, 18 unsupervised)

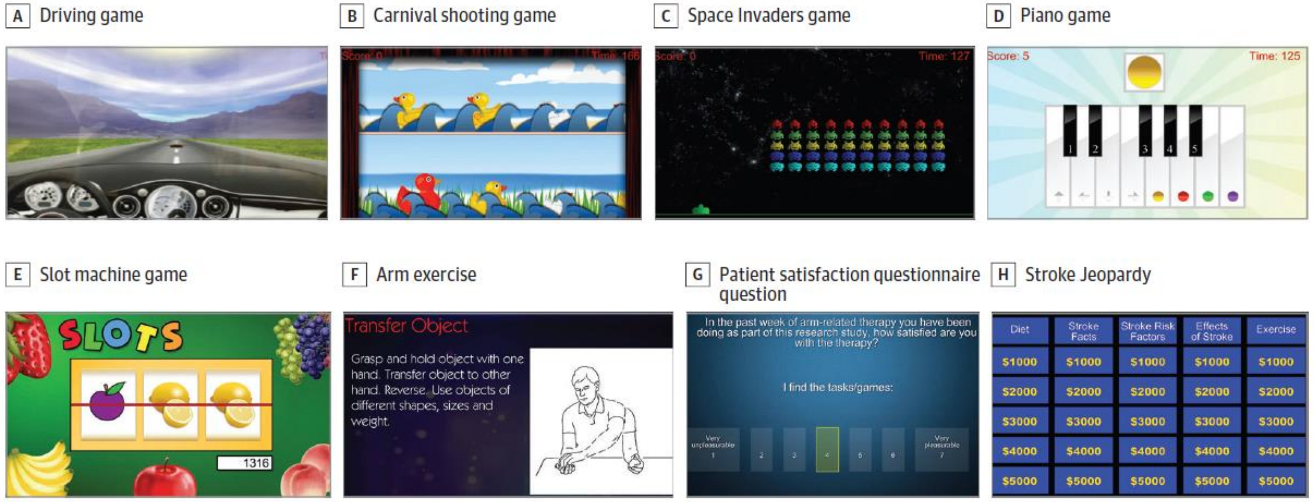
Groups: Home versus In-clinic



Finding 1:
Significant improvement for both groups

points). Both groups showed significant treatment-related motor gains, with a mean (SD) unadjusted FM score change from baseline to 30 days after therapy of 8.36 (7.04) points in the IC group ($P < .001$) and 7.86 (6.68) points in the TR group ($P < .001$). The adjusted mean change in FM score was 0.06

Figure 2. Examples of Telerehabilitation Therapy Content



Cramer et al., JAMAN, 2019

Finding 2
<u>**Similar**</u> improvement for both groups

Table 2. Treatment-Related Change in FM Motor Score[a]

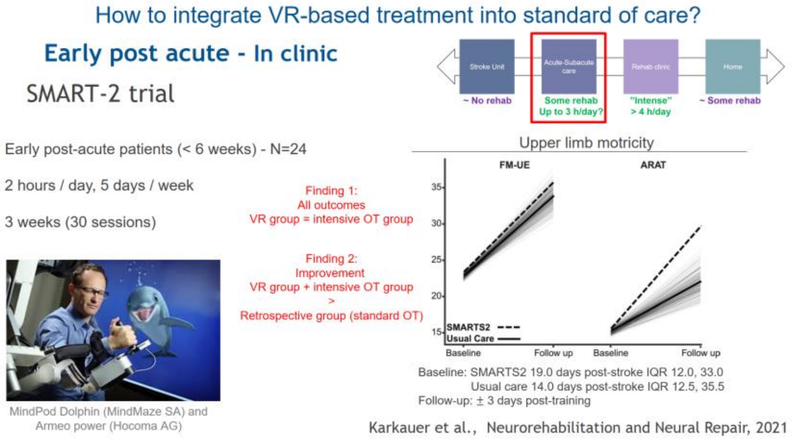
Model	Patients, No. TR	IC	Total	FM Score for IC Group, Mean Change	FM Change (TR-IC), Difference Between Groups (95% CI)[b]
Primary analysis					
ITT with multiple imputation of missing outcomes	62	62	124	8.23	0.06 (−2.14 to 2.26)
Secondary analyses					
ITT with substitution of "worst-best-case" missing outcomes	62	62	124	8.58	−0.19 (−2.29 to 1.92)
Complete case ITT	59	55	114	8.36	0.00 (−2.27 to 2.27)
Complete case PP	58	55	113	8.36	−0.15 (−2.41 to 2.10)

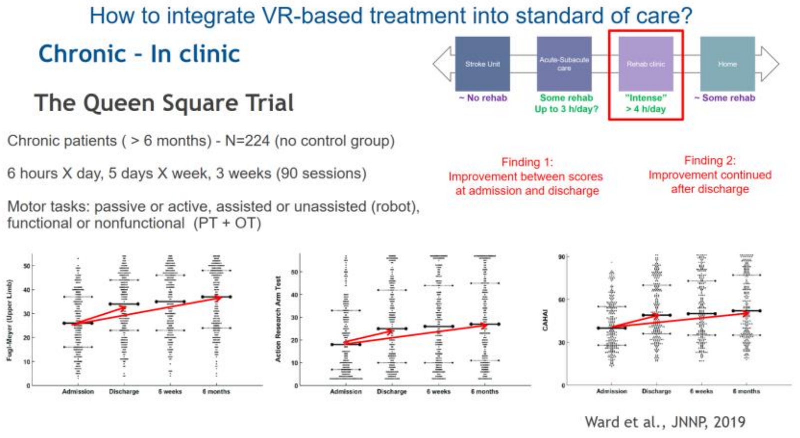
Abbreviations: FM, Fugl-Meyer; IC, in-clinic; ITT, intent to treat; PP, per protocol; TR, telerehabilitation.

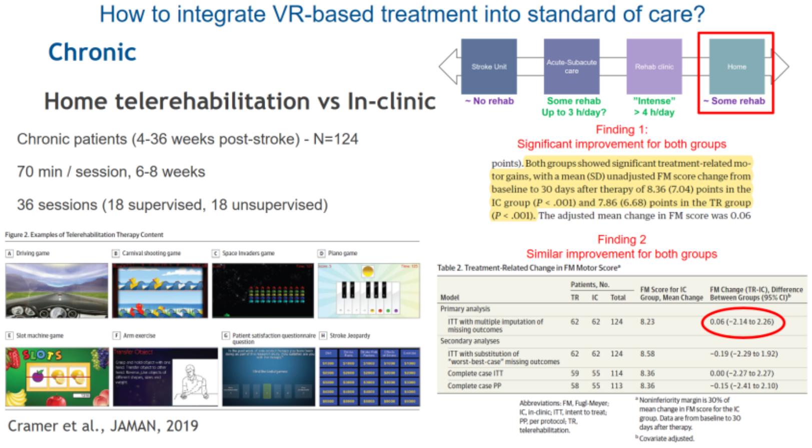
[a] Noninferiority margin is 30% of mean change in FM score for the IC group. Data are from baseline to 30 days after therapy.

[b] Covariate adjusted.

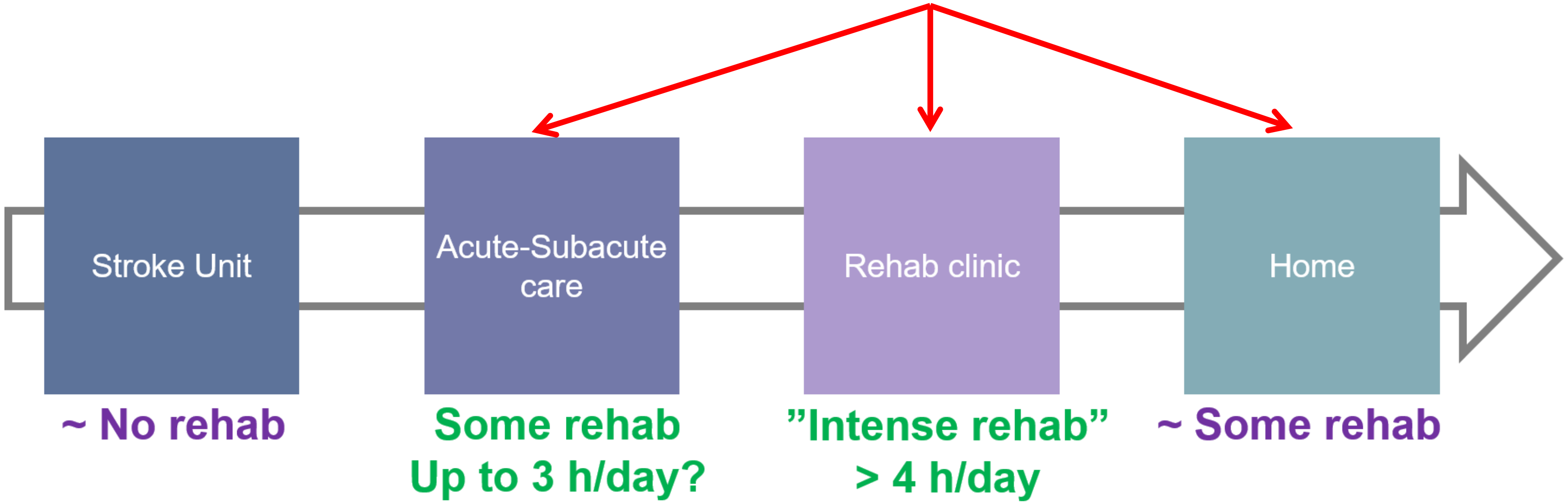
How to integrate VR-based treatment into standard of care?







VR in addition to standard therapy



Virtual reality, a new therapeutic tool for neurological care

Outline

- What is virtual reality based rehabilitation?
- Examples of treatments using virtual reality
- Is virtual reality effective for (stroke) rehabilitation?
- How to integrate VR-based treatment into standard of care?
- Conclusion, added value of VR-based rehabilitation

Conclusion, added value of VR-based rehabilitation

Increase dose therapy

(intensity, frequency and/or duration of session)

Standard motor rehabilitation (OT): upper limb training 30 repetitions/session

Lang et al., Arch Phys Med Rehabil., 2009

Non-human primates: upper limb training 600 repetitions/session

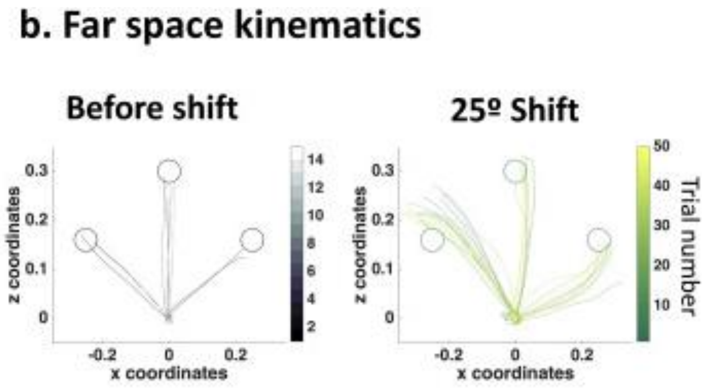
Nudo et al., Science, 1996

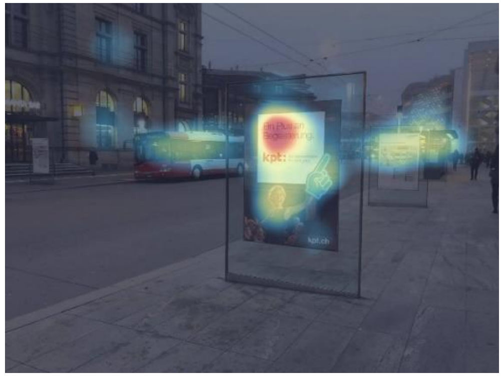
Conclusion, added value of VR-based rehabilitation?

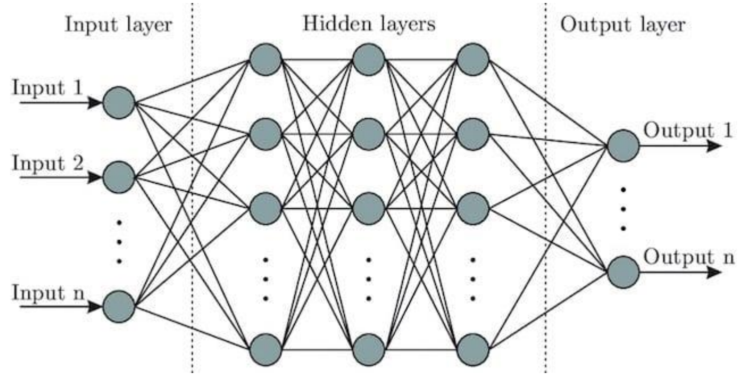
- **Increase dose**
- **Increase motivation, attractiveness of the training**

- 3D and 360° countless new and well controlled environments
- Real-time feedback and monitoring (remote)
- Lower cost for additional VR-based sessions (?)
- Digital output from sensors
- Ease of eye tracking measures

→ Easily included in machine learning analyses
(e.g. prediction of responders)







Conclusion

VR in neurorehabilitation

Effective therapy → high intensity

VR based therapy → can provide additional therapy sessions
→ done in addition to standard of care, not to replace it
→ in subacute and chronic stages
→ in clinic or at home